

Dear Editors,

We are pleased to submit for review the attached manuscript that reports a unique longitudinal study involving two chronic tetraplegic spinal cord injury patients (ASIA A) trained to operate an electroencephalography (EEG)-based, self-paced brain-computer interface (BCI) in order to participate in the BCI race discipline of the international Cybathlon event, the first bionic special Olympics held in Zurich Switzerland on October 8th 2016.

Despite the high profile of recent human BCI studies (Collinger et al., 2013; Bouton et al., 2016; Vansteensel et al., 2016; Pandarinath et al., 2016), it is rare to report longitudinal studies in realistic (home-use) conditions and with minimal expert support (Vansteensel et al., 2016). Furthermore, although all these works required brain implants, it is also believed that non-invasive approaches have an important role to play in order to achieve large-scale clinical translation (Ajemian, 2017). We believe our study supports this view. Specifically, our study leverages the experiences acquired during the Cybathlon in order to demonstrate the—so far, scarce and inconclusive—existence and efficacy of operant learning effects during BCI training, thus pinpointing our mutual learning methodology as the key to translational non-invasive BCI applications. Please find below a short summary of the study.

The BCI application performances achieved by both users and, especially, their Cybathlon competition outcomes (gold medal, record setting) substantiate the main finding of our study: unique, strong evidence of operant conditioning leading to considerable maturity and translational impact of non-invasive, sensorimotor rhythm (SMR)-based BCI. More than the impressive performances, our study distinguishes in that it is one of very few BCI training and control works with end-users that is longitudinal enough and has been conducted under realistic (home-use) and even adverse (crowded arena) conditions, thus justifying a claim on real translational potential for this type of interfaces. Our work provides the most complete and reliable proof to date of the existence and efficacy of instrumental learning taking place during online motor imagery BCI training, showcasing the presence of long-lasting learning effects at the neuroimaging, interface and application level. In particular, we show how our mutual learning protocol and user-centered BCI design can be credited with the aforementioned successful outcomes. These results touch upon issues currently in the spotlight of BCI research. Consequently, we believe that the insights provided and the conclusions reached in our work are of paramount importance to the state-of-the-art and clinical translation. We thus expect that this work could significantly shape the field's future and contribute to the critical transition of BCI from the laboratory to everyday home use, providing a viable and competitive alternative to invasive approaches.

We would like to suggest Prof. Karunesh Ganguly as the expert Academic Editor and Dr Gabriel Gasque as the Associate Editor of this manuscript. Furthermore, we would like to propose the following expert reviewers:

- Prof. Nick Ramsey (N.F.Ramsey@umcutrecht.nl)
- Prof. Eric Sellers (SELLERS@mail.etsu.edu)
- Prof. Niels Birbaumer (niels.birbaumer@uni-tuebingen.de)
- Prof. Jonathan Wolpaw (jonathan.wolpaw@health.ny.gov)

Ajemian, R. (2017). Neurosurgery: Gentler alternatives to chips in the brain. *Nature*, 544, 416–416.

Bouton, C. E., et al. (2016). Restoring cortical control of functional movement in a human with quadriplegia. *Nature*, 533, 247–250.

Collinger, J. L., et al. (2013). High-performance neuroprosthetic control by an individual with tetraplegia. *The Lancet*, 381, 557–564.

Pandarinath C., et al. (2017). High performance communication by people with paralysis using an intracortical brain-computer interface. *eLife*, 6, e18554.

Vansteensel M.J., et al. (2016). Fully implanted brain–computer interface in a locked-in patient with ALS. *N. Engl. J. Med.*, 375, 2060–2066.

Looking forward to your reply,
JdR Millán