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ORIGINAL RESEARCH

Pilot Study: Evaluation of the Effect of Functional Electrical Stimulation Cycling on Muscle Metabolism in Nonambulatory People With Multiple Sclerosis

Mary Ann Reynolds, MS,[a] Kevin McCully, PhD,[a] Blake Burdett, BS,[b] Christine Manella, PT,[b] Laura Hawkins, BS,[b] Deborah Backus, PT, PhD[b]

From the [a]Department of Kinesiology, University of Georgia, Athens, GA; and [b]Shepherd Center, Atlanta, GA.

Abstract

Objective: To investigate the changes in muscle oxygen consumption ($m\dot{V}O_2$) using near-infrared spectroscopy (NIRS) after 4 weeks of training with functional electrical stimulation (FES) cycling in nonambulatory people with multiple sclerosis (MS).

Design: Four-week before-after trial to assess changes in $m\dot{V}O_2$ after an FES cycling intervention.

Setting: Rehabilitation hospital.

Participants: People (N = 8; 7 men, 1 women) from a volunteer/referred sample with moderate to severe MS (Expanded Disability Status Scale score > 6.0).

Intervention: Participants cycled 30 minutes per session, 3d/wk for 4 weeks or a total of 12 sessions.

Main Outcome Measures: $m\dot{V}O_2$ of the right vastus lateralis muscle was measured with NIRS before and within 1 week after the intervention. Six bouts of 15-second electrical stimulation increasing from 2 to 7Hz were used to activate the muscle. $m\dot{V}O_2$ was assessed by analyzing the slope of the NIRS oxygen signal during a 10-second arterial occlusion after each electrical stimulation bout.

Results: Significant FES training by electrical stimulation frequency level interaction was observed ($P = .031$), with an average increase in $m\dot{V}O_2$ of 47% across frequencies with a main effect of training ($P = .047$).

Conclusions: FES cycling for 4 weeks improved $m\dot{V}O_2$, suggesting that FES cycling is a potential therapy for improving muscle health in people with MS who are nonambulatory.

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Multiple sclerosis (MS) is the most prevalent cause of neurologic disability in young adults. This inflammatory demyelinating disease of the central nervous system leads to impairments that can severely limit a person's activity, participation in daily activities, and quality of life.[1] Although there are a variety of medical therapies successful at reducing the number of relapses during MS and delaying disease progression, the question of how to address the remaining and evolving motor and sensory deficits in a safe manner remains unclear.[2] Recent studies have shown that exercise, both aerobic and resistance, can induce marked improvements in variables (eg, muscle strength, fatigue, cardiorespiratory function, ambulation).[3,4] These improvements suggest that not all functional impairments are a result of nonreversible tissue injury, but rather that a large proportion may be a result of low fitness caused by decreased activity as impairments become more severe. Although exercise may improve function through a host of avenues (eg, increased levels of neurotrophic factors, improved coordinated function),[4,5] skeletal muscle function may also be improved and has been shown to have a significant impact on fatigue, ambulation, and overall function.[3,6]

One proposed physiological mechanism that could play a role in exercise-related changes in muscle function is skeletal muscle mitochondrial function. The mitochondrion is a dual-membrane organelle that is vital for maintaining proper cell function. Specific to muscle function, mitochondria are responsible for oxidative

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phosphorylation, which produces energy used in sustained physical activity.[7] Exercise has been shown to increase mitochondrial density in healthy able-bodied participants, whereas inactivity results in the opposite effect.[8,9] However, research is still needed to determine if mitochondrial function is a contributor to functional disability in people with MS. It is possible that inactivity resulting from the initial motor and sensory loss directly caused by MS could cause downregulation of mitochondria, which would decrease the ability to do sustained physical activity, resulting in further inactivity. People who are nonambulatory as a result of their MS are at an even greater risk of these secondary changes because they are generally dependent on their wheelchair for mobility. In fact, mitochondrial capacity is impaired in people with MS similar to or worse than its impairment in deconditioned able-bodied individuals.[10] This impairment in muscle function may contribute to fatigue, which will further decrease participation in daily activities and ultimately quality of life.[11-13]

Traditionally, mitochondrial function has been studied using both invasive and noninvasive methods. The noninvasive criterion standard to assessing skeletal muscle mitochondrial function has been 31 phosphorous magnetic resonance spectroscopy (^{31}P-MRS), which measures resynthesis of phosphocreatine after exercise.[14] However, ^{31}P-MRS has limitations in terms of cost and availability. Another approach that can measure skeletal muscle mitochondrial function noninvasively is near-infrared spectroscopy (NIRS).[15] Our laboratory has designed a protocol that uses NIRS in combination with a rapid cuff inflation system, which blocks oxygen delivery and venous return, to measure kinetic changes in skeletal muscle oxygen consumption ($m\dot{V}O_2$) after submaximal exercise. The advantage to using NIRS over ^{31}P-MRS is that it is relatively inexpensive (~$10,000–$70,000 vs $2 million) and more accessible. NIRS has been shown to be reproducible,[15] independent of exercise intensity,[16] and able to identify changes caused by training status[15] or disability.[17]

The evidence provides support that exercise is a necessary part of rehabilitation strategy to combat both primary motor and sensory loss and the secondary deconditioning that occurs because of decreased activity in people with MS. In those who are wheelchair dependent, there are few exercise options that are available. Functional electrical stimulation (FES) cycling is an intervention that allows people with severe lower-limb weakness or paralysis an avenue for exercise (eg, those with moderate to severe MS). Studies with FES cycling in people with spinal cord injury have demonstrated improvements in blood flow,[18] exercise capacity,[19] body composition,[20] metabolism,[21,22] muscle mass,[23,24] and muscle strength.[25-27] Impairments observed in people with spinal cord injury are similar to those seen in people with MS. Therefore, it is possible that people with MS will receive the same or similar benefits from FES cycling. The purpose of this article is to examine the effects of an FES cycling intervention on muscle function, specifically muscle metabolism using NIRS, in people with moderate to severe MS who are nonambulatory.

List of abbreviations:

FES	**functional electrical stimulation**
MS	**multiple sclerosis**
$m\dot{V}O_2$	**muscle oxygen consumption**
NIRS	**near-infrared spectroscopy**
^{31}P-MRS	**31 phosphorous magnetic resonance spectroscopy**
RPM	**revolutions per minute**

Methods

This was a prospective pre-post design to determine the muscle response, specifically muscle metabolism of the right vastus lateralis, to FES cycling in people with moderate to severe MS who were nonambulatory. Testing occurred before and within 1 week after a 4-week FES cycling training intervention. Testing consisted of NIRS measurements of muscle metabolism during a progressive work test in which measurements were made at progressively increasing frequencies of electrical stimulation.

Participants

Participants with MS were recruited from a nonprofit rehabilitation hospital in the United States. The study was approved by the institutional review boards of all involved institutions. We certify that all applicable instructional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research. All participants provided written informed consent prior to data collection. Data were collected from December 2012 to August 2013.

Participants were included if they were >18 years of age, unable to ambulate farther than household distances (≥200m), not using FES cycle or receiving weekly applications of electrical stimulation intervention in the lower limb, medically stable with approval from a physician to participate in exercise studies, and able to follow >3-step commands and comply with procedures and follow-up. Participants were excluded if they had experienced a diagnosed relapse in the last 6 months or if they were diagnosed with cardiovascular disease, uncontrolled hypertension, history of epileptic seizures, lower motor neuron disease, or peripheral neuropathy in the lower limbs. Other exclusion criteria included the inability to electrically stimulate leg muscles; presence of a pacemaker, implanted defibrillator, or other implanted electronic or metallic devices (exception being a baclofen pump); unstable long bone fractures of the lower limb or trunk; inability to tolerate sitting upright for at least 1 hour; and allergy to surface electrodes.

Muscle metabolism assessment

Muscle metabolism was assessed using NIRS before and after the 4-week FES cycling training intervention. Resting metabolism and exercise metabolism during a progressive work test using electrical stimulation were measured. Participants were positioned supine on a padded therapy table. The NIRS probe[a] was placed over the surface of the right vastus lateralis muscle and secured on the leg with biadhesive tape and 2 snapped straps. Two electrodes used on the right quadriceps during the FES cycling protocol were positioned over the vastus lateralis muscle and attached to the Theratouch 4.7 stimulator.[b] One electrode was placed proximal to the NIRS probe, and 1 electrode was placed distal to the NIRS probe. A blood pressure cuff attached to a Hokanson AG101 Rapid Cuff Inflator[c] was wrapped around the upper thigh, as high as anatomically possible, proximal to the NIRS probe. The experimental setup is shown in figure 1. Adipose tissue thickness can influence quantification of NIRS measurements.[28] To account for this, skinfold thickness was assessed by a trained rater at the beginning of each NIRS protocol. Metabolic rates were calculated from the slopes of the NIRS oxygenated hemoglobin signal using linear regression as previously published.[29]

The muscle metabolism assessment was performed as previously published by Erickson et al.[29] Briefly, the assessment began with approximately 1 minute of rest to assess baseline muscle