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Conveying Temporal Information to the Auditory System via Transcranial Current Stimulation

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Summary

This review paper investigates whether non-invasive application of electric current to the human scalp can be utilized to convey perceptually relevant temporal information to the auditory system. Recent studies have corroborated this notion by demonstrating that transcranial current stimulation (TCS) with temporally structured (sinusoidal and/or sound envelope-shaped) current biases neural processing and auditory perception toward the temporal pattern of the applied current. However, the perceptual benefits achieved with TCS so far are fairly modest. In sum, the temporally specific modulatory ability of TCS makes it a useful scientific tool for identifying temporal mechanisms for auditory perception. Practical or clinical applications (e.g., to enhance or restore auditory functions in normal or hearing-impaired populations) are currently still premature and require further optimization of stimulation parameters.

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1. Introduction

TCS is a non-invasive and soundless brain stimulation technique that is becoming increasingly popular in auditory research, as reflected by a rapidly growing body of published studies over the last years [1, 2]. TCS involves the non-invasive and harmless application of low-intensity current (typically within ±2 mA) via scalp electrodes. Current-flow simulations and intracranial recordings in humans [3, 4] have shown that the induced current spreads mainly along the highly conductive skin and to a smaller amount into the cranium, where it propagates widely across the brain. Extracellular electric fields applied to pyramidal neurons in vitro almost instantaneously elevate (or reduce, depending on the relative field orientation) spontaneous neural firing (e.g., [5]). Thus, intracranial stimulation with temporally structured (alternating or complex-shaped) current can entrain neural excitability to the temporal pattern of that current [6]. Application of the current at the scalp (TCS) is thought to induce corresponding excitability changes at the neural population level [7, 8]. Neural oscillations in neocortex align their high-excitability phases to expected relevant sensory events, thereby providing a mechanism for temporal filtering of sensory input [9]. If TCS with temporally-structured current was also able to control the timing of neural excitability, then this technique could be utilized (in analogy to neural oscillations) to provide the brain with temporal information that is critical for extracting specific events from the sensory environment. The presumed ability of TCS to entrain neural oscillations [10] would be evidenced by demonstrating that neural excitability—and therewith the neural processing of sensory stimuli—covaries with the temporal pattern of TCS. Similarly, the presumed ability of TCS to convey perceptually relevant temporal information would require showing that perception of sensory stimuli covaries with the temporal pattern of TCS. Such evidence would have interesting consequences for both scientific research and clinical/practical application: It would confirm that TCS can effectively manipulate specific temporal activity patterns (including neural oscillations), which would enable to experimentally identify causal roles of these patterns in auditory functions, such as hearing, auditory scene analysis, and speech comprehension. Moreover, it would suggest that TCS can be utilized to enhance or restore these functions in normal and hearing-impaired populations [11].

The goal of this review paper is to assess whether TCS can be utilized to provide the human auditory system with perceptually relevant temporal information. The focus is on auditory studies that have applied TCS with temporally structured currents. Auditory studies using TCS variants that seem less suited for conveying temporal information (direct currents, random noise currents, or alternating cur-

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rents bearing no temporal relationship to acoustic input) have been reviewed elsewhere [1, 2].

2. TCS can entrain neural oscillations

Electric stimulation with alternating current can entrain spontaneous neural firing (measured intracranially) in animal neocortex, even when the alternating current is applied transcranially (TACS) [12]. Studies attempting to translate these animal findings to humans found that TACS elevates power at the TACS frequency in subsequent scalp magneto-/electroencephalographic recordings (M/EEG) [13]. However, these aftereffects more likely reflect TACS-induced synaptic plasticity than oscillatory phase entrainment [14]. More convincing evidence of TACS-induced entrainment would show that oscillations follow the applied current waveform *during* the stimulation. Using sophisticated approaches to reduce TACS-induced artefacts in simultaneous M/EEG recordings (e.g., [15, 16]), several studies have indeed shown an *online* increase in both power at the TACS frequency [17, 18] and phase-locking between TACS waveform and M/EEG oscillation [16, 17, 19]. While the minimum current intensity required to reliably entrain human neocortical oscillations is still being debated [3, 4, 20, 21], the aforementioned studies strongly suggest that TACS can entrain neural oscillations and thereby convey temporal information to sensory systems. In future studies, it needs to be shown whether TCS with more complex- shaped (aperiodically fluctuating) currents resembling naturally occurring sensory signals (e.g., speech) can align endogenous neural activity as well [6].

3. TCS can modulate auditory perception in a temporally specific manner

Several studies have shown that TCS applied above temporal cortex can modulate auditory perception in a temporally specific manner. Neuling *et al.* [22] applied direct current modulated at 10 Hz. They reported that the threshold for detecting tone pips in a simultaneous noise masker depends on the relative phase of the simultaneously applied 10-Hz electric stimulation. The size of this *phase-effect* on simultaneous-masked threshold was ∼0.3 dB. Using a similar paradigm, Riecke *et al.* [23] found that detection of 4-Hz click trains in silence depends on the relative phase of the click train and simultaneously applied 4-Hz TACS (size of phase effect on click-detection accuracy: ∼2%). Consistent with these click-detection results, Riecke *et al.* [24] found that the perceptual buildup of 4Hz-modulated complex tones in informational maskers (i.e., the time required for listeners to perceptually segregate a rhythmic target stream from background noise) depends on the relative phase of the target stream and 4-Hz TACS (size of phase effect on buildup time: ∼40 ms). Because the applied current carried temporal cues regarding the occurrence of the target stream constituents, this observation supports the notion that TCS can provide perceptually relevant temporal information to the auditory system.

Temporal information might be of particular importance for speech processing, as a rapid sequence of densely structured information has to be precisely deciphered. The amplitude envelope of the speech signal is critical for this, as its disruption strongly impairs speech comprehension (e.g. [25]). Indeed, several recent studies show that speech processing can be manipulated by applying external stimulation carrying speech-envelope information. E.g., Riecke *et al.* [26] investigated speech comprehension under 4-Hz TACS in a cocktail party-like two-talker situation. Speech envelopes were artificially fixed at 4 Hz and enhanced, and the two simultaneous speech signals were mixed so that their envelopes alternated. Consistent with results on click- and tone-detection, speech-recognition accuracy was found to depend on the relative phase of the target-speech envelope and TACS (size of phase-effect on speech-recognition accuracy: ∼3%). Zoefel *et al.* [27] combined TACS at 3.125 Hz with functional magnetic resonance imaging (FMRI) while participants listened to rhythmic sentences (spoken at the TACS frequency) that were modified with vocoders to resemble either intelligible speech or only broadband noise fluctuating at the speech rhythm. Speech-evoked FMRI responses in superior temporal gyrus were found to depend on the relative phase of the auditory speech rhythm and TACS. Strikingly, this effect was only observed for intelligible speech, but not fluctuating noise. Moreover, certain relative phases resulted in suppression of speech-evoked responses (compared with sham stimulation). Importantly, these results provide a potential neural mechanism underlying the aforementioned TACS-phase effects on speech recognition [26].

Two recent studies also applied TCS at different time lags relative to speech sounds; however, current waveforms matched the envelope of the natural speech stimuli. Wilsch *et al.* [28] observed that speech-in-noise recognition at listeners' individual "best" time lag (the lag revealing the smallest threshold) is better than under sham stimulation, with a threshold difference between individual best lag and sham of ∼0.4dB. In a second experiment, Riecke *et al.* [26] removed the low-frequency envelope from auditory speech stimuli and applied it via TCS to restore this "aurally missing" temporal information in the brain. Speech comprehension was found to depend on the lag between envelope-reduced speech and envelope-shaped TCS. The maximal benefit was observed when TCS led the acoustic input by 375ms, with a difference in word-recognition accuracy of ∼4% (average best lag vs. average worst lag). In sum, these studies show consistently that TCS applied above temporal cortex can convey perceptually relevant temporal information to the auditory system.

4. TACS frequency modulates perceptual sampling frequency

It is conceivable that TACS transmits temporal information via not only its relative phase but also its *frequency* – in form of a sampling rhythm that affects the temporal resolution of perception. Based on the observation that gap-detection thresholds correlate negatively with listeners' gamma resonance frequency in auditory cortex (defined as the modulation frequency within 20–70 Hz that evokes the strongest auditory steady-state EEG response), Baltus *et al.* used TACS near individual gamma-resonance frequency to manipulate the temporal resolution of the auditory system [29, 30]. They found that TACS with a frequency slightly above (vs. below) resonance frequency reduced gap-detection threshold. This indicates that TACS can modulate the rate at which the human auditory system samples acoustic input.

5. Clinical utility of TCS and current limitations

There currently exists only little evidence to support an effective clinical/practical utilization of rhythmic auditory TCS. TCS effects observed so far are rather modest (see section 3) and their actual size and direction (benefit vs disruption) are difficult to estimate. E.g., most studies correct for inter-individual differences in the best time lag (presumed to originate from anatomical variations [19]) to improve the power of group-level analyses. However, this approach requires sacrificing the listeners' maximum-performance data, which inevitably results in an underestimation of both average effect sizes and potential benefits. Indeed, beyond the effects of TCS timing, only few studies could validly detect significant differences between TCS and sham stimulation. Thus, it remains to be shown whether TCS can reliably provide sufficiently strong auditory perceptual benefits, as required for a clinical or practical application.

Potential benefits may be strengthened by systematically improving TCS parameters to promote the specific spatiotemporal brain-activity patterns that underlie normal auditory functions [31]. While the TCS studies reviewed here have primarily considered basic temporal parameters, future research may focus on complementary (spatial and spectral) parameters, e.g., by comparing the benefits of different electrode shapes, locations, and numbers. Clinical TCS utilization also requires more basic research on the mechanisms underlying the observed TCS effects, which are still being debated [20, 21, 32]. While it seems safe to conclude that TACS with sufficient intensity can entrain endogenous neural activity and modulate auditory perception (sections 2 and 3), it is still unclear how this entrainment originates: directly in the cortex, indirectly via rhythmic peripheral responses elicited by the current, or both. An exclusive mediating role of peripheral responses seems unlikely because TACS applied above the mastoids does not entrain otoacoustic emissions [33] and TACS-phase effects on auditory cortical speech processing have been observed exclusively for auditory stimuli that can be identified as speech [27]. Nevertheless, even though the TCS studies reviewed here attempted to reduce potential tactile or visual sensations [34], the applied currents might have induced subliminal tactile or visual temporal cues that potentially facilitated (or disrupted) neural activity. Future studies need to rule out this possibility by applying TCS also to non-auditory control locations (e.g., near the eyes or on the hand).

6. Conclusions

Our review shows that the timing of TCS modulates endogenous neural activity, auditory cortical speech processing, and various perceptual auditory functions (hearing in silence or noise, auditory streaming, and speech comprehension). This converging evidence indicates that TCS can convey temporal information to the auditory system (by entraining slow endogenous neural activity) and therewith alter processing and perception of acoustic input. This makes TCS a highly useful scientific tool for identifying causal dynamic mechanisms underlying perceptual auditory functions. However, perceptual benefits achieved with current stimulation settings are still modest, indicating that any clinical or practical utilization of TCS (e.g., in assisted hearing) still requires substantial methodological improvement.

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