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Exercise Interventions Targeting Obesity in Persons With Spinal Cord Injury

David W. McMillan, PhD,[1,2] Jennifer L. Maher, PhD,[3] Kevin A. Jacobs, PhD,[4] Mark S. Nash, PhD,[1] and David R. Gater, MD, PhD, MS[1,2]

[1]Christine E. Lynn Rehabilitation Center for the Miami Project to Cure Paralysis, UHealth/Jackson Memorial, Miami, Florida; [2]Department of Physical Medicine & Rehabilitation, University of Miami Leonard M. Miller School of Medicine, Miami, Florida; [3]Department of Health, University of Bath, Claverton Down, Bath, United Kingdom; [4]Department of Kinesiology and Sport Sciences, University of Miami, Coral Gables, Florida

Abstract: Spinal cord injury (SCI) results in an array of cardiometabolic complications, with obesity being the most common component risk of cardiometabolic disease (CMD) in this population. Recent Consortium for Spinal Cord Medicine Clinical Practice Guidelines for CMD in SCI recommend physical exercise as a primary treatment strategy for the management of CMD in SCI. However, the high prevalence of obesity in SCI and the pleiotropic nature of this body habitus warrant strategies for tailoring exercise to specifically target obesity. In general, exercise for obesity management should aim primarily to induce a negative energy balance and secondarily to increase the use of fat as a fuel source. In persons with SCI, reductions in the muscle mass that can be recruited during activity limit the capacity for exercise to induce a calorie deficit. Furthermore, the available musculature exhibits a decreased oxidative capacity, limiting the utilization of fat during exercise. These constraints must be considered when designing exercise interventions for obesity management in SCI. Certain forms of exercise have a greater therapeutic potential in this population partly due to impacts on metabolism during recovery from exercise and at rest. In this article, we propose that exercise for obesity in SCI should target large muscle groups and aim to induce hypertrophy to increase total energy expenditure response to training. Furthermore, although carbohydrate reliance will be high during activity, certain forms of exercise might induce meaningful postexercise shifts in the use of fat as a fuel. General activity in this population is important for many components of health, but low energy cost of daily activities and limitations in upper body volitional exercise mean that exercise interventions targeting utilization and hypertrophy of large muscle groups will likely be required for obesity management. **Key words**: *body composition, body fat, energy expenditure, lifestyle interventions, physical activity*

Introduction

Spinal cord injury (SCI) profoundly impacts the structure and function of many body systems, as evidenced by the breadth and depth of associated secondary complications. Recent advancements in medical practice[1] have increased life expectancy[2] consequentially increasing risk of developing cardiometabolic comorbidities.[3-19] Specifically, persons with SCI experience accelerated risk for accumulating adipose tissue[20-33] and developing lipid[34-43] and glucose[44-58] metabolism disorders. Accordingly, the Consortium for Spinal Cord Medicine (CSCM) recently released clinical practice guidelines for cardiometabolic disease (CMD) in persons with SCI.[3] The CSCM CMD guidelines recommend physical exercise as a primary treatment strategy for the management of CMD in SCI. Furthermore, AGREE II evidence-based activity guidelines[59] were recently updated[60] and state with moderate to high confidence that exercise benefits CMD in persons with SCI.[60] However, neither of these guidelines contain details about how to deliver exercise to specifically target the component risk(s) that comprise the CMD disease state. Efforts to tailor exercise to address obesity in SCI are warranted, as obesity is the most prevalent CMD risk factor in this population.[3] This review starts by summarizing current guidelines on exercise and obesity in persons with SCI. We then present considerations for the implementation of exercise as a strategy for managing obesity in SCI. In doing so, we view obesity through the lens of calorie balance and focus principally on the ability for exercise to increase energy expenditure (EE). We acknowledge that no behavior occurs in a vacuum, and energy deficits induced by exercise can readily

Corresponding author: David W. McMillan, 1611 NW 12th Avenue, Room 3.163, Miami, FL 33136; email: dmcmillan@med.miami.edu

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be negated by concomitant increases in intake and/or decreases in nonexercise activity. However, this issue of Topics in Spinal Cord Injury Rehabilitation extensively covers other behavioral contributions to obesity in SCI, so this review will focus specifically on designing exercise for maximizing EE for the management of obesity in SCI.

Considerations for Exercise and Obesity

Obesity is the most common CMD risk factor in persons with SCI,[3] with the SCI-specific body mass index (BMI) cutoff (≥22 kg/m^2), revealing an obesity prevalence of ~75%.[3] The population-specific BMI cutoff is used because SCI results in dysregulation of muscle,[61-69] bone,[70-73] and adipose[20-33] tissue that renders profound changes in body composition. The CSCM CMD guidelines allow for the use of BMI ≥22 kg/m^2 to diagnose obesity in SCI, but there are notable limitations to the use of BMI in persons with SCI. Population-specific BMI cutoffs are derived from persons with chronic SCI and thus are not calibrated for person in the earlier (acute and subacute) phases of SCI. There are practical limitations in accessibly and accurately determining height and weight. Furthermore, regional (e.g., sublesional) changes in body composition warrant the use of multicompartment modeling of body composition whenever possible. In SCI, obesity is classified as a whole-body fat (BF) percentage of >22% BF for adult men and >35% BF for adult women.[3] Multiple methods are available for determining body composition. Still, there are specific considerations and constraints for persons with SCI.[74] Unique regional changes due to SCI, such as atrophy of sublesional skeletal muscle and encroachment of fat deposits into the viscera,[28-32] paralyzed muscle,[32,33] and bone marrow,[71,72] increase the utility of assessment techniques that determine regional tissue composition. Furthermore, SCI imparts methodological constraints on standard methods such as bioelectrical impedance and skinfold thickness (both designed to be conducted with the patient/participant standing). Four-compartment modeling, dual-energy x-ray absorptiometry (DXA), and a recently validated prediction equation using abdominal skin fold appear to have the most significant utility for assessing body composition, and thus obesity, in SCI.[75]

Evidence-based guidelines have well established the use of activity to increase cardiorespiratory fitness and muscular strength in persons with SCI.[59] Recently, North American guidelines have included activity as a viable treatment strategy for CMD in SCI.[3,60] These guidelines recommend "at least 30 min of moderate to vigorous intensity aerobic exercise 3 times per week"[60] or "at least 150 minutes per week […] satisfied by sessions of 30-60 minutes performed three to five days per week, or by exercising for at least three, 10-minute sessions per day."[3] Current CMD guidelines are designed primarily around volume and frequency of activity but give vague or no recommendations for intensity and mode of the activity. Recommendations targeting nonspecific benefits, such as the Exercise and Sport Science Australia (ESSA) position statement on exercise and SCI, do provide intensity categories (i.e., 150 min/week moderate intensity or 60 min/week vigorous intensity) similar to recommendations for persons without SCI from governmental health authorities (e.g., Centers for Disease Control and Prevention[76] and World Health Organization[77]). However, the specific tailoring of exercise intensity to target CMD-related outcomes has yet to be adopted into recommendations despite calls for recognition of the importance of intensity in this context.[78] Furthermore, while certain guidelines have differentiated between exercise and physical activity (PA),[60] because of the low energy cost of PA (discussed later) it is our opinion that a greater emphasis should be placed on the distinction between targeted exercise and unstructured PA when managing obesity in persons with SCI. The result is that the current guidelines do not offer recommendations for the tailoring of exercise to address the specific component risk(s) that comprise the CMD state. The high prevalence of obesity in SCI and the pleiotropic nature of this body habitus warrant specific strategies for management. There are two primary goals for exercise as a treatment for obesity: primarily to induce a negative calorie balance and secondarily to increase the utilization of fat as a fuel source. Inducing a negative calorie balance is most readily achieved through reduced calorie intake, but exercise can facilitate a negative balance via increases in EE. Exercise potentially has a multifaceted impact on EE, with acute increases

during and after exercise and chronic increases in EE if exercise imparts changes in the mass and/or activity of metabolically active tissues. It should be remembered that changes in EE due to exercise can be readily offset by compensatory and substitution behaviors, as has been demonstrated in SCI.[79] However, the following sections will focus principally on using exercise to increase EE in the context of obesity management in SCI.

Exercise Energy Expenditure

In general, EE during exercise is the most modifiable component of total daily EE in persons without SCI ranging from 100 to 8500 kcal/day.[80] This thermic bandwidth imparts exercise with the potential to have a great influence on the achievement and/or maintenance of optimal body weight, composition, and overall health. However, this ability for exercise to modify EE is greatly diminished by SCI due to large reductions in the skeletal muscle mass that can be voluntarily contracted, depending on the level and completeness of injury. Often those with SCI are limited to arm activity that involves a two- to three-fold smaller muscle mass than the legs[81] and, therefore, is less capable of expending energy. Additionally, the upper extremity musculature is inherently less oxidative. This is evident in elite cross-country skiers who have equally trained arms and legs and yet the arms compared to the legs are less capable of extracting oxygen due to greater variability in blood flow and diffusion limitations[81,82] and less capable of oxidizing lipids[82,83] due to lower beta oxidative enzyme activities.[84]

Given reduced muscle mass and oxidative capacity, rates of EE during exercise in persons with SCI are low ranging from 2.2 to 4.2 kcal/min during arm crank ergometry,[85] circuit resistance exercise,[86,87] moderate intensity continuous exercise,88 and high-intensity interval exercise.[88-90] Furthermore, these values, already relatively low, scale with level of injury, resulting in the need for tetraplegia-specific considerations.[91] Across a wide range of activities, those with motor complete SCI expended 1.7 to 4.0 kcal/min during activities of daily living and PA and 1.7 to 8.1 kcal/min during exercise.[92,93] The use of functional electrical stimulation (FES) to contract lower extremity muscles during tasks such as leg cycling,[94-100] rowing,[95,101-104] or other exercise[69,105,106] allows for increased muscle mass to contribute to exercise EE. FES cycling and rowing elicit maximum EE rates of approximately 5 and 10 kcal/min, respectively.[95] Unfortunately, transcutaneous neuromuscular electrical stimulation has inherent limitations[107] that lead to rapid fatigue.[108] With the current state of this technology, rapid fatigue results in a reduced number of consecutive active contractions that can be induced by FES, reducing the volume of active exercise that can be completed with FES. Combining lower extremity FES and arm crank ergometry modestly increases exercise EE above these modes alone[95-98] and could be especially beneficial for persons with higher level injuries.[109] However, steady-state EE with this mode still does not exceed approximately 6 kcal/min. During volitional exercise, persons with cervical SCI have further limitations to exercise EE, with steady-state arm cycling having a cost as low as 0.9 kcal/min.[91] For perspective, aerobically fit individuals without SCI expend 11.1 to 16.6 kcal/min during cycling ergometry at 65% to 75% VO_{2peak}[110,111] and approximately 20 kcal/min during combined upper and lower body exercise at 76% VO_{2max}.[82]

The American College of Sports Medicine[112] and the US Department of Health and Human Services Centers for Disease Control and Prevention[76] general-population guidelines recommend that individuals perform 75 to 150 min/week of moderate to vigorous intensity aerobic exercise to reduce the risk of cardiovascular disease. This volume of exercise is associated with minimum goal of 1000 kcal/week of caloric expenditure, with 2000 kcal/week being put forth as a more optimal weekly expenditure by an authoritative position statement.[113] Although persons with SCI may be capable of achieving appropriate volumes of activity, the associated expenditure goals are impractical, with the minimum 1000 kcal/week requiring more than 250 minutes of exercise (assuming an average rate of exercise EE of 4 kcal/min) and experimental evidence showing 4 to over 20 hours a week for persons with tetraplegia to achieve the 2000 kcal/week target. Thus meeting general-population expenditure goals requires a substantially greater volume compared to the population-specific SCI guidelines (90 min/week of moderate-to-vigorous

activity[60] or 150 min/week of general activity[3]). The low rates of exercise EE in persons with SCI warrant a multiple intervention approach to cardiometabolic health, and a strong emphasis should be placed on dietary changes in the management of obesity in this population.[114,115]

While expenditure of energy is paramount to obesity abatement, the source of the calories is also an important consideration. Interventions such as aerobic exercise that may stimulate fat oxidation are particularly relevant to persons with SCI. However, those with SCI have markedly reduced mobilization, delivery, and uptake of fat during FES cycling compared to those without SCI performing voluntary leg cycling.[116] These effects of SCI may be partially responsible for the reduced oxidation of fat during voluntary upper body exercise compared to those without SCI.[85,111,117,118] However, the limited ability to oxidize fat during exercise in persons with SCI may be largely due to the mode of voluntary exercise available to them rather than their injury per se.[85] A heavy reliance on carbohydrates during exercise does not encompass the full effect of a bout of exercise on fat metabolism, as fat sources such as intramuscular triglycerides may not be utilized until hours to days after an intense exercise session.[119] Therefore, limited contributions of fat oxidation to exercise EE does not reduce the importance of exercise in the management of obesity in persons with SCI as this intervention may have significant effects on fat use during several hours of postexercise recovery.

Postexercise and Resting Energy Expenditure

Exercise has acute and chronic effects on EE at rest that must be considered when designing exercise interventions to manage obesity. After an acute session of exercise, EE does not immediately return to preexercise levels, but it decays in a manner dependent on exercise volume and intensity.[120] This phenomenon was originally identified as excess postexercise oxygen consumption,[121] and postexercise EE in persons without SCI can be elevated for hours to days after an exercise session.[120] The few studies that have reported postexercise EE in SCI after arm cycling[122] and FES leg cycling[94] have shown a limited (<30 min) elevation of postexercise EE in SCI. However, it should be noted that postexercise EE was not a primary outcome, and therefore neither study employed exercise designed to maximize postexercise EE. Studies are currently underway to determine the effect of exercise mode and intensity on postexercise EE in this population (ClinicalTrials.gov NCT03545867).[123] Although direct data pertaining to postexercise EE in SCI are limited, indirect evidence suggests that variables beyond exercise EE contribute to the beneficial effects of exercise on fat metabolism in SCI. For example, it has been shown that 36 sessions of circuit resistance training (CRT), costing approximately 400 kcal/week,[86,87] improved the clinical lipid profile in persons with paraplegia.[124] Similarly, FES leg cycling for 135 to 180 minutes per week has been shown to benefit body composition and cholesterol.[125] The exercise EE during these studies was well below the posited threshold of 900 to 1200 kcal/week thought to be required to alter the blood lipid profile.[126,127] While indirect, these findings suggest that optimizing exercise for managing obesity in SCI requires the consideration of variables beyond exercise EE. The effect of exercise on fat utilization is of utmost importance as stored fat has been shown to predict cardiovascular disease risk factors in persons with SCI independent from measures of activity and fitness.[128]

Along with increasing postexercise EE, a session of exercise also results in changes in substrate partitioning during postexercise recovery during which there is a robust increased reliance on fat oxidation.[129,130] Glycogen utilization during exercise increases postexercise fat oxidation due to lowered postexercise glycogen levels resulting in a shift in the use of glucose away from oxidation and toward glycogen resynthesis.[131] The relative decrease in glucose oxidation results in an opportunistic increase in use of fat as a fuel. Accordingly, exercise intentionally designed to maximize glycogen depletion has the greatest potential to boost postexercise fat oxidation. Multiple exercise approaches can result in meaningful relative glycogen depletion, but strategies with intermittent high intensity contraction (e.g., interval exercise, resistance exercise, etc.) achieve this goal in a time-efficient manner. For example, resistance exercise has been shown to have a similar beneficial effect on postexercise fat utilization as

endurance exercise despite having a lower calorie cost.[132] The shifts in postexercise fat oxidation may explain the aforementioned benefits of CRT[124] and FES[125] because these modes of exercise are highly glycolytic, and the benefits seen in these studies seem to exceed what would be expected based on exercise EE. Exercise is also known to acutely affect the metabolism of the macronutrients in a meal, with pre-meal exercise decreasing postprandial glycemia[133] and lipemia[134] in persons without SCI. Little is known about the interaction of feeding and activity in SCI, but studies are underway to examine if peri-meal exercise influences postprandial metabolism in SCI (e.g., NCT03545867 and NCT03691532).

Exercise resulting in skeletal muscle hypertrophy results in multiple benefits to EE. First, hypertrophy of muscles involved in exercise, such as increases in leg muscle mass in response to FES training,[69,105,125,135] results in increased exercise EE throughout training.[99,100] Increased lean mass also has the potential to increase resting and basal EE. A recent trial in SCI showed that testosterone combined with FES resistance training resulted in a 221 to 250 kcal/day increase in basal EE.[105] These findings are encouraging; given reduced resting and basal EE[136] in SCI, even small changes in these variables can induce meaningful relative increase in total daily EE. However, it should be noted that inactive skeletal muscle has a relatively low specific metabolic rate (13 kcal/kg/day) compared to tissues like the heart and kidneys (440 kcal/kg/day), brain (240 kcal/kg/day), and liver (200 kcal/kg/day).[137] Accordingly, small organs with high specific metabolic rates account for ~60% to 70% of resting EE despite having a combined weight of <6% of total body weight,[137-142] with inactive skeletal muscle comprising ~40% to 50% of body weight but accounting for ~20% to 30% of resting EE.[137-140] Therefore, only large increases in muscle mass will be meaningful if the hypertrophied muscles remain sedentary, highlighting the importance of long-term behavior modification and sustainable access to optimal exercise equipment.

Breaking Up Sedentary Time

Despite the known benefits of exercise, the adoption of a physically active lifestyle has remained low among those with SCI.[143] Compared with noninjured individuals and those with other chronic disorders, individuals with SCI have long ranked at the lowest end of the human fitness spectrum.[144,145] Independent of PA, prolonged periods of sedentary behavior, which can be typical for many individuals with SCI, have been shown to decrease lean mass and negatively affect overall metabolic and cardiovascular health of persons without SCI.[146-148] Further, the health protective effects of moderate-to-vigorous PA may not be able to counteract the detrimental effects of prolonged sedentary time[149,150] and may even be negated by long periods of sedentary time.[151] Research in noninjured adults reports that brief interruptions of sedentary time led to significant improvements in metabolic health, regardless of the activity's intensity.[149,150,152] A recent study in adults with chronic paraplegia reported similar findings.[153] This suggests that brief, low-intensity interruptions of sedentary time may be an important clinical intervention for improving metabolic health, especially in a population known to spend large amounts of time being sedentary. However, there are population-specific considerations for breaking up sedentary time in SCI. Current research practices in the general population rely heavily on seated time as a proxy for sedentary time, and wheelchair users are in a constant state of sitting. Unfortunately, alternative definitions of sedentary time among persons with SCI have yet to be developed. Wearable devices used to quantify sedentary time in community-dwelling individuals with SCI show a high proportion (~87%) of the day spent in sedentary time,[154] emphasizing the need for understanding sedentary behavior in this population as well as the potential for interventions targeting sedentary time. An alternative approach could involve setting a minimum cutoff for EE, where a task with an energy cost below this level qualifies as sedentary behavior. However, the low energy cost of most activities of daily living[92,93] draw into question the utility of interrupting sedentary behavior as a means for weight management.

Several studies in adults without SCI quantified the EE of various light-intensity activities performed intermittently during sedentary periods.[155-157] Walking at a self-selected pace for 2 to 5 minutes once per hour was reported to increase total EE

by 60 to 132 kcal over 8 hours.[155,157] Another study reported that simply accumulating 2 to 4 hours of standing time throughout an 8-hour workday can significantly increase EE (up to 57 kcal/day) compared with sitting alone.[156] The low calorie cost of these studies from persons without SCI is promising, as large changes in EE might not be required for small breaks in sedentary time to make an impact on overall health. However, it should be noted that the modest increases in EE in these studies occurred due to walking or standing; persons with SCI will need to find other, likely less costly, activities by which to break up sedentary time. The low requirements of PA and activities of daily living in individuals with SCI[92,93] suggest that unstructured activity in persons with SCI has an even lower potential to meaningfully contribute to a calorie deficit.

The current population-specific activity guidelines,[3,60] which encourage moderate-to-vigorous PA, should be promoted as a means for improving physical capacity. However, modifications may be necessary for managing obesity. In persons with SCI, unstructured PA appears to have low utility in increasing EE due to the low calorie cost of most PA tasks,[92,93] but future research should investigate the independent effect of sedentary behavior to determine an inclusive representation of the requirements for inducing clinically relevant improvements in metabolic health and, specifically, obesity.

Conclusion

Identification of accessible and affordable treatments for obesity are warranted, as obesity is the most common CMD risk factor in SCI,[3] and secondary health complications have a negative impact on quality of life in this population.[158-160] Exercise is a primary treatment strategy for CMD in SCI,[3] but there are important considerations for tailoring exercise to manage obesity in SCI. Exercise for obesity management should primarily aim to induce a negative energy balance and secondarily increase the use of fat as a fuel source. Unfortunately, in SCI reduced muscle mass and oxidative capacity result in a limited ability for activity to induce a negative energy balance, with calories expended primarily from carbohydrates. These constraints must be considered when designing activity for obesity management in SCI, especially in higher level injuries, but certain forms of exercise have a greater therapeutic potential in this population. We suggest that exercise for obesity in SCI should target large muscle groups and aim to induce hypertrophy to increase total EE in response to training. Furthermore, exercise that maximizes the use of glycogen might induce meaningful postexercise shifts in the use of fat as a fuel. Future research should aim to determine the importance of breaking up sedentary time in SCI. However, the low energy cost of PA in this population likely limits the range of useful activity strategies for obesity management and calls into importance combinatorial approaches that achieve calorie deficit via modifications of multiple different behaviors.

Conflicts of Interest

The authors report no conflicts of interest.

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