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What is it about old muscles?

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The World Health Organization has recognized ageing as one of the most important bio-psycho-social challenges of the 21st century (World Health Organization, 2015). Advanced adult age is associated with an increased incidence and prevalence of impairment, reduced physical activity, restricted participation in leisure and work-related activities, higher mortality, and increased utilization of health services with obvious consequences for national health systems. These observations provide ample justification for research that attempts to explain the physiological changes that accompany the highly variable process we call ageing.

It has been recognized by many that some of the most prominent features of the ageing human phenotype are the loss of skeletal muscle mass, strength and power. A plethora of scientific research studies, both cross-sectional and longitudinal in design, have shown the degree to which muscles atrophy and become weaker in elderly men and women. The term sarcopenia was initially used to refer to the loss of muscle mass with advanced adult age but its conceptual and operational definitions have been modified to include a functional component (strength and physical performance) (Cruz-Jentoft *et al.* 2010). During the last 30 years many of the contributing factors to the age-associated loss of muscle mass and function in general, and to sarcopenia in particular, have been identified and the role of determinants, such as the level of physical activity, in slowing down those losses have been explored.

An interesting aspect of this research is the debate about the proportional contribution of quantitative *vs.* qualitative adaptations in muscle. In other words, how much of the functional loss can be explained by the amount of tissue lost (quantity) and how much is due to the modification of normal tissue that becomes impaired or dysfunctional because of molecular alterations in muscle proteins (quality). There is no good scientific evidence to suggest that one mechanism would exclude the other; in other words, both quantitative and qualitative alterations can and do co-exist. However, while the presence of smaller and weaker muscles is relatively easy to demonstrate, evidence to support the second explanation, that older muscles have a limited ability to generate force and power even after adjusting for differences in size, has been more controversial and difficult to obtain. This interest in understanding qualitative changes in muscle parallels the changes in our conceptual model of sarcopenia to include performance although research in both areas has advanced, to a significant degree, independent from each other.

Variability in age-related changes adds to its complexity and a thorough understanding of the process may require evidence obtained from multiple biological levels, simultaneously, in the same group of individuals, and after eliminating, to the degree it is possible, confounding effects of illness and physical inactivity. In this issue of *The Journal of Physiology*, Brocca *et al.* (2017) report on a very comprehensive analysis of age-related changes in skeletal muscle in healthy and physically active individuals. Taken together, their findings demonstrate that age-related sarcopenia is much more than a quantitative challenge and that various cellular mechanisms contribute to a decline in muscle fibre function that is independent of the decline of muscle fibre size. The strength of this argument is the inclusion in the study of reliable measurements of *in vivo* muscle strength and size, including measurements of whole muscle and tendon function, *in vitro* experiments of single muscle fibre mechanical properties including force generation and shortening velocity, an analysis of the expressions of various proteins, and determinations of post-translational modifications of myoproteins. It is interesting that a similar argument may apply when considering the cell (as opposed to the individual) as the system of study because the concentration (quantity) of myosin did not decline but the degree of post-translational modifications in the form of oxidation and phosphorylation of myosin (quality) was higher in elderly.

The reasons why *in vivo* measurements of specific force did not mirror the changes at the level of single muscle fibres remain to be determined. Further, longitudinal measurements are needed to show that the reported effects are due to ageing and not differences between age groups due to other factors. These limitations notwithstanding, the authors have presented compelling evidence to support a major role for changes in muscle quality, particularly in contractile and regulatory myoproteins, as a mechanism for age related muscle dysfunction and sarcopenia.

Research on ageing and related topics should have a higher priority (Frontera *et al.* 2017). From a clinical perspective these important findings reported by Brocca *et al.* (2017) indicate that in order to reverse or slow down age-related changes in skeletal muscle, it will not be enough to induce hypertrophy using rehabilitative interventions such as strength training, protein-based dietary strategies, or anabolic agents. Future clinical interventions for the rehabilitation of older individuals must address the decline in muscle quality.

References

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Additional information

Competing interests

None declared.