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Searching for the mechanisms of consciousness in epilepsy

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Defining and understanding consciousness is often assumed to be similar to searching for the Holy Grail. The term consciousness has many ambiguous meanings and often, in medicine, awareness or responsiveness (or lack thereof) are used as surrogate markers. Epileptic seizures provide an opportunity to study these types of changes as part of the consciousness experience. In the *Lancet Neurology*, Jennifer Guo and colleagues¹ report the results of their study aimed at discovering the potential neuronal underpinnings of impaired consciousness, as depicted by alterations in awareness or responsivity, in presumed typical absence epilepsy using functional MRI (fMRI) and electroencephalography (EEG), and behavioral testing in children and adolescents aged 5–19 years. The investigators propose that the impairments identified are the result of widespread involvement of the brain, implicating suspension of the default mode network in conjunction with reduced sensory perception, and not because of focal changes. They also suggest that the behavioural impairments might happen at the onset of the seizures.

To collect an adequate number of patients, the investigators expanded the criteria for absence seizures and probably included patients with different syndromes, as discussed by Panayiotopoulos.² The International League Against Epilepsy is proposing a classification of seizures and epilepsies^{3,4} and Guo and colleagues provide new insights that might help classification. Their findings suggest a different way of interpreting how changes in impairment of consciousness occur in absence seizures. It is often assumed that the

impairment of consciousness occurs if the seizures last more than 3 s, based on the reaction times tested with EEG monitoring.⁵ This cutoff was included in the study of the effectiveness of antiseizure medications to define an electroclinical seizure as lasting more than 3 s;⁶ the medications were considered effective if there were no seizures or EEG discharges longer than 3 s.⁶ Other researchers have considered 6 s,⁷ whereas Stefan⁸ suggests that changes in eye movements can predict the alteration in consciousness. Guo and colleagues' data suggest that brief absence seizures (ie, 3.8 s [SD 3]) are more likely to spare consciousness than more prolonged ones, and suggest that absence seizures that impair consciousness do so at their electrographic onset. Browne and colleagues⁹ have reported that almost half of patients with absence seizures have impaired auditory reaction times within 0.5 s of the spike-wave discharge onset.

The study by Guo and colleagues does not necessarily identify neuronal underpinnings, it only provides evidence for changes in the intensity of the measured signals. The suggestion that the impairment of consciousness happens early in association with the spike-wave discharge raises the question of what comes first: the predisposition to impaired consciousness or the onset of the EEG absence seizure discharge. Guo and colleagues propose the emergence of a susceptible state, manifested by the early appearing abnormal fMRI signals followed by increased power, hypersynchronous EEG activities, that lead to the impairment of consciousness—ie, absence seizures with altered consciousness are not provoked by but rather predispose to prolonged spike-wave discharges. The caveat is that surface EEG cannot localise changes that might have occurred in deep structures, and therefore the possibility that early deep electrographic seizure discharges contributed to the altered fMRI signal cannot be excluded. Because the impairment of consciousness did not happen with every spike-wave discharge, these data might suggest another mechanism different to the spike-wave discharge. The investigators suggest that the impairment is related to the intensity of the response as measured by the fMRI and power in the EEG, but this intensity might be an epiphenomenon. Additionally, the data do not necessarily exclude the possibility that the impairment of consciousness is greater in those seizures that last longer. The morphology of the recorded seizures is different between the seizures with impairments in consciousness versus those in which consciousness was spared, suggesting that the EEG discharge might contain information that needs to be further explored, including the actual frequency of the discharge and its evolution.

Concerns exist about whether data obtained in an fMRI scanner and EEG are directly related, especially in view of the finding that not all the seizures in each patient had alterations in consciousness. However, because of the artifacts produced by the fMRI during the EEG collection, it was not possible to do the analysis simultaneously. As our ability to use more sophisticated methods improves, the investigation of why responses are not uniform from seizure to seizure will be a step to further understand the substrates of consciousness. This compelling study creates a new set of questions. The clinical considerations are that not all brief spike-wave discharge bursts might be silent and that use of functional tests will be paramount in establishing whether spike-wave discharges impair responsiveness.

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