International Journal of EXERCISE SCIENCE

Original Research

Mobility Improvements After a High-cadence Dynamic Cycling Intervention in an Individual with Motor Neuron Disease: A Case Study

KRISTIN NOLL†, BRIAN T. DOWDELL†, and ANGELA L. RIDGEL‡

Exercise Science and Physiology Program, Kent State University, Kent, OH, USA

†Denotes graduate student author, ‡Denotes professional author

ABSTRACT

International Journal of Exercise Science 14(3): 791-801, 2021. Previous exercise studies in individuals with motor neuron disease have shown some positive benefits but the stress of regular exercise could result in overuse weakness in this population. The purpose of this case study is to determine the efficacy, and tolerability of a high-cadence dynamic cycling intervention in an individual with motor neuron disease. A 67-year-old male with significant lower extremity weakness and a diagnosis of idiopathic motor neuron disease completed six 30-minute sessions of high cadence dynamic cycling over a two-week period using a custom-built motorized ergometer with the motor speed set at 80 revolutions per minute. This intervention resulted in an 80.4 m increase in walking distance during the six-minute walk test (21% increase), with a lower rating of perceived exertion than at baseline. Amyotrophic Lateral Sclerosis Functional Rating Scale- Revised scores improved slightly (2.4%) suggesting that the intervention was tolerated, and it did not compromise the participant's physical function. These data show that this intervention can improve mobility, is well-tolerated and minimizes the risk of overuse weakness in an individual with motor neuron disease.

KEY WORDS: Rehabilitation, exercise, motor weakness, amyotrophic lateral sclerosis

INTRODUCTION

Motor neuron diseases (MND) are differentiated by the degree of upper and lower extremity involvement, specifically lower motor neuron only, upper motor neuron only or a combination between upper and lower motor neuron (31). Amyotrophic Lateral Sclerosis (ALS) commonly presents as mixed upper and lower motor neuron findings and is one of the most common forms of motor neuron disease (11). Average age of onset is 55 years old with a median survival rate of approximately three years following diagnosis. ALS is a progressive disease that causes muscular weakness, which leads to increased fatigue, loss of balance, and spasticity (7).

The primary non-pharmacological treatments for motor neuron diseases focus on relieving the symptoms (31). A recent meta-analysis suggested that exercise may be helpful for relieving

spasticity associated with MND, but there are no large randomized controlled studies to support this suggestion.

In addition, past recommendations have cautioned exercise due to the thought that the physical strain of exercise was harmful in MND and could potentially cause an increased loss of MNs and overuse weakness (32). However, avoiding physical activity can result in cardiovascular deconditioning, as well as disuse weakness (12). More recently, there is growing evidence that moderate intensity aerobic and strength training can be helpful for reducing spasticity, fatigue, and muscle function without causing additional muscle damage (21, 29). A pilot study by Sanjak et al. (28) supported that treadmill ambulation training improved rating of perceived exertion and fatigue in individuals with ALS. Nevertheless, there is a limited amount of evidence-based therapeutic exercise data to guide therapists with techniques to slow the progression of motor neuron loss or improve the survival rate and evidence of exercise-related slowing of disease progression in clinical populations is limited (21).

Studies with animal models have provided positive evidence that exercise can slow progression of MND and provide neuroprotection (8, 13, 17). Interestingly, the effects of exercise on models of ALS depend on the exercise type and intensity. For example, a forced exercise (FE) intervention in the ALS rodent model, where the animals are forced to maintain an exercise rate that is greater than their preferred pace, enhanced motor function, slowed disease progression, and extended the survival rate (8, 13). Furthermore, MN density in the lumbar spinal cord of these animal models was significantly greater after moderate intensity training on a treadmill and high intensity training in a pool, compared to lower intensity exercise. These findings suggest that exercise mode and intensity are important factors in neurorecovery.

Differential effects of exercise mode and intensity on neurorecovery have also been documented in stroke (15, 19) and Parkinson's disease (24-27). For example, high-cadence cycling promoted improvements in walking capacity in individuals with chronic stroke (19) and a reduction in Parkinson's disease motor symptoms (24-27). High-cadence cycling studies in Parkinson's disease suggested that repetitive rhythmic aerobic exercise promotes changes in neural drive (24, 26). High-cadence cycling provides three features which could have driven these improvements: augmented exercise, intermittent breaks, and unweighting characteristics. The potential value of high-cadence leg cycling in the ALS/motor neuron disease population is that the rider is mechanically assisted by the motor, allowing them to pedal at rates higher than they could voluntarily achieve. Only one pilot study has examined the effects of treadmill training in ALS, and to our knowledge, there has been no research to date that has attempted to investigate the effects of high cadence cycling in individuals with ALS (28). The purpose of this case report was to test tolerability of two weeks (six sessions) of high cadence cycling and the effects on gait, muscle strength, and daily activity function in an individual with motor neuron disease.

METHODS

Participants

Written informed consent was provided by the participant according to the guidelines of the Kent State University IRB. The research was carried out fully in accordance to the ethical standards of the International Journal of Exercise Science (23). The subject of this case study was a 67-year-old right-hand dominant Caucasian male with progressive left foot drop. He was a recreational runner, but stopped 2.5 years ago due to an unstable left hip. He received a hip stability/strengthening program from a physical therapist, which reduced the hip pain, but leg weakness continued. The patient noted moderate to severe leg weakness after climbing one flight of stairs, cycling for more than 30 minutes, and while walking more than five minutes. The patient reported no difficulty with speech, swallowing, or breathing.

In the physical exam, the subject presented with marked wasting of the anterior tibialis, gluteus maximus, and gluteus medius. Manual Muscle Test (MMT) of the biceps and triceps revealed normal strength bilaterally. MMT was *good to normal* for the left lower extremity, including the hip flexor, knee extensors, knee flexors, and adductors and for the right hip flexor, knee extensors, knee flexors, and hip extensors. MMT was *fair to poor* for the left lower extremity, including the dorsi flexors, plantar flexors, hip extensors, and hip abductors and right dorsi flexors, plantar flexors, hip adductors, and hip abductors. Mental status was reported as essentially normal. Cranial nerve examination was unremarkable.

In the single leg stance test, the subject was able to stand for 3.53 seconds with his right lower extremity and 1.59 seconds with his left lower extremity, which is much less than the average for healthy 60 to 69 year olds (22.5 ± 8.6 seconds) (6). Average ambulation speed during the 25 foot walk test was 5.99 seconds (speed = 4.17 ft/sec or 127.21 cm/sec), which was below the normal value of 212.7 ± 42.1 cm/sec (5). The subject was only able to complete one repetition of the 5-Repetition Sit to Stand Test without assistance (normal value for males age 60-69 = 5-repetitions of sit to stand in 11.4 sec) (4). With assistance, he was able to complete five repetitions in 10.12 seconds. Gait assessment revealed a marching gait pattern with increased left hip flexion compared to the right and left foot drop. Compensatory Trendelenburg was present bilaterally with the right greater than the left.

The lower extremities showed greater strength loss than the lower extremities, and the distal extremities were weaker than the proximal extremities (Table 1). Force output values for elbow flexors, elbow extensors, and hip flexors were within normative value ranges (1). However, knee flexor, knee extensor and dorsiflexors showed force output values that were 44%, 37% and 95% less than normative values. Modified Ashworth Spasticity Scale Scores were 0 for both arms and for both lower extremities suggesting that muscle tone is normal (2).

Table 1. Subject and normative reference values (males 60-69 years old) for force obtained with hand-held dynamometer and reported by muscle action and side (1).

Muscle Action	Side [a]	Subject Force (lb)	Normative Ranges for Force (lb)
Elbow Flexion	N	50	47.8-63.8
	D	51	47.6-68.8
Elbow Extension	N	35.5	27.8-43
	D	38.5	27.4-46
Hip Flexion	N	34.5	31.9-50.9
	D	42	30.7-51.3
Knee Flexion	N	21.5	40-61.2
	D	25.5	42.5-62.1
Knee Extension	N	41	69.5-100.7
	D	44	65.4-97.6
Ankle Dorsiflexion	N	2	41-68
	D	2	39.5-66.3

[a] N= nondominant, D= dominant.

Electromyogram and nerve conduction studies revealed scattered chronic motor axon loss in C6-7 innervated muscles and fasciculation potentials in four out of 14 muscles of the cervical segment. Active motor axon loss was also noted in the right deltoid muscle. The patient showed normal sensory responses of the bilateral median, ulnar, and radial nerve. From T6-T11, fasciculation potentials were noted along with chronic motor axon loss changes in the mid thoracic paraspinals, and active axonal loss in the lower thoracic paraspinals. Needle examination of thoracic paraspinal muscles (T7 and T11 levels), indicated evidence of widespread disorder of anterior horn cells like that seen with evolving motor neuron disease/ALS. Evaluation of L2-S1 revealed axon loss changes of bilateral nerve roots (left > right) along with minimal active denervation of bilateral gastrocnemius and left tibialis anterior muscle. Follow-up tests completed one year later showed progression of previous abnormalities and active motor axon loss changes in the cervical segments. Specifically, chronic motor axon loss changes in C5-T1 innervated segments with scattered active denervation changes were seen in C7-T1, biceps, and lower thoracic paraspinals. In addition, acute and chronic motor axon loss changes were seen in all muscles examined throughout the left lower extremity (L3-S1) with most prominent motor axon loss noted in the gluteus medius. Blood work showed elevated creatine kinase levels.

Deep Tendon Reflexes showed hyporeflexia in both ankles (1+) and hyperreflexia in both biceps (3+), bilateral brachioradialis (3+), and bilateral knee extensor (3+). The patient showed positive signs for Hoffman's, Tromner's, Venderovich's, and negative signs for Romberg's and clonus. Sensory examination was normal and symmetric in perception of light touch, pinprick, temperature, vibration, and proprioception. Based on the overall clinical picture, the subject was diagnosed with ALS, Stage II per Sinaki and Mulder's Clinical ALS Staging (30).

Protocol

The high cadence cycling exercise intervention was administered over two weeks (three times weekly, six total sessions) using a custom motorized cycle (dynamic cycle) developed in the lab

(22). The dynamic cycling paradigm uses a motorized stationary cycle to assist individuals with PD to pedal the legs at a cadence faster than they can (or would) pedal on their own. This rehabilitation paradigm is dynamic because the motor rotates the pedals at a high speed with a slight, but prescribed, variation. The motor speed was set at 80 revolutions per minute and the participant was encouraged to keep up with the motor by pushing on the pedals and producing positive power. This motor speed was chosen based on previous studies in individuals with Parkinson's disease (24, 26). To avoid overwork muscle weakness, the training paradigm included a 30-minute dynamic cycling session with three intervals of five minutes of cycling interspersed with five minutes of rest resulting in 15 minutes of total exercise. A physical therapist supervised the subject during all exercise sessions. The participant's level of exertion was assessed prior to starting the exercise and every minute using Borg's RPE scale 6-20. If the subject reported a level greater than 13, then the research personnel adjusted the intensity by lowering the motor speed to avoid excessive fatigue. Muscle strength and functional status was assessed before the first cycling session (pre-test) and immediately after the last session (post-test). Gait performance was assessed at baseline and immediately after each exercise session.

Gait performance was measured using the six-minute walk test (6MWT). This test was completed on a treadmill and the subject wore a support harness (Biodex® Standard Harness and Unweighing System) to lower the risk of a fall. The subject was instructed to walk as fast as he could for 6 minutes. Total distance and average speed were recorded. In addition, walking tolerability was assessed, using the methods of Sanjak et al. (28), by recording RPE every minute during the 6MWT and by calculating the percent change in the highest score for each session.

Changes in muscle strength were measured by asking the subject to perform a maximal voluntary isometric contraction **(**MVIC) against a hand-held digital push-pull dynamometer (Baseline™ universal digital push-pull dynamometer) at baseline and immediately after the two-week intervention period. During the MVIC evaluation, perpendicular resistance was applied to a pre-marked location on the subject's extremity and the subject was instructed to hold the position for approximately three to five seconds. Muscular strength of the ankle (dorsiflexion/plantarflexion), knee (flexion/extension), and hip musculature (flexion/extension) was measured twice by a trained physical therapist and averaged (16). Global muscle strength was also assessed using Manual Muscle Testing (MMT) of the lower limbs. The Great Lakes Study Group concluded that MMT was a reliable and sensitive measure of global strength in individuals with ALS (14). MMT of the ankle, knee, hip flexors\extensors, and hip abductors\adductors was evaluated at baseline (pre-test) and after the last cycling session (post-test) by a physical therapist using standard protocols (18).

Functional status was evaluated at baseline (pre-test) and after the last cycling session (post-test) using the ALSFRS-R score (amyotrophic lateral sclerosis functional rating scale revised) (10). Sanjak et al. (28) reported that ALSFRS scores are regularly used to report disease progression and treatment efficacy.

RESULTS

Cycling performance: The subject showed similar heart rates, RPE and performance (as measured by power) throughout the six sessions (Table 2). Positive power values show that the subject was not passive but produced positive effort while cycling. RPE values were rated as light (10-11), but average heartrate ranged between 83-90% of maximum heart rate (as calculated by 200 - age).

Table 2: Exercise Performance and Rating of Perceived Exertion (RPE).

	Session 1	Session 2	Session 3	Session 4	Session 5	Session 6
Heartrate (bpm)	135.3	137.3	127.8	136.2	139.1	132.3
RPE (6-20)	10.4	11.3	10.7	10.9	10.9	10.7
Power	24.3	27.6	26.9	31.7	27.7	26.3
Cadence (rpm)	83.8	84.1	84.5	84.9	85.3	79.5

Muscle Strength: Both MVIC and MMT showed minimal changes over the course of the intervention (Table 3). To the author's knowledge, there are no published minimally clinically important difference (MCID) for MVIC or MMT for individuals with ALS or motor neuron disease. However, a study in inflammatory myopathies suggested that ≥ 15% improvement in MMT would be clinically relevant (3).

Mobility and Functional Status: The subject showed improvements after the cycling intervention on several gait parameters, including distance and speed during treadmill ambulation (Table 3) (Figure 1A-C). Maximum distance walked during the 6MWT improved by 80.4 m (21%) from baseline to after the last session and showed progressive improvement over two weeks (Figure 1A). This change was within the minimally clinically important difference (MCID) of 14% or 25m reported by Sanjak et al. (28). There was a slight decrease in distance walked from session three to four, which is likely reflective of the two-day break between these sessions (i.e., session three was on a Friday and session four was on a Monday). In addition, gait velocity increased by 0.4 m/s (27%) and showed steady improvement over the intervention (Figure 1B). Interestingly, the improvements in walking speed were accompanied by a decrease in the RPE scores in sessions three and four (Figure 1C).

The participant's ALSFRS-R scores slightly improved (2.4%), implying that the intervention did not compromise his physical function (Table 3). Furthermore, this change was less than the MCID of 20% (or 4 points) (9). Lastly, there were no adverse events during the intervention and the subject noted that he enjoyed the exercise and felt like it provided positive benefits. These outcomes show that a high cadence dynamic cycling program over two weeks was tolerated did not compromise physical function and elicited improvements in gait for an individual with motor neuron disease.

Table 3. Percentage change and responsiveness of outcome measures.

	Pre-test	Post-test	% change	MCID
Disease-specific functional rating scale				
ALSFRS-R score (max= 48)	41	42	2.4%	20% (4 or higher) (9)
Static Isometric tests (ankle, knee, hip)				
MMT*	56	57	2%	N/A
MVIC*	563.1	554.6	-2%	N/A
Locomotor capacities				
Gait velocity (m/s)	1.1	1.5	27%	N/A
Maximum distance (m, 6MWT)	305.8	386.2	21%	14% or 25 m (28)
Rating of perceived exertion (6MWT)	14	13	-7%	N/A

MMT: manual muscle test, MVIC: maximum voluntary isometric contraction, 6MWT: 6-minute walk test, MCID: Minimally clinically important difference, N/A: Not Applicable, *= total lower extremity score, -%= improvement

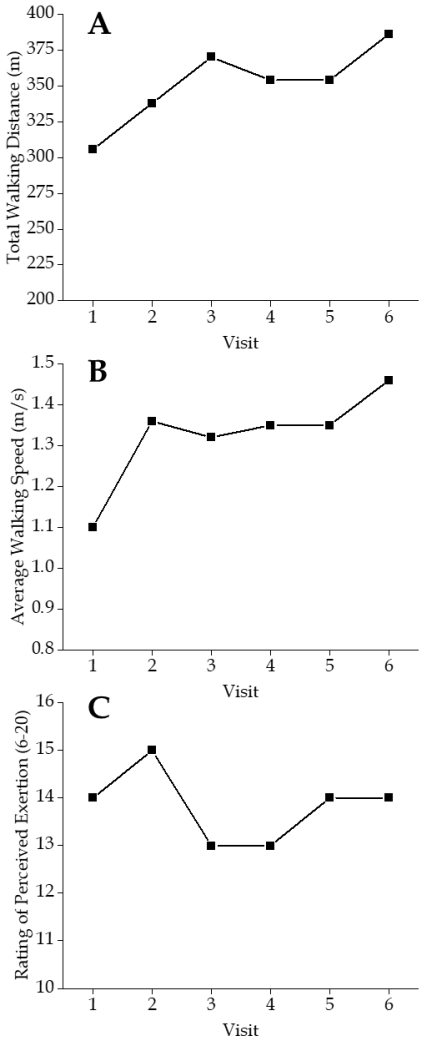

Figure 1. 6MWT distance (A), speed (B), and RPE (C) over the six-session intervention. The participant showed progressive improvement in walking speed and distance, with lower rating of perceived exertion (RPE) during some of the sessions.

DISCUSSION

The purpose of this case report was to test tolerability of two weeks (six sessions) of high cadence cycling and the effects on gait, muscle strength, and daily activity function in an individual with motor neuron disease. These results show that an ambulatory individual with motor neuron disease can tolerate and show favorable training responses over a two-week intervention of dynamic cycling.

Although the exact mechanisms of functional improvements are not clear, several features of the dynamic cycle may have contributed to these improvements. A recent electroencephalographic (EEG) spectral analysis study with healthy cyclists suggested that high cadence cycling reduced EEG spectral power, and that this decrease is likely attributed to neural efficiency in brain function (20). The underlying mechanism for the reduction in EEG spectral power in the high-cadence cycle group was attributed to less activation of cortical/neuronal circuitry or the optimization of cerebral metabolism. This data could explain why the subject with motor neuron disease reported lower RPE scores over the intervention. Therefore, it is plausible that dynamic cycling increased the activation of proprioceptors and promoted neural efficiency which delayed central fatigue and improved ALS symptoms.

The pathophysiology of ALS limits sustained high effort exercise which impedes biochemical and neuronal responses. However, we incorporated intermittent rest breaks during the 30-minute intervention to protect the participant from overwork weakness. Sanjak et al. (28) demonstrated that intermittent rest breaks along with five-minute exercise intervals provided a safe and sufficient method to administer moderate intensity aerobic exercise to ALS subjects. Lastly, the dynamic cycle provided the participant an "unweighing activity" which may have minimized the risk of injury. Previous ALS animal model research showed that swimming (unweighted activity) significantly delayed disease onset and spinal motor neuron death, as well as increased survival compared with treadmill training (13).

This case study has a few limitations. First, there was a slight decrease in MVIC values post-intervention, which was an unexpected finding considering the improvements that were seen in the 6MWT. Since the subject's manually muscle tested knee flexors/extensors and hip flexors showed good to normal strength, the task of matching the subject's lower extremity strength during MVIC with a hand-held dynamometer was difficult for the physical therapist, and this could have led to increased data variability. Although a 2% change is small and may also reflect a negative effect of high-cadence cycling on this population. Second, the ALFSRS-R scale likely underestimated disease severity (33). Future studies should use isokinetic dynamometry and a more robust severity scale (i.e., Appel ALS) to assess changes in muscle strength, fatigue, and disease progression. Third, it is likely that repeated testing in the 6MWT provided beneficial effects on gait that were added to the benefits from high-cadence dynamic cycling. Lastly, although the medical evaluation was consistent with symptoms of ALS, it may also be that this individual had idiopathic motor neuron disease (34). However, this case study was intended to provide a basis for support of future exercise studies in this broad population of individuals.

In conclusion, a two-week intervention of dynamic cycling was a well-tolerated and safe exercise modality in an individual with motor neuron disease. Although the results from a single case report cannot be generalized to all individuals with motor neuron disease, the positive effects revealed encouraging results concerning the use of dynamic cycling in this population. Findings from this case study may support future research examining the potential benefits of this exercise paradigm in the reduction of ALS or idiopathic motor neuron disease symptoms. Future research should examine if high-cadence cycling can improve daily fatigue over a longer period, slow progression of weakness and improve quality of life in individuals with motor neuron disease.

ACKNOWLEDGEMENTS

The authors would like to thank the research volunteer for his time.

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