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Effects of acetylcholine and electrical stimulation on glial cell line-derived neurotrophic factor production in skeletal muscle cells

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Effects of acetylcholine and electrical stimulation on glial cell line-derived neurotrophic factor production in skeletal muscle cells

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Abstract

Glial cell line-derived neurotrophic factor (GDNF) is a neurotrophic factor required for survival of neurons in the central and peripheral nervous system. Specifically, GDNF has been characterized as a survival factor for spinal motor neurons. GDNF is synthesized and secreted by neuronal target tissues, including skeletal muscle in the peripheral nervous system; however, the mechanisms by which GDNF is synthesized and released by skeletal muscle are not fully understood. Previous results suggested that cholinergic neurons regulate secretion of GDNF by skeletal muscle. In the current study, GDNF production by skeletal muscle myotubes following treatment with acetylcholine was examined. Acetylcholine receptors on myotubes were identified with labeled alpha-bungarotoxin and were blocked using unlabeled alpha-bungarotoxin. The question of whether electrical stimulation has a similar effect to that of acetylcholine was also investigated. Cells were stimulated with voltage pulses; at 1 and 5 Hz frequencies for times ranging from 30 min to 48 h. GDNF content in myotubes and GDNF in conditioned culture medium were quantified by enzyme-linked immunosorbant assay. Results suggest that acetylcholine and short-term electrical stimulation reduce GDNF secretion, while treatment with carbachol or long-term electrical stimulation enhances GDNF production by skeletal muscle.