Calcium homeostasis in motor nerve terminals of Smn-deficient mice

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Calcium ions play a key role in the regulation of neurotransmission. One of the most important organelles in charge of cytosolic calcium clearance in motor nerve terminals is the mitochondria.

Spinal muscular atrophy (SMA) is a genetic disease caused by loss or mutations of the Survival of Motor Neuron (SMN1) gene, characterized by motor impairment of axial and proximal limb muscles. In mouse models of the disease, synchronous neurotransmitter release is half reduced while asynchronous release increases by 300%. Moreover, studies of the mitochondria shown alterations both at the structural and metabolic level. Together, these data suggest possible alterations in the calcium homeostasis of motor nerve terminals in SMA.

In this work, we used an SMA mouse model, which severity can be controlled by changing the number of copies of the SMN2 transgene, representing different degrees of the disease (SMA type 1 and 2). We used a fluorescent calcium indicator (Rhod 2-AM) and live imaging to record the changes in mitochondrial calcium upon electrical stimulation in nerve terminals at different postnatal ages (P7-P14). In controls, we found that the calcium signal rises very fast until reaching a plateau. After stimulation, the decrease in calcium is slow (half decay time, one minute). In SMA mutants, we found an apparent correlation between the mouse phenotype and the amplitude of the mitochondria calcium signals, with almost normal parameters in less affected mice. For example, in SMA type 2 mice, at P7, the kinetics of the calcium signals are not altered, although basal fluorescence showed a tendency of being higher than in control animals. We also examined the number of active calcium spots and their mean area per nerve terminal, finding no differences between controls and SMA type 2 mice.

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