A new view of fibre type transformations in elderly skeletal muscles

P.W. Sheard,[1] N. Lal[1] and J. Cornwall,[2] [1]Department of Physiology, University of Otago, Dunedin 9016, New Zealand and [2]Department of Anatomy, University of Otago, Dunedin 9016, New Zealand.

Sarcopenia is the age-related progressive muscle weakness and loss of skeletal muscle mass that contributes significantly to morbidity and mortality, affecting all people beyond late middle age. Typical histological features of elderly mammalian skeletal muscles include increased variation in fibre diameter, the emergence of slow twitch (type I) fibre clumping, and increase in slow fibre abundance. These changes are widely thought to be driven by a progressive denervation of fast myosin-containing fibres followed by their reinnervation by sprouts from nearby motor nerve terminals on slow fibres. Here, we present data from two different muscles and species that are not consistent with that mechanism and which therefore motivate a re-evaluation of the cellular events that drive sarcopenia.

First, we examined 26 anterior cervical muscles from five embalmed elderly human cadavers. Tissue sections were processed immunohistochemically using antibodies against type I and type II myosins, and sections were examined under a compound microscope and digitally photographed. Type II (fast) fibre clustering (clusters of >10 adjacent fibres) was observed in 64% of sections, with *longus colli* having the highest frequency (89%) of fast fibre clusters. Second, we wished to critically examine the “slow terminal sprouting” hypothesis by examining age-related changes in a muscle that normally has no slow fibres, the mouse cleidomastoid. Mice in 3-6 month (young adult) and 22-26 month (elderly) age groups were deeply anaesthetized with pentobarbitone and transcardially perfused with 4% paraformaldehyde. Muscles were snap frozen and tissue sections were processed immunohistochemically as outlined above. Cleidomastoid muscles from young adult mice had no type I myosin-positive fibres, but such fibres were present in elderly muscles. In this case the appearance of slow fibres cannot be caused by fibre transformation after slow nerve terminal sprouting since no “slow” motoneurons normally innervate this muscle. Instead, we suggest that the slow fibre accumulation in this case is due to long-term denervation of fast fibres that then express both slow and fast myosin isoforms.

Together, our results show that the widely described mechanism driving progressive age-related changes in skeletal muscles should not be considered to apply universally. We argue that slow-to-fast fibre clumping and transformation may also be a common manifestation of sarcopenia, and that fibre type clumping and transformation may sometimes be due to long-term denervation rather than to motor nerve sprouting and reinnervation.

Human tissues were retrieved and utilized in accordance with the NZ Human Tissues Act, 2008. Use of animal tissue was with prior approval of the University of Otago Animal Ethics Committee.