Brain Stimulation 17 (2024) 550–552

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.journals.elsevier.com/brain-stimulation

Reduced VR motion sickness by applying random-phase transcranial alternating current stimulation to the left parietal cortex

Dear Editor,

With the increasing spread of consumer-friendly VR headsets in our daily life, VR motion sickness (VRMS) is approximately affecting 40–70 % of the VR users [1]. Although brain stimulation-based VRMS mitigation techniques exist [2], it is still unclear whether the mitigated VRMS symptoms in these previous studies could be observed in an online manner. In other words, whether or not reduced VRMS could be perceived while tACS was applied concurrently with the VR environment. Furthermore, the true attribution of mitigated VRMS symptoms to targeted brain interventions or other factors, such as the side effects of brain stimulation and their potential impacts on cognitive aspects, remains ambiguous.

Based on an open dataset (https://doi.org/10.5281/zenodo.6373681), we found that EEG-based inter-trial coherence (ITC) at 18Hz within a left parietal region (electrode P3) were positively correlated with VRMS ratings based on Fast Motion Sickness Scale (FMS [3]) ($p = 0.026$ and $r = 0.496$, see Supplementary Fig. S1). Therefore, as a follow-up, this study aimed to employ a non-invasive transcranial alternating current stimulation technique (tACS) to deliver a random phase waveform (Fig. 1A) that may disrupt the endogenous phase information of VRMS-linked 18Hz neural oscillations at P3. The stimulation montage was configured as follows: the stimulation electrode was positioned at P3, while the return electrodes were placed at CP1, TP7, and O1. All electrode placements were based on the 10–20 electrode coordinate system (refer to Fig. 1B). The current amplitude was set to 0.999 mA (baseline to peak) for P3 and 0.333 mA for CP1, TP7, and P1, respectively. Impedance was maintained below 10 kΩ. The simulated electric field and current density, illustrated in Fig. 1C, indicate values of 0.189 V/m and 0.052 A/m^2, respectively, around our stimulation electrode, P3. Throughout this study, tACS was administered via 4 Ag/AgCl electrodes (3.14 cm^2) at 18 Hz using a Starstim8 system (Neuroelectrics, Spain). We hypothesized that applying random phase tACS would rapidly disrupt the VRMS-linked brain activity pattern (i.e., P3 ITC at 18Hz) and thus mitigate VRMS. If observed, we aimed to investigate whether this mitigation effect could be attributed to differences in side effects of the tACS protocols. Also, we explored whether this mitigation effect was associated with the participants' cognitive abilities. This was assessed through two cognitive tasks: one is online (VR multitasking paradigm during tACS; see Supplementary text and Fig. S3); another is offline (Non-VR working memory 2-back task pre/post tACS; see Supplementary text).

We recruited eighteen young adults aged between 20 and 30 y and conducted a single-blinded, sham-controlled, counter-balanced, within-subject, multi-visit tACS study. The within-subject factor, as shown below, was the stimulation type which had three levels (or conditions) that were counter-balanced across lab visits with at least one-week time interval between each visit.

1) Active tACS with a random phase waveform where the phase of the sine wave is randomly shifted (inversed) between 3 and 9 cycles.
2) Sham tACS with a random phase waveform for a 20-s duration (10-s ramping up/down).
3) Control tACS with a regular sinusoidal waveform (i.e., no phase shifts) and the same duration and amplitude as the active tACS protocol.

Detailed experimental procedure for each condition can be found in Supplementary text and Fig. S2.

Analyses of repeated measures of online VRMS severities, such as FMS ratings, self-reports of perception of the stimulation and cognitive performance (i.e., RT, RTV, d-prime), utilized Generalized Linear Mixed Model (GLMM) with treatment (active/control/sham tACS), time (runs 1 to 4 for the 2-back task, runs 1 to 5 for all others) and time × treatment as fixed factors.

As hypothesized, the analyses of GLMM show that 18Hz-random-phase tACS applied to the left parietal cortex reduced VRMS. Specifically, significant results of time × treatment were found between active tACS and control tACS at run 2 ($M_{FMS} = 0.222 \pm 0.126$ vs $M_{FMS} = 0.722 \pm 0.205$, $t(148) = 2.030$, $p = 0.039$) as well as between active tACS and sham tACS at run 3 ($M_{FMS} = 0.167 \pm 0.088$ vs $M_{FMS} = 0.778 \pm 0.201$, $t(95) = 2.784$, $p = 0.006$), as shown in Fig. 1E and F (All p-values were Bonferroni corrected). These results indicated a 69.25 % reduction in nausea compared to the control tACS and a 78.53 % reduction compared to the sham control tACS. We did not observe any significant changes in our cognitive assessments of VR multitasking during tACS or working memory performance pre/post tACS (see Supplementary Fig. S4 and S5). Also, no side effects of tACS were associated with the mitigated VRMS found during the active tACS treatment (see Supplementary Fig. S6). Taken together, these results suggest that 18Hz random-phase tACS applied to the left parietal cortex could mitigate VRMS, even though its effectiveness was not prominent until the 10th min after tACS started and only could last for approximately 6 mins.

Although a recent study developed a 10 Hz regular tACS applied on bilateral parietal areas to mitigate VRMS [4], this is the first phase-dependent brain stimulation study that clearly demonstrates a significant online reduction in VRMS and its independence from stimulation side effects and cognitive manipulation. More importantly, our brain-centric stimulation is more rapid than a current state-of-the-art vestibular apparatus stimulation technique. For example, Weech and his colleagues found that applying noisy galvanic stimulation on vestibular inner ear sensory organs through mastoids presented an 30-min delayed mitigation effect in VRMS [5]. Moreover, the magnitude

https://doi.org/10.1016/j.brs.2024.04.015
Received 12 December 2023; Received in revised form 11 April 2024; Accepted 22 April 2024
Available online 25 April 2024

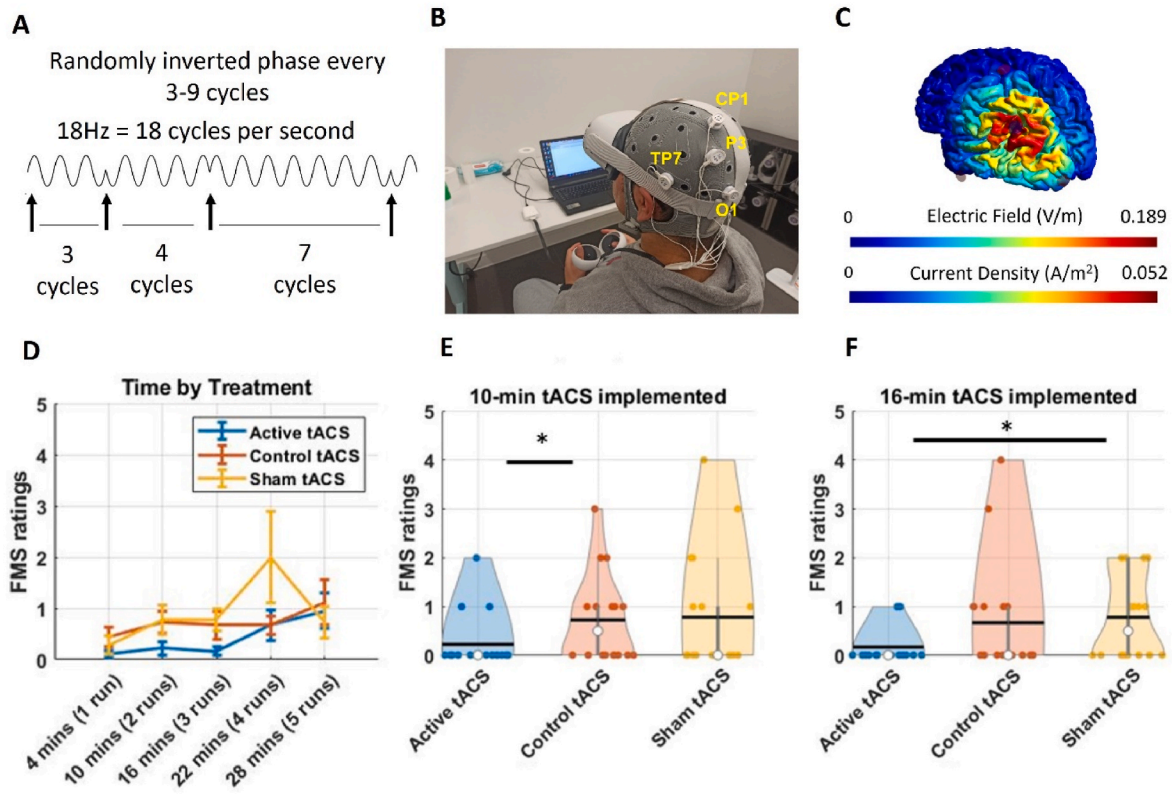

Fig. 1. (A) An example of the random phase sine waveform where we selected 3 cycles, 4 cycles and then 7 cycles before a phase shift. (B) An example of the tACS montage. (C) Simulated electric field and current density by SimNIBS 4.0. (D) An increasing trend in FMS ratings over time. (E) and (F) Reduced VRMS found at the 10th and 16th min during the active tACS intervention. $^{*}P < 0.05$.

of mitigation of our study is more effective (70–78 % improvement) than galvanic stimulation (approximately 35 % improvement). However, it is worth noting that the beneficial effects of this stimulation were short lived and only delayed the onset of VRMS. We speculate that the short-lived mitigation may be attributed to the weak stimulation. It is conceivable that longer-term online effects and more enduring outcomes could be attained with stronger stimulation – as higher current intensities often result in greater tACS effects [6,7]. Similarly, 'stronger' may pertain to the extent of phase shifting. It is possible that an increase in the frequency of phase shifts (such as every 3 to 6 cycles, as opposed to the current 3 to 9 cycles) may result in a more disrupted VRMS-linked brain activity pattern, thereby leading to more effective reduction of VRMS effects.

A widely accepted explanation for motion sickness is the sensory-conflict theory [8], which posits that discrepancies between visual and vestibular sensory information may lead to motion sickness. Recent fMRI and EEG studies have proposed that the parietal cortex is involved in the integration of visual and vestibular sensory information prior to the determination by the motion sickness control center in the brain (which has yet to be identified) of whether the integrated information contains mismatches in visual-vestibular sensory signals [9–11]. Therefore, we speculate that the 18Hz neural oscillations at the left parietal cortex (represented by the electrode P3) indicates key brain activity for the integration of mismatched visual and vestibular signals that can cause the ensuing perception of VRMS. Thus, random phase tACS at P3 disrupted the procedure of integration, resulting in incomplete perception of VRMS and reduced VRMS-related symptoms. At least, through this EEG-informed tACS study, we were able to show that VRMS is causally related to beta band phase synchrony in the left parietal cortex, presented by P3. However, additional research will be required to fully understand the effects of random phase tACS on neural activity and to stimulate control regions to understand the regional specificity of these effects. Moreover, additional research will be needed to understand why the control tACS did not show the opposite effect. It is likely that the control tACS was not strong enough to make a noticeable difference beyond the neural activity that was driven by the sensory stimuli. Indeed, previous research has indicated that tACS does not modulate neural activity when the stimulating frequency matches strong endogenous oscillatory activity [12].

Ethics

This procedure was approved by the ethics panel of the University of Glasgow (No. 200210220), College of Medical, Veterinary and Life Sciences. The details about this VR-based multitasking paradigm and 2-back working memory task can be found in attached supplementary materials. The core inclusion criteria were: 1) a moderate VRMS susceptibility, as previously defined [13] through the assessments of self-reported Motion Sickness Susceptibility Questionnaire scores (that is, 10–36), 2) no tACS contraindications and 3) no more than 2hr per month engaging in VR and/or PC first-person shooting games.

Funding sources

This work was supported in part by the European Research Council (ERC) through the European Union's Horizon 2020 Research and Innovation Programme under Grant 835197, and in part by the Royal Society of Edinburgh (RSE) International Joint Project under Grant 1764 and the Medical Research Council Impact Account Acceleration (MRC IAA) under Grant MR/X502807/1.

CRediT authorship contribution statement

Gang Li: Writing – original draft, Software, Resources, Project

administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Theodore Zanto:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2024.04.015.

References

[1] Meeri Kim. Cybersickness: why people experience motion sickness during virtual reality. Inside Science 2019. https://insidescience.org/news/cybersickness-why-people-experience-motion-sickness-during-virtual-reality. [Accessed 4 April 2022].
[2] Li G, McGill M, Brewster S, Pollick F. A review of electrostimulation-based cybersickness mitigations. 2020 IEEE international conference on artificial intelligence and virtual reality (AIVR). 2020. p. 151–7. https://doi.org/10.1109/AIVR50618.2020.00034.
[3] Keshavarz B, Hecht H. Validating an efficient method to quantify motion sickness. Hum Factors 2011;53:415–26. https://doi.org/10.1177/0018720811403736.
[4] Benelli A, Neri F, Cinti A, Pasqualetti P, Romanella SM, Giannotta A, et al. Frequency-dependent reduction of cybersickness in virtual reality by transcranial oscillatory stimulation of the vestibular cortex. Neurotherapeutics 2023;20:1796–807. https://doi.org/10.1007/s13311-023-01437-6.
[5] Weech S, Wall T, Barnett-Cowan M. Reduction of cybersickness during and immediately following noisy galvanic vestibular stimulation. Exp Brain Res 2020;238:427–37. https://doi.org/10.1007/s00221-019-05718-5.
[6] Wischnewski M, Schutter DJLG, Nitsche MA. Effects of beta-tACS on corticospinal excitability: a meta-analysis. Brain Stimul 2019;12:1381–9. https://doi.org/10.1016/j.brs.2019.07.023.
[7] Zanto TP, Jones KT, Ostrand AE, Hsu W-Y, Campusano R, Gazzaley A. Individual differences in neuroanatomy and neurophysiology predict effects of transcranial alternating current stimulation. Brain Stimul: Basic, Translational, and Clinical Research in Neuromodulation 2021;14:1317–29. https://doi.org/10.1016/j.brs.2021.08.017.
[8] Reason JT. Motion sickness—some theoretical considerations. Int J Man Mach Stud 1969;1:21–38. https://doi.org/10.1016/S0020-7373(69)80009-X.
[9] Frank SM, Greenlee MW. The parieto-insular vestibular cortex in humans: more than a single area? J Neurophysiol 2018;120:1438–50. https://doi.org/10.1152/jn.00907.2017.
[10] Ventre-Dominey J. Vestibular function in the temporal and parietal cortex: distinct velocity and inertial processing pathways. Front Integr Neurosci 2014;8:53. https://doi.org/10.3389/fnint.2014.00053.
[11] Donaldson PH, Rinehart NJ, Enticott PG. Noninvasive stimulation of the temporoparietal junction: a systematic review. Neurosci Biobehav Rev 2015;55:547–72. https://doi.org/10.1016/j.neubiorev.2015.05.017.
[12] Neuling T, Rach S, Herrmann CS. Orchestrating neuronal networks: sustained after-effects of transcranial alternating current stimulation depend upon brain states. Front Hum Neurosci 2013;7. https://doi.org/10.3389/fnhum.2013.00161.
[13] Li G, Varela FM, Habib A, Zhang Q, McGill M, Brewster S, et al. Exploring the feasibility of mitigating VR-HMD-induced cybersickness using cathodal transcranial direct current stimulation. In: 2020 IEEE international conference on artificial intelligence and virtual reality (AIVR); 2020. p. 123–9. https://doi.org/10.1109/AIVR50618.2020.00030.

Gang Li*
Perception, Action & Cognition Lab, School of Psychology and Neuroscience, University of Glasgow, G12 8QB, UK

Theodore Zanto
Neuroscape, Department of Neurology, University of California, San Francisco, CA, 94158, USA

* Corresponding author.
E-mail address: Gang.Li@glasgow.ac.uk (G. Li).