TRPV4 CHANNEL EXPRESSION IN THE HIPPOCAMPUS IS MAINLY CONFINED TO ASTROCYTES

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Purpose: Transient receptor potential (TRP) channels are a family of cell membrane proteins classified in 3 main groups: TRPC, TRPV and TRPM. Many of these Ca²⁺-permeable cationic channels are expressed in the CNS but their gating mechanisms and function are not fully understood. TRPV4 channels, expressed both in the periphery and in the brain, have recently attracted considerable attention due to their sensitivity to changes of temperature within the physiological range, activation by low pH and cell swelling, and mechanosensitive properties. Our aim was to examine cellular expression of these channels within the hippocampus in the context of our work suggesting that TRP channels may be activated during ischemia and that their closure by mild hypothermia is neuroprotective (Lipski et al., PANS, 2006). Methods: RT-PCR, immunocytochemistry and western blotting were used to study hippocampal TRPV4 expression in slices from juvenile rats (n=12) and in organotypic slice cultures (n=9). Results: The presence of TRPV4 mRNA and protein was consistently demonstrated in both preparations using RT-PCR and western blots. In acute slices, strongly TRPV4-immunoreactive cells were seen in all hippocampal regions except the CA1/CA3 pyramidal and dentate granule cell layers. In both preparations, double labelling for TRPV4 and GFAP confirmed that the strongly labelled cells were astrocytes, while little or no TRPV4 staining was found in cells labelled for GAD or MAP2. TRPV4 immunoreactivity was also observed outside the hippocampus, for example in GFAP-positive cells of the cerebral cortex, in leptomeninges, and in ependyma and choroid plexus of the cerebral ventricles. Conclusion: These data provide the first evidence that TRPV4 is expressed in hippocampal and extrahippocampal astrocytes, suggesting a specific role.