

Histology of the long term denervated rat muscle

Nicoletta Adami, Donatella Biral, Susy Caccavale, Katia Rossini

*Translational Myology Lab of the Interdepartmental Research Center of Myology,
Department of Biomedical Science, University of Padua, Italy.*

E-mail: katia.rossini@unipd.it

Abstract

We studied long term denervation of rat muscles after permanent sciectomy. Three phases can be distinguished: an early phase of fast progressive atrophy, an intermediate phase (4-6 months of denervation) characterized by the slowing down of the atrophic process and a final phase (after additional 3-5 months) during which fibrous and adipose tissues substitutes muscle fibers. Some regenerative myogenetic events randomly appear as demonstrated by anti-MHCemb monoclonals (myotubes are seen around atrophic fibers in severely atrophic muscles. NCAM, an adhesion molecule restricted to the synapse in innervated myofibers, is expressed along all atrophic fibers early after denervation. It also marks myotubes and early regenerated myofibers. It seems to be lost in severely atrophic myofibers.

Key Words: rat muscle, long term denervation, MHCemb, N-CAM, muscle regeneration.

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We studied long term denervation of rat muscles after permanent bilateral sciectomy. Like widely demonstrated by previous studies [1, 2], three phases distinguishes long term muscle rat denervation: an early phase, of rapid increase of muscular atrophy; an intermediate phase in which there is a slow down of the atrophic process and the final phase during which the gross muscle mass seems to be stable, the decreasing number of myofibers, being substituted by fibrous and adipose tissues.

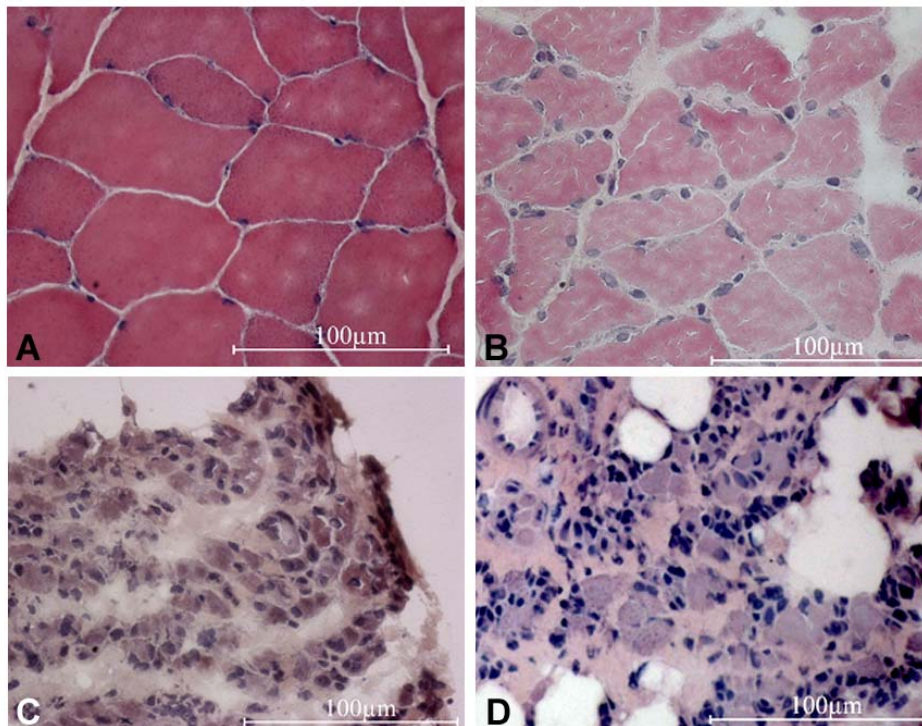


Figure 1. Hematoxylin and eosin stain of A, normal rat soleus muscle; B, 21-days denervated soleus; C, 4-month denervated muscle; D, 7-month denervated soleus

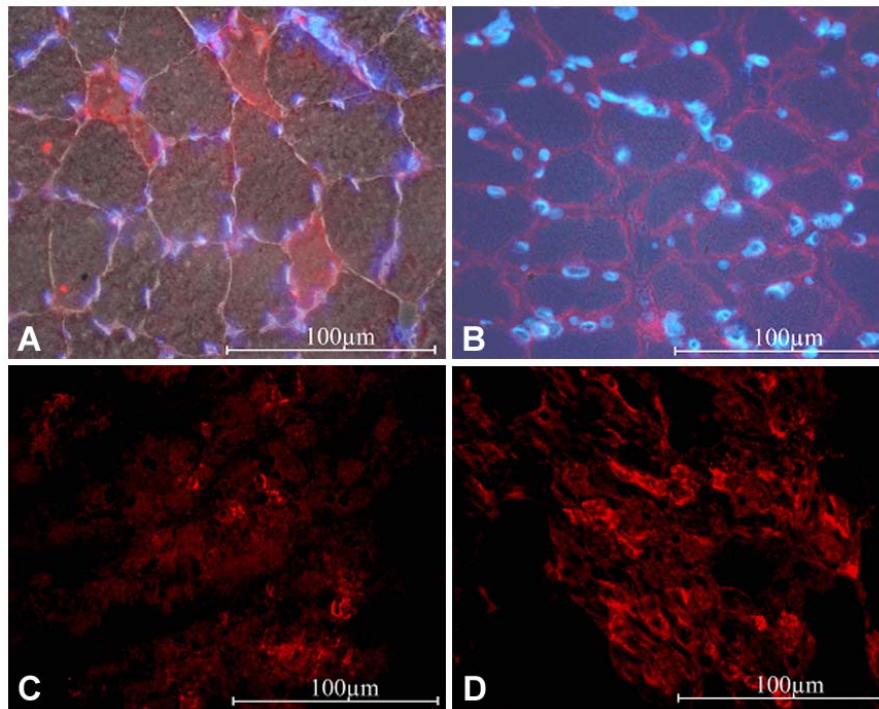


Figure 2. Long-term denervation of soleus rat: NCAM immunostaining. A, 4-days denervated muscle; B, 21-days denervated soleus; C, 4-month denervated muscle; D, 7-month denervated soleus.

Following permanent sciectomy, the distal-leg muscles undergo a severe atrophy during the first 4-6 months of denervation, which ends in tissue degeneration after additional 3-5 months. After 1 month of denervation the myofiber diameter decreases to 50% of normal fibers. Progressively it reaches values of less than 20% during additional 2 months. Then a steady-state severe atrophy characterizes the surviving myofibers, whose number begins to decrease from 6 months. At 9-11 months of permanent denervation the normal fascicular architecture of the muscle is lost and interstitial tissue, which includes adipocytes and sheets of collagen, dramatically increases at the expenses of the myofibers.

The ATPases demonstrate expression of a fast-like type of myosin (not shown), suggesting that fiber type differentiation is lost. In particular slow myosin disappears and only a fast-like myosin is present in the surviving fibers. Histochemical SDH, a marker of mitochondria of oxidative myofibers, decreases and finally disappears in both slow and fast myofibers (not shown). On the other hand, some regenerative myogenetic events randomly appear as demonstrated by anti-MHCemb monoclonals. Myotubes are also seen around atrophic fibers in very atrophic muscles.

NCAM, an adhesion molecule restricted to the synapse in innervated myofibers, is expressed along all atrophic fibers early after denervation [3]. It also marks myotubes and early regenerated myofibers. It seems to be lost in the very atrophic myofibers at 9-11 months of denervation.

Acknowledgements

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