



Theta-burst-induced seizures reported by Lenoir et al.: Anterior or posterior insular seizures?



Dear Editor,

Lenoir et al. [1] recently reported two cases of epileptic seizures as adverse events of continuous theta burst stimulation. They targeted the dorsal-posterior operculo-insular cortex in order to modulate somatosensory sensations in healthy volunteers, including those mediated by thermo-nociceptive input received by this region. Although the principal objective of this report is to call for attention for the potential risk of this procedure, the authors may have been unaware of important information which provide insights into the insular subregion activated by their stimulation technique. In particular, the fact that both Case 1 and Case 2 showed *euphoric thoughts* at the onset of their seizure events is inconsistent with a primary seizure origin in the posterior operculo-insular cortex. Clinically, this manifestation is commonly called “ecstatic seizure” (also known as Dostoevsky’s epilepsy after his description of his own epileptic aura), and is a rare entity in the field of epilepsy [2,3]. Ecstatic seizures were once considered to originate from the temporal lobe [2,4], but growing availability of stereotactic EEG recording and electrical cortical stimulation using intracortically-implanted electrodes have allowed to identify an origin in the anterior insula [3,5]. Indeed, euphoric states were never detected after more than 300 stimulus sites in the posterior operculo-insular region [6], and the incidence of ecstatic auras, rarely reported in intracortical stimulation studies [3,7,8], always involved stimulation of the anterior insula. The occurrence of this symptom is therefore considered to depend on a widely-distributed cortical network requiring the activation of a vast region of the anterior insula [3,8,9], that is rarely achieved by focal stimulation with intracortical electrodes. The incidence of ecstatic aura in the report of Lenoir et al. [1] appears high (two out of only 18 participants), and thus strongly suggests that their procedure effectively and widely activated the anterior insula. Indeed, the chronological sequence of ictal symptoms in Case 1 supports the seizure onset within the anterior insula with later involvement of its posterior sectors or the parietal operculum (i.e., paresthesias occurred later than the ecstatic aura), in contrast with the authors’ intention to stimulate primarily the dorsal-posterior operculo-insular cortex. Of note, the sensations of laryngeal constriction that is described in Case 1 also strongly points to a location in the anterior insula [6]. Thus, although the stimulating coil was theoretically positioned “over the dorsal-posterior operculo-insular cortex”, the stimulation appears to have been effectively delivered to more anterior sectors. It is indeed hard to determine the appropriate coil orientation and position for a particular insular subregion,

since the insular cortex has a complex pyramidal shape with differentially-oriented gyri, –an anatomical circumstance that is greatly different from that of the primary motor cortex. We therefore would like to suggest that the neuromodulatory effects of this procedure, if achieved in future studies using an identical technique, must be carefully interpreted in the light of the significant involvement of the affective-cognitive network centered around the anterior insula.

Conflicts of interest

The authors declare no competing financial interests.

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