Federation of European Neuroscience Societies

.: Scientific Highlights

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.: Scientific Highlight of the Year

Presented by:

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Differential distribution of NCX1 contributes to spine-dendrite compartmentalization in CA1 pyramidal cells

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Summary:

The distribution of calcium in dendritic compartments of neurons is thought to be crucial in regulating postsynaptic function. The compartmentalized distribution of calcium offers the basis for selective regulation of single synapses and synaptic plasticity. Several mechanisms are known to contribute to the clearance of calcium from neurons, but the distinct contribution of different extrusion mechanisms to calcium compartmentalization in dendritic spines versus shafts remains elusive.

We used a novel combination of methods in order to explore the contribution of a Na^+/Ca^{2+} exchanger (NCX) molecule in the calcium clearance across the plasma membrane in dendrites. High resolution, ultrastructural immunocytochemistry was combined with two-photon imaging to assess the subcellular distribution and role of NCX1 in rat CA1 pyramidal cells. NCX1 immunolabelling was predominantly found in the somatodendritic, but not along the axonal domain of pyramidal cells. Quantitative electron microscopic analysis of the preembedding immunogold reactions revealed comparable densities of NCX1 within dendritic shafts and spines sampled in different layers. However, the density of NCX1 in dendritic shafts was ~ 7 times higher than in dendritic spines and somata. In dendritic shafts a slight accumulation of gold particles was found around the base of spines, suggesting a role for NCX1 in the restriction of spatial spread of synaptic Ca^{2+} signals. In line with the relatively low density of NCX1 in spines, we

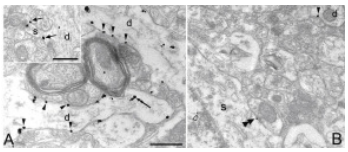


Figure 1. Quantitative electron microscopic analysis of gold particles (arrows and arrowheads) labeling NCX1 on different subcellular domains. The density of NCX1 in dendritic shafts (A) was ~ 7 times higher than in dendritic spines (A, inset) and somata (B).

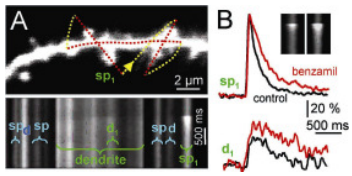
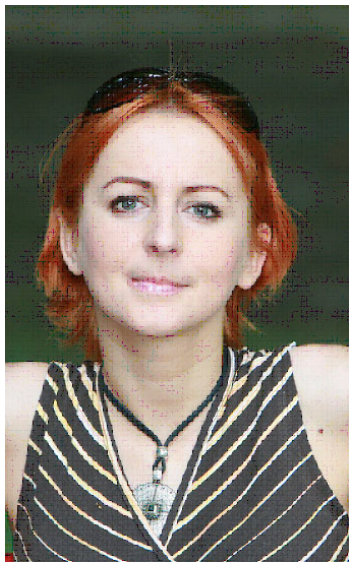


Figure 2. NCX1 activity shapes Ca2+ transients in dendritic shafts and spines only during repeated (7 stimul at 200 Hz) stimulation of single synapses. (A) Top, Confocal Z-stack of a dendritic segment imaged with the red parts of the overlayed scanning path. Bottom, Average of 4 single traces. Only one spine (sp1) and the corresponding parent dendritic segment were responding. (B) Normalized Ca2+ transients in the spine (sp1) and parent dendrite (d1) in control and benzamil.

could not detect significant changes in the decay kinetics of Ca^{2+} transients in dendritic spines, when NCX activity was inhibited during small intensity synaptic stimulation resulting in Ca^{2+} signals restricted to spines. The involvement of NCXs in Ca^{2+} extrusion was significant only at longer repetitive activation of synaptic NMDA receptors, producing a larger and longer Ca^{2+} influx to dendritic spines. Ca^{2+} transients could invade from spine to dendritic shafts only at long, repetitive synaptic activity, and the amplitude, decay time constant as well as the spatial spread of dendritic Ca^{2+} signals were increased in the presence of the NCX blocker benzamil.

Our results suggest a subcellular compartment-dependent distribution of NCX1 in the plasma membrane of CA1 pyramidal cells with preferential expression in dendritic shafts. Moreover, the distribution did not depend on the distance from the soma, thus our results also indicate a distance- and excitatory input-independent distribution of NCX1. Two-photon imaging of synaptically activated Ca^{2+} transients during NCX blockade showed preferential action localized to the dendritic shafts for NCXs in regulating spine-dendrite coupling.


Andrea Lörincz


Rózsa Balázs

Curriculum Vitae:

Andrea Lőrincz obtained her MSc degree at the University of Szeged in biology in 2000. As an undergraduate, Dr. Lőrincz joined the laboratory of Dr. Gábor Tamás where she mastered sophisticated light- and electron microscopic techniques and received a PhD scholarship after her graduation. During her PhD studies, Andrea joined the laboratory of Dr. Zoltán Nusser in 2001 for one year to gain experience in high-resolution immunohistochemical techniques and discovered the polarized distribution of HCN channels in cortical pyramidal cells (Lőrincz et al., 2002, Nature Neurosci). In 2003 she was awarded the Young Investigator Prize by the Hungarian Foundation for Electron Microscopy and the Ferenc Joó Prize. In 2004 Andrea started her postdoctoral years in the laboratory of Prof. Shigemoto in Okazaki, Japan. She gained experience in several new techniques, the most important being the newly developed SDS-digested freeze fracture replica labeling technique. In 2006 she joined Dr. Nusser`s group.

Balazs Rozsa obtained his MD degree at Semmelweis University in 1999 and his MSc at Eötvös Loránt University in theoretical physics in 2002. During his studies he learned

mechanical and electrical engineering at University of Technology and Economics as well. He got several awards on national competitions in the field of mathematics, biology and physics. Using his multidisciplinary knowledge he developed and patented new technologies in the field of nonlinear microscopy and 3 dimensional scanning. Using their microscopes they made 17 publications and patents in the last 4 years. In 2007 he was awarded the Junior Prima Primissima Prize. In 2002-2007 he was doing his PhD under the guidance of Prof. Vizi Sylvester, Budapest. Balazs interest is involved in studying the dendritic physiology of interneurons (Rózsa et al., 2004). He started his lab in 2005 to study signal integration and regenerative activity in interneuron dendrites as well as their network activity using their 3D microscopes.

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