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MEETING ABSTRACT

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Changes in the expression of histone deacetylase 1–11 mRNAs in the hippocampus in two mouse models of temporal lobe epilepsy

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Background: Histone modifications involve deacetylation of histone proteins by HDAC families of enzymes contributing to transcriptional silencing of gene expression. There are four different classes, comprising 11 HDAC isoforms. We investigated changes in the expression of HDAC mRNAs in an animal model of temporal lobe epilepsy (TLE).
Methods: C57BL/6N mice were injected unilaterally with kainic acid (KA; 0.350 nmol/70 nl) into the dorsal hippocampus (CA1). EEGs were continuously recorded subdurally for 4 weeks and revealed an initial status epilepticus, followed by about 2 severe spontaneous seizures per day. In the injected hippocampus, losses in CA1 and CA3 pyramidal cells were observed after 24 h and granule cell dispersion after 7 days. Expression levels of HDAC 1–11 mRNAs were investigated by *in situ* hybridization 2, 4, 6, 12, 24 and 48 h, and 7, 14 and 28 days after KA.
Results: In the dentate gyrus, HDAC 1, 2, 4, 7 and 11 mRNAs were significantly decreased 4 h after KA ipsi- and contralateral to the injection relating to increased seizure activity during the initial status epilepticus and presumably contributing to increased expression of different genes. In contrast, HDAC5 mRNA levels were significantly increased 4 and 12 h after KA presumably resulting in silencing of certain genes. HDAC3 mRNA levels were transiently increased (contralaterally) and those of HDAC4 mRNA decreased after 24 to 48 h. Most interestingly, 7 to 28 days after KA injection we observed also a pronounced increase in HDAC9 mRNA expression in granule cells of the injected hippocampus correlating with the concomitantly developing granule cell dispersion.
Discussion: Decreases in HDAC 1, 2, 4, 7 and 11 during the status epilepticus may initiate augmented gene expression of various genes and may induce epileptogenesis. Specific upregulation of HDAC 5 and 9 in granule cells may be related to granule cell dispersion.
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