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The GAD65 KO mouse model of reduced GABAergic synthesis: changes in hippocampal network oscillations and single cell properties

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Mice with targeted disruption of the gene for glutamic acid decarboxylase (GAD65 KO mice) display a postnatal deficit in γ-aminobutyric acid (GABA) synthesis, increased fear and anxiety. In the current study I examine GABAergic network activities and single cell properties in the ventral hippocampus (vHP) that may be involved in the emergence of this phenotype.
For this reason, I performed local field potential recordings from acute horizontal brain slices including the vHP and examined the spontaneous sharp-wave ripples (SW-R), the carbachol-induced gamma oscillations from Cornu Ammonis 1 (CA1) and 3 (CA3) and the synaptic plasticity of the circuit CA3-CA1. I found that the power and the peak frequency of gamma oscillations were significantly increased both in CA3 and CA1 subregions of GAD65 KO mice in comparison to wild-types (WT). In line, spontaneous SW- and Ripple- components of the SW-R activity were altered and wave propagation failure from CA3 to CA1 was observed.
Additionally, I performed patch clamp recordings in CA1 pyramidal neurons in order to investigate possible alterations in single cells properties, that may contribute to the network alterations. These experiments, revealed unaltered intrinsic properties of CA1 pyramidal cells but moderate changes in their excitatory and inhibitory post-synaptic currents. Finally, in order to see if these post-synaptic currents are altered in time, my next experiments involve their distribution in time and specifically in relation to the network oscillations.
These findings suggest that reduced GABA availability in GAD65 KO mice may trigger long-term alterations in vHP network oscillations, which in turn may underlie the fear- and anxiety-phenotype of GAD65 KO mice. Augmented network oscillations in the vHP might be a risk factor for the development and persistence of fear memories and stress-related disorders.