Divergent Ca^{2+} signaling pathways mediated by Stress-Inducible Protein 1 in hippocampal neurons and astrocytes

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The cellular prion protein (PrP^C) is a highly conserved cell surface glycoprotein expressed in the Central Nervous System. Its conformationally modified isoform is associated with the Transmissible Spongiform Encephalopathies or prion diseases. Recently, multiple and diverse functions of PrP^c have been reported. Among several PrP^C-binding partners, our group identified Stress Inducible Protein 1 (STI 1), which promotes neuronal differentiation and survival in wild-type ($Prnp^{+/+}$), but not in PrP-null ($Prnp^{0/0}$) hippocampal neurons (*Lopes et al., 2005)*. However, in astrocytes STI1 induces differentiation and survival independently of PrP^C. Using an intracellular Ca^{2+} probe, Fluo- 3 AM, we evaluated the STI1 effect on Ca^{+2} signaling in both, neurons and astrocytes. Our data demonstrated that in hippocampal neurons, STI1 induced an increase in intracellular Ca^{2+} levels through extracellular Ca^2 influx, dependent on PrPc. Moreover, Ca^{2+} influx promoted MAPK activation. Additionally, STI1 also promoted Ca^{+2} mobilization from intracellular stocks (endoplasmic reticulum) in both $Prnp^{+/+}$ and $Prnp^{0/0}$ cells in astrocytes. Our data suggest that STI1 induces PrPc-independent cellular signaling in astrocytes whereas in hippocampal neurons STI1 interaction with PrPc is crucial for cell signaling. Notably, cell signaling triggered by STI1 in astrocytes and neurons differ, since Ca^{+2} is mobilized from different cellular sources, leading to diverse biological functions.

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