## **Decreased Brain Functional Connectivity in VR Users During Cybersickness**

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<u>Significance</u>: The rise of consumer-friendly virtual reality (VR) systems has led to related research to develop and deliver gamified cognitive and rehabilitation therapies in VR. However, some participants withdraw from the therapy due to VR-induced motion sickness (cybersickness). Moreover, approximately 60% of the general population experience some level of cybersickness, which may limit therapeutic efficacy even in those who do not drop out. Therefore, it is necessary to explore a new method to alleviate cybersickness and realize a "side-effect-free" VR-based therapy training platform that will help users maintain a sustainable behavioral performance.

<u>Background and Objective</u>: A handful of studies have explored the potential of electrostimulation-based cybersickness mitigations (Li, Varela, et al., 2020; Takeuchi et al., 2018; Weech et al., 2020), however neither the stimulation method (direct or alternating current) or the stimulation area (brain area) is clear yet. Therefore, the aim of the present study was to clarify the neural (EEG) indicators of cybersickness in order to build a foundation for the development of EEG-guided neurostimulation for cybersickness mitigations.

Method: A total of 20 healthy right-handed young adults attended this study. Given the close relationship between the vestibular network and the etiology of cybersickness, 5-channel scalp EEG signals were recorded from each participant's vestibular network (primarily involving the frontal midline cognitive and left and right sensorimotor domain, (Arshad et al., 2015; Ferrè & Haggard, 2020; Kyriakareli et al., 2013; Li, Anguera, et al., 2020; Takeuchi et al., 2018)) during passively watching an all-in-one VR (Oculus Quest 2) based 10-min tunnel travel application. The tunnel travel application required the participant to travel in an abstract tunnel, and produced a perception of moving in-depth. A digital version of the Fast Motion Sickness Scale (FMS) was used to directly collect cybersickness ratings inside the scenes at 1-min intervals. To extract neural indicators in the widespread vestibular network, a brain functional connectivity measure (Anguera, Boccanfuso, et al., 2013), the phase locking values (PLVs) of the inter-electrode coherence (IEC) at delta to beta frequency bands were calculated. To be more specific (see Figure. 1), we created 1 frontal (Fz) and 2 parietal composite electrodes of interest (EOI) from the average of the following electrodes: left temporoparietal junction (TPJ) and parieto-insular vestibular cortex (PIVC)-based CP5 and P3 as well as right TPJ and PIVC-based CP6 and P4, with PLVs calculated for each frontal-parietal EOI combination separately. If a significant linear regression relationship between the PLVs and cybersickness ratings could be established, then phase difference would be further calculated to investigate the nature of the PLVs (that is, in-phase or anti-phase), with an attempt to determine the specific brain oscillation-based neurostimulation method. We also investigated whether advanced machine learning techniques could detect cybersickness severity based on the PLVs and conventional power spectrum-based EEG features (), with an attempt to build the foundation of the development of an AI-driven closed-loop neurostimulation method for cybersickness mitigation.

Please note that IEC-based PLV is a commonly-used measure of phase consistency across electrodes in EEG (Anguera, Lyman, et al., 2013). A long-range IEC (e.g., the frontoparietal IEC in this study or frontal-to-

posterior IEC in (Anguera, Boccanfuso, et al., 2013)) was usually used to avoid the volume conduction issue. Regarding the data pre-processing, a low-pass filter with a cutoff frequency of 40 Hz and high-pass filter with a cutoff frequency of 0.1 Hz were applied to remove power line noise and DC drift, respectively. The filtered EEG data were then corrected using the mean of each channel and Electrooculography (EOG)based independent component analysis (ICA). The present study adopted 8-channel EEG rather than medium or high-density EEG, since these reduced EEG channels were carefully selected by our previous study for the cognitive domain (Fz, Cz, Pz (Li, Anguera, et al., 2020)) and other researchers' studies for TPJ and PIVC (Arshad et al., 2015; Kyriakareli et al., 2013; Takeuchi et al., 2018). The three domains were recently proposed to constitute the human vestibular network (Ferrè & Haggard, 2020), where we believe is highly correlated with cybersickness level, according to the widely-accepted etiology of motion sickness, that is, the sensory-conflict theory (Reason, 1969).



(a)



Figure 1. (a) The comparison of the FMS ratings and EEG indicators in the first and last minute during moderate CS-inducing task (tunnel travel). Note: the first and last minute stand for the first and last minute of each participant's run. The grand average data is shown by the bar charts (The p values were obtained by paired t-test). An example from a representative participant who required withdraw at the 8<sup>th</sup> minute of tunnel travel task is shown by the curve graphs. The PLV stands for the phase locking value (Min:0;

Max:1) for IEC. A value of 1 reflects perfect phase-locking across trials and a value of 0 reflects perfectly randomly distributed phases. The F2L<sub>Beta</sub> stands for the frontal cognitive to left sensorimotor IEC at beta frequency. (b) The circular histogram shows the specific phase difference from that representative participant. The labels "1000", "2000", "3000" and "4000" and the four blue bars indicate the number of phase difference that falls into the corresponding bins of the degrees. (c) The EEG montage used in this study, where EXT was used to collect EOG data for ICA-based EEG denoising processing.

<u>Results and Conclusion</u>: The results showed that there was a significant and inverse regression relationship between cybersickness ratings and frontoparietal neural phase-locking (that is, the PLVs of frontal to left parietal at beta frequency, see Figure. 1(a)), indicating the possibility of applying transcranial alternating current stimulation (tACS)-based frontoparietal neurostimulation to promote phase-locking to reduce cybersickness. Further analysis found that there was less phase difference (< 30°) in the majority of the participants (16 out of 20, see Figure. 1(b)), indicating the necessity of using in-phase rather than antiphase tACS to mitigate cybersickness. Regarding the machine learning techniques, we found that the PLVs could achieve the best regression performance (adjusted  $R^2$ =0.43) if compared to traditional power spectrum features (adjusted  $R^2$ =0.32) by using neural networks (NN) under the 10-fold cross validation condition. Here, the architecture of the NN was 1 hidden layer with 50 units with Relu activation function. This result indicates that indeed the IEC-based PLVs have the potential to be the primary neurofeedback biometrics in closed-loop EEG-guided neurostimulation for cybersickness mitigations.

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