Signalling pathways involved in the pathogenesis of epileptic hippocampus

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We can find hippocampal sclerosis in patients with mesial temporal lobe epilepsy. The pathology of hippocampal sclerosis consists of neuronal cell death, enhanced neurogenesis, axonal sprouting and reactive gliosis. Previously, the epilepsy research on hippocampal sclerosis has been focused on morphological and electrophysiological changes but not underlying signaling mechanisms. Signaling pathways means the intracellular cascade that is activated in response to extracellular signal and that ultimately acts on the cell nucleus and thereby result in long-term changes in brain functions. Therefore, the elucidation of the signaling molecules activated abnormally in the epileptic hippocampus would be valuable in understanding pathomechanisms of epilepsy and searching for the potential therapeutic targets.

Recently, we found that c-AMP response element binding protein (CREB) and 90-kDa ribosomal S6 kinase (p90RSK) are actively expressed in surgically obtained epileptic hippocampus revealing hippocampal sclerosis. Activation of CREB and p90RSK was noted in the whole subfields of hippocampus with hippocampal sclerosis representing a distinctive cellular distribution, but the common major changes were present in proliferating reactive astrocytes. Their activation revealed regional specificities to epileptic hippocampus; not significant in adjacent temporal lobes despite the presence of a number of astrocytes expressing high levels of GFAP. However, our results were based on cross-sectional examination of surgical materials, so it is insufficient to know the significance of the chronic activation of CREB and p90RSK in epileptic hippocampus. To elucidate their possible roles in the epileptogenesis the further studies using experimental seizure models are needed.