

## Brainwave entrainment for the treatment of chronic pain: comment on *Br J Pain* 2020; 14: 161–70

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Dear Editor

We read with interest the article by Locke and colleagues: ‘Acceptability and Usability of Smartphone-Based Brainwave Entrainment Technology Used by Individuals With Chronic Pain in a Home Setting’.<sup>1</sup> The article is inspired by the important question of how to treat chronic back pain with therapeutic strategies beyond the use of pharmacological agents that have inherent shortcomings. The authors focus on ‘brainwave entrainment’ of alpha oscillations with rhythmic sensory stimulation. This is where we share the authors’ fascination with this approach and also feel that a note of caution is appropriate.

We agree with Locke and her colleagues in their emphasis on the importance of brain oscillations in the alpha frequency to pain physiology. In their report, they give a detailed report of how their smart phone application for ‘brainwave entrainment’ via visual impulses and binaural beat was accepted and included in the daily lives of their research participants. Characteristic feedback quotes from the participants are offered in a qualitative fashion, balanced to desirable effects (e.g. relaxation) and undesirable effects (e.g. headaches). While evaluating implementation of a potentially beneficial technique in the lives of patients in dire need of new therapeutic approach is laudable, we feel that this is a situation where the cart was put before the horse.

‘Brainwave entrainment’ is a poorly defined term that we assume refers to entrainment of neural oscillations by periodic (in this case, sensory) input. In our reading of the literature, it is not established that binaural beats reproducibly succeed in entraining neural oscillations. For example, a recent carefully performed study using electroencephalography (EEG) failed to demonstrate a measurable effect of binaural beats on alpha oscillations.<sup>2</sup> Even if a rhythmic sensory input stream creates a periodic signature in the EEG, it is not clear if actual entrainment has occurred or whether the observed structure is simply the superimposition of event-related potentials. Furthermore, even if entrainment occurs, there are complex questions about

whether the effect of stimulation persists and by what mechanism. This is particularly relevant since it is not clear whether the generalization from effects of modulation of alpha oscillations on acute pain<sup>3,4</sup> translates to the case of chronic pain. Rather, it is important to demonstrate durable restoration of altered alpha oscillations beyond stimulation application. It may be worth mentioning that transcranial alternating current stimulation in the alpha frequency increased alpha power that was correlated with symptom improvement in patients with chronic low back pain in a double-blind placebo-controlled study.<sup>5</sup>

Of note, the authors are in the process of publishing a randomized trial using visual flashes of various frequencies: 1, 7 and 10 Hz.<sup>6</sup> The authors here demonstrate enhancement of 10 Hz neural oscillations in midline posterior electrodes. Intriguingly, this study finds that while sitting comfortably entrainment from 10 Hz visual flashes shows the greatest reduction in self-reported ‘unpleasantness’ aspect of pain (65% of participants with a minimal clinically important difference (MCID)) compared to 40% with 1 Hz and 30% with 7 Hz. However, the authors do not find a significant reduction in pain ‘intensity’ (50% MCID with 10 Hz, 45% with 1 Hz and 30% with 7 Hz). This experiment investigates target engagement and utilizes a randomized trial. Thus, these findings are promising and lay a foundation for future research. We feel that demonstrating such neural effects of stimulation should be the priority and reports such as the one by Locke and colleagues may lead to misunderstandings about the state of the technology and contribute to the skepticism by neuroscientists about the value of modulating brain oscillations for clinical purposes.

In addition, we note that the study allowed participants to self-administer binaural beats and flashing visual stimuli at different frequencies that were self-selected. Thus, it is challenging to understand why alpha frequency is discussed, but not the focus of the intervention. Furthermore, there is no control group, and the qualitative findings might have arisen from a placebo effect derived from perceived value and

expectation. Finally, we thought that the fact that a third of the participants reported ‘exacerbation of existing headaches or a new headache’ did not receive sufficient attention. We feel one of the main conclusions of this qualitative research could easily be a general note of caution about the potential side effects of rhythmic sensory stimulation instead of the proposed conclusion about acceptability and usability.

In conclusion, we applaud the integration of qualitative research that queries the perspective of patients but argue that the report by Locke and colleagues should be contextualized to avoid a premature and possibly harmful misinterpretation of modulation of brain activity by rhythmic sensory stimulation.

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### Conflict of interest

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### Guarantor

F.F. (flavio\_frohlich@med.unc.edu) is the guarantor of the paper.

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