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In Vivo recordings in a model for human absence epilepsy

Promotionsfach: Physiologie
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The gamma2(R43Q) mouse model carries a point mutation in the gamma2 subunit of the GABA-A receptor, a widely distributed ligand-gated Chloride channel in the central nervous system. This mutation was first characterized in humans and is associated with autosomal dominant inheritance of childhood absence epilepsy (CAE) and febrile seizure (FS). CAE has a typical onset during school age with clinical symptoms like sudden behavioral arrest, facial automatisms and a loss of consciousness. These episodes usually last only a few seconds, can occur several hundred times a day and are accompanied by typical 3-Hz-Spike-and-Wave discharges on the EEG. Mice carrying the gamma2(R43Q) point mutation show a similar phenotype.
In this study extracellular recordings of thalamocortical relay neurons and in vivo whole-cell recordings of cortical pyramidal neurons were used to assess their electrophysiological properties in the gamma2(R43Q) mouse model. The barrel system was chosen as a model for thalamocortical interaction. Data was acquired in a randomized, blinded study design.
Thalamocortical relay neurons in gamma2(R43Q) mice did not reveal any significant increase in terms of firing frequency, action potential precision or spontaneous activity (n=12, both groups). Cortical whole-cell recordings in layer 2/3 and layer 5/6 pyramidal neurons (n(wildtype)=14, n(R43Q)=10) showed a higher resting membrane potential on trend level and significantly higher spontaneous activity upon PTZ injection in gamma2(R43Q) mice compared to littermate controls (p-value: 0.02). No significant difference in terms of response amplitudes could be observed.
This study is the first in vivo study in a knock-in mouse model for human absence epilepsy. The findings support a cortical defect leading to the observed phenotype. It can be hypothesized that altered tonic inhibition through GABAergic synapses contributes in the pathophysiology of the gamma2(R43Q) mouse model. Data supporting the idea of altered GABAergic fast inhibition in cortex could not be found.