Calcium extrusion protein expression in the hippocampal formation of chronic epileptic rats after kainate-induced status epilepticus

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The plasma membrane Ca^{2+}-ATPase (PMCA) and (potassium-dependent) sodium-calcium exchange (NC(K)X) represent two main calcium extrusion mechanisms that are important for the restoration of $[Ca^{2+}]_i$ levels after electrical activity. To investigate whether the expression of these calcium extrusion proteins is altered in the course of epileptogenesis, we compared the hippocampal-parahippocampal protein expression of NCX1, 2, and 3, PMCA1-4, and NCKX2 at an early and late stage after kainate-induced status epilepticus (SE), with that in control rats using immunocytochemistry. Several alterations were found in chronic epileptic rats: (i) NCX1 was permanently downregulated in the inner molecular layer (iml) of the dentate gyrus (DG) and entorhinal cortex layer III (ECIII), related to neuronal loss in hilus and ECIII, respectively; (ii) PMCA and NCKX2 expression was transiently upregulated in the iml, and downregulated in several areas where cell loss had occurred, (iii) NCX3 expression, which in control rats is abundant in presynaptic terminals of mossy fibers (mf), was extensively and permanently decreased in stratum lucidum and hilar region. In addition, newly formed mf sprouts that project to the DG iml did not noticeably express NCX3; (iv) NCX2 and NCKX2 were (transiently) upregulated in astrocytes of epileptic rats throughout the hippocampal formation, including ECIII. Our results show regional-specific changes of calcium extrusion proteins in epileptic rats that contribute to altered calcium homeostasis in the diseased state. More importantly, some alterations in calcium extrusion protein expression are already present at an early stage of epileptogenesis and could therefore be involved in this process.

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