Progression of epileptogenesis in chronic epileptic rats: studies on parahippocampal synaptic reorganization

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In patients with mesial temporal lobe epilepsy (MTLE), the superficial part (layers I-III) of the entorhinal cortex presents marked cell loss particularly noticeable in layer III. This characteristic cell loss has been reproduced in rat models of MTLE after induction of a status epilepticus (SE) and is confined to the medial portion of the entorhinal cortex (MEA). The main input to MEA-III arises from the presubiculum. An anatomical tracing study in chronic epileptic rats, 2-5 months after kainic acid (KA) induced SE, revealed that presubicular fibers still project to MEA-III, despite extensive loss of layer III neurons. In order to investigate how the function of the MEA is affected in chronic epileptic rats, we performed in vivo electrophysiological recordings using a 16-channel silicon-probe in the MEA of anesthetized rats 2-4 months after KA-induced SE. Stimulations were performed in either the presubiculum or the subiculum which project to superficial and deep layers of the MEA, respectively. Both after presubiculum and subiculum double pulse stimulation, oscillations in the β/γ-frequency range were observed in the superficial part of MEA in epileptic rats that displayed MEA-III loss. Oscillations were never observed in control rats or KA rats with minor MEA-III loss. Interestingly, layer III GABAergic interneurons, that in normal rats provide strong inhibition in MEA layer II/III, are well preserved after chronic epilepsy in rats. We hypothesize that the observed oscillations are the result of specific alterations in the superficial MEA resulting in an impairment of inhibition. Such alterations may involve changes in synaptic connections and/or cellular properties that influence the excitability of local neuronal networks. The occurrence of oscillations in superficial MEA in chronic epileptic rats likely provides an increased excitatory drive to the hippocampus. Whether spontaneous seizures also originate in the superficial MEA layers will be subject of future studies.

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