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Amyotrophic Lateral Sclerosis, Resistance Training, Endurance Exercise, Tolerance, and Compliance

Clawson LL, Cudkowicz M, Krivickas L, Brooks BR, Sanjak M, Allred P, Atassi N, Swartz A, Steinhorn G, Uchil A, Riley KM, Yu H, Shoenfeld DA, Maragakis NJ. A randomized controlled trial of resistance and endurance exercise in amyotrophic lateral sclerosis. Amyotrophic Lateral Scler Frontotemporal Degene. 2018;19(3–4):250–8.

Amyotrophic lateral sclerosis (ALS) is classified as a neurodegenerative disease that results in destruction of motor neurons in the brain and spinal cord (1). The cause of this disease is unknown, with 90% of all cases being nonfamilial (1). As ALS progresses, it results in cachexia, loss of muscle mass and movement coordination, paralysis, and eventual death (1). It is estimated that 30,000 people in the US (1) and 1,400 people in Australia (2) are living with ALS.

According to the American Academy of Neurology the current standard of care for persons with ALS includes static stretching and passive range of motion to offset muscle and joint stiffness caused by neurologic decline (3). Low powered studies and conflicting research results of the effect of resistance (weights lifting) and/or aerobic exercise on ALS have led to difficulty determining recommendations for these modes of exercise (3). Some researchers indicate that vigorous aerobic or intense resistance training may increase the risk of (4) or exacerbate the progression (3) of ALS. Because of this, some clinicians instruct patients to avoid these forms of exercise. On the contrary, authors of several studies in mice (5) and humans (6) suggest resistance and aerobic exercise have multiple benefits for ALS, including delayed onset of symptoms, slowed progression, and improved quality of life, without being a major risk factor (7). The aim of this study was to determine the tolerance and compliance of exercise when comparing resistance, aerobic, and stretching or passive range of motion exercises in persons with ALS.

MANUSCRIPT REVIEW

This 24-week, randomized controlled trial included persons with ALS who met these inclusion criteria: (a) classified as having lab-supported probable or definite ALS, confirmed by a neurologist and (b) willingness to participate in this study. Exclusion criteria were not mentioned. Due to difficulty with the recruitment of persons with ALS who were willing to perform exercises, this study began in April 2012, with the last participant enrolled in September 2015.

Fifty-nine participants were randomly assigned to resistance training (n = 21), aerobic exercise (n = 18), or static stretching or passive range of motion [S-ROM] (n = 20). Tolerability was defined as each participant completing ≥50% of total repetitions assigned for resistance training and S-ROM and ≥50% of aerobic exercise duration programmed at a specific heart rate and perceived exertions scale (Borg 6–20) rating. Compliance was defined as each participant attempting ≥50% of all exercise sessions for the 24-week period. Broad compliance measures were implemented with anticipation of rapid progression of ALS and inability to perform higher intensity or longer duration exercise. As a result, broad compliance measures afforded participants greater consistency with exercise completion at each session. To improve retention and avoid travel to treatment center, home-based exercise was programmed for all participants. The participants' "home exercise partner" was initially trained by a physical therapist, and appropriate exercise form was evaluated at follow-up visits throughout the course of the intervention. Outcome measures included exercise compliance and tolerance with secondary measures, including ALS Functional Rating Scale-Revised, ALS Scale for Quality of Life-Revised (3), Fatigue Severity Scale, Ashworth Spasticity Scale (6), and Visual Analog Scale. Follow-up measures were taken at weeks 12 and 24. Training logs and teleconferences were used to track at-home exercise compliance and tolerance.

All groups performed 3 exercise sessions per week. Resistance training included 2 sets of 8 repetitions with use of ankle or wrist weights. Initial intensity was 40% 1 repetition maximum (1RM) and was increased to 50% 1RM at week 4 and 70% 1RM at week 6. 1RM testing was conducted at baseline. Aerobic exercise included the use of a minicycle with 10 min of upper and lower body cycling, respectively, at 50%–70% heart rate reserve and 13–15 on the Borg scale. S-ROM exercise included 4 sets of 30-second static stretches for each exercise. For a list of exercises, see the Supplemental Material (https://www.tandfonline.com/doi/suppl/10.1080/21678421.2017.1404108).

Analysis of all primary and secondary outcomes was conducted at 12 and 24 weeks. Over the course of the study, there were 4 serious adverse events resulting in withdrawal from the study, none of which were deemed a direct result of the exercise intervention or resulted in death. In addition, another 11 participants were lost to follow up (n = 4), co-enrollment in another study (n = 1), difficulty with travel (n = 1), or complication associated with disease progression (n = 2). Minor adverse events that are frequently seen in persons with ALS included musculoskeletal injury, fatigue, and falling, which did not differ between the groups.

When assessing the proportion of participants that were able to tolerate exercise, the S-ROM, resistance, and aerobic groups were 77%, 65%, and 51% compliant. These results indicated all 3 modes of exercise are well tolerated by persons with ALS and safe to perform, with greatest compliance occurring in the S-ROM and resistance groups. There were no differences at 12 or 24 weeks regarding any of the secondary measures, which suggests that resistance and aerobic training did not exacerbate or cause accelerated progression of disease, reduce quality of life, or increase fatigue in this sample of participants.

CLINICAL IMPLICATIONS

This is one of the first studies to demonstrate that resistance and aerobic exercise is safe and well tolerated for persons with ALS, and compliance with resistance training is comparable with standard care (S-ROM). The findings of this study are supported by previous researchers (6,8) that demonstrate short-term improvement in disability associated with supervised resistance and aerobic training. It is possible that differences in exercise adherence can be attributed to the intensity parameters being too low for resistance training or too high for aerobic training, resulting in lower compliance rates associated with the S-ROM, respectively. Future researchers will need to focus on specific frequency, intensity, type, and volume of exercise programming for the management of ALS. Although the clinical exercise physiologist should interpret the results of this study with caution, the use of resistance and aerobic training should be considered as a management technique for patients diagnosed with ALS.

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RESEARCH HIGHLIGHTS

Huntington's Disease, Resistance Training, Aerobics, Feasibility, Adherence, and Physical Fitness

Quinn L, Hamana K, Kelson M, Dawes H, Collett J, Townsen J, Raymund R, van der Plas AA, Reilmann R, Frich JC, Rickards H, Rosser A, Busse M. A randomized, controlled trial of a multimodal exercise intervention in Huntington's disease. Parkinsonism Relat Disord. 2016;31:4–52.

Huntington's disease (HD) is a genetically linked neurodegenerative disease that is progressive and results in neuronal damage to the substantia nigra and cerebral cortex of the brain (1). HD is associated with nonmotor symptoms such as cognitive impairment, dementia, memory loss, and disorientation, as well as motor symptoms including chorea (irregular or rapid) and athetosis (slow or writhing involuntary) movements of the hands, feet, face, and trunk (1). Currently, there are approximately 30,000 people in the US (1) and 1,500 people in Australia (2) who are living with HD.

The effectiveness of exercise as a management technique for HD is a relatively new research focus with limited studies. It is suggested that multimodal rehabilitation programs can improve physical function, quality of life (3), and possibly cognition (4) in persons with HD. Many challenges exist with determining the effectiveness of exercise-based interventions on HD, including level of supervision, appropriately programmed intensity, variability of cognitive impairment, exercise preference or tolerance, and comfort with exercise settings (5,6). These factors can lead to reduced initiation and adherence to exercise for persons with HD. Therefore, the aim of this study is to determine the effectiveness of a multimodal exercise program on persons with mild to moderate HD to determine safety, feasibility regarding retention and adherence, and improvement of physical fitness, motor control, physical function, and cognition.

MANUSCRIPT REVIEW

This was a randomized, controlled, multicenter trial, that assigned 32 of 312 screened participants to an exercise (n = 17) or control (n = 15) group for a 12-week intervention and 26-week follow up. Inclusion criteria were (a) genetically confirmed cases of HD, (b) ≥18 years of age, and (c) stable medication regime of antichoreic drugs for 4 weeks. Participants were excluded if they were (a) unable to use an exercise bike, (b) had psychological or physical limitation precluding exercise testing, and (c) currently in an exercise program. All participants who met inclusion criteria were screened for cardiovascular risk factors and underwent electrocardiogram testing to ensure safety with initiation of exercise.

The control (CT) group was instructed to carry on with normal activity for the full duration of the intervention. Participants in the exercise (EX) group participated in three 50-min exercise sessions per week for a total of 12 weeks. Follow-up assessment occurred at week 13 and was compared with the baseline. Exercise included 25 min of cycling at 55%–85% age-predicted maximum heart rate (APMHR), 10–15 min of resistance training (2 sets of 15 repetitions), and 5 min of static stretching. For full details on the exercise program, see the Supplemental Material (https://www.prd-journal.com/article/S1353-8020(16)30243-7/fulltext#supplementaryMaterial). Participants could choose between their home or a medical fitness center to perform the exercise. An exercise professional provided gym-based supervision and at-home exercise for all 3 sessions during weeks 1–2, which was then tapered to 2 sessions for weeks 3–6, and 1 session for the final 6 weeks.

Primary outcome measures included retention (completion of intervention) and adherence (completion of sessions), which was predetermined as >75% of supervised and unsupervised sessions and maintaining APMHR intensities for >75% (19/25 min) of the cycling duration. A series of secondary measures were also collected at baseline and follow-up assessment to determine improvement in motor control, quality of life, and physical and cognitive function (7–10).

Three participants from the EX group dropped out before the 13-week assessment due to concomitant conditions, and 10 (n = 5 EX and n = 5 CT) were unable to be contacted at the 26-week period. Two serious adverse events occurred in the CT group, both attempted suicides, with 1 possibly being related to the week 13 assessment. A total of 97% of the EX group completed the intervention. Ninety-three percent of the EX group were able to complete the required sessions of the intervention, with only 75% achieving APMHR at each exercise session. Blunted heart rate response can be attributed to autonomic dysfunction commonly associated with HD, resulting in the inability to reach a predetermined percentage for APMHR (1). The EX and CT groups showed no differences in fall occurrence, suggesting that supervised exercise does not incur a greater fall risk in this population.

The EX group improved aerobic fitness ($VO_{2\ MAX}$), motor function, and reduced body weight compared with the CT group. A reduced body weight may not be considered a positive finding because HD can lead to rapid weight loss in some people, resulting in cachexia and negative health outcomes (11). Follow-up assessment at 26 weeks indicated that all EX participants returned to low levels of physical activity after the intervention was terminated, and there were no differences in measured health outcome between groups.

CLINICAL IMPLICATIONS

This is the first study to demonstrate that a multimodal exercise program is safe and that persons with mild to moderate HD can adhere to exercise with and without supervision and in different settings. The authors of this study showed improvement in aerobic fitness and motor control, but no improvement in strength, physical function, or cognition, which can all reduce quality of life in persons with HD (3). The exclusion of those with cognitive deficit and mental health disease, which is commonly associate with HD, may have resulted in reduced applicability of this study. The resistance training protocol may have used an intensity and/or volume that was too low for improvement in strength. Future researchers might investigate the effects of resistance versus aerobic training and allow for a more robust sample of participants with and without HD-related cognitive impairment. The clinical exercise physiologist should encourage persons with HD to remain physically active using a multimodal program when safe and appropriate for an individual.

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