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WHICH HIPPOCAMPAL CELLS DIE AFTER CRH-INDUCED STATUS EPILEPTICUS

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3.12 WHICH HIPPOCAMPAL CELLS DIE AFTER CRH-INDUCED STATUS EPILEPTICUS? Charles E. Ribak¹ and Tallie Z. Baram², Dept. Anatomy & Neurobiology, University of California, Irvine, CA¹ and Dept. Neurology, Children's Hospital Los Angeles and University of Southern California, Los Angeles, CA².

Objective: Previous studies of CRH-induced status epilepticus in infant rats demonstrated neuronal loss in several limbic structures, including the CA3 region of the hippocampus. In addition, mossy fiber sprouting occurred in the dentate gyrus of such rats indicating a loss of target neurons. The goal of the present study was to identify the neurons affected by CRH-induced seizures using both light and electron microscopy.

Methods: Infant rats were injected with CRH i.c.v. two times a day on postnatal days 10 and 11. Following a 24 hour survival time after the last injection, rats were perfused with a combined aldehyde solution. Brain sections including the hippocampus were osmicated, dehydrated and embedded in plastic for electron microscopy.

Results: Clusters of neurons in the CA3 region of the hippocampus and a few in the hilus of the dentate gyrus showed dense osmiophilic staining in thick sections. Semi-thin 2 μ m sections showed dark osmiophilic neurons in the pyramidal cell layer of CA3. These cells were shrunken but still displayed apical and basal dendrites. Electron microscopy revealed densely-stained degenerating pyramidal cells with intact cell membranes and electron dense nuclei and cytoplasm. Dendrites of these cells were shrunken, had spines and were postsynaptic to large immature-appearing mossy fibers.

Conclusion: The hippocampal cells that are dying subsequent to CRH-induced status epilepticus are CA3 pyramidal neurons that are linked via mossy fibers to the tri-synaptic excitatory hippocampal circuit. The shrunken appearance and selective loss of these neurons are incompatible with necrosis as the mechanism of degeneration.

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