Impairment of GABA release in the hippocampus at the time of the first spontaneous seizure in the pilocarpine model of temporal lobe epilepsy

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The alterations in GABA release have not yet been systematically measured along the natural course of temporal lobe epilepsy. In this work, we analyzed GABA release (using in vivo microdialysis under basal and K^+ evoked conditions) and loss of two major GABA interneuron populations (parvalbumin and somatostatin neurons) in the ventral hippocampus at different time-points after pilocarpine-induced status epilepticus in the rat, i.e. during development and progression of epilepsy. We found that (i) during the latent period (between the epileptogenic insult, i.e. status epilepticus, and the first spontaneous seizure) there is a loss of GABA cells and the basal GABA release is reduced, but the system seems still capable to effectively counteract seizures, because an increased GABA release takes place in response to stimulation; (ii) at the time of the first spontaneous seizure (i.e., when the diagnosis of epilepsy is made in humans) this increased responsiveness to stimulation of the GABA release system disappears and no compensation for GABA cell loss is anymore available; (iii) thereafter, this dysfunction remains constant until a late phase of the disease. These data suggest that a GABAergic hyper-responsiveness compensates for GABA cell loss and protects from occurrence of seizures during latency, whereas impaired GABA release favors the occurrence of spontaneous recurrent seizures and the maintenance of an epileptic state.