BDNF is a mediator of glycolytic fiber-type specification in mouse skeletal muscle

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Brain-derived neurotrophic factor (BDNF) influences the differentiation, plasticity, and survival of central neurons and likewise, affects the development of the neuromuscular system. Besides its neuronal origin, BDNF is also a member of the myokine family. However, the role of skeletal muscle-derived BDNF in regulating neuromuscular physiology in vivo remains unclear. Using gain- and loss-of-function animal models, we show that muscle-specific ablation of BDNF shifts the proportion of muscle fibers from type IIB to IIX, concomitant with elevated slow muscle-type gene expression. Furthermore, BDNF deletion reduces motor end plate volume without affecting neuromuscular junction (NMJ) integrity. These morphological changes are associated with slow muscle function and a greater resistance to contraction-induced fatigue. Conversely, BDNF overexpression promotes a fast muscle-type gene program and elevates glycolytic fiber number. These findings indicate that BDNF is required for fiber-type specification and provide insights into its potential modulation as a therapeutic target in muscle diseases.
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