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Ischemia-induced increase in the expression of the regulators of G-protein signaling subtype7 (RGS7) in gerbil hippocampus

Stroke is one of the leading causes of death in the United States. Ischemic stroke accounts for most stroke events. Transient global ischemia induced to gerbils is a well-studied animal model of neuronal death in the hippocampus. The hippocampus is a brain region responsible for learning and memory and one of its subregion called CA1 is the most vulnerable area to ischemic damage in the brain. Neurons in other hippocampal subregions, especially in CA3 and in the dentate gyrus, will survive the ischemic insult. So, differences in the reaction of neurons to ischemic insult in distinct hippocampal subregions will inform us about pathways related to neuronal death and/or survival. Signal transduction is the fundamental biological process for relaying extracellular information to intracellular changes. One important class of signal transduction pathways with profound clinical significance is that controlled by the G-protein coupled receptors (GPCRs). More than 600 GPCRs exist, and they comprise the second-largest protein family in the mammalian genome. Recently, a newly discovered family of proteins, called Regulators of G protein Signaling (RGS) proteins, has been shown to regulate GPCR functions. Activation of GPCRs catalyzes the exchange of G alpha bound GDP for GTP to cause dissociation of G alpha from the G beta-gamma dimer and initiate down stream signaling propagation. RGS proteins are responsible for terminating this signaling. The goal of this study was to investigate the temporal and spatial pattern of RGS7 (one subtype of RGS proteins) mRNA distribution after transient global cerebral ischemia induced to gerbils. Animals were given an ischemic insult by ligation of both common carotid arteries for five minutes that was followed by 4 or 16 hr reperfusions. Control animals underwent the same surgical procedure as for ischemia except that the arteries were not clamped. The brains were frozen and twelve-micrometer coronal sections were cut in a cryostat. Quantitative in situ hybridization was used to measure RGS7 mRNA levels in four hippocampal subregions. RGS7 mRNA level in the dentate gyrus was significantly increased after ischemia. The mRNA levels were 50-60% and 20-25% (n=8/group) higher in the ischemic hippocampus 4 hr and 16 hr after reperfusion, respectively. Other subregions (CA1, CA3, hilus) of the hippocampus did not show changes. These results suggest that upregulation of RGS7 expression may be one of the possible mechanisms involved in neuronal survival in the dentate gyrus. The rapid increase in RGS7 expression could represent an adaptation of the granule cells to reduce excitability in order to protect these neurons against ischemic damage.