The interaction of macronutrients and body composition among individuals with chronic spinal cord injury

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ABSTRACT

Background: Changes in body composition and dietary intake occur following spinal cord injury (SCI). The Geometric Framework for Nutrition (GFN) is a tool that allows the examination of the complex relationships between multiple nutrition factors and health parameters within a single model. This study aimed to utilize the GFN to examine the associations between self-reported macronutrient intakes and body composition in persons with chronic SCI.

Methods: Forty-eight individuals with chronic SCI were recruited. Participants completed and returned 3- or 5-day self-reported dietary recall sheets. The mean macronutrient masses (g) for fats, proteins, and carbohydrates were analyzed. Circumferential anthropometric measures, dual-energy x-ray absorptiometry (DXA), and magnetic resonance imaging (MRI) were used to assess body composition.

Results: Associations between all the circumferential anthropometric measures and carbohydrates were observed (p ≤ 0.01). Among the MRI measures, only significant associations between subcutaneous adipose tissue and protein*carbohydrate (p = 0.0402) as well as carbohydrates (p = 0.0046) were identified. Carbohydrates were negatively associated with total percent fat mass (%total FM; p = 0.0017), total fat mass (Total FM [g]; p = 0.0042), trunk percent fat mass (%trunk FM; p = 0.0095), trunk fat mass (Trunk FM [g]; (p = 0.0086), lower extremity percent fat mass (%LE FM; p = 0.0121), and lower extremity fat mass (LE FM [g]; p = 0.0211).

Conclusions: Carbohydrates appear to play an important role in body composition among individuals with SCI. Higher carbohydrate intake was associated with lower fat mass. Additional research is needed to determine how carbohydrate intake influences body composition and cardiometabolic health after SCI.

CLINICAL TRIAL REGISTRATION
Registered with clinicaltrials.gov: NCT01652040 and NCT02660073.

KEYWORDS: Spinal cord injury; Geometric framework for nutrition; Carbohydrates; Macronutrients; Nutrition; Body composition.
ABBREVIATIONS

SCI: spinal cord injury; NMES-RT: neuromuscular electrical stimulation evoked resistance training; LOI: level of injury; MRI: magnetic resonance imaging; DXA: dual-energy x-ray absorptiometry; AIS: American Spinal Injury Association Impairment Scale; Sup-WC: supine waist circumference; Sup-AC: supine abdominal circumference; Sup-HC: supine hip circumference; Sit-WC: seated waist circumference; Sit-HC: seated hip circumference; SAT: skin adipose tissue; VAT: visceral adipose tissue; VAT:SAT: ratio of VAT to SAT; Total LM: total body lean mass; Total FM: total body fat mass; %total FM: total body percent fat mass; Trunk LM: trunk lean mass; Trunk FM: trunk fat mass; %trunk FM: trunk percent fat mass; LE LM: lower extremity lean mass; LE FM: lower extremity fat mass; %LE FM: lower extremity percent fat mass; GFN: geometric framework for nutrition; NDSR: Nutrition Data System for Research.
1. INTRODUCTION

Stark changes in body composition and dietary behaviors occur following spinal cord injury (SCI); furthermore, these adaptations directly influence one another [1, 5, 58]. Following SCI, adiposity throughout the body increases while lean mass (LM) below the level of injury (LOI) decreases, resulting in neurogenic obesity [1, 58]. The loss in LM along with decreases in activity levels and impaired sympathetic nervous system activity results in a lowering of basal metabolic rates (BMR) and daily energy needs following SCI [2,3]. Nutrition reporting among those with SCI reveals total caloric intakes lower than able-bodied individuals [3,4, 5], in addition to lower measured BMR and calculated total energy expenditure [5–7]. Despite these factors, obesity is still more prevalent among persons with chronic SCI compared to able-bodied persons [8–12]. Persons with chronic SCI also have an increased risk for obesity-related cardiometabolic diseases [13], including dyslipidemia [14–16], glucose intolerance and diabetes mellitus [15,17–23], central obesity [24–27], systemic inflammation, [19,28–31] and mitochondrial dysfunction [32,33].

To mitigate these adverse effects it is recommended that those with SCI not only engage in physical activity but also modify their dietary habits [34,35]. Higher dietary fat intake is reported after SCI [36,37] and is associated with increased adiposity [6]. However, the precise role of macronutrient intake on body composition after SCI is not fully understood, which is partly due to traditional approaches which investigate the effect of one variable at a time (e.g., effects of one macronutrient on one metabolic or body composition outcome). Previous research has shown that macronutrient intake is associated with visceral and subcutaneous adiposity as well as fasting insulin levels in men with motor complete SCI [38]. Furthermore, the percentage of fat intake has been shown to account for 29-34% of whole and regional body fat mass, while the percentage of carbohydrate intake was positively related to whole-body LM and negatively associated with fat mass in men with chronic SCI [6]. However, these reports have relied on traditional statistical techniques to examine these associations.

The Geometric Framework for Nutrition (GFN) has emerged as a tool to better understand the complex relationships between nutrition and health [39,40]. As opposed to more reductionist methods, the GFN allows the examination of complex interactions among multiple nutrients and health outcomes [39]. The GFN enables researchers to examine broad multidimensional interactions between variables of interest across multiple domains.
Subsequently, the dynamic relationships between nutrition and health outcomes can be mapped on n-dimensional nutrient state-spaces, where n is the number of nutritional parameters [39–41]. Therefore, this powerful tool allows the consequences of ingesting combinations of nutrients to be represented graphically, which provides a visual representation of how nutrient intakes are related to markers of health. While this tool has been used to examine the influence of nutrition on several health-related outcomes among multiple non-human organisms [42], including aging [43] and liver disease [44], only a few human studies have utilized the GFN to examine the relationships between nutrition and health outcomes [40,42,45–47]. Therefore, the purpose of the current work was to use the GFN to examine the associations between self-reported macronutrient intakes and body composition in persons with chronic SCI. Body composition assessment was conducted using three different levels of measurement, including circumferential anthropometrics, dual energy x-ray absorptiometry (DXA), and magnetic resonance imaging (MRI).

2. MATERIALS AND METHODS
2.1 Participants

Individuals were recruited to participate in two different clinical trials (registered with clinicaltrials.gov: NCT01652040 and NCT02660073) broadly aimed at exploring the effects of lower extremity neuromuscular electrical stimulation evoked resistance training (NMES-RT) following chronic (≥ 1-year post-injury) traumatic and non-traumatic SCI (level of injury [LOI] ranged between C5-L2). Importantly, the current study consisted of a retrospective analysis of baseline data from each study. All procedures were in accordance with the ethical standards of the Helsinki Declaration of 1964 and its later amendments. The McGuire Veteran Affairs Investigation Research Board and the Virginia Commonwealth University (VCU) Office of Research and Innovation approved the current study. For Study 1 (NCT01652040, n=16), men between 18 and 50 years of age with motor complete SCI (American Spinal Injury Association Impairment Scale [AIS]-A: complete motor and sensory loss below the LOI; or AIS-B: complete motor loss and incomplete sensory loss below the LOI) were recruited. For study 2, men and women aged between 18 and 65 years with motor complete or incomplete SCI (AIS-A; AIS-B; or AIS-C: incomplete motor and sensory loss with less than half of the muscles tested below the LOI graded ≥ 3) were recruited (NCT02660073, n=32). Those presenting with cardiovascular
disease, uncontrolled type 2 diabetes (or requiring insulin), hematocrit > 50%, or symptoms of a urinary tract infection were excluded from participating in either study. Additional exclusion criteria for Study 1 included individuals with pressures sores ≥ stage 2 and serum testosterone levels > 34.7 nmol·L⁻¹. Similarly, pregnant women, those with pressure sores ≥ stage 3, or osteoporosis as determined using dual-energy X-ray absorptiometry (DXA; T-scores ≤ -2.5) were also excluded from Study 2. All potential participants received a physical exam from an SCI certified physician to ensure eligibility. Interested and qualified individuals provided informed written consent approved by the Hunter Holmes McGuire Veterans Affairs Medical Center IRB.

2.2 Dietary Recall

Throughout Study 1 and Study 2, participants completed and returned 5- or 3-day dietary recall logs, respectively, which included at least one weekend day [6]. Our lab has previously shown no difference between caloric intake and percentages of macronutrients from 3- or 5-day recalls [6]. Participants and their caregivers (as available) were educated on properly completing the recall form; capturing the amount and type of foods consumed during the weekdays for every meal and snack. Once returned to the lab, each participant’s data was entered into dietary tracking and analysis software (Nutrition Data System for Research [NDSR], versions 2012-2018; University of Minnesota, USA). The first week of self-reported dietary data (either 3 or 5-days of recalls) was averaged for each individual. The mean macronutrient masses (g) for fats, proteins, and carbohydrates were used for analysis. Due to the relatively small sample size, we limited our model to examine macronutrients as opposed to more detailed foods groups (e.g., simple vs. complex carbohydrates and saturated vs. unsaturated fat).

2.3 Circumferential Anthropometric Measures

Several circumferential anthropometric measures were captured while participants were seated in their wheelchairs and lying supine on the DXA scanner as previously described [31]. Briefly, these measures were collected at baseline prior to any intervention by an experienced technician. Waist circumferential measures were taken from the narrowest point between the lowest ribs and the iliac crests in both the seated (Sit-WC) and supine positions (Sup-WC). Abdominal circumferential measures were captured at the level of the umbilicus, also while
participants were seated (Sit-AC) and lying supine (Sup-AC). Finally, supine hip circumferential measures (Sup-HC) were acquired from the widest part of the buttocks (often traversing the greater trochanters). At least three separate measurements within 0.5 cm of each other were captured for each circumferential anthropometric measure. The average of these three measures was used for analysis.

2.4 Magnetic Resonance Imaging (MRI) Measures

MRI was performed before any intervention at baseline for participants in both studies (1.5T; General Electric Signa, Milwaukee, WI, USA). Twenty-five – 33 transverse images (slice thickness: 0.8 cm; and interslice spacing: 1.2 cm) were captured between each individual’s xiphoid process and their femoral heads using an abdominal coil (fast spin-echo sequence: axial in-phase/out-phase; repetition time: 140 ms; echo time: 4.3 ms in-phase, 2 ms out-phase; field-of-view: 42 cm; matrix size: 256 × 256; number of excitations: 1; and acquisition time: 2 mins) [27,31].

Images were first processed using ImageJ (version 1.52a; National Institutes of Health, Bethesda, MD, USA) to identify an abdominal area of interest for each participant. Anatomical consistency of the abdominal region was maintained among the participants by only including images between the upper poles of the kidneys and the femoral heads. Win Vessel (version 2; Ronald Meyer, Michigan State University, MI, USA) was then used for additional image processing and analysis as previously described [60]. Based on pixel signal intensity, tissue segmentation (adipose, skeletal muscle, and bone) for each image within the abdominal region was achieved. Next, manual tracing of the adipose tissue between the skin and the abdominal muscles (subcutaneous adipose tissue; SAT), and the adipose within the abdominal walls and surrounding the viscera (visceral adipose tissue; VAT) were identified during segmentation. Once traced, the cross-sectional area (CSA; cm²) for both the VAT and SAT was measured, and the ratio between them (VAT:SAT) was calculated.

2.5 Dual X-ray absorptiometry (DXA) Measures

Full-body DXA scans were conducted at baseline for both studies (GE Healthcare Lunar Prodigy, WI, USA) as previously reported [50]. Briefly, each participant was placed in a supine position with the lower extremities strapped together above the knee joint in a neutral position.
The upper extremities were stabilized close to the body in neutral, and the pelvis/trunk was aligned in a neutral position as well. Lean body mass (kg), fat mass (kg), and the percent body fat mass (%) were assessed for the total body (respectively: Total LM, Total FM, %total FM) along with specific regions of interest: the trunk (respectively: Trunk LM, Trunk FM, %trunk FM) and the combined lower extremities (respectively: LE LM, LE FM, %LE FM). Each image was analyzed using GE Healthcare encore (version 16, Madison, WI, USA). These regions of interest were first automatically identified and then manually adjusted to improve reliability [50].

In the current study, we used a combination of anthropometric measurements (circumferences), DXA, and MRI to capture a complete picture of body composition. Circumferences offer a practical clinical tool to assess fat mass and are strongly correlated with cardiometabolic markers in chronic SCI [31]. In addition, DXA is a surrogate gold standard tool to evaluate whole body composition and fat-free mass, while MRI represents the gold standard to assess regional adiposity [31,51]. Therefore, the combination of these measurements allowed for a more complete examination of body composition.

### 2.6 Statistical Analysis

A cross-sectional analysis utilizing the GFN approach was employed. Not all macronutrient intakes were normally distributed. General additive models using thin-plate smoothing spines were used to form response surfaces for each anthropometric, MRI, and DXA measure over the self-reported macronutrient intake spaces [52,53]. These models were built using single factors (proteins; carbohydrates; fats) and 2-factor interactions (protein*carbohydrate; protein*fat; carbohydrate*fat) in the R mgcv package (version 1.8-31). Graphical representations of these models were then generated as previously described [43,44,54]. Briefly, two-dimensional response surfaces representing the three-dimensional nutrient state-spaces of each outcome measure were developed in triplicate, providing multiple perspectives for each relationship. In addition to these plots, Pearson correlations were conducted to examine bivariate associations between macronutrient intakes. Our sample size was selected to provide sufficient power (0.80) for the primary aim, examining the relationships between macronutrient intake and measures of body composition. Due to the exploratory nature of the study, no adjustments for covariates were performed to ensure sufficient statistical power. All GFN analyses and images were produced using RStudio (version 1.3.959; R: version 4.0.0, The
Accepted manuscript

R Foundation for Statistical Computing). Regression analyses and bivariate statistics were performed using SPSS (SPSS statistics version 24, IBM corp. Armonk, USA). An α of 0.05 was chosen for all analyses.

3. RESULTS

3.1 Participants

A total of 54 individuals participated in both studies; however, six persons who contributed to Study 1 later engaged in Study 2. For those participating in both studies, their data collected during Study 2 was excluded from analysis. Demographic and injury information for the remaining 48 participants is provided in Table 1. All participants completed baseline testing for Study 1 and Study 2 without experiencing any adverse events.

3.2 Dietary Recall Results

All participants in Study 2 provided self-reported dietary recall information for each of the 3 requested days, while 3 participants in Study 1 only reported dietary information for 4 out of the 5 requested days. However, the data for these individuals in Study 1 were still included in analysis, and no special steps were taken to address this negligible data loss [6].

A wide variety of dietary patterns were observed. A mean of 1615±704 kcals (mean±SD; range: 329 – 4354 kcals) per day was reported. On average these calories were derived from 18.6±5.3% (range: 9.8% – 40.5%) protein, 43.8±8.4% (range: 27.6 – 68.9%) carbohydrates, and 36.6±6.4% (range: 21.2 – 49.4%) fat. This amounted to a reported average of 69.3±28.2 g (range: 11.6 – 156.9 g) of protein, 180.8±83.4 g (range: 29.8 – 449.2 g) of carbohydrates, and 67.8±34.6 g (range: 18.4 – 222.2 g) of fat being consumed by the participants daily. A Pearson correlation matrix (n=46) revealed a significant inverse association between the percentage of carbohydrates and fat consumed (r= -0.753, p<0.01).

3.3 Circumferential Anthropometric Results

The Supine-WC for 1 participant was not measured as they presented with scoliosis, which interfered with accurate measurement. Mean anthropometric results are shown in Table 2. The general additive models revealed significant associations between carbohydrates and
circumferential anthropometric measures (Sit-WC, Sit-AC, Sup-WC, Sup-HC, and Sup-AC; see Table 3 and Figures 1 and 2).

3.4 MRI Results

MRI was not conducted for 4 participants due to procedure contraindications. Mean results for the MRI measures are also presented in Table 2. Significant associations between SAT and protein*carbohydrate as well as carbohydrates were identified; however, no significant associations were observed for VAT or VAT:SAT ratio (see Table 3 and Figure 3).

3.5 DXA Results

All participants completed DXA scans. Table 2 presents the mean DXA variables observed among the participants. Only measures of LM were not found to be significantly associated with any macronutrient combination. Carbohydrates were significantly associated with %total FM, Total FM, %trunk FM, Trunk FM, %LE FM, LE FM (see Table 3 and Figure 3). Additionally, significant interactions between carbohydrate*fat for LE-FM and between protein*carbohydrate for %LE FM and LE FM (see Table 3 and Figure 4). Additionally, linear regressions were performed to further explore the relationships between carbohydrate intake and measures of fat mass after controlling for total caloric intake (see Table 4). Accounting for total caloric intake did not influence the relationship between carbohydrate intake and measures of fat mass.

4. DISCUSSION

4.1 Major Findings

Overall, the results demonstrate an inverse association between the amount of carbohydrates individuals with SCI consume and measures of their body fat. This pattern was consistently demonstrated despite employing different tools used to assess body composition among those with SCI, which included circumferential anthropometric measurements, MRI, and DXA. Specifically, carbohydrate intake was negatively associated with all anthropometric measures, SAT as measured by MRI, and all DXA measures of fat mass. These results suggest that higher carbohydrate intake was associated with lower measures of FM. There were also notable interactions for protein*carbohydrates for SAT and DXA measures of LE FM, as well as an interaction for carbohydrates*fat for LE FM; however, these interactions may be driven by
carbohydrate intake. Furthermore, lean body mass, VAT, and VAT:SAT ratio were unrelated to these dietary macronutrients in the current study.

4.2 Macronutrient intake following SCI

Two-thirds of persons with SCI are likely to be obese and are at risk for metabolic complications related to obesity [7,12,20,55,56]. Dietary factors strongly influence the prevention and management of these risk factors [57–60]. However, only a few studies have investigated individuals' dietary intakes with chronic SCI [6,36,57–61], and little is known regarding how specific macronutrients impact body composition and cardiometabolic health after SCI. The recommended macronutrient distribution range for able-bodied adults consists of caloric intake from protein (10-35%), fat (20-35%), and carbohydrate (45-65%) [36]. Previous research has found evidence of dietary inadequacy in adults with chronic SCI [5,36,62]. Total caloric intake is often below recommended levels [6,36], with low fiber intake [57,63,64] and deficiencies in certain vitamins and minerals [57,63,64], but with high carbohydrate and fat intake [36]. In the current study, calories were derived from 18.6±5.3% (range: 9.8% – 40.5%) protein, 36.6±6.4% (range: 21.2 – 49.4%) fat, and 43.8±8.4% (range: 27.6 – 68.9%) carbohydrates. These results suggest the average fat intake was high in the current study relative to recommendations for able-bodied adults, similar to previous findings from our laboratory [5]. Previous literature showed that persons with chronic SCI consume fat that approaches or exceeds USDA recommendations [36,37,57,63,65–67], as do the amounts of carbohydrates consumed [5,66]. Specifically, an excess intake of simple carbohydrates [63] and saturated fat [36] but low fruit and vegetables [57,65] has been reported.

4.3 Carbohydrate intake following SCI

It has been proposed that excess carbohydrates may be stored as fat in visceral, subcutaneous, intermuscular, and intramuscular locations [61], which could contribute to obesity and disorders of carbohydrate metabolism [2,7,68]. In contrast, previous research showed that the percentage of carbohydrate intake was negatively related to the percentage of whole-body FM, leg FM, and trunk FM but positively related to the percentage of whole-body LM, trunk LM, and BMR adjusted to body weight in persons with SCI [5]. For all circumferential measures, lower carbohydrate intake was associated with increased FM (as denoted by the red
regions of Figures 1 & 2). Specifically, carbohydrate intake below 150 grams per day was associated with the largest abdominal, waist, and hip circumferences. This pattern was also seen for DXA measures of FM, with carbohydrate intake below 150 grams per day being associated with the largest amounts of LE FM, trunk FM, and total body FM (as denoted by the red regions of Figure 4). This pattern was also true for SAT, with carbohydrate intake below 150 grams per day being associated with the largest SAT CSA (as denoted by the red regions of Figure 3). While there were no significant associations between macronutrient intake and VAT, this threshold of carb intake was not seen with VAT. The lack of significant association with VAT may be due to the level of physical activity rather than dietary intake - previous research shows a negative association between the physical activity levels and visceral adiposity in persons with SCI [69]. These results may also support previous research showing a protective role of SAT on metabolic profile [70,71].

4.4 Fat intake following SCI

Although fat intake was not significantly associated with measures of FM in the current study, previous work has suggested that the percentage of dietary fat was negatively related to the percentage of whole-body LM, trunk LM, and BMR adjusted to body weight [6]. Persons with SCI are likely to consume a high fat diet, which is a predisposing lifestyle factor for dyslipidemia, central adiposity, and insulin resistance [6,36,72,73]. Previous work has found that persons with paraplegia and tetraplegia consume 81.4g and 82.7g of fat per day, respectively, while the recommended daily intake for able-bodied individuals is 40-70g/d [36]. Additionally, dietary fat intake has been found to explain 29 to 34% of whole-body and regional FM in chronic SCI [6]. The lack of a significant association between fat intake and body composition in the current study could be due to many factors, including the level of physical activity, which was not accounted for in this exploratory study. Interestingly, while fat intake was not significantly associated with measures of body composition in the current study, there was a significant inverse bivariate association between the percentage of carbohydrates and fat consumed. This suggests that individuals who consumed higher amounts of carbohydrates also consumed lower fat, which may indicate that lower fat intake is partially responsible for the favorable body composition seen with higher carbohydrate intake.
4.5 Interactions among macronutrient intake and body composition following SCI

While neither fat nor protein consumption alone or in combination were significantly related to any measures, carbohydrate*fat and protein*carbohydrate interactions were significantly related to LE FM. Indeed, significant relationships were found only when carbohydrate intake was considered. Therefore, dietary carbohydrate intake appears to be driving these interactions. In this preliminary report, dietary fat and protein alone do not significantly impact body composition, but rather their influence depends on dietary carbohydrates. This is potentially related to the changes in fat and carbohydrate metabolism following SCI. Persons with SCI have a reduced ability to use stored fat as a substrate even during exercise due to the dysfunction of the autonomic nervous system and thus rely on carbohydrate utilization [74]. Moreover, increased carbohydrate utilization and decreased fat utilization across a range of exercise intensities during arm cycling have been demonstrated in men with paraplegia [75]. Additionally, as previously stated, traditional approaches have examined the associations of one dietary factor at a time as opposed to examining the complex interactions among many nutritional factors, which may lend credence to these novel findings using the GFN. Therefore, future research should further investigate macronutrient intake on health outcomes following SCI using the GFN to validate these findings.

As previously mentioned, we used a combination of anthropometric measurements (circumferences), DXA, and MRI in the current study to capture a complete picture of body composition. Central adiposity characterized by increasing waist circumference, VAT CSA or VAT:SAT ratio is tightly associated with cardiometabolic disorders after SCI. Both seated and supine waist and abdominal circumferences are strongly related to VAT and VAT:SAT ratio as measured by the gold standard MRI. Furthermore, our lab has previously established SCI-specific anthropometric and VAT thresholds associated with impaired cardiometabolic health [31]. The MRI VAT CSA cutoff was identified as 100cm$^2$. The cutoffs for anthropometric measurements were 86.5cm and 88.3cm for supine waist and abdominal, respectively, and 89.1cm and 101cm for seated waist and abdominal, respectively. The current sample, on average, were below the cutoffs for VAT CSA (81.5±65.1cm$^2$), supine waist (82.9±12.9cm) and abdominal circumference (83.3±14.0cm), as well as seated waist (88.1±11.7cm) and abdominal circumferences (95.1±15.3cm). Therefore, this sample represents a relatively lean group of individuals with SCI. As expected, our sample had higher fat mass and less lean mass as
compared to the general able-bodied population [8,9,25,76]. Additionally, anthropometric measurements are a clinical surrogate measure to estimate VAT accumulation in persons with SCI, DXA represents a surrogate gold standard to assess whole-body fat mass and fat-free mass, and MRI breaks down these compartments further into regional muscle and fat mass [31,51]. Therefore, the combination of these techniques allowed the examination of practical clinical tools (circumferences), as well as validated measures of regional adiposity and fat free mass (MRI and DXA, respectively).

4.6 Limitations

It should be noted that this study does not identify any type of causal relationship between dietary choices among those with SCI and body composition. The associations observed also do not clearly indicate how those with SCI might leverage one or more macronutrient(s) over another to influence body composition. One notable limitation of this work is that these conclusions rely entirely on the self-reported dietary data of our participants. In addition, this data set includes few females, and the exclusion criteria of both studies preclude the participation of those with commonly comorbid conditions. Such factors limit sub-group analyses using GFN methodologies and the scope of this report’s findings. Additionally, the sample in the current study represents a younger and leaner group of individuals living with SCI. The sample’s average age was 38±12 years, average BMI was 23.6±4.6, and the average waist circumference was 82.9±12.9 cm. On average, the sample was well below the aforementioned cutoffs for individuals with SCI, suggesting that their body fat is lower than is observed among older individuals with SCI. Also not accounted for in our report was the fact that few of our participants reported alcohol consumption which is ignored in our analysis as the NDSR software treats alcohol independently. This may be relevant due to the reported high alcohol consumption in SCI and its association with increased adiposity, especially central adiposity [77–82]. While seemingly a small sample for this type of analysis, it is a relatively large sample when considering this specific population [83]. However, this relatively large sample did not allow for a sufficient sample size to control for covariates such as LOI or time since injury.

Therefore, the results of this study should be viewed as exploratory results that can inform future work in larger trials. Moreover, physical activity levels were not measured in the current study. Because physical activity is a determining factor of body composition, this should be considered...
a major limitation of the current study. Lastly, distinct types of macronutrients were not investigated in the current study (e.g., saturated vs. unsaturated fat and simple vs. complex carbohydrates). Due to the aforementioned limitations, caution should be used when interpreting these findings. Future work should further examine the relationships between physical activity levels, body composition, and macronutrient and micronutrient intake in persons with chronic SCI.

4.7 Conclusions

Carbohydrates appear to play an important role in body composition among individuals with SCI, and lower carbohydrate intake seems to be associated with higher fat mass. This may be related to the changes in fat and carbohydrate metabolism as well as the reported increase in fat consumption that occurs following SCI. Traditional approaches have examined the associations of one dietary factor at a time as opposed to examining the complex interactions among many nutritional factors. Using the GFN, we examined associations between several dietary factors and multiple measures of body composition. Regardless of the body composition measure used, carbohydrates were consistently inversely related to measures of body fatness. Therefore, these results using the GFN lay the foundation to more holistically address dietary behaviors and body composition changes among individuals with chronic SCI. Because carbohydrate intake appears so influential in this population, additional research is needed to determine how carbohydrate type and physical activity influence body composition and cardiometabolic health after SCI.

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STATEMENT OF AUTHORSHIP

Jacob A. Goldsmith: Helped write the original draft, reviewed scientific evidence and scientific writing, summarized research findings, helped with writing and editing, developed figures, and organized and approved the final version.
Matthew E. Holman: Helped writing the original draft, assisted with the development of the research hypothesis, helped with data curation, provided formal analysis, provided critical feedback, developed figures, reviewed scientific evidence, helped edit and approve the final version.

Puneet Puri: Provided critical feedback, helped edit, and approved the final version.

Refka E. Khalil: Provided critical feedback and data curation, helped with editing and approved the final version.

Areej N. Ennasr: Provided critical feedback, helped edit, and approved the final version.

Ashraf S. Gorgey: Provided funding acquisition, developed the research hypothesis, submitted the initial proposal, reviewed scientific evidence, helped with writing and editing, and approved the final version.

CONFLICT OF INTEREST

The authors have no conflicts to report.

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DATA AVAILABILITY

Anonymized individual data will be available immediately after study publication upon request from those who wish to access the data. If anonymized data is provided, it should be done after proposals to Ashraf.Gorgey@va.gov. Raw data (including personal information and participant codes) will be stored in a locked cabinet at the McGuire VA Research Institute for this time period.
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https://doi.org/10.1038/sc.2008.134.


Figure 1. Supine anthropometric measures. Two-dimensional representations of each GFN response surface within macronutrient intake state-spaces are provided. The median value of the third factor (identified with parentheses on each x-axis) limits each response surface. Red regions represent increased anthropometric circumferences and blue regions represent reduced anthropometric circumferences. 1A and 1B represent supine abdominal circumference (cm); 1C and 1D represent supine waist circumference (cm); 1E and 1F represent supine hip circumference (cm). In all examples, lower carbohydrate intake is associated with increased circumferences. Nutrient intake is quantified in grams. Kcal quantities can be calculated using conversion factors: 9 kcals per gram (fat) and 4 kcals per gram (protein and carbohydrates).
Figure 2. Seated anthropometric measures. Two-dimensional representations of each GFN response surface within macronutrient intake state-spaces are provided. The median value of the third factor (identified with parentheses on each x-axis) limits each response surface. Red regions represent increased anthropometric circumferences and blue regions represent reduced anthropometric circumferences. 2A and 2B represent seated waist circumference (cm); 2C and 2D represent seated abdominal circumference (cm). In all examples, lower carbohydrate intake is associated with increased circumferences.
Figure 3. Magnetic resonance imaging (MRI) measures of fat mass. Two-dimensional representations of each GFN response surface within macronutrient intake state-spaces are provided. The median value of the third factor (identified with parentheses on each x-axis) limits each response surface. Red regions represent increased fat mass and blue regions represent reduced fat mass. 3A, 3B, and 3C represent subcutaneous adipose tissue area (cm$^2$); 3D, 3E, and 3F represent visceral adipose tissue area (cm$^2$). In all examples, lower carbohydrate intake is associated with increased fat mass.
Figure 4. Dual-energy x-ray absorptiometry (DXA) measures of fat mass. Two-dimensional representations of each GFN response surface within macronutrient intake state-spaces are provided. The median value of the third factor (identified with parentheses on each x-axis) limits each response surface. Red regions represent increased fat mass and blue regions represent reduced fat mass. 4A and 4B represent lower extremity fat mass (kg); 4C and 4D represent trunk fat mass (kg); 4E and 4F represent total fat mass (kg). In all examples, lower carbohydrate intake is associated with increased fat mass.
Table 1. Baseline demographics and spinal cord injury characteristics for 48 participants

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<tr>
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<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity</td>
<td>White:</td>
<td>African American:</td>
</tr>
<tr>
<td></td>
<td>n = 16</td>
<td>n = 29</td>
</tr>
<tr>
<td></td>
<td>African American:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 19</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male:</td>
<td>Female:</td>
</tr>
<tr>
<td></td>
<td>n = 42</td>
<td>n = 6</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>38 ± 12</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72.6 ± 14.1</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>176.2 ± 7.9</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.6 ± 4.6</td>
<td></td>
</tr>
<tr>
<td>Level of Injury (range)</td>
<td>C5 – L1</td>
<td></td>
</tr>
<tr>
<td>Time Since Injury (yr)</td>
<td>10 ± 10</td>
<td></td>
</tr>
<tr>
<td>AIS (score)</td>
<td>A: n = 30</td>
<td>B: n = 13</td>
</tr>
<tr>
<td>SCI Classification</td>
<td>Paraplegia: n = 19</td>
<td>Tetraplegia: n = 29</td>
</tr>
</tbody>
</table>

**BMI**: body mass index; **AIS**: American Spinal Injury Association Impairment Scale; **AIS-A**: complete motor and sensory loss below the level of injury; **AIS-B**: complete motor loss and incomplete sensory loss below the level of injury; **AIS-C**: incomplete motor and sensory loss with less than half of the muscles tested below the LOI graded ≥ 3. Mean ± SD unless otherwise noted.
Table 2. Mean anthropometric, MRI, and DXA measures

<table>
<thead>
<tr>
<th>Anthropometric Measures</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sit-WC (cm)</td>
<td>88.1 ± 11.7</td>
</tr>
<tr>
<td>Sit-AC (cm)</td>
<td>95.1 ± 15.3</td>
</tr>
<tr>
<td>Sup-WC (cm)*</td>
<td>82.9 ± 12.9</td>
</tr>
<tr>
<td>Sup-HC (cm)</td>
<td>95.7 ± 10.1</td>
</tr>
<tr>
<td>Sup-AC (cm)</td>
<td>83.3 ± 14.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MRI Measures</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>SAT (cm(^2))*</td>
<td>148.5 ± 95.0</td>
</tr>
<tr>
<td>VAT (cm(^2))*</td>
<td>81.5 ± 65.1</td>
</tr>
<tr>
<td>VAT:SAT*</td>
<td>0.67 ± 0.46</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DXA Measures</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total-FM (%)</td>
<td>30.6 ± 10.9</td>
</tr>
<tr>
<td>Total-FM (Kg)</td>
<td>23.1 ± 10.8</td>
</tr>
<tr>
<td>Total-LM (Kg)</td>
<td>46.6 ± 7.6</td>
</tr>
<tr>
<td>Trunk-FM (%)</td>
<td>31.9 ± 13.7</td>
</tr>
<tr>
<td>Trunk-FM (Kg)</td>
<td>12.7 ± 6.9</td>
</tr>
<tr>
<td>Trunk-LM (Kg)</td>
<td>22.5 ± 3.5</td>
</tr>
<tr>
<td>LE-FM (%)</td>
<td>32.4 ± 10.6</td>
</tr>
<tr>
<td>LE-FM (Kg)</td>
<td>7.2 ± 3.5</td>
</tr>
<tr>
<td>LE-LM (Kg)</td>
<td>13.5 ± 3.0</td>
</tr>
</tbody>
</table>

*n = 47; **n = 44; DXA, dual-energy X-ray absorptiometry; MRI, magnetic resonance imaging; SAT, Sit-WC, seated waist circumference; Sit-AC, seated abdominal circumference; Sup-WC, supine waist circumference; Sup-HC, supine hip circumference; Sup-AC, supine abdominal circumference; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue; Total-FM, total body fat mass percentage; Total-FM, total body fat mass; Total-LM, total body lean mass; Trunk-FM, trunk fat mass percentage; Trunk FM, trunk fat mass; Trunk-LM, trunk lean mass; LE-FM, lower extremity fat mass percentage; LE-FM, lower extremity fat mass; LE-LM, lower extremity lean mass; Kg, kilograms.
Table 3. General additive model p-values for measures of body composition among the macronutrient intake state-space

<table>
<thead>
<tr>
<th>Macronutrients</th>
<th>Protein</th>
<th>Carb</th>
<th>Fat</th>
<th>Protein*Carb</th>
<th>Protein*Fat</th>
<th>Carb*Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anthro</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sit-WC</td>
<td>0.3991</td>
<td><strong>0.0007</strong></td>
<td>0.9806</td>
<td>0.7210</td>
<td>0.8629</td>
<td>0.8139</td>
</tr>
<tr>
<td>Sit-AC</td>
<td>0.3662</td>
<td><strong>0.0100</strong></td>
<td>1.0000</td>
<td>0.7596</td>
<td>0.4227</td>
<td>0.8411</td>
</tr>
<tr>
<td>Sup-WC</td>
<td>0.8395</td>
<td><strong>0.0003</strong></td>
<td>1.0000</td>
<td>0.3281</td>
<td>0.8418</td>
<td>0.4025</td>
</tr>
<tr>
<td>Sup-HC</td>
<td>0.7865</td>
<td><strong>0.0019</strong></td>
<td>0.9356</td>
<td>0.1478</td>
<td>0.9091</td>
<td>0.0801</td>
</tr>
<tr>
<td>Sup-AC</td>
<td>0.6251</td>
<td><strong>0.0039</strong></td>
<td>0.9980</td>
<td>0.5184</td>
<td>0.8397</td>
<td>0.5266</td>
</tr>
<tr>
<td><strong>MRI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAT</td>
<td>1.0000</td>
<td><strong>0.0046</strong></td>
<td>0.9994</td>
<td><strong>0.0402</strong></td>
<td>0.9965</td>
<td>0.1231</td>
</tr>
<tr>
<td>VAT</td>
<td>0.0609</td>
<td>0.5405</td>
<td>0.6956</td>
<td>0.6156</td>
<td>0.1636</td>
<td>0.6557</td>
</tr>
<tr>
<td>VAT:SAT</td>
<td>0.1579</td>
<td>0.5666</td>
<td>0.7819</td>
<td>0.5922</td>
<td>0.3007</td>
<td>0.6102</td>
</tr>
<tr>
<td><strong>DXA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total-F</td>
<td>0.7037</td>
<td><strong>0.0017</strong></td>
<td>0.9985</td>
<td>0.1441</td>
<td>0.7369</td>
<td>0.2794</td>
</tr>
<tr>
<td>Total-FM</td>
<td>0.9233</td>
<td><strong>0.0042</strong></td>
<td>1.0000</td>
<td>0.1683</td>
<td>0.7994</td>
<td>0.2365</td>
</tr>
<tr>
<td>Total-LM</td>
<td>0.3564</td>
<td>0.4249</td>
<td>0.3702</td>
<td>0.4426</td>
<td>0.3849</td>
<td>0.4182</td>
</tr>
<tr>
<td>Trunk-F</td>
<td>0.4295</td>
<td><strong>0.0095</strong></td>
<td>0.9998</td>
<td>0.5786</td>
<td>0.9665</td>
<td>0.6495</td>
</tr>
<tr>
<td>Trunk-FM</td>
<td>0.5450</td>
<td><strong>0.0086</strong></td>
<td>0.9887</td>
<td>0.6804</td>
<td>0.8684</td>
<td>0.7561</td>
</tr>
<tr>
<td>Trunk-LM</td>
<td>0.6225</td>
<td>0.6143</td>
<td>0.7742</td>
<td>0.4646</td>
<td>0.6499</td>
<td>0.4697</td>
</tr>
<tr>
<td>LE-F</td>
<td>1.0000</td>
<td><strong>0.0121</strong></td>
<td>0.8587</td>
<td><strong>0.0124</strong></td>
<td>0.5798</td>
<td>0.1675</td>
</tr>
<tr>
<td>LE-FM</td>
<td>1.0000</td>
<td><strong>0.0211</strong></td>
<td>1.0000</td>
<td><strong>0.0397</strong></td>
<td>0.8477</td>
<td><strong>0.0051</strong></td>
</tr>
<tr>
<td>LE-LM</td>
<td>0.4075</td>
<td>0.4094</td>
<td>0.2315</td>
<td>0.5580</td>
<td>0.4067</td>
<td>0.4812</td>
</tr>
</tbody>
</table>

p-values ≤ 0.05 are in bold. Anthro, anthropometrics; Carb, carbohydrates; DXA, dual-energy X-ray absorptiometry; MRI, magnetic resonance imaging; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue; Sit-WC, seated waist circumference; Sit-AC, seated abdominal circumference; Sup-WC, supine waist circumference; Sup-HC, supine hip circumference; Sup-AC, supine abdominal circumference; Total-F, total body fat mass percentage; Total-FM, total body fat mass; Total-LM, total body lean mass; Trunk-F, trunk fat mass percentage; Trunk FM, trunk fat mass; Trunk-LM, trunk lean mass; LE-F, lower extremity fat mass percentage; LE-FM, lower extremity fat mass; LE-LM, lower extremity lean mass.
**Table 4:** Linear regression analyses examining carbohydrate intake (g) and measures of fat mass (FM) with and without controlling for total caloric intake

<table>
<thead>
<tr>
<th>Marker</th>
<th>Without total calories</th>
<th>Total Calories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trunk FM</td>
<td>0.137 (.010)</td>
<td>0.106 (.025)</td>
</tr>
<tr>
<td>Leg FM</td>
<td>0.154 (.006)</td>
<td>0.061 (.093)</td>
</tr>
<tr>
<td>Total FM</td>
<td>0.172 (.004)</td>
<td>0.111 (.022)</td>
</tr>
<tr>
<td>Seated WC</td>
<td>0.174 (.004)</td>
<td>0.134 (.011)</td>
</tr>
<tr>
<td>Supine WC</td>
<td>0.226 (&lt;.001)</td>
<td>0.124 (.017)</td>
</tr>
<tr>
<td>SAT-MRI</td>
<td>0.228 (.001)</td>
<td>0.163 (.007)</td>
</tr>
</tbody>
</table>

Weighted least squares regressions between carbohydrate intake (g) and measures of fat mass with and without controlling for total caloric intake (kcals). FM, fat mass; WC, waist circumference; SAT, subcutaneous adipose tissue.