Sudden unexpected death in epilepsy (SUDEP) is the leading cause of death for patients with refractory epilepsy, and there is increasing evidence for a centrally mediated respiratory depression as a pathophysiological mechanism. The brain regions responsible for a seizure's inducing respiratory depression is unclear—the respiratory nuclei in the brainstem are thought to be involved, but the involvement of forebrain structures is not yet understood. The aim of a study of Nobis et al. was to analyze intracranial EEGs in combination with the results of respiratory monitoring to investigate the relationship between seizure spread to specific mesial temporal brain regions and the onset of respiratory dysfunction and apnea.

The authors reviewed all invasive electroencephalographic studies performed at Northwestern Memorial Hospital (Chicago) since 2010 to identify those cases in which 1) multiple mesial temporal electrodes (amygdala and hippocampal) were placed, 2) seizures were captured, and 3) patients' respiration was monitored. They identified 8 investigations meeting these criteria in patients with temporal lobe epilepsy, and these investigations yielded data on a total of 22 seizures for analysis.

The onset of ictal apnea associated with each seizure was highly correlated with seizure spread to the amygdala. The onset of apnea occurred  $2.7 \pm 0.4$  (mean  $\pm$  SEM) seconds after the spread of the seizure to the amygdala, which was significantly earlier than after spreading to the hippocampus (10.2  $\pm$  0.7 seconds; p < 0.01).

The findings suggest that the activation of amygdalar networks is correlated with central apnea during seizures. This study builds on the authors' prior work that demonstrates a role for the amygdala in voluntary respiratory control and suggests a further role in dysfunctional breathing states seen during seizures, with implications for SUDEP pathophysiology <sup>1</sup>.

## 1)

Nobis WP, González Otárula KA, Templer JW, Gerard EE, VanHaerents S, Lane G, Zhou G, Rosenow JM, Zelano C, Schuele S. The effect of seizure spread to the amygdala on respiration and onset of ictal central apnea. J Neurosurg. 2019 Apr 5:1-11. doi: 10.3171/2019.1.JNS183157. [Epub ahead of print] PubMed PMID: 30952127.

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