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MEETING ABSTRACT

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Postsynaptic calcium signalling controls presynaptic differentiation at the neuromuscular synapse

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Abstract: Correct formation of synapses requires reciprocal communication between presynaptic neurons and their postsynaptic target cells. At the neuromuscular junction (NMJ), nerve-induced regulation of the postsynaptic differentiation is well-studied, whereas retrograde mechanisms, by which the muscle controls the presynaptic motor neuron differentiation, are still poorly understood. We have recently shown that $Ca_V1.1$-driven calcium signals regulate patterning of postsynaptic AChRs and outgrowth of the motor axons during NMJ formation. Here we utilized two genetic mouse models, both of which lack $Ca_V1.1$-driven calcium signals, and report a central role of activity-induced skeletal muscle calcium signaling in the retrograde regulation of presynaptic differentiation at the NMJ. In mice lacking $Ca_V1.1$ expression and thus activity-dependent calcium signals, correct fasciculation and navigation of the motor nerves were perturbed during early NMJ development. Motor axons failed to recognize their termination territory and motor axon endings grew beyond postsynaptic AChR clusters. Moreover, in the absence of postsynaptic activity-dependent calcium signaling, proper accumulation of the synaptic vesicles and active zones at nerve terminals failed to occur. Together these observations strongly suggest that postsynaptic muscle calcium signaling functions upstream of multiple retrograde pathways to induce complete differentiation of the motor neurons.

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Keywords: calcium channels – synapse formation – neuromuscular junction – motor neurons

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