Regeneration of the long term denervated human muscle

Ugo Carraro

Translational Myology Lab of the Interdepartmental Research Center of Myology, Department of Biomedical Science, University of Padua, Italy.
E-mail: ugo.carraro@unipd.it

Abstract

Light and electron microscopy and antibody for embryonic myosin show that myogenic regenerative events are present in human muscle up to 37-year post-spinal cord injury. After 5 years of Functional Electrical Stimulation (FES) in the recovered muscles regenerative events are present, but at a lower rate than in long-term denervated muscles. We conclude that the FES-training of paraplegic subjects is safe (it does not induce more muscle damage/regeneration than denervation per se) and effective (the mean size of the myofibers went from 15.4 to 27.0, that is, a 76% increase after two years of FES).

Key Words: human muscle, permanent denervation of the lower extremity, FES, muscle recovery, prevention of secondary diseases.

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Morphologic characteristics of the long-term denervated muscle in animals suggest that some original fibers are lost and some of those seen are the result of repeated cycles of fiber regeneration (Figue 1 and 2).
Muscle biopsies from lower motoneuron denervated spinal cord injury (SCI) patients enrolled in the EU Project RISE show the characteristics of long-term denervation. They present a few atrophic or severely atrophic myofibers dispersed among adipocytes and connective tissue (denervated degenerated muscle, DDM), while after 2- to 10-year FES-training the muscle cryosections present mainly large round myofibers.
Monoclonal antibody for embryonic myosin shows that regenerative events are present from 1- to 37-year post- SCI (Figure 3).
In the FES-trained muscles the regenerative events are present, but at a lower rate than long-term denervated muscles (myofiber per mm2 of cryosection area: 0.8+/-1.3 in FES vs. 2.3+/-2.3 in DDM, mean+/- SEM, p = 0,011).

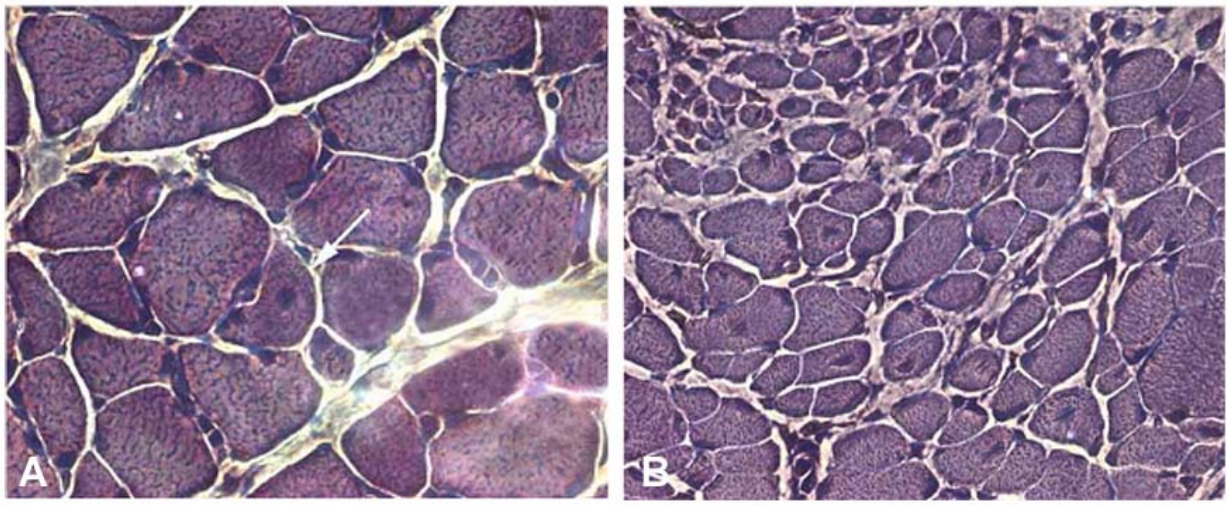

Figure 1. *Hematoxylin-eosin staining of denervated (A) and aneurally regenerated rat muscle (B). Note the incremental size of the fibers and the presence of central nuclei in myofiber of a 1-month regenerated muscle in the permanent absence of the nerve (A). B shows that spontaneous regeneration is also present in a 1-month denervated muscle, as demonstrated by the central nucleus in several muscle fibers.*

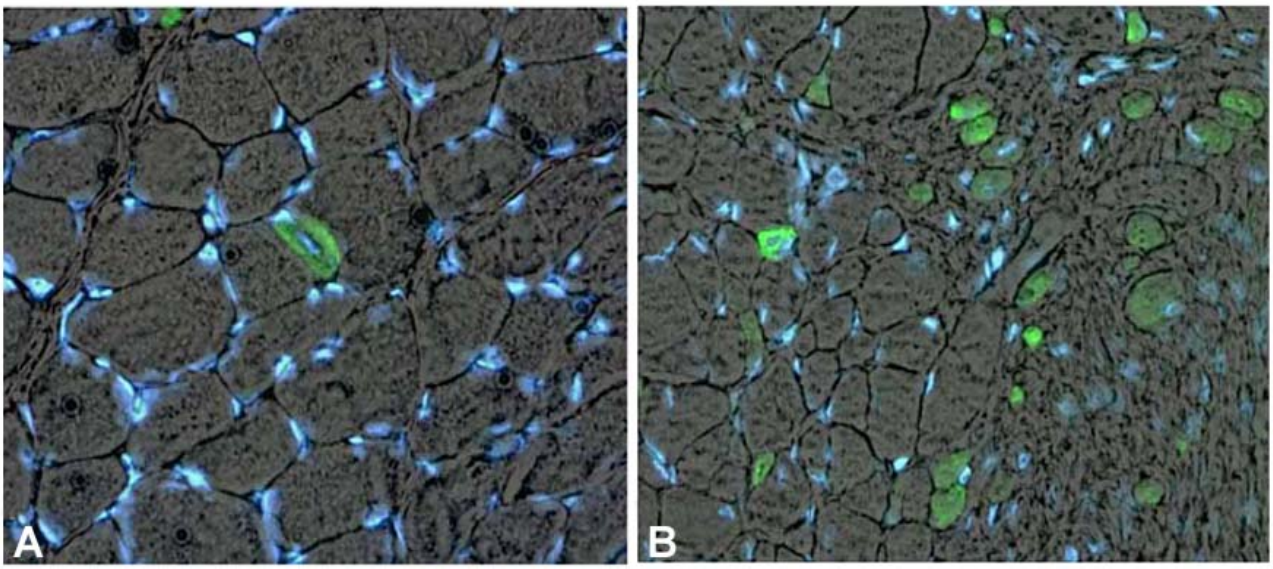

Figure 2. *Double exposure anti-MHCemb (green) & Hoechst (blue staining for nuclei) under bright-field illumination at contrast phase. A, 30 days denervated muscle showing a myofiber with central nucleus positive for MHCemb; B, 30 days aneurally regenerated muscle with some still positive myofibers for MHCemb.*

Muscle biopsies from lower motoneuron denervated patients enrolled in the EU Project RISE show the characteristics of long-term denervation. They present a few atrophic or severely atrophic myofibers dispersed among adipocytes and connective tissue (denervated degenerated muscle, DDM). Monoclonal antibody for embryonic myosin shows that regenerative events are present from 1- to 37-year post-spinal cord injury (SCI). After 2- to 10-year FES-training the muscle cryosections present mainly large round myofibers (not shown).

In the FES-trained muscles the regenerative events are present, but at a lower rate than long-term denervated muscles (myofiber per mm2 of cryosection area: 0.8+/-1.3 in FES vs. 2.3+/-2.3 in DDM, mean+/- SEM, p = 0,011).

In our opinion this is a sound additional evidence of safety of the Kern's electrical stimulation protocol for FES of DDM. The results demonstrate that FES-training is safe: indeed it does not induce more myofiber damage/regeneration than denervation per se.

We conclude that the FES-training of paraplegic subjects is safe (it does not induce more muscle damage/regeneration than denervation per se) and effective (the mean size of the myofibers went from 15.4 to 27.0, that is, a 76% increase after two years of FES).

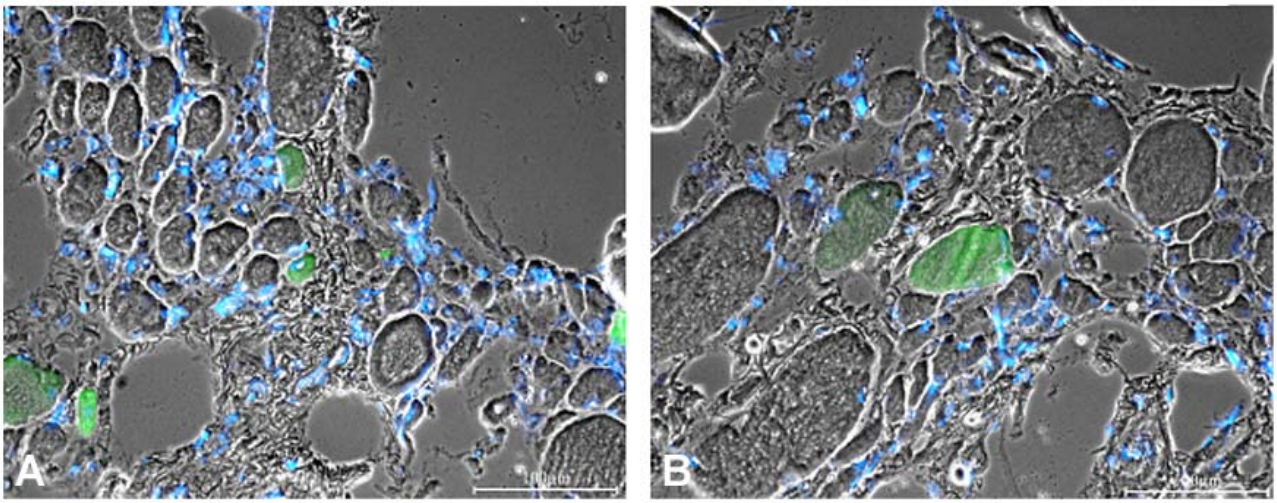

Figure 3. *Long-term Denervated Human Muscle. Lower Motor Neuron Lesion. The anti-MHCemb positive fibers(green) are myofibers regenerated during the last two weeks before biopsy harvesting.*

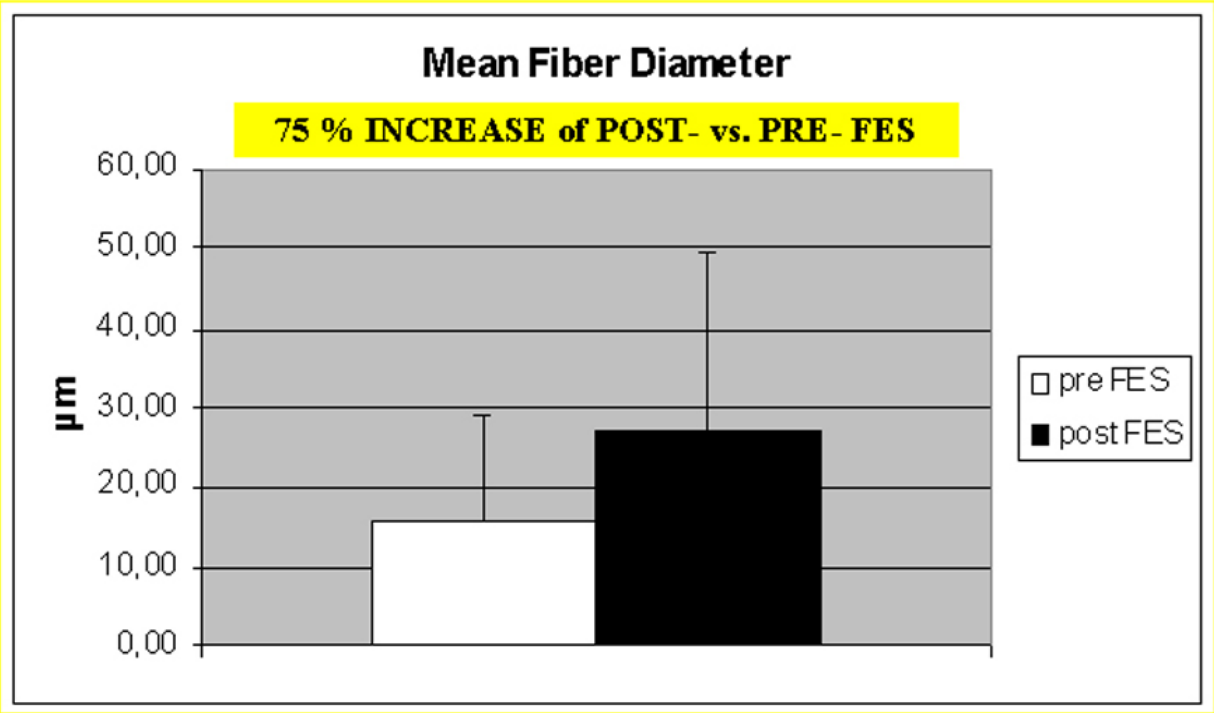

Figure 4. *FES of Long-term Denervated Human Muscle. RISE Project - Preliminary results.*

Acknowledgements

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