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The Expression and Activity of K_V3.4 Channel Subunits are Precociously Upregulated in Astrocytes Exposed to Aβ Oligomers and in Astrocytes of Alzheimer's Disease Tg2576 Mice

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Astrocyte dysfunction emerges early in Alzheimer's disease (AD) and may contribute to its pathology and progression. Recently, the voltage gated potassium channel K_V3.4 subunit, which underlies the fast-inactivating K^+ currents, has been recognized to be relevant for AD pathogenesis and is emerging as a new target candidate for AD. In the present study, we investigated both in *in vitro* and *in vivo* models of AD the expression and functional activity of K_V3.4 potassium channel subunits in astrocytes. In primary astrocytes biochemical, immunohistochemical, and electrophysiological studies demonstrated a time-dependent upregulation of K_V3.4 expression and functional activity after exposure to amyloid-β (Aβ) oligomers. Consistently, astrocytic K_V3.4 expression was upregulated in the cerebral cortex, hippocampus, and cerebellum of 6-month-old Tg2576 mice. Further, confocal triple labeling studies revealed that in 6-month-old Tg2576 mice, K_V3.4 was intensely coexpressed with Aβ in nonplaque associated astrocytes. Interestingly, in the cortical and hippocampal regions of 12-month-old Tg2576 mice, plaque-associated astrocytes much more intensely expressed K_V3.4 subunits, but not Aβ. More important, we evidenced that the selective knockdown of K_V3.4 expression significantly downregulated both glial fibrillary acidic protein levels and Aβ trimers in the brain of 6-month-old Tg2576 mice. Collectively, our results demonstrate that the expression and function of K_V3.4 channel subunits are precociously upregulated in cultured astrocytes exposed to Aβ oligomers and in reactive astrocytes of AD Tg2576 mice.

Biography:

Anna Pannaccione is the assistant Professor of Pharmacology at the Department of Neuroscience of the University of Naples Federico II, School of Medicine from 2004.

His main research themes are focused on the functional, pathophysiological and pharmacological role(s) of diverse classes of ionic channels and transporters. Throughout the years, these themes have been pursued by means of an integrated approach using electrophysiological, biochemical, genetic, and pharmacological techniques. In particular, the following research themes have been addressed to the characterization of the involvement of ionic homeostasis dysregulation in Alzheimer's disease with particular attention to the study of sodium/calcium exchanger, voltage-gated potassium K_V3.4/mirp2, and sodium Na_V1.6 channels.