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INVITED COMMENTARY

Quantitative EEG and Brain Network Analyses in Patients with Early Consciousness Disorder Following Acute Large Hemispheric Infarction

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Consciousness is one of the greatest human mysteries, and it has been the focus of the work of many neuroscientists, mathematicians, philosophers, and neurologists. The leading existing theories for explaining consciousness range from global workspace theory where the brain parts joint participation and coordination result in consciousness, integrated information theory which attributes consciousness to the capacity a system of integrated information and quantum theory that assumes consciousness is constituted by discrete events corresponding with varying oscillation frequencies of distinct brain regions [1]. Nevertheless, consciousness experiences in healthy individuals have been consistently found to correlate with synchronized changes in brain activity that are organized in distinct cerebral networks [2, 3]. In addition, various neurological pathologies ranging from stroke to neurodegenerative diseases result in impairment of these brain connectivity signatures and cerebral networks [4]. In particular, patients with disorders of consciousness (DOC) or consciousness impairment have been found to have a decreased level of resting-brain activity in certain brain regions and reduced degree of functional connectivity within hubs of default mode network such as the posterior cingulate cortex and precuneus [5]. Furthermore, early changes in these resting-state brain networks in patients with anoxic brain injury predicted the long term functional outcome [6]. These studies suggest the potential roles of utilizing resting-brain networks as markers of the level of consciousness and as predictors of future recovery of consciousness in patients hospitalized in the intensive care unit (ICU). These studies, however, involved patients with diffuse brain injury such as in the cases of anoxic or traumatic brain injuries. Patients with focal brain injury due to stroke also often develop early consciousness disorder (ECD) even within 24 h of stroke in approximately 35% of the cases [7]. While the mechanisms of ECD in these patients are not clear, a study of resting-state functional MRI (fMRI) in stroke patients with ECD has shown decreased resting-brain activity and decrease in the strength of the default mode network connectivity in the precuneus and posterior cingulate cortex compared to normal subjects [8]. This suggests the potential role of brain activity and connectivity in understanding the differences in consciousness level among patients with stroke. Electroencephalography (EEG) offers an alternative option to fMRI in studying brain connectivity in the ICU setting due to its lower costs, higher temporal resolution and ease of application in the ICU patients [9, 10].

In this issue of *Neurocritical Care*, Huang et al. perform extensive analysis of the brain activity and networks based on EEG data in patients with acute large hemispheric infarction who had ECD [11]. They enrolled 30 patients who were admitted to a neurointensive care unit with large hemispheric stroke within one month of onset. Among these patients, 22 patients had ECD. First, they performed quantitative analysis of the EEG data

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by using power spectrum and entropy analyses. Subsequently, they completed a brain network connectivity analyses by utilizing coherence, phase synchronization and finally graph theory analyses to describe the characteristics of brain networks. Additionally, they performed detailed analysis based on the laterality of the stroke (left hemisphere versus right hemisphere) and the affected versus non-affected cerebral hemispheres by the stroke. Their main results show that the conscious group had higher beta relative spectral power across the whole brain, higher alpha spectral power on the infarction contralateral side in certain lobes according to the infarction side compared to the ECD group. In addition, conscious group had lower theta and delta spectral power on the infarction contralateral side than the ECD group. Entropy analysis similarly showed higher approximate entropy and permutation entropy across the whole brain in the conscious group than the ECD group. Analysis of the brain connectivity showed higher alpha and beta frequency band coherence in several brain lobes in the conscious group than ECD group. Additionally, alpha and beta phase synchronization were also higher in several brain areas in conscious group versus ECD group. Graph analysis of the brain networks showed that the conscious group had higher small-worldness than the ECD group. Interestingly, small-wordlness properties were not different on the infarction side. But, they were higher on the infarction contralateral side in the conscious group versus ECD group. This study suggests that utility of quantitative EEG measures and connectivity metrics analyses in stroke patients with ECD. Importantly, it also highlights the role of the contralateral infarction hemisphere in maintaining consciousness in patients with large hemispheric stroke.

The strength of this study is that it provides a comprehensive and in-depth analysis of functional connectivity and quantitative EEG metrics in stroke patients in the ICU setting. There are, however, several limitations of this study. First, it is a single center study with a small sample size. Second, the inclusion criteria included patients within the first 30 days of stroke which may have resulted in various degrees of cerebral edema that could have impacted the study results. Third, the study does not investigate the relationship of connectivity changes with patients' functional outcomes or recovery of ECD. Finally, the lack of quantitative accompanying imaging analysis adjusting for stroke volume and changes of the brain structure due to cerebral herniation could have also added additional bias affecting the EEG data acquisition. Nevertheless, this study provides additional evidence to the growing body of literature suggesting the utility of brain connectivity analysis in patients with ECD in the ICU setting to better understand consciousness level or as a monitoring tool. Particularly, due to the ease of EEG application and low cost, EEG connectivity derived measures have the potential to be utilized in future large multicenter prospective studies in the ICU setting aiming to improve prognostication of comatose patients and enhance their functional recovery.

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Competing interest
Authors report no conflict of interests in relationship to the content of this work.

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