Abstract

Visinin-like protein-1 (VILIP-1) is a neuronal EF-hand Ca^{2+}-binding protein. Here, I describe the distribution of the immunoreactivity detected by specific antibodies against VILIP-1 protein in rat peripheral tissue and in the brain at the light microscopic level. VILIP-1 antibodies stain neurons, but not glial cells, in the whole rat hippocampal formation, including principal cells in the CA1 and CA3 region of the Ammon's horn and in the dentate gyrus. Moreover, to analyze the precise distribution of VILIP-1 in hippocampal interneurons, immunofluorescence co-staining of VILIP-1 with the GABAergic neuronal marker, glutamic acid decarboxylase 67 (GAD67), and with different well defined neurochemical markers for perisomatic inhibitory cells (parvalbumin, PV), dendritic inhibitory cells (calbindin-D28k), and interneurons specialized to innervate other interneurons (calretinin, CR), were performed in rat hippocampal slices. Additionally, the co-localization of VILIP-1 with one of its interaction partners, the α4β2 nicotinic acetylcholine receptor (nAChR) has been studied.

The α4β2 nAChR is the most abundant nAChR subtype with high-affinity for nicotine in the brain. The α4β2 nAChR is crucial for nociception, nicotine addiction and the beneficial effects of nicotine on cognition. VILIP-1, recently shown to affect clathrin-dependent receptor trafficking, interacts with the cytoplasmic loop of the α4 subunit. VILIP-1 enhances ACh responsiveness of hippocampal neurons, possibly comprising a novel form of physiological up-regulation of α4β2 nAChR. In the hippocampal formation VILIP-1 is co-localized with α4β2 nAChR in a distinct neuronal subpopulation consisting particularly of interneurons. Furthermore, enhancement of α4β2 nAChR induced by VILIP-1 leads to enhancement of inhibitory postsynaptic currents (IPSCs). Thus, VILIP-1 in conjunction with the α4β2 receptor might play an important role in modulating hippocampal network activity and synaptic plasticity.

Interestingly in this context, induction of long term potentiation in the hippocampus correlates with increased expression levels of neuronal calcium sensor (NCS) proteins. We have investigated mGluR- and time-dependent changes in the expression of two different NCS proteins. Following DHPG application *in vivo* NCS-1 and VILIP-1 expression increased, with significant levels reached after 8 and 24h. Furthermore, the physiological effects of VILIP-1 upregulation were studied using patch-clamp recording from rat hippocampal neurons *in vitro*, indicating effects of VILIP-1 on neuronal excitability of hippocampal neurons.