Abstract:

The polymodal transient receptor potential vanilloid 4 (TRPV4) channel, a member of the TRP channel family, is a calcium-permeable cationic channel that is gated by cell swelling, low pH and high temperature may be involved in neuronal and glia pathophysiology. In the present study, we examined the impact of cerebral hypoxia/ischemia (H/I) on the functional expression of astrocytic TRPV4 channels in the adult rat hippocampal CA1 region. Hypoxia/ischemia was induced by a bilateral 15-minute occlusion of the common carotids combined with hypoxic conditions. Our immunohistochemical analyses revealed that 7 days after H/I, the expression of TRPV4 is markedly enhanced in hippocampal astrocytes of the CA1 region and that the increasing TRPV4 expression coincides with the development of astrogliosis. Adult hippocampal astrocytes in slices or cultured hippocampal astrocytes respond to the TRPV4 activator 4-alpha-phorbol-12,-13-didecanoate (4αPDD) by an increase in intracellular calcium and the activation of a cationic current, both of which are abolished by the removal of extracellular calcium or exposure to TRP antagonists, such as Ruthenium Red or RN1734. Following hypoxic/ischemic injury, the responses of astrocytes to 4αPDD are significantly augmented. Collectively, we show that TRPV4 channels are involved in ischemia-induced calcium entry in reactive astrocytes and thus, might participate in the pathogenic mechanisms of astroglial reactivity following ischemic insult.