Live Ratiometric Ca^{2+} Imaging in a Zebrafish Model for Spinal Muscular Atrophy

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Spinal Muscular Atrophy (SMA) is a progressive neurodegenerative disease specifically affecting lower motor neurons in the spinal cord. Homozygous loss of ubiquitously expressed Survival of Motor Neuron 1 (SMN1) gene, which encodes a protein implicated in snRNP assembly, is causative of this disease but detailed molecular mechanisms for the motor neuron (MN) specific phenotype are currently unclear. Immaturity of the Neuromuscular Junction (NMJ) and abnormal synaptic transmission have been reported in mouse models of SMA [1,2] using electrophysiology in tissue slices or in vitro cultivated neurons [3]. However, to date, there have been no reports comparing the Ca^{2+} levels or activity of MNs under SMN deficient conditions in the context of a living animal. Here, we have undertaken an approach of using in vivo ratiometric Ca^{2+} imaging to serve as a non-invasive reporter for MN and Schwann cell (SC) function in a live anesthetized animal model. Two novel zebrafish stable transgenic lines have been established, which make use of a FRET based Ca^{2+} sensor [4, 5] to detect changes in intracellular Ca^{2+} levels in primary MNs as well as their enveloping SCs. We provide evidence that there are significant changes in the evoked Ca^{2+} response of MNs and SCs in the SMA zebrafish model. Furthermore, the MN specific transgenic line facilitates live monitoring of Ca^{2+} influx into the presynaptic terminal at the NMJ synapse during synaptic activity. These novel lines serve as a platform to assess MN activity and glia excitability in live zebrafish, which may be extended to research in other neurodegenerative diseases and neurobiology.

References:


