

Decline in titin content in rat skeletal muscle after denervation

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摘要

Abstract

Titin, an elastic and giant myofibrillar protein, is responsible for generating passive tension and maintaining sarcomere structure in striated muscles. Several studies have reported attenuation of passive tension and disorganization of sarcomere in atrophic muscles, but the changes of titin have not been investigated after denervation. For this purpose, we used sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and immunofluorescent staining to examine titin in innervated and denervated tibialis anterior (TA) muscles of the rat. With increasing denervation time, we found a greater loss of titin than myosin heavy chain (MHC) and actin contents in atrophic TA muscle. The ratios of titin/MHC and titin/actin gradually decreased following denervation. In contrast, ratios of MHC/actin in the denervated groups showed no significant differences with the controls even at 56 days postdenervation. The ultrastructure of myofibrils also showed disturbed arrangements of myofilaments and a disorganized contractile apparatus in denervated muscle. Immunofluorescent staining displayed translocation of the titin epitope from the Z-line to the I-band, suggesting that the apparent cleavage of titin occurred near the Z-line region during the atrophying process. Our study provides evidence that titin is more sensitive to degradation than MHC and actin after denervation. Moreover, the titin decline results in the loss of titin-based sarcomeric integrity in atrophic muscle.