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Editorial

P300 jitter latency, brain-computer interface and amyotrophic lateral sclerosis

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The development of disability is an invariable clinical feature of amyotrophic lateral sclerosis (ALS), significantly impacting on the ability of patient to interact with their environment, activities of daily living, and ultimately life quality (Dharmadasa et al., 2017). While commercially available augmentative and communication devices may be useful for anarthric ALS patients that have some residual motor control, alternative methodologies are required in advanced stages of ALS, where motor control is completely lost, and patients are locked-in. Non-invasive brain-computer interface (BCI) technologies, which rely on detection of electroencephalography (EEG) signals and don't require physical movements, have shown utility in ALS patients within the home environment (Farwell and Donchin, 1988, Nijboer et al., 2008, Sellers et al., 2010). Most BCI technologies rely on detection of the P300 response, an event related potential generated by an "oddball paradigm", and represented as a positive deflection in background voltage with variable latency, ranging between 250-to-500 ms (Polich, 2007). The P300 response is recorded by electrodes overlying the parietal lobe (frontocentral electrodes) and reflects processes involved in stimulus evaluation and categorization. A potential limitation of P300 based BCI in ALS patients relates to within-user and between-user latency variability, termed latency jitter, which could impact on BCI performance (Polich and Herbst, 2000, Blankertz et al., 2011, Mak et al., 2012).

In this issue of *Clinical Neurophysiology*, Zisk and colleagues (Zisk et al., 2020) report that P300 latency jitter is significantly increased in ALS patients and negatively correlates with BCI performance. In addition, the event-related potential (ERP) amplitudes were significantly smaller in ALS patients and were correlated with jitter. Interestingly, the degree of jitter was not correlated with functional disability or behavioral abnormalities. Importantly, P300 latency jitter should be taken into consideration when designing BCI technologies in order to improve performance in ALS patients.

While the P300 based BCI techniques may offer a novel manner of communication in severely disabled ALS patients, the major challenge to effective translation relates to the low signal-to noise ratio of ERPs in routine EEGs. This may be further compounded in visually impaired ALS patients, such as those that have lost eye-gaze control. Altering the stimulation paradigm design, such as utilizing auditory- or functional near-infrared spectroscopy-based BCIs, could enhance BCI performance and needs further validation (Schettini et al., 2015, Borgheai et al., 2020). Additionally, using classifier score series, adaptive filters to better assess single-trial responses and thereby correct for latency jitter, as well as color stimuli, are likely to reduced excessive jitter and thereby improve BCI performance (Mowla et al., 2017). Separately, the pathophysiological implication of increased latency jitter in ALS warrant further assessment. Specifically, increased jitter did not correlate with functional decline or behavioral abnormalities in ALS, thereby questioning the pathophysiological importance of this finding. Given the evolution of cortical dysfunction in ALS (de Boer et al., 2020), it seems plausible to conclude that increased jitter may reflect underlying cortical pathology. Longitudinal studies assessing the evolution of P300 latency jitter, and relating this to anatomical integrity (measured by quantitative MRI techniques) and cortical dysfunction (utilizing transcranial magnetic stimulation) will help confirming whether increased latency jitter is a useful surrogate biomarker in ALS. Finally, awareness of ERP latency jitter may be instrumental in optimizing BCI technology in the management of advanced ALS patients.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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