Modulation of the slow transition to seizure process by interictal discharges *in vitro*.

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Rationale: Previous studies have demonstrated that the slow transition to seizure process *in vitro* is associated with dynamical changes in the properties of high-frequency activity (HFA). These changes reflect a progressive loss in the dynamical stability of neuronal populations as the seizure approaches. It is well established that interictal discharges have the capacity to delay or abort the transition to seizure. In this study we examined the impact of interictal discharges on the slow transition process and HFA properties.

Methods: The experiments were performed *in vitro* in rat hippocampal slices perfused with artificial CSF containing high potassium (>8 mM). Field potentials from the hippocampal CA1 and CA3 regions were recorded using multiple extracellular electrodes.

Results: Spontaneous seizure-like events were generated within the CA1 region with a mean inter-seizure interval of 60.4±4.4 s. Seizures did not occur abruptly, but were preceded by a progressive buildup of low-amplitude HFA at ~200 Hz. The CA3 region generated interictal discharges, which propagated to CA1 where they interfered with the dynamics of HFAs. Each discharge was preceded by a buildup of HFA and followed by period with suppression or absence of HFA. Removal of interictal discharge interference by disconnecting the CA3 region shortened the inter-seizure period (40.3±2.0 s)

Discussion: This study suggests that the seizure-delaying effect of interictal discharges could be attributed to their ability to modify the slow dynamics of the transition to seizure. This can occur via modulation of the mechanisms underlying the transition, which are involved in the genesis of interictal HFA.

This study was supported by the grants of the Ministry of Health of the Czech Republic (NT/13357, NT/14489-3), AZV 15-29835A), Neuron Fund for Support of Science (001/2012) and the Czech Science Foundation (GACR 14-02634S).