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Single mutation causes seizure disorder

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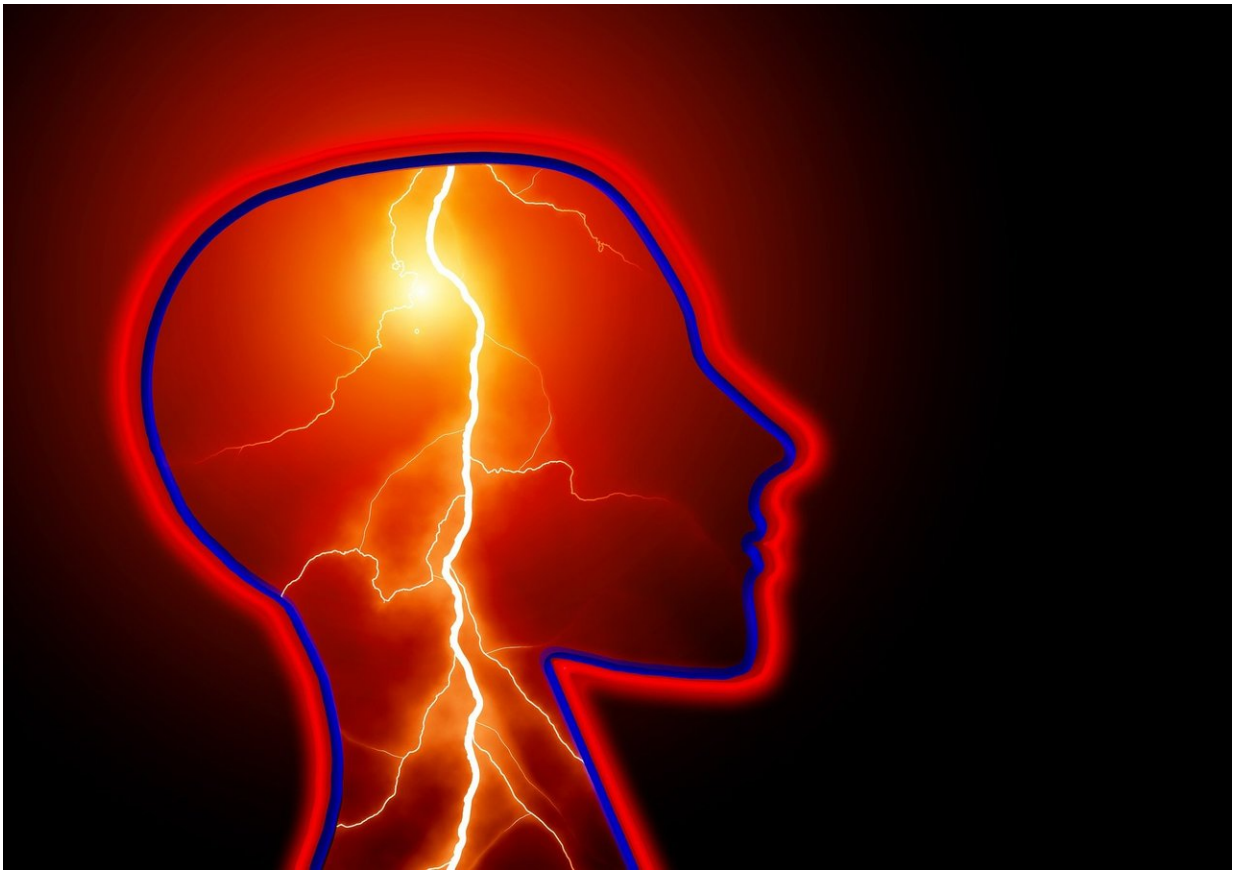

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Lennox-Gastaut syndrome is a severe early-onset seizure disorder that includes cognitive and behavioral abnormalities. Its pathophysiology is largely unknown.

Recent whole-exome sequencing in patients with Lennox-Gastaut syndrome identified a spontaneous mutation in the gene encoding a GABA-A receptor subunit implicated in other childhood epilepsies.

Robert Macdonald, MD, PhD, and colleagues have now generated a mouse model with the human mutation in the GABA-A receptor subunit gene. The mice have spontaneous atypical absence seizures and other types of seizures, with EEG characteristics consistent with Lennox-Gastaut syndrome. The mice also have abnormal behaviors observed in patients with Lennox-Gastaut syndrome, including impaired learning, memory, and social interaction, increased anxiety and hyperactivity.

The findings, reported in the journal *Brain Communications*, demonstrate that a single mutation in one gene can impair inhibitory GABA signaling in the brain and cause multiple types of seizures and behavioral abnormalities. The mouse model will be useful for further characterization of Lennox-Gastaut syndrome pathophysiology and for the development of novel therapies.

More information: Shimian Qu et al. GABAA receptor β3 subunit mutation D120N causes Lennox–Gastaut syndrome in knock-in mice, *Brain Communications* (2020). DOI: 10.1093/braincomms/fcaa028

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