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Presentation Abstract

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Title:	In vivo calcium imaging in α-synuclein transgenic model of Parkinson's disease
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Abstract:	α-synuclein (α-syn) is one of the most abundant presynaptic proteins involved in neurotransmitter release and synaptic plasticity. In Parkinson's disease there is an abnormal aggregation of α-syn and formation of toxic α-syn oligomers. While the mechanisms behind these processes are not completely clear, our recent studies *in vitro* suggest that oligomers of α-syn form ring-like structures that might penetrate into the membranes forming non-specific ionic channels and facilitating influx of calcium into the cytosol. However it is unclear if such alterations in calcium levels occur *in vivo*. In the present study, we investigated calcium homeostasis in transgenic mice expressing human α-syn under the mThy-1 promoter. Using 2-photon microscopy *in vivo*, we investigated spontaneous and evoked neuronal calcium activity with respect to frequency, amplitude, distribution and shape of calcium transients. Neuronal response to a sensory stimulus was mapped using surface potential recordings with a silver ball electrode. Following the mapping, a mixture of calcium dye Oregon Green BAPTA-1 AM and astrocytic marker SR101 were pressure injected ~500 μm below the cortical surface at the center of the neuronal response. Our results indicate that α-syn mice with a fully developed disease (6 months of age) exhibit abnormal calcium activity including spontaneous and evoked calcium plateaus and prolonged responses lasting seconds after the termination of the stimulus. Taken together with recent 2-photon calcium imaging studies in APP mice [1],

these data suggest that disruption of calcium homeostasis might be a common theme in Alzheimer's and Parkinson's disease-related neurodegeneration. Moreover, our previous findings from neuronal tissue culture show that co-exposure to α-syn and amyloid β protein facilitates an increase in intracellular calcium concentration [2]. The synergistic role of these two proteins in the disruption of calcium homeostasis might explain the fact that populations of Alzheimer's and Parkinson's disease patients overlap (having Parkinson's disease increases the chances of getting Alzheimer's disease by ~25%).

[1] Busche, M. A. et al., *Science* 321 (5896), 1686 (2008); Kuchibhotla, K. V., Lattarulo, C. R., Hyman, B. T., and Bacskai, B. J., *Science* 323 (5918), 1211 (2009).

[2] Tsigelny, I. F. et al., *PLoS ONE* 3 (9), e3135 (2008).

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