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Involvement of fast-spiking cells in ictal sequences during spontaneous seizures in rats with chronic temporal lobe epilepsy.

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Recommendations:

★★ Very Good — 27 Oct 2017

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CONFIRMATION

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The paradoxical role played by GABAergic networks in seizure initiation is well established and the role of $GABA_A$-receptor mediated signaling in promoting epileptiform synchronicity and in triggering seizures has been documented in several studies performed *in vitro* by employing the 4-aminopyridine model. Specifically, it was reported that ictal discharge onset is associated with a synchronous GABAergic event {1} and increased interneuron firing {2-4}; see {5} for a review. Moreover, in this model, the optogenetic stimulation of GABAergic interneurons can trigger ictal discharges {6,7}. However, few studies have explored *in vivo* the role of interneurons in the generation of seizures in experimental models of temporal lobe epilepsy.

Here, Neumann et al. used two animal models of temporal lobe epilepsy -- the perforant path stimulation model and the intrahippocampal kainic acid model -- to study the activity of single units in the hippocampus between and during seizures in animals implanted with tetrode wires 4 weeks after the induction of a *status epilepticus*. The main findings obtained in this study are that in the hippocampal CA1 area, ictal spikes during the initial and late phase of seizures are more strongly associated with the activity of fast-spiking inhibitory interneurons compared to that of principal cells. Moreover, the strength of entrainment of neuronal activity during ictal spikes correlates with the strength of coupling before the onset of the seizure, indicating that fast-spiking GABAergic interneurons firing together and in a strong correlated pattern with field oscillations between seizures form clusters that are likely to be activated during seizures. During an ictal spike, single units from the same cluster also fire in given temporal sequences that are repeated from one ictal spike to another as well as from one seizure to another.

The *in vivo* results reported by Neumann et al. support previous findings on the pivotal role played by interneurons and GABAergic inhibition in seizure generation (see {5} for a review). They also suggest that the temporal relations between single units occurring during the interictal period are preserved when seizures occur; this evidence suggests that establishing the activity of single units between seizures should predict their activity during ictogenesis.

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Disclosures

None declared

Add a comment

Abstract:

ABSTRACT

See Lenck-Santini (doi:10.1093/awx205) for a scientific commentary on this article. Epileptic seizures represent altered neuronal network dynamics, but the temporal evolution and cellular substrates of the neuronal activity patterns associated with spontaneous seizures are not fully understood. We used simultaneous recordings from multiple neurons in the hippocampus and neocortex of rats with chronic temporal lobe epilepsy to demonstrate that subsets of cells discharge in a highly stereotypical sequential pattern during ictal events, and that... more »
these stereotypical patterns were reproducible across consecutive seizures. In contrast to the canonical view that principal cell discharges dominate ictal events, the ictal sequences were predominantly composed of fast-spiking, putative inhibitory neurons, which displayed unusually strong coupling to local field potential even before seizures. The temporal evolution of activity was characterized by unique dynamics where the most correlated neuronal pairs before seizure onset displayed the largest increases in correlation strength during the seizures. These results demonstrate the selective involvement of fast spiking interneurons in structured temporal sequences during spontaneous ictal events in hippocampal and neocortical circuits in experimental models of chronic temporal lobe epilepsy.

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