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4-Hz Transcranial Alternating Current Stimulation Phase Modulates Hearing

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ABSTRACT

Background: Non-invasive brain stimulation with transcranial alternating currents (tACS) has been shown to entrain slow cortical oscillations and thereby influence various aspects of visual perception. Much less is known about its potential effects on auditory perception.
Objective: In the present study, we apply a novel variant that enables near-equivalent stimulation of both auditory cortices to investigate the causal role of the phase of 4-Hz cortical oscillations for auditory perception.
Methods: We measured detection performance for near-threshold auditory stimuli (4-Hz click trains) that were presented at various moments during ongoing tACS (two synchronous 4-Hz alternating currents applied transcranially to the two cerebral hemispheres).
Results: We found that changes in the relative timing of acoustic and electric stimulation cause corresponding perceptual changes that oscillate predominantly at the 4-Hz frequency of the electric stimulation, which is consistent with previous results based on 10-Hz tACS.
Conclusion: TACS at various frequencies can affect auditory perception. Together with converging previous results based on acoustic stimulation (rather than tACS), this finding implies that fundamental aspects of auditory cognition are mediated by the temporal coherence of sound-induced cortical activity with ongoing cortical oscillations at multiple time scales.

Introduction

Periodic fluctuations between relatively depolarized and hyperpolarized neuronal states are ubiquitous throughout the brain and form the basis of neural oscillations [1,2]—a topic of ongoing interest in the cognitive neurosciences [3–6]. Several auditory studies found consistently that the phase of slow (0.5–12 Hz) spontaneous neural oscillations is coupled with neural excitability in the auditory cortex [7,8] as well as various auditory cognitive phenomena such as target detection [9–11], selective attention [12–17], and speech comprehension [18–20]. Complementary to these correlational studies, few studies used a modulatory approach that allowed obtaining causal evidence for a functional role of the phase of slow cortical oscillations in auditory perception. Specifically three studies manipulated cortical oscillatory phase and tested the effects on auditory detection performance: Neuling et al. [21] applied transcranial alternating current stimulation (tACS) [22–24] at 10 Hz, and found that tone detection performance fluctuated along with the phase of the ongoing tACS. Henry et al. [25,26] applied auditory stimulation, not tACS, that was modulated periodically at 3 Hz or 5 Hz, and found consistently that gap detection performance fluctuated along with the phase of this ongoing auditory modulation. All three studies attributed the observed covariations between (electric or auditory) stimulation and perception to neural entrainment, i.e., phase alignment of cortical oscillations (at the frequency of the ongoing external stimulation) to the stimulation itself. In sum, the phase of cortical oscillations in the range of 3 Hz, 5 Hz, and 10 Hz seems to be crucial for auditory perception. It is still unclear whether such a causal link also holds for other frequencies.

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Advantages of the modulatory approach over the correlational approach are that it allows drawing stronger theoretical inferences and possibly offers some practical benefits due to its potential to influence perception via neural entrainment. In fact, without prior neural entrainment to periodic stimulation, oscillatory phase-dependent modulations in auditory perception seem to be more difficult to obtain in human listeners [27,28]. Compared with ongoing auditory stimulation, tACS is arguably the preferred modulatory approach for auditory studies as it can be applied both in silence and at selected scalp position, thereby allowing experimenters to bypass the peripheral auditory system and entrain local spontaneous cortical oscillations while reducing possible confounding by auditory-evoked spiking activity [29–33]. The only auditory tACS study so far [21] targeted electric stimulation on the auditory cortices in the two cerebral hemispheres using bilateral electrodes placed above the ears. Unfortunately, the alternating currents induced with this approach flow in opposite directions in the two cortical hemispheres (from medial to lateral in one hemisphere vs. from lateral to medial in the other hemisphere). This asymmetry introduces an inter-hemispheric phase shift of 180° in bilateral structures, which may be detrimental especially to auditory perception considering that sound processing in the auditory cortices is normally associated with bilateral synchronous neural phase-locking (see e.g., Ref. [34]), except perhaps for spatially specific stimuli and tasks.

In the present study, we investigated whether the phase of tACS in the delta/theta range can modulate auditory perception. Frequencies in this range may serve several aspects of auditory perception and cortical processing: Firstly, delta/theta amplitude fluctuations in speech signals are critical for speech comprehension [35] and can entrain auditory cortical oscillations in human cortex [15,16,18,19,36]. Secondly, these frequencies constitute dominant spectral components of auditory-evoked cortical potentials (e.g., Ref. [37]). Finally, sounds modulated at these frequencies are highly effective in exciting neurons in the middle superior temporal gyrus and lateral Heschl's gyrus in both cerebral hemispheres [38]—thus these bilateral auditory cortical regions were chosen as target regions in the present study. We specifically chose 4 Hz because it is well separated from and harmonically unrelated to the previously explored 10-Hz frequency in the alpha range [21].

To avoid inter-hemispheric phase shifts, we used a novel bilateral dual-channel variant of tACS that allows applying near-equivalent (in terms of both phase and intensity) electric stimulation to bilateral homolog structures. Using this approach, we sought to induce neural entrainment at matched 4-Hz oscillatory phases in the bilateral auditory cortical target regions and directly tested our hypothesis that the phase of experimentally-entrained delta/theta oscillations would modulate auditory perception. We assessed the effect of the oscillatory phase on auditory perception by measuring human listeners' detection performance for near-threshold auditory stimuli presented at various moments (phase angles) within the ongoing oscillatory tACS [21]. We expected that tACS would entrain neural oscillations in the target regions and hypothesized that this would influence auditory perception such that performance for auditory stimuli presented at phase angles within one tACS half-cycle would differ significantly from performance at phase angles spanning the opposite half-cycle. In line with this hypothesis, the results indeed show that performance varied significantly across tACS half-cycles. A spectral analysis corroborates the notion that this effect on perception takes the form of an oscillation predominantly at the applied 4-Hz tACS frequency.

Material and methods

Participants

Fourteen paid volunteers (seven females, ages: 22–38 years) participated in the study. They reported no history of neurological, psychiatric, or hearing disorders, were suited to undergo non-invasive brain stimulation as assessed by prior screening, and gave their written informed consent before taking part. They had normal hearing (defined as hearing thresholds of less than 25 dB HL at 250, 500, 750, 1000, 1500, 3000, and 4000 Hz), except for one participant who had mild hearing loss in the left ear for the two highest frequencies. Excluding the data of this participant from the analyses did not alter the conclusions of the study.

Acoustic stimulation

Auditory stimuli were comprised of repetitive acoustic pulses. When presented sufficiently loud, such click trains can evoke excitation patterns along the cochleotopic axis that are more widespread and possibly more strictly phase-locked than those evoked by tones, due to their broader spectra and more concise temporal structure, rendering them suitable for studying temporal processing in the auditory system in the absence of a clear pitch percept [39]. In the present study, a train of four clicks presented at the same rate as tACS (4 Hz, see next section) was used. While single clicks or tones might have been suitable as well, these repetitive clicks were deemed a more effective probe for phase-dependent auditory perception, because they may allow detecting the overall sound by perceptually tracking its amplitude envelope; i.e., based on *multiple* perceptual snapshots and the additional overall temporal pattern that may arise from these snapshots. The repetition rate of the clicks was chosen to match specifically the tACS frequency to ensure that acoustic and electric stimuli would share a common amplitude envelope; i.e., the putative snapshots would be sampled at the same phase angle on consecutive tACS cycles. To reduce the potential of individual clicks to evoke neural responses that could possibly reset the neural oscillatory phase, the sound level was set individually to a low value near click detection threshold (see below, Procedure section). The click train was generated by summing all harmonics of a 4-Hz fundamental frequency within the range from 112 to 3976 Hz. The starting phase and amplitude of the sinusoidal harmonics were fixed, thus the resulting sound waveform resembled a periodic sequence pulsating at the fundamental frequency of 4 Hz. The waveform was bandpass-filtered between 224 and 1988 Hz (3 dB cutoff frequencies, fourth-order Butterworth filter with zero phase shift). The portion between 125 and 1125 ms was extracted to obtain a train of four clicks centered on a 1-s interval. The auditory stimuli were presented diotically via a high-fidelity soundcard (Focusrite Forte) and insert earphones (EARTone 3A).

Electric stimulation

Figure 1 schematizes the applied tACS approach. Square rubber electrodes were attached to the scalp with conductive gel at positions defined by the International 10-20 system. The stimulation electrodes (size: 5 × 5 cm) were placed over the temporal cortices (centered on positions T7 and T8), whereas the return electrodes (size: 5 × 7 cm) were placed symmetrically to the left and right side of the midline (respectively) so that their long sides were centered on the vertex (position Cz) and bordering each other. This configuration was chosen to produce relatively strong currents in the target