Type of presentation: Poster

LS-10-P-2608 Effect of an adapted physical exercise on satellite cells from skeletal muscles of old mice: ex vivo and in vitro analyses at light and electron microscopy

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During aging, a progressive loss of skeletal muscle mass and a concomitant decrease in muscle strength and endurance take place. This condition, termed sarcopenia, has important health-care and socioeconomic implications, since it contributes to frailty, disability and premature death (1). The mechanisms leading to sarcopenia are probably manifold and still incompletely elucidated, although the decline in muscle regeneration efficiency is thought to play a crucial role. Still in the absence of specific therapies, many studies have stressed the importance of physical exercise as an effective approach to prevent/limit the sarcopenic drive (2,3).

In this study, the effects of an adapted exercise on the number and myogenic properties of satellite cells (SCs) were investigated in quadriceps femoris and gastrocnemius muscles of old male mice (28 months). Both muscles contain a high proportion (about 90%) of type II fibers, which are specifically affected by sarcopenia (4). We compared old exercised mice (OE) versus old sedentary mice (OS), using adult sedentary mice (12 months, A) as a control: SCs were identified (Figs. 1) and quantified ex vivo; in addition, the proliferation and differentiation potential of SC-derived myoblasts from the same groups of mice was studied in vitro (Figs. 2 and 3). Ultrastructural morphology and immunocytochemical techniques at light and electron microscopy were used with special attention to some molecular markers of SC activation, and to some protein factors involved in RNA transcription and splicing.

Our results demonstrated that: 1) physical exercise induces an increase in the total number and in the activated fraction of SCs compared with sedentary old sample; 2) myoblasts from exercised muscles show morphological features and nuclear activity quite similar to myoblasts from adult subjects, whereas myoblasts from non-exercised muscles exhibit structural and functional alterations suggestive of a reduced metabolic activity; 3) myotubes differentiated from myoblasts of exercised muscles resemble the myotubes from adult myoblasts, whereas myotubes from non-exercised muscles show marked morphological alterations.

The present study provides convincing evidence that physical exercise not only induces numerical increase and activation of SCs in old animals but can also improve their capability to differentiate into structurally and functionally correct myotubes. Adapted physical exercise may actually represent a non-pharmacological approach to stimulate SCs in the attempt to enhance muscle quality even at very advanced age.

1. Ryall et al. Biogerontol 9:213, 2008
2. Zancanaro et al. Eur J Histochem 51:305, 2007
3. Bautmans et al. Acta Clin Belg 64:303, 2009
4. Larsson et al. Acta Physiol Scand 103:31, 1978

Acknowledgement: Acknowledgements - MC is a PhD student of the Doctoral Program “Multimodal Imaging in Biomedicine” (University of Verona).

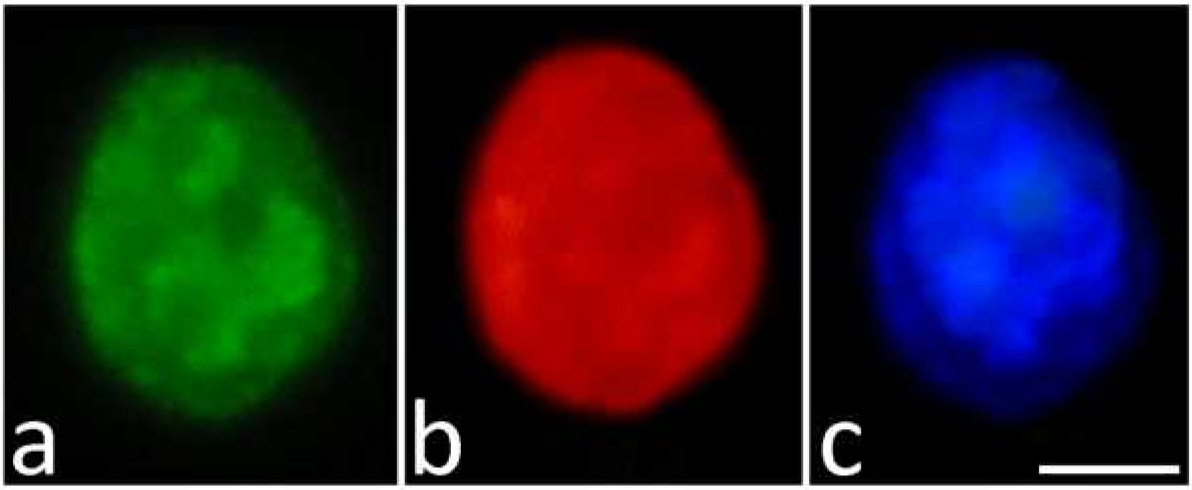

Fig. 1: Fluorescence microscopy: the nucleus of a SC after immunolabelling for Pax7 (a SC molecular marker) (a) and MyoD (a marker of SC activation) (b); nuclear DNA was stained with Hoechst 33258 (c). Bar, 10 µm

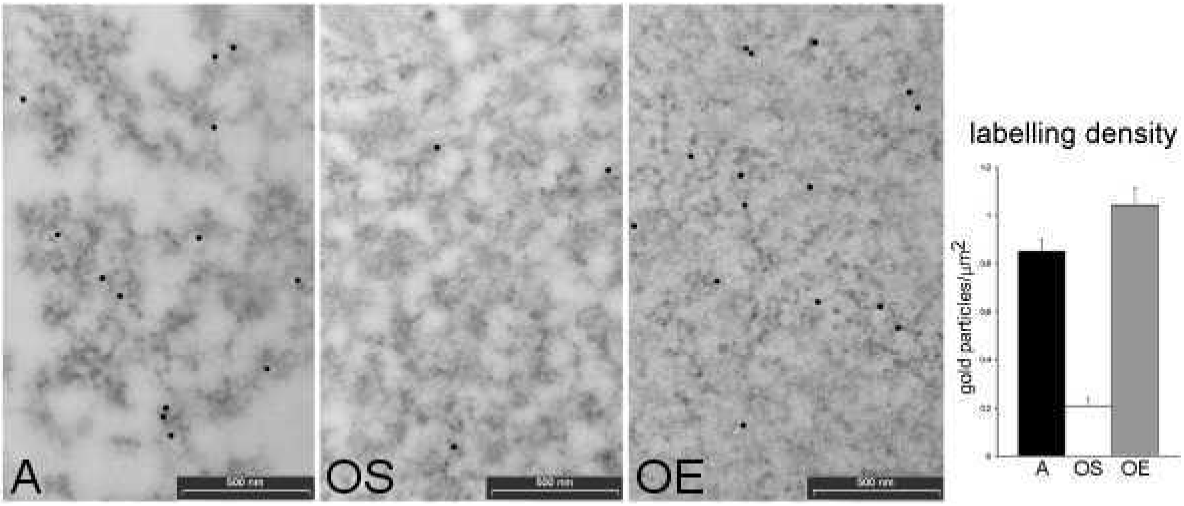

Fig. 2: Immunoelectron microscopy: nuclei of SC-derived myoblasts from A, OS ad OE mice after labelling for activated RNA-polymerase II. Bars, 500 nm. Quantitative evaluation demonstrates similar values (mean±SE) in A and OE mice, while OS mice show significantly lower values (Mann Whitney test).

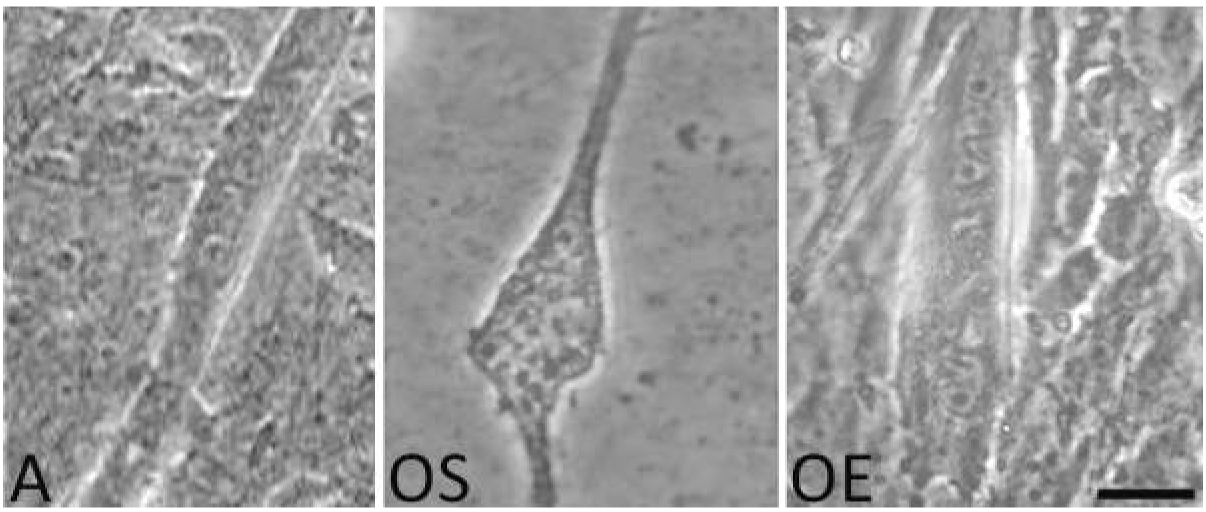

Fig. 3: Phase contrast microscopy: the myotubes differentiated from myoblasts of OS mice show irregular shape and clustered nuclei, whereas the myotubes of OE mice resemble those of adults (A). Bar, 10 µm.