

P069 Induction of intrinsic mitochondrial cell death pathway following experimentally-evoked seizures and in human temporal lobe epilepsy.

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Seizures are capable of causing neuronal death. Previous studies have demonstrated that experimental seizures can activate the intrinsic mitochondrial cell death pathway and activate caspases and that components of these pathways are altered in involved brain structures in patients with temporal lobe epilepsy. We recently developed a mouse model of seizure-induced neuronal death with features of programmed cell death. Presently, we examined the activation of the mitochondrial apoptotic pathway in this model and contrasted this to events within human epilepsy brain. Seizures evoked by intraamygdala kainic acid in C57BL/6 mice caused ipsilateral death of CA1 and CA3 neurons within the hippocampus. Western blotting revealed seizures induced cleavage of Bid, overexpression of Bax, cytochrome c release and activation of caspase-9 and -7. Expression of anti-apoptotic Bcl-2 and Bcl-xl was not significantly altered but seizures did reduce levels of the inhibitor of apoptosis protein cIAP2. Analysis of hippocampi from patients with intractable epilepsy revealed Bid was also cleaved and caspases 9 and 7 were processed. These data suggest seizures activate the mitochondrial apoptotic cell death pathways and as such may be targets for neuroprotection following status epilepticus and in epilepsy.