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Effects of combined endurance and resistance training in Amyotrophic Lateral Sclerosis: A pilot, randomized, controlled study

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Due to an error, some paragraphs of the Discussion section were omitted from this article (published in Eur J Transl Myol 2018;28(1):132-40. DOI: 10.4081/ejtm.2018.7278).

The revised Discussion section is now available below.

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Discussion

The positive effects of exercise in healthy people are, in general, well documented and have been largely demonstrated. Accordingly, physical inactivity is associated with increasing risk of many adverse health conditions.²⁹ This is more relevant in the process of aging or some neuromuscular disorders where a progressive degradation of the neuromuscular system manifests by a steady decline in muscle mass and strength. In fact, at the level of the single motor unit, aging and disease can be associated with

muscle atrophy. Furthermore, recent data show that physical activity promotes reinnervation of muscle fibers in aging.³⁰⁻³⁵

In ALS, conflicting results have weakened the role of physical exercise, though a growing number of researchers indicates the safe and the beneficial effects of physical activity.^{3,36,37}

Among the benefits, we found an overall improvement of the score on functional independence scale in all patients, independently of the type of exercise conducted (specific programme or standard neuromotor rehabilitation treatment). In

addition, improvements in muscle power (expressed by the MRC scale), oxygen consumption (measured by VO₂submax) and fatigue were specifically observed in the EP group, all hallmarks of a training effect for the specific exercise programme.

As for physical activity in general, improvements can potentially reduce the strains of daily living by increasing reserve capacities.³⁸ This would allow ALS patients to meet the physiological demands required for activities of daily living more effectively, reflecting an increase of their score on functional independence scale.

Examining our combined exercise programme, our purpose was to assess the clinical efficacy of a programme of moderate aerobic and isometric exercises, through an objective assessment of muscle strength, fatigue and cardiovascular parameters, in the early stage of ALS.

The specific exercise programme was based on a standardized training consisting of an aerobic workout of moderate entity and muscle contractions. As for the aerobic exercise, treadmill or cycloergometer training is a highly repetitive form of gait training that promotes specific practice and can provide an aerobic training stimulus. Similarly, to a recent study on fitness reserve after aerobic training in stroke patients,³⁹ we found that our specific exercise programme could decrease submaximal oxygen consumption determining better economy of motion at the end of the

period of training. As long as the patient is able, a sub-maximal recumbent cycle, all-extremity ergometer, or bike test may be performed to estimate aerobic capacity. Caution should be taken if maximal aerobic capacity has to be assessed, as high-intensity exercise may promote dangerous oxidative stress in persons with ALS. Aerobic training can primarily increase aerobic capacity through cardiorespiratory reconditioning and promote cardiovascular function, improving cardiovagal modulation. Although there are no data on ALS patients, it has been shown that an increase in neuromuscular activity (e.g. repeated exercise), results in a fast-to-slow transition, and that the lack of activity (e.g. resulting from denervation), induces a slow-to-fast transition.⁸ These considerations suggest that aerobic exercise might be the best option for exercise prescription.

In parallel to aerobic training, resistance exercises were set accurately, defining the type of contraction, the muscle segments to be reinforced, and the number of repetitions per session. In our study, a submaximal isometric contraction was chosen to avoid muscle damage from mechanical and bioelectrical overload, or metabolic stress, especially to the fast twitch fatigable muscular fibers. During isometric exercise, in fact, the muscle is activated, maintaining a constant length, and reaches a state of maximum tension safely. Recent studies have also shown that isometric exercises can maximize motor unit activity in

terms of increase of the firing rates of active motor units and recruitment of other motor units that usually are inactive.⁴⁰ This mechanism can be crucial in strengthening a denervated muscle and could explain the improvement of MRC muscle scale that we observed in our patients after the five-week training programme.

In summary, the use of a combined protocol of aerobic and resistance training (below maximal effort) seems to have positive effects in terms of energy and fatigue required to perform activities of daily living, and is associated with increased function and independence. A lower requirement for oxygen by the working muscle during submaximal tasks indicates better walking economy. However, the significant increase in muscular strength expressed by the MRCSS not supported by a change of dynamometric measures of the examined muscles could indicate that the submaximal isometric contractions used were too mild and precautionary.

We found our combined exercise programme feasible and well tolerated in patients at the early stages of ALS. It appears to be beneficial for those muscles, which were not profoundly weak, and to contrast cardiovascular deconditioning and muscle atrophy due to the ALS disease and the resulting progressive inactivity. This programme appears to be most effective when implemented before the onset of significant

muscle atrophy. Therefore, these preliminary data suggest that specific rehabilitation programs can counter out the progressive motor deficit of ALS. We believe that moderate exercise can be a reasonable recommendation to establish specific exercise therapy and to improve clinical practice in ALS Centers.

Integration with bio molecular data and/or biopsy and a longer exercise programme would be useful to evaluate the effect of exercise on motoneuron efficiency, evidencing cellular and metabolic changes and to verify the effect of rehabilitative intervention on the natural history of the disease.