Mossy cell excitability is reduced in a pre-symptomatic genetic mouse model of epilepsy

Epilepsy is a widely encountered brain disorder affecting a significant proportion of the population. It presents itself in several subtypes, associated with other disturbances or alone, and is often untreatable or managed unsatisfactorily through currently existent therapy/medication. This study intends to extend the knowledge regarding the state of the pre-epileptic brain, by using a genetic model for epilepsy, i.e. a Synapsin II knockout mouse. Synapsin II is a neuronal phosphoprotein that covers synaptic vesicles and clusters them, by tethering to the actin cytoskeleton. The main morphological finding in Synapsin II KO mice is the dramatic decrease of the reserve pool of synaptic vesicles. Synapsin II KO mice seem completely normal before the age of 2 months, when they become highly susceptible to epileptic seizures. Here, I focused on the young, pre-symptomatic mouse, to investigate possible changes in a specific hippocampal microcircuit, namely the granule-mossy circuit, in acute brain slices. The dentate gyrus (DG) is thought to have a gate role, filtering the information that enters the hippocampus. In particular the excitatory hilar mossy cells of the DG, that receive input from up to 10,000 granule cells, and send axonal projections to target other granule cells, are suitable candidates for seizure spread throughout the hippocampus. Indeed, a specific hippocampal morphological characteristic of temporal lobe epilepsy is the loss of hilar neurons, and several theories involving mossy cell alterations have emerged to explain this phenomenon.

The main findings of this study are the decreased release of neurotransmitter from the granule cell terminals and decreased excitability of the excitatory hilar mossy cells. These results suggest a role of the mossy cells in activating inhibitory interneurons, thus maintaining the normal physiological excitatory hippocampal state.