Congenital myopathies: disorders of excitation-contraction coupling and muscle contraction.


Abstract
The congenital myopathies are a group of early-onset, non-dystrophic neuromuscular conditions with characteristic muscle biopsy findings, variable severity and a stable or slowly progressive course. Pronounced weakness in axial and proximal muscle groups is a common feature, and involvement of extraocular, cardiorespiratory and/or distal muscles can implicate specific genetic defects. Central core disease (CCD), multi-minicore disease (MmD), centronuclear myopathy (CNM) and nemaline myopathy were among the first congenital myopathies to be reported, and they still represent the main diagnostic categories. However, these entities seem to belong to a much wider phenotypic spectrum. To date, congenital myopathies have been attributed to mutations...
in over 20 genes, which encode proteins implicated in skeletal muscle Ca\(^{2+}\) homeostasis, excitation-contraction coupling, thin-thick filament assembly and interactions, and other mechanisms. RYR1 mutations are the most frequent genetic cause, and CCD and MmD are the most common subgroups. Next-generation sequencing has vastly improved mutation detection and has enabled the identification of novel genetic backgrounds. At present, management of congenital myopathies is largely supportive, although new therapeutic approaches are reaching the clinical trial stage.

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