

No evidence for modulation of outer hair-cell function by 4-Hz transcranial alternating current stimulation

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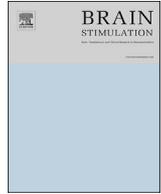
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Keywords:

TACS
Hearing
Otoacoustic emission
Entrainment

Dear Editor,

A growing number of studies show that transcranial stimulation with direct current (TDCS) or alternating current (TACS) applied above the auditory cortex can alter auditory cognition (for reviews, see Refs. [1–3]). These auditory effects are often interpreted as being mediated by neural excitability changes under the temporal electrodes and as reflecting a causal role of auditory cortex in the studied auditory phenomenon. A widely neglected alternative is to attribute this causal role, partially or fully, to neuronal structures belonging to earlier stages of the auditory stimulus processing hierarchy. In support of this possibility, a large proportion of the TDCS/TACS current applied to the scalp propagates along the highly conductive skin [4] by which it might reach receptors in the peripheral sensory system [5,6]. Moreover, the small current fraction that directly penetrates the brain may spread along corticofugal projections by which it might reach subcortical and peripheral structures (for a review on such projections, see Ref. [7]). In the present study, we tested whether TACS can modulate the function of outer hair cells (OHCs) in the human cochlea. We applied 4-Hz TACS to nineteen normally-hearing participants and recorded distortion-product otoacoustic emissions (DPOAEs; see [Supplementary Material S1](#)) from their right ear. We predicted that a modulation of DPOAE occurs during (online) and after (offline), but not before TACS.

The experimental design ([Fig. 1A](#)) included four independent variables: To assess online effects, we used a within-subject experimental design where participants underwent two sessions involving either both TACS and sham stimulation (main session) or neither (control session). To assess offline effects, we presented sham stimulation two times, before and after TACS (Sham_{pre} and Sham_{post}). To assess electrode-ear distance effects [5,6], we applied TACS at two different distances from the test ear using the electrodes above the ipsilateral (T8 and Cz; TACS_{near}) or contralateral auditory-motor cortex (T7 and Cz; TACS_{far}), respectively. This allowed us to test whether OHCs are more vulnerable to TACS when the latter is applied at a nearby scalp region. Finally, to avoid

a ceiling effect, we probed DPOAEs at four different *test levels* near the participant's DPOAE threshold (see [Supplementary Material S1.2](#)). Together, this yielded two sessions, each with four blocks (20 min) resembling four conditions. Each block comprised four sub-blocks (5 min) resembling four different test levels. The order of sessions, blocks and sub-blocks was counterbalanced across participants.

The obtained OAE recordings were transformed into the frequency domain and measures of interest were extracted for each condition and each participant (see [Supplementary Material S2](#)). The relevant measures were the level of the DPOAE, the average level of its spectral sidebands (the DPOAE frequency \pm the TACS frequency), and the noise floor (average level at neighboring frequencies, for control). The DPOAE-sideband level was taken to measure the strength of the periodic modulation of DPOAE, the level of the DPOAE itself was taken to measure more sustained (non-periodic) DPOAE changes, and the level of the noise floor was taken to measure general (frequency-unspecific) effects on the OAE recording.

To test for an online TACS effect, a three-way repeated-measures ANOVA including factors *session*, *distance* (near and far), and *test level* was used, which revealed no main effect of *session* on any of the aforementioned measures (DPOAE sideband: $P = 0.11$, $F_{1, 18} = 2.92$; DPOAE: $P = 0.89$, $F_{1, 18} = 0.02$; noise floor: $P = 0.14$, $F_{1, 18} = 2.35$) and no significant interaction (see [Fig. 1B](#) left). Thus, TACS had no instantaneous periodic or sustained effect on DPOAE or OAE recording.

To test for an offline TACS effect, a two-way ANOVA including factors *time* (pre and post) and *test level* was used, which also revealed no main effect of *time* on any measure (DPOAE sideband: $P = 0.28$, $F_{1, 18} = 1.26$; DPOAE: $P = 0.46$, $F_{1, 18} = 0.56$; noise floor: $P = 0.23$, $F_{1, 18} = 1.58$) and no significant interaction (see [Fig. 1B](#) center). Thus, TACS had no periodic or sustained aftereffect on DPOAE or OAE recording.

To test for an electrode-ear distance effect, a two-way ANOVA including factors *distance* (near and far) and *test level* was used. As already suggested by the lack of a significant online TACS effect above, this revealed no main effect of *distance* on any measure (DPOAE sideband: $P = 0.31$, $F_{1, 18} = 1.11$; DPOAE: $P = 0.79$, $F_{1, 18} = 0.08$; noise floor: $P = 0.29$, $F_{1, 18} = 1.19$) and no significant interaction (see [Fig. 1B](#) right).

In sum, these results provide no evidence for our hypothesis that TACS affects OHC function. They allow two mutually exclusive interpretations: On the one hand, it is conceivable that TACS alters OHC function as we hypothesized, but that we failed to detect it due to a lack of statistical power or current intensity. However, our sample size was comparable to that of previous studies that have

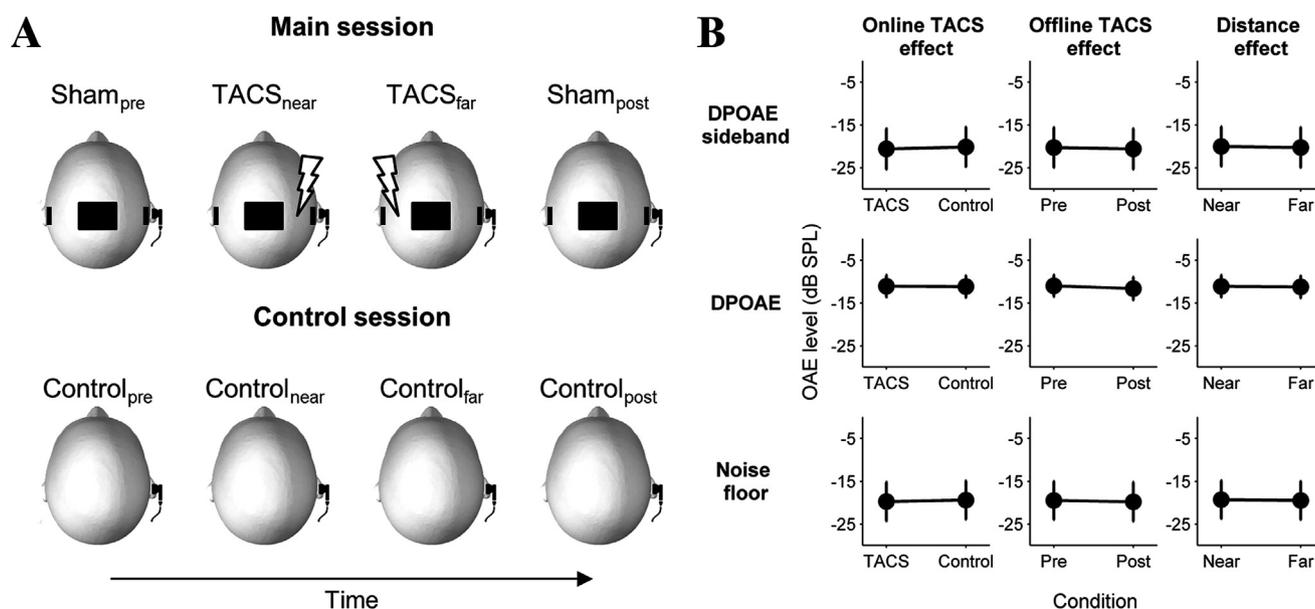


Fig. 1. Experimental Design and Results.

A) During the main session (top), TACS was applied at two different distances from the test ear: above the ipsilateral or contralateral auditory-motor cortex (conditions TACS_{near} and TACS_{far}). Sham stimulation was applied before and after TACS. During the control session (bottom), no stimulation was applied.

B) Results show no significant online (left), offline (center), or distance effect (right) of TACS on the levels of DPOAE sidebands (top), DPOAE (middle), or noise floor (bottom).

successfully detected auditory effects using similar TACS parameters. On the other hand, it is possible that our hypothesis that TACS at conventional intensities alters OHC function is false. We think this latter interpretation is more plausible, because it agrees with recent results showing no effect of galvanic vestibular stimulation on DPOAE [8,9]. It remains to be investigated whether auditory effects of TACS originate at a different auditory processing stage than OHCs, for example, the auditory nerve, brainstem, or cerebral cortex (see [Supplementary Material S3](#)).

Authors' contributions

L.R., S.B., E.G., and D.B. designed research.
S.B. performed research.
E.F. and L.R. contributed materials/analytic tools.
L.R. and S.B. analyzed the data.
S.B. and L.R. wrote the paper and made the figures.
E.F., E.G., and D.B. commented on drafts.

Conflicts of interest disclosure

The authors declare no competing financial interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.brs.2019.01.022>.

References

- [1] Heimrath K, Fiene M, Rufener KS, Zaehle T. Modulating human auditory processing by transcranial electrical stimulation. *Front Cell Neurosci* 2016;10:53. 53.
- [2] Zoefel B, Davis MH. Transcranial electric stimulation for the investigation of speech perception and comprehension. *Lang. Cogn. Neurosci.* 2017;32:910–23.
- [3] Riecke L, Zoefel B. Conveying temporal information to the auditory system via transcranial current stimulation. *Acta Acustica united Acustica* 2018;104:883–6.
- [4] Miranda PC, Lomarev M, Hallett M. Modeling the current distribution during transcranial direct current stimulation. *Clin Neurophysiol* 2006;117:1623–9.
- [5] Schutter DJ, Hortensius R. Retinal origin of phosphenes to transcranial alternating current stimulation. *Clin Neurophysiol* 2010;121:1080–4.
- [6] Kar K, Krekelberg B. Transcranial electrical stimulation over visual cortex evokes phosphenes with a retinal origin. *J Neurophysiol* 2012;108:2173–8.
- [7] Terreros G, Delano PH. Corticofugal modulation of peripheral auditory responses. *Front Syst Neurosci* 2015;9:134. 134.
- [8] Cevette MJ, Cocco D, Pradhan GN, Galea AM, Wagner LS, Oakley SR, et al. The effect of galvanic vestibular stimulation on distortion product otoacoustic emissions. *J Vestib Res* 2012;22:17–25.
- [9] Ueberfuhr MA, Braun A, Wiegrebe L, Grothe B, Drexler M. Modulation of auditory percepts by transcutaneous electrical stimulation. *Hear Res* 2017;350:235–43.

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