Differences in resting metabolic rate between paraplegic and able-bodied subjects are explained by differences in body composition1–3

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ABSTRACT

Background: Little is known about the relation between body composition and energy metabolism in paraplegia.

Objective: We investigated the relation between body composition and energy metabolism in healthy paraplegics as compared with able-bodied control subjects. We hypothesized that paraplegics would have lower fat-free mass (FFM), body cell mass (BCM), resting metabolic rate (RMR), and thermic effect of feeding (TEF).

Design: This cross-sectional study included 34 control subjects and 28 paraplegics (mean age: 29.1 ± 7.6 and 33.9 ± 9.2 y, respectively) with body mass indexes (in kg/m²) of 23.5 ± 1.8 and 24.3 ± 6.0, respectively. We measured RMR and TEF with indirect calorimetry, total body water with deuterium dilution, and extracellular water with corrected bromide space. We calculated FFM (total body water/0.732) and BCM [(total body water - extracellular water)/0.732].

Results: FFM was higher in control subjects than in paraplegics (77.2 ± 7.2% and 69.2 ± 8.7%, respectively; P = 0.0002), as were BCM (47.4 ± 6.7% and 35.9 ± 8.1%, respectively; P < 0.0001) and RMR (7016 ± 935 and 6159 ± 954 kJ/d, respectively; P = 0.0007). FFM was the single best predictor of RMR in both groups (r² = 0.83 for control subjects and 0.70 for paraplegics, P < 0.0001 for both). RMR adjusted for FFM did not differ significantly between control subjects and paraplegics (6670 ± 504 and 6588 ± 501 kJ/d, respectively). TEF also did not differ significantly between control subjects and paraplegics (6.25 ± 2.2% and 5.53 ± 1.8% of energy intake, respectively).

Conclusions: FFM, BCM, and RMR, but not obligatory TEF, are lower in paraplegics than in control subjects. RMR does not differ between control and paraplegic subjects after adjustment for FFM, indicating similar metabolic activity in the fat-free compartment of the body. Am J Clin Nutr 2003;77:371–8.

KEY WORDS Paraplegia, disability, spinal cord injury, body composition, fat-free mass, resting metabolic rate, thermic effect of feeding

INTRODUCTION

Obesity is one of many secondary complications found in the paraplegic population. Similar to obesity in the able-bodied population, obesity in spinal cord injury (SCI) is associated with numerous metabolic sequelae, including glucose intolerance and insulin resistance (1, 2), hyperlipidemia (3), and coronary artery disease (4). Additional sequelae unique to the SCI population include pulmonary emboli (5), reduced function below the level predicted by the neurological lesion (6), pain (7), and compromised mobility (8).

Positive energy balance increases the risk of obesity. Total daily energy expenditure comprises resting metabolic rate (RMR), thermic effect of feeding (TEF), and physical activity. RMR in able-bodied individuals accounts for ≈65% of total daily energy expenditure and is largely determined by body size and composition. We and others have shown that fat-free mass (FFM) explains 70–85% of the variation in RMR (9–11). A low RMR, expressed in relation to FFM, was found to be a risk factor for weight gain (12). Therefore, the relation between these 2 variables was investigated to explain differing rates of weight gain in various clinical populations (13–17). A limited number of studies indicate that persons with chronic SCI have low absolute resting or basal metabolic rates (18–21). Only one study adjusted RMR for body composition and found that RMR adjusted for FFM, fat mass (FM), and age was 678 kJ/d lower in SCI patients than in able-bodied subjects (P < 0.01) (18). However, the generalizability of the results from the above studies is limited, because of either small sample sizes (18, 19), lack of able-bodied control subjects for comparison (19–21), or inclusion of men only (18, 19, 21). Also, to the best of our knowledge, no study has related body cell mass (BCM) to energetics in this population. FFM includes both extracellular mass and the metabolically active BCM (skeletal muscle and organs); the latter is responsible for all of the oxygen consumption, carbon dioxide production, and work performed by the body. It is not known whether RMR adjusted for body composition, including FFM and BCM, is lower in men and women with paraplegia than in those who are able-bodied.

TEF accounts for 3–10% of total daily energy expenditure and may play a role in the development and maintenance of obesity...
(22). Only 2 studies have investigated TEF in the SCI population. One found that TEF (expressed as a percentage of total daily energy intake) in male SCI subjects was lower than that of able-bodied control subjects (18), whereas the other study found no differences in TEF, expressed as a percentage of either test energy intake or RMR (23).

Our objective was to investigate factors that influence RMR and TEF in a group of healthy adult men and women with paraplegia. We hypothesized that paraplegia would result in lower FFM, BCM, RMR, and TEF.

SUBJECTS AND METHODS

Subjects

Able-bodied men and women (n = 34) were recruited from the University of Toronto, Ryerson University, and the staff of The Hospital for Sick Children in Toronto. Paraplegic men and women (n = 32) were recruited from The Toronto Rehabilitation Institute, Ontario Wheelchair Sports Association, Ontario March of Dimes, Canadian Paraplegic Association, and Spina Bifida and Hydrocephalus Association of Toronto. The subjects were group-matched on the basis of body mass index (in kg/m²). Four subjects with paraplegia were excluded from the analyses because of technical difficulties with our indirect calorimeter, resulting in a total of 28 paraplegic subjects. The most common cause of paraplegia in these remaining 28 subjects was motor vehicle accident (n = 11), followed by hemorrhage (n = 4), spina bifida (n = 4), and falls (n = 3). The remaining causes were mixed and included transverse myelitis (n = 2), gunshot wound (n = 1), bacterial infection (n = 1), scuba diving accident (n = 1), and Von Hippel Lindau syndrome (n = 1). The mean number of years since the onset of paraplegia was 11.4 ± 9.5 (range: 1.5–39 y). Eighteen of the 28 paraplegic subjects (11 men and 7 women) had complete lesions (no sensory or motor function in the sacral segments) and 10 subjects (6 men and 4 women) had incomplete lesions (partial sensory function, motor function, or both below the lesion and sensory or motor function in the S4–5 sacral segments) (24). All subjects underwent a screening health history, and none reported a history of diabetes, Crohn’s disease, renal disease, heart disease, hypothyroidism, or hyperthyroidism. None of the subjects had any active decubitus ulcers. Women were in the follicular phase (days 1–12) of their menstrual cycles according to their self-reports.

Data collection began in January 2000 and was completed in August 2001. The study was approved by the Research Ethics Board of The Hospital for Sick Children and The Toronto Rehabilitation Institute. Subjects were given a small honorarium for their participation.

Procedures

Studies were carried out during a 1-d visit to the Clinical Investigation Unit of The Hospital for Sick Children. Subjects were told that they should not exercise or consume alcohol or caffeine for the 24 h preceding the study day. Subjects arrived in the morning after a 12-h fast, provided informed consent, and completed a second health history. All measures were obtained by the same investigator (ACB) with subjects wearing light clothing and no shoes.

First, subjects were asked to empty their bladders so that a urine sample could be analyzed for nitrogen and metanephrine contents. For each subject, between 0830 and 1030, a urine sample was collected into a plastic container and treated with 4 mL of a 30% HCl solution to prevent microbial growth. Body weight was measured to the nearest 0.1 kg on a beam balance scale (Detecto Model; Cardinal Scales, Web City, MO) for the control subjects and on a digital wheelchair scale (Scale-Tronix 6006; Wheaton, IL) for the paraplegic subjects. The CV between the 2 instruments was determined in a subsample of 6 able-bodied control subjects, and was found to be 0.36 ± 0.15%. Height was measured to the nearest 0.1 cm with a wall-mounted stadiometer (Holtain Ltd, Crymych, United Kingdom) for the control subjects and on an adult-sized Plexiglas length board (made specifically for the study by the Medical Engineering Department of The Hospital for Sick Children) for the paraplegic subjects. Subjects were asked to transfer from their wheelchairs, first to a bed and then onto the length board. With the subject’s head resting against the immovable headboard, legs outstretched and feet in dorsiflexion, the movable foot board was pressed against the heels. Subjects looked up at the ceiling during the measurement, while the investigator ensured that the hips were straight and centered on the board. The CV between the stadiometer and the length board in the able-bodied subsample was 0.78 ± 0.23%.

After a baseline blood sample was obtained (15 mL, drawn into a heparin-containing syringe), each subject was given an oral dose of water labeled with 2H2O for the measurement of total body water (TBW) and with sodium bromide for the measurement of extracellular water (ECW). The dosages were as follows: 0.25 g 99.9 atom percent (AP) 2H2O (CDN Isotope, Pointe-Claire, Quebec) per kg estimated TBW (60% of body weight) and 1.0 mL 30% NaBr (Fisher Scientific, Nepean, Ontario) per kg body weight. The container was then rinsed with ~15 mL deionized water, which the subject subsequently drank to wash any remaining isotope from the mouth into the stomach. A plateau blood sample (15 mL) was obtained 3 h after administration of the 2H2O and NaBr (25, 26). Subjects continued to fast during the equilibration period. Blood samples were centrifuged (Beckman J6B Centrifuge; Beckman Coulter Inc, Fullerton, CA) at 1200 × g for 10 min at −4 °C, and the plasma samples were subsequently stored at −20 °C until analyzed.

Body composition

Plasma samples were analyzed for their 2H2O content by using an isotope ratio mass spectrometer (CF-IRMS, model ANCA GSL; Europa Scientific Inc, Crewe, United Kingdom) after equilibration with hydrogen gas (27). The following equation was used to calculate TBW:

\[
TBW (kg) = \frac{[(\text{dose} \times 99.9)/20] \times (18.02/\text{atom percent excess}) \times 10^{-3}] / 1.04
\]

where dose is the dose of 2H2O in g, 99.9 is the AP of 2H2O, 20 is the molecular weight of 2H2O, 18.02 is the molecular weight of unlabeled water, atom percent excess is \(AP_{\text{plateau}} - AP_{\text{baseline}}\), and 1.04 is the correction for hydrogen dilution space. The intraassay CV was 0.11 ± 0.07% for a standard 200-ppm deuterium solution and was 0.06 ± 0.04% for a 300-ppm solution. The intraindividual CV for plasma deuterium AP was 0.45 ± 0.22%. FFM was calculated as TBW/0.732, where 0.732 represents the hydration constant of lean tissue (28), and FM was calculated as weight − FFM.

ECW was estimated as corrected bromide space from plasma samples by means of the bromide dilution technique (26). Bro-
mide concentration in the ECW space was determined from plasma samples by neutron activation of stable \(^{79}\text{Br}\) to \(^{80}\text{Br}\) (29) and by using the following equation:

\[
\text{Corrected bromide space} = (\text{Br dose/plasma enrichment at 3 h}) \times 0.90 \times 0.95 \times 0.94
\]

where 0.90 is the correction factor for nonextracellular bromide distribution, 0.95 is the Donnan equilibrium factor, and 0.94 is the correction for water in the plasma. The intraassay CV for standard 0.005%, 0.01%, and 0.02% bromide solutions was 1.45 ± 0.94% and the intraindividual CV for plasma bromide concentration was 5.19 ± 3.8%. Intracellular water was calculated as TBW – ECW, and BCM was calculated as intracellular water/0.732.

Energy expenditure

RMR was measured during the \(^{7}\text{H}_{2}\text{O}\) and NaBr equilibration period by using continuous open-circuit indirect calorimetry (2900 Energy Expenditure Unit; Sensormedics, Yorba Linda, CA) in a thermoneural environment. External validity of the instrument was tested regularly for the duration of the study by oxidation of 5 mL (3.94 g) ethyl alcohol. The CV between expected and observed carbon dioxide production was 1.23 ± 0.10% and for oxygen consumption, it was 1.52 ± 0.14%. The instrument was calibrated before each measurement against standard mixed reference gases (4% CO\(_2\), 16% O\(_2\), and 80% N\(_2\)). Expired air was collected by using a ventilated canopy for 60 min; only the last 40 min of data were used in the calculations. During the measurement period, subjects remained supine, were instructed not to talk or fidget, and watched television to reduce boredom and prevent sleeping. Data were carefully reviewed after each measurement, and an average of 1.13 ± 2.7 min were deleted, resulting in a total of ≥34 min of steady state data for 61 of the 62 subjects (1 subject dozed on and off for 19 min, resulting in 21 min of steady state data). The deleted data points were deleted because subjects either moved, laughed, spoke, fell asleep, or had spasms. RMR was predicted by using the equations of Schofield (30), and the percentage of predicted RMR was calculated as (RMR\(_{\text{measured}}\)/RMR\(_{\text{predicted}}\) × 100.

TEF was measured with indirect calorimetry for 120 min after the plateau blood sample and after consumption of a mixed liquid meal consisting of 55% carbohydrate, 30% fat, and 15% protein (Carnation Instant Breakfast; Nestle Canada Inc, Toronto). The dose of the meal was calculated as 30% of RMR. Subjects were given a 10-min break after the first 55 min to relieve pressure and to allow them to stretch. TEF was calculated as a percentage of the test energy intake (EI) and as a percentage of RMR as follows:

\[
\%\text{EI} = \left[\frac{\text{average kJ above RMR/min} \times 120 \text{ min}}{\text{EI}}\right] \times 100
\]

\[
\%\text{RMR} = \left[\frac{\text{average postprandial energy expenditure}}{\text{RMR/min}}\right] \times 100
\]

where EI was expressed in kJ, and postprandial energy expenditure was in kJ/min.

Laboratory analysis

The Core Laboratory at The Hospital for Sick Children measured thyroid stimulating hormone and thyroid hormone concentrations in 300 μL plasma from the baseline blood samples. Thyroid stimulating hormone was determined by using a sandwich magnetic separation immunoassay (31, 32), and triiodothyronine (T\(_3\)) and free thyroxine (T\(_4\)) were measured with a competitive magnetic separation immunoassay (33, 34; R Vunnam, J Craine, C Marx, C Bianca, A Spadaro, S Matthies, J Junjulas, and A Akerkar, unpublished observations, 1984) by using a Technicon Immuno 1 immunoassay analyzer (Bayer Corp, Tarrytown, NY). Urinary nitrogen concentration was determined in diluted urine samples (100 μL urine:10 mL deionized water) by using pyro-chemiluminescence with an ANTEK 7000 nitrogen/sulfur analyzer (Mandel Scientific Co Ltd, Houston) (35). Nitrogen concentration was used to determine the nonprotein respiratory quotient (RQ) and protein oxidation in the fasted state. Fat and carbohydrate oxidation were calculated from the nonprotein RQ by using the tables of Lusk (36). Metanephrine concentration in 10-mL urine samples was determined by using an LC-4C BAS Amperometric detector (Bioanalytical Systems Inc, West Lafayette, IN).

Statistical analyses

A power analysis indicated that 20 able-bodied and 20 paraplegic subjects were needed to detect a 15% difference in RMR with 80% power at α = 0.05; we recruited additional subjects to allow for attrition. The SAS program (version 8.1; SAS Institute Inc, Cary, NC) was used for all computations. Results were considered significant at P < 0.05. Nonnormal data were log transformed. Data are presented as means ± SDs.

A chi-square analysis was performed to determine whether there were significant differences in sex distribution between the control and paraplegic groups. Differences between the 2 groups and between subgroups (male control subjects compared with male paraplegics, female control subjects compared with female paraplegics, and paraplegics with trauma compared with nontrauma etiologies) were determined by using t tests and, when warranted, P values for unequal variances. Differences between control subjects, paraplegics with complete lesions, and paraplegics with incomplete lesions were determined by using analysis of variance with a Tukey post hoc test. Pearson’s product-moment correlation coefficients were used to quantify the univariate associations between FFM and years since onset of paraplegia and between RMR and selected predictor variables. The latter associations were evaluated further by using the multivariate technique of all possible regressions and forward stepwise regression. RMR was the outcome variable; possible predictors included years since onset of paraplegia, age, sex, height, body mass index, FFM, BCM, FM, T\(_3\) concentration, and metanephrine concentration. Analysis of covariance was used to adjust the indexes of energy metabolism for selected predictor variables if there was no evidence of a significant interaction between group and the predictor variable.

RESULTS

Age and body-composition characteristics of the 2 groups are shown in Table 1. There was no significant difference in the sex distribution between the 2 groups. Control subjects were slightly younger than were paraplegic subjects. Weight and body mass index did not differ significantly between groups, but control subjects were taller. Expressed as a percentage of body weight, TBW, FFM, intracellular water, and BCM were higher in the control group, and FM and ECW were lower in the control group. Differences in all of the above parameters were maintained when we compared male control and paraplegic subjects and female control and paraplegic subjects, with one exception. Male control subjects were slightly younger than were male paraplegics (29.1 ± 8.5 and 36.3 ± 10.1 y, respectively; P = 0.0119), whereas age did not differ significantly between female control and paraplegic subjects.
(29.2 ± 5.4 and 30.3 ± 6.6, respectively; \( P = 0.7458 \)). There was no significant correlation between years since onset of paraplegia and FFM (\( r^2 = 0.047, P = 0.2681 \)).

### Thermogenic hormones and energy metabolism

There were no significant differences between the control and paraplegic groups in any of the hormon’s measured. The values for the control and paraplegic groups, respectively, were as follows: thyroid stimulating hormone, 1.75 ± 0.74 and 1.57 ± 0.66 mIU/L (\( P = 0.3442 \)); \( T_3 \), 1.57 ± 0.32 and 1.57 ± 0.33 nmol/L (\( P = 0.9746 \)); free \( T_3 \), 15.5 ± 2.4 and 16.1 ± 1.4 pmol/L (\( P = 0.2535 \)); and metanephrine, 1.16 ± 0.63 and 1.07 ± 0.53 \( \mu \)mol/L (\( P = 0.6346 \)). The parameters of energy metabolism are shown in Table 2. The Schofield equation (30) closely predicted RMR in the control group (\( \Delta = 99 \) kJ/d, \( P = 0.2633 \)) but significantly overestimated RMR in the paraplegic group (\( \Delta 339 \) kJ/d, \( P = 0.0025 \)). As expected, measured RMR was significantly higher (by 14%) in the control group than in the paraplegic group. This difference remained significant when RMR was adjusted separately for age, weight, FM, \( T_3 \), and metanephrine but was reduced to < 2% when adjusted for FFM (\( P = 0.5467 \)), both FM and FFM (\( P = 0.3692 \)), and BCM (\( P = 0.5780 \)).

Similar results were obtained when the groups were divided by sex: RMR was significantly higher in male control subjects than in male paraplegics (7415 ± 737 and 6649 ± 749 kJ/d, respectively; \( P = 0.0023 \)) and in female control subjects than in female paraplegics (6056 ± 609 and 5401 ± 721 kJ/d, respectively; \( P = 0.0373 \)). The differences were no longer significant when RMR was adjusted for FFM [7197 ± 503 and 6957 ± 514 kJ/d for men (\( P = 0.1643 \)) and 5440 ± 461 and 5873 ± 447 kJ/d for women (\( P = 0.0820 \)]. Protein oxidation did not differ significantly between the 2 groups. There were trends toward lower fat oxidation and higher carbohydrate oxidation and fasting RQ in the control group. Postprandial RQ was significantly higher in the control group (\( P < 0.0001 \)). TEF (expressed either as a percentage of RMR or as a percentage of test energy intake) was not significantly different between the 2 groups.

Partial correlation coefficients between RMR and selected predictor variables for both groups are shown in Table 3. The best single predictor of RMR was FFM, which accounted for 83% of the variation in RMR in control subjects and 70% of the variation in paraplegics (\( P < 0.0001 \) for both).

The relation between unadjusted RMR and FFM for both groups is shown in Figure 1. FM was not predictive of RMR in the control group (\( P = 0.4267 \)) but was predictive of RMR in the paraplegic group (\( P = 0.0223 \)). The most statistically significant prediction equation for RMR in the paraplegic group, as determined by forward stepwise regression, was as follows:

\[
\text{RMR (kJ/d)} = 3618 - 795(\ln \text{age}) - 731(\text{sex}) + 3170 \\
\text{(in weight)} - 794(\ln T_3) + 261(\ln \text{metanephrine})
\]

(5)

where age is in y, sex = 0 for men and 1 for women, weight is in kg, \( T_3 \) is in mmol/L, and metanephrine is in \( \mu \)mol/L (\( r^2 = 0.89, \text{SEE} = 388 \text{ kJ/d}, \text{and} \ P < 0.0001 \)).

The most clinically useful equation for RMR in the paraplegic group was as follows:

\[
\text{RMR (kJ/d)} = 10682 - 1238(\ln \text{age}) - 521(\text{sex}) \\
- 24(\text{height}) + 87(\text{FFM})
\]

(6)

where height is in cm and FFM is in kg (\( r^2 = 0.82, \text{SEE} = 435 \text{ kJ/d}, \text{and} \ P < 0.0001 \)).

### Nature of injury and completeness of lesion

Within the paraplegic group, there were no significant differences in any of the parameters between those subjects whose paraplegia was caused by trauma (\( n = 16 \)) and those whose paraplegia was not caused by trauma (\( n = 12 \)).

Analysis of variance indicated that there were no significant differences in weight, body mass index, TEF, or concentrations of thyroid stimulating hormone, \( T_3 \), free \( T_3 \), or metanephrine between the control subjects, complete paraplegics, and incomplete paraplegics. ECW was higher in control subjects than in incomplete paraplegics (\( P = 0.0138 \)). Intracellular water and BCM were higher in control subjects than in either complete or incomplete
paraplegics ($P < 0.0001$), whereas FFM was higher in control subjects than in complete paraplegics only ($P = 0.0007$). FM was higher in complete than in incomplete paraplegics ($32.0 \pm 8.6\%$ and $28.6 \pm 8.9\%$, respectively), but this difference was not significant. Only the complete group had significantly higher FM than did control subjects ($P = 0.0007$). Absolute RMR was not significantly different between the complete and incomplete paraplegics ($6153 \pm 804$ and $6170 \pm 1228$ kJ/d, respectively), but both values were significantly lower than that of control subjects ($P = 0.0035$).

There were no significant differences in fasting protein oxidation between the 3 groups. Fat oxidation accounted for $54.0 \pm 15.2\%$ of RMR in the complete paraplegics, which was higher than in the incomplete paraplegics ($39.2 \pm 16.3\%$) and the control subjects ($41.2 \pm 15.0\%$) ($P = 0.0112$). Carbohydrate oxidation accounted for $36.0 \pm 15.1\%$ of RMR in the complete paraplegics, which was lower ($P = 0.0073$) than in the incomplete paraplegics ($51.3 \pm 15.2\%$) and the control subjects ($49.2 \pm 14.9\%$). The difference in carbohydrate oxidation remained significant when adjusted for all parameters of body composition and T3 concentration, but became nonsignificant when adjusted for metanephrine concentration ($37.6 \pm 15.9\%$ and $42.0 \pm 16.1\%$ in complete and incomplete paraplegics, respectively; $P = 0.5074$). Fasting RQ was lower ($P = 0.0085$) in the complete paraplegics ($0.82 \pm 0.04$) than in the incomplete paraplegics ($0.86 \pm 0.04$) and control subjects ($0.86 \pm 0.04$) and control subjects ($0.86 \pm 0.04$).

### TABLE 3

Pearson's product-moment partial correlation coefficients between resting metabolic rate and selected predictor variables in able-bodied control subjects and paraplegic subjects

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Control subjects ($n = 34$)</th>
<th>Paraplegic subjects ($n = 28$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r$</td>
<td>$P$</td>
</tr>
<tr>
<td>Age (y)</td>
<td>0.13</td>
<td>0.4643</td>
</tr>
<tr>
<td>Time since onset of paraplegia (y)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>0.79</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>0.71</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.45</td>
<td>0.0078</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td>0.91</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>−0.14</td>
<td>0.4267</td>
</tr>
<tr>
<td>Body cell mass (kg)</td>
<td>0.87</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Triiodothyronine (nmol/L)</td>
<td>0.02</td>
<td>0.9129</td>
</tr>
<tr>
<td>Metanephrine (µmol/L)</td>
<td>−0.23</td>
<td>0.1867</td>
</tr>
</tbody>
</table>

1Predicted by using the method of Schofield et al (30).
2By $t$ test.
3Reference range: < 6.6 µmol/L.
4Reference range: 0.8–5.4 nmol/L.
5RMR was adjusted for each body-composition variable by using analysis of covariance and was adjusted for fat-free mass and fat mass by using multiple linear regression.
6Reference range: <6.6 µmol/L.
DISCUSSION

The 2 major findings of this study were that the obligatory phase of TEF is not lower in persons with paraplegia and that absolute RMR is lower in persons with chronic paraplegia than in able-bodied persons, but is not different when adjusted for FFM. This suggests that the metabolic activity of the fat-free body is similar in paraplegic subjects and able-bodied control subjects.

As expected, persons with chronic paraplegia had significantly lower FFM and BCM and higher FM than did able-bodied control subjects. Despite the loss of metabolically active tissue, a significant amount of variation in RMR in the paraplegic group was explained by FFM ($r^2 = 0.70, P < 0.0001$) and BCM ($r^2 = 0.46, P = 0.0001$). Furthermore, the difference in absolute RMR was reduced from 14% to < 2% when RMR was adjusted for FFM and BCM ($P = 0.5467$ and $P = 0.5780$, respectively). These findings differ from those of Monroe et al (18), who found that RMR adjusted for FFM, FM, and age was 678 kJ lower per day in persons with SCI than in able-bodied persons ($P < 0.01$). This may reflect methodologic differences between the 2 studies, because there were no significant differences in T3 or T4 concentrations. The latter finding was unexpected, but may reflect the fact that we studied persons with paraplegia. We might have seen altered sympathetic activity in persons with tetraplegia, as a result of a higher level of interruption of the sympathetic pathways (37).

TEF was not significantly lower in the paraplegic group. This agrees with the findings of Aksnes et al (23), who measured TEF for 2 h after ingestion of a mixed liquid meal (similar in composition to the one used in the present study) in 9 tetraplegic and 6 able-bodied men. However, our results do not agree with those of Monroe et al (18), who found that TEF was lower ($P < 0.05$) in 10 men with SCI than in 59 able-bodied men. This may reflect methodologic differences between our 2 studies. Monroe et al (18) measured TEF for 14 h in a respiratory chamber and calculated TEF as a percentage of test energy intake as follows:

$$\frac{[(EE_{0\ activity} - BMR)/EI] \times 840 \times 100}{840}$$

where $EE_{0\ activity}$ is the intercept of the linear regression between energy expenditure and physical activity (kcal/min), BMR is basal metabolic rate (kcal/min), and 840 is the duration of measurement (min). Ravussin et al (38), and more recently Tataranni et al (39), found that intraindividual variability of TEF measured with the above method varied from 43% to 125%. Tataranni et al (39) noted that this may have resulted from the large variability of the terms used in the computation of TEF, including BMR and the intercept of the regression line, and concluded that measuring TEF in a respiratory chamber is not ideal. Nonetheless, by extending the measurement period to 14 h, Monroe et al (18) were able to capture both the obligatory and facultative phases of TEF. This is in keeping with the recommendation by Reed and Hill (40) that TEF be measured for $\geq 5$ h. For practical reasons, we could not extend our postprandial measurement period past the obligatory phase (2 h), and so we may have missed differences that might have become apparent later.

There were trends toward higher fasting fat oxidation, lower carbohydrate oxidation, and lower RQ in the paraplegic group. Postprandial RQ was significantly lower in the paraplegic group, suggesting similar patterns of substrate oxidation in the fasted and fed states. These results are not unexpected, because substrate oxidation is influenced by body composition. As a result of increased circulating fatty acids, obesity is associated with a high ratio of fat oxidation to carbohydrate oxidation, and consequently a decreased RQ (41, 42). This may result in insulin resistance with subsequent impairment of glucose storage and oxidation (41–43), which are known consequences of SCI (1–3, 44, 45). Within the SCI population, evidence indicates that persons with complete lesions as compared with incomplete lesions are at higher risk of developing the metabolic syndrome (46, 47).

In a subanalysis by completeness of lesion, postprandial RQ and fasting carbohydrate oxidation were significantly lower, and fasting fat oxidation was higher, in the complete paraplegics. Adjusting carbohydrate oxidation for body composition did not reduce the difference between the 2 subgroups, but adjusting for metanephrine concentrations did, suggesting that the difference in sympatheic activity was suf-
cient to affect substrate oxidation. The results of the present study provide additional evidence of metabolic impairment in persons with complete lesions as compared with incomplete lesions, independent of body composition.

Our study contributes knowledge where certain gaps in the literature existed, but a few limitations should be mentioned. First, we recognize that a prediction equation devised in a sample of 28 paraplegics may be of limited generalizability. Nonetheless, our sample was representative of the larger paraplegic population because we were careful to include men and women with complete and incomplete lesions and trauma- and nontrauma-related etiologies. Also, to the best of our knowledge, ours is the first study in this population to relate energetics to thermogenic hormone activity and to report alterations in substrate oxidation. Second, we used the Pace and Rathbun (28) lean tissue hydration constant of 73.2% to determine FFM and BCM. This may or may not be appropriate for the paraplegic population. To determine the hydration constant, we would have had to measure TBW as well as FFM with an independent method such as dual-energy X-ray absorptiometry, which was beyond the scope of our study. However, there is no reason to believe that the hydration constant of lean tissue in this population should differ from that of an able-bodied population, except perhaps in the most extreme cases of leanness and obesity. Wang et al (48) reported that the hydration constant is quite robust, even in situations of varying adiposity, and concluded that the change in the ratio of TBW to FFM may be too small to identify with the available in vivo methods. Also, in isolating BCM, we quantified intracellular water, which is independent of the hydration constant. Both were lower in the paraplegic group and both explained a significant amount of variation in RMR in the control and paraplegic groups; thus, we are confident that we isolated the body compartments most relevant to energy metabolism.

In conclusion, FFM, BCM, and RMR are lower in chronic paraplegia. RMR does not differ between paraplegic and able-bodied subjects after adjustment for FFM and BCM, suggesting similar amounts of metabolic activity in the fat-free compartment of the body. Paraplegia does not have an apparent effect on the obligatory phase of TEF, but possible differences in facultative thermogenesis still need to be ruled out. Future studies may prospectively cross-validate the RMR prediction equation generated by the current study. Also, physical activity levels should be quantified and related to body composition in this population.

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