Pannexin 1 restricts dendritic branching and formation of dendritic spines in hippocampal neurons: possible role of small Rho GTPases and F-actin.

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The morphological integrity and plastic properties of neurons depend on the dynamics of the neuronal cytoskeleton and involve changes in synaptic morphology and electrical signaling. Dendrites and dendritic spines are the major locus for excitatory synapses, and the actin cytoskeleton is their principal structural and regulatory component. Hence, actin reorganization places a central role in regulating of dendritic arborization and dendritic spines formation and maturation. In this regard, the family of small Rho GTPases, RhoA, Rac1, and Cdc42 play an essential role in regulating structural plasticity by controlling the assembly and stability of the actin cytoskeleton. However, the signals that control the activation or inhibition of the different small Rho GTPases in neuronal development and plasticity are relatively unknown.

Pannexin 1 (Panx1) is a membrane protein that forms non-selective channels implicated in actin-dependent processes in neurons such as cell migration and neurite extension, suggesting that Panx1 also be involved in other structural changes such as those associated with synaptic plasticity.

Here, we investigate if Panx1 channels modulate F-actin remodeling-dependent structural plasticity in hippocampal neurons through a mechanism that involves small Rho GTPases activity. We observed that the absence or blockade of Panx1 channels upon resting conditions increased the length and complexity of the dendritic arbor of hippocampal neurons. Similarly, under the induction of long-term chemical potentiation by glycine stimulation, hippocampal neurons exhibited a higher dendritic spines density than control neurons.

Interestingly, the absence or blockade of Panx1 channels stimulated the content of F-actin and increased the expression and activity of Rac1 and Cdc42 Rho GTPases. Consistently, the inactivation of Rac1 prevents the effect of Panx1 channels inhibition on dendritic arborization and the density of dendritic spines.

Our results provide evidence that the role of Panx1 channels in neuronal morphology and structural synaptic plasticity relies on actin organization and dynamics by regulation of RhoA and Rac1 GTPase activity.