

Active acetylcholine receptors prevent the atrophy of skeletal muscles and favor reinnervation

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Denervation of skeletal muscles induces severe muscle atrophy, which is preceded by cellular alterations such as increased plasma membrane permeability, reduced resting membrane potential and accelerated protein catabolism. The factors that induce these changes remain unknown.

Conversely, functional recovery following denervation depends on successful reinnervation. Here, we show that activation of nicotinic acetylcholine receptors (nAChRs) by quantal release of acetylcholine (ACh) from motoneurons is sufficient to prevent changes induced by denervation.

Using in vitro assays, ACh and non-hydrolysable ACh analogs repressed the expression of connexin43 and connexin45 hemichannels, which promote muscle atrophy. In co-culture studies, connexin43/45 hemichannel knockout or knockdown increased innervation of muscle fibers by dorsal root ganglion neurons. Our results show that ACh released by motoneurons exerts a hitherto

unknown function independent of myofiber contraction. nAChRs and connexin hemichannels are potential molecular targets for therapeutic intervention in a variety of pathological conditions with reduced synaptic neuromuscular transmission. © 2020, The Author(s).