



EDITORIAL

The role of exercise in neuromuscular diseases

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Regular physical activity, appropriately dosed in volume and frequency, has a wide-ranging beneficial function on the physical and mental health of humans. In fact, the scientific literature demonstrates, incontrovertibly, that physical exercise can perform a powerful preventive function on numerous serious and often chronic and deadly diseases such as type 2 diabetes, stroke, hypertension, and cancer (and in particular breast and colon cancer), osteoporosis, neurodegenerative diseases, depression and pathological anxiety (1). This silent protective action is accompanied by a significant improvement in the quality of life and the level of self-esteem, a slowing down of cellular muscle ageing processes (sarcopenia) and is associated with a reduction in the risk of cognitive decline and development of dementia. The holistic effect of the benefit of physical activity is demonstrated by the fact that it ends up impacting on human longevity by increasing its average survival, or by postponing the onset of potentially deadly diseases (2).

It is of absolute importance that for all these pathological situations and for others, such as inflammatory diseases, physical activity can also perform a curative function and not only a preventive one. And therefore, the focus of the scientific community, slowly but consistently, moves towards a more adequate use of physical exercise as an additional therapeutic element to the common therapeutic approach, often capable of preventing or delaying pharmacological interventions. In short, many people begin to internalize that the exercise is itself a drug that is often more effective than many and has therapeutic indications that are apparently unrelated to each other. As such, it should be administered by competent personnel who know how to manage, above all, the dose.

Although this premise highlights a fundamental role of physical exercise to prevent and treat a *plethora* of human diseases (1, 3), in neuromuscular diseases populations, notwithstanding the great interest, particularly for prevention

of excessive fatigue and maintenance of the patient's quality of life, this indication is still lacking (4). In fact, until now, scientists and clinicians thought that, having these diseases ultimately deal with skeletal muscles, as a precautionary measure it was better to ask the subject not to perform exercise, in order to avoid accelerating the degenerative process or determine exercise-induced muscle damage leading to pain, rhabdomyolysis and myoglobinuria. The attitude to precaution has additional fundamentals in a whole series of knowledge gaps regarding the physiopathology of diseases, how this can intersect with the physiological plastic effects of qualitative and quantitative different physical exercise, the outcome measures to be considered, how to proceed for a highly personalized approach, and the impact of new technologies for monitoring temporal evolution of diseases and approach efficacy.

However, in the presence of a neuromuscular disease, a crucial time ridge for the purpose of establishing the ultimate significance of the level of physical activity for disease progression and evolution is represented by the time of diagnosis. In fact, if, on one hand, it is fundamental to establish whether physical activity turns out to be a factor that can accelerate or decelerate the onset of the clinical symptoms of the disease, on the other, it is also of great importance to establish, once the symptoms begin to manifest, whether regular physical activity may change its natural evolution over time. The existence of this ridge defines the importance of future retrospective and prospective studies, possibly on a large scale. Therefore, considering that diagnose often occurs after the age of 30, it is crucial, first to establish whether early physical activity, of high or moderate intensity, is dangerous or beneficial. Some initial retrospective studies have involved, with opposite results, the limb girdle muscular dystrophy 2I (LGMD2I) and the dysferlinopathies (LGMD2B and Myoshy myopathies). In the first case, the retrospective approach allowed to estab-

lish how the level of physical activity prior to the diagnosis is not able to negatively impact on the onset of the disease (5). In the second case, instead, in full agreement with the physiological significance of the dysferlin in the cellular repair processes from exercise-induced micro lesions, retrospective studies have shown an increased risk of an early onset of the disease (6).

Both in retrospective and perspective studies quality of exercise should be taken into consideration. As known, two different kinds of exercise paradigms can be distinguished at the extremes of a wide range of possibilities: resistance and endurance. Resistance exercise is based on the repeated application of external loads, followed, in the long run, by changes in muscle size (hypertrophy) leading to changes in muscle strength. Following resistance exercise, phenotypical muscular changes mostly depend on the eccentric components of contractions intrinsically linked to muscle damage, particularly at ultra-microscopical level. Endurance exercise includes low load-long lasting activities followed by increased maximal oxygen consumption, increased capillarization and improvement in cardiovascular fitness.

To date, safety of supervised training, mostly including endurance type paradigms which appear to be well tolerated (7, 8), is widely accepted, but precise guidelines of exercise interventions related to neuromuscular diseases' aetiology are still lacking. Indeed, safety and efficacy of resistance type exercise in myopathies have not been sufficiently investigated (9).

To take stock of the knowledge gaps and necessary scientific developments to ascertain the role of exercise in neuromuscular diseases, last June, the first satellite symposium of the National Congress of the Italian Myology Association (AIM), entirely dedicated to the topic with participation of leading exponents in the field of applied muscle physiology and neurology was held at Mondino Foundation in Pavia (Italy).

In the current special issue of *Acta Myologica* three papers (10-12) summarize what emerged during the symposium, dealing with fundamental physiological acquisitions, known effects in certain myopathies, and open issues to be addressed, with the aim to stimulate future clarifying investigations.

Berardinelli and D'Antona report on the main physiological aspects of muscle adaptation to physical exercise with the aim of intersecting the effects of muscle exercise adaptation with the pathophysiology of some neuromuscular diseases of known etiology. The second paper, by Sheikh and Vissing, deals with evidences of efficacy of exercise in muscle and lower motor neuron diseases, highlighting that, although moderate exercise appears to be safe and effective in muscular diseases, efficacy and safety in lower motor neurone diseases is still a matter of debate. The third paper by Voet highlights how the vicious circle

of inactivity represents a fundamental element at the base of the progressive deterioration of the neuromuscular function of the patient and how the interruption of this circle can lead to a significant improvement of the cardiometabolic fitness and the quality of life of the patients.

All authors agree that future research must consider an accurate evaluation of the overall impact of exercise, both retrospectively and prospectively, with a focus on quality, intensity, frequency and duration, and a strict consideration of the pathophysiology of diseases and their evolution.

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