

## The relationship between energy expenditure and lean tissue in monozygotic twins discordant for spinal cord injury

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**Abstract**—Energy expenditure and fat-free mass (FFM), as well as the relationships between these parameters, were investigated in thirteen pairs of monozygotic twins discordant for SCI. Basal energy expenditure (BEE) and resting energy expenditure (REE) were determined by indirect calorimetry. Measurements for FFM and fat mass were obtained by dual-energy x-ray absorptiometry. Total body potassium was determined by a 4-Pi whole-body counting chamber. Values are expressed as mean  $\pm$  standard deviation. BEE and REE of the twins with SCI were significantly less than those of the able-bodied co-twins ( $1387 \pm 268$  vs.  $1660 \pm 324$  kcal/d,  $p < 0.005$ , and  $1682 \pm 388$  vs.  $1854 \pm 376$  kcal/d,  $p < 0.05$ , respectively). Regardless of the group, direct and highly significant relationships were evident between BEE or REE and FFM or TBK. In summary, twins with SCI had lower energy expenditure than their able-bodied co-twins. Regardless of paralysis, direct linear relationships existed between energy expenditure and measures of lean mass.

**Key words:** energy expenditure, fat-free mass, paraplegia, spinal cord injury, total body potassium.

### INTRODUCTION

Persons with chronic spinal cord injury (SCI) have been reported to have a reduction in metabolic rate [1,2]. Lean tissue is the most metabolically active body tissue, and muscle mass, a predominant component of lean tis-

sue, appears to be lost over time in those with SCI at a rate exceeding that of the able-bodied population [3,4]. The loss of lean tissue and associated energy expenditure changes in persons with chronic SCI would be expected to have profound implications on carbohydrate and lipid metabolism, as well as an impact on cardiovascular risk [5–8]. The ability to gauge accurately the reduction in energy expenditure in a person with chronic paraplegia is

**Abbreviations:** BCM = body cell mass, BEE = basal energy expenditure, DXA = dual-energy x-ray absorptiometry, FECO<sub>2</sub> = fraction of mixed expired carbon dioxide, FEO<sub>2</sub> = fraction of mixed expired oxygen, FFM = fat-free mass, FM = fat mass, IGF-I = insulin-like growth factor-I, IPD = intrapair difference, pBEE = predicted basal energy expenditure, REE = resting energy expenditure, SCI = spinal cord injury, SD = standard deviation, TBK = total body potassium, VCO<sub>2</sub> = carbon dioxide production, VO<sub>2</sub> = oxygen consumption.

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limited because of the relatively large variance in energy requirements known to be present in the general population. With the use of a monozygotic twin model discordant for SCI, an indirect but fairly convincing appraisal of the individual reductions in energy expenditure and losses of lean body tissue, as well as their interrelationships, may be assessed.

## METHODS

### Subjects

Thirteen pairs of monozygotic twins discordant for SCI were recruited by referral from their physicians for study (**Table 1**). Nine pairs were males and four were

females (**Table 2**). Of the co-twins with SCI, 11 had paraplegia and 2 had tetraplegia; all were nonambulatory. The twins with SCI were in good health without comorbidities at the time of study. The duration of injury ranged from 3 to 26 years (**Table 2**). Genetic testing for zygosity was performed in all pairs at six independent, highly polymorphic loci (Lifecodes, Stamford, CT). All 13 pairs were found to be strongly consistent with monozygosity, with a probability of being nonidentical of 1 in 4,096. Institutional Review Board approvals from the Veterans Affairs Medical Center, Bronx, NY, and the Mount Sinai School of Medicine, New York, NY, were obtained before the study began. The subjects were provided with verbal and written information about the study, and written consent was obtained.

**Table 1.**  
Characteristics of subjects.

Characteristics	SCI Twins ( <i>n</i> = 13)	Non-SCI Twins ( <i>n</i> = 13)	Paired <i>t</i> -test	<i>p</i> Value
Height (m)	1.74 ± 0.12	1.76 ± 0.10	-1.462	—
Weight (kg)	69.9 ± 18.0	78 ± 17.6	-3.224	<0.01
Body Mass Index (kg/m <sup>2</sup> )	22.7 ± 4.0	24.4 ± 3.5	-4.105	<0.005
Body Surface Area (m <sup>2</sup> )	1.82 ± 0.27	1.94 ± 0.26	-3.570	<0.005

**Table 2.**  
Individual characteristics of twins with SCI.

Subject	Age (yr)	Duration of Injury (yr)	Gender	Level of Lesion	Completeness of Lesion
1	47	26	Male	L1-2	Incomplete
2	39	22	Male	T12-L1	Incomplete
3	25	11	Male	T10-12	Complete
4	37	3	Male	T6	Complete
5	40	8	Male	T12-L1	Complete
6	37	16	Male	C5-7	Incomplete
7	32	2	Female	T10-12	Complete
8	36	5	Female	T7	Complete
9	34	11	Male	T7-8	Incomplete
10	21	21	Female	T10-12	Incomplete
11	49	27	Female	T12-L1	Incomplete
12	43	25	Male	T9	Complete
13	45	19	Male	C6-7	Incomplete
Mean ± SD	37 ± 8	15 ± 9	—	—	—

SD = standard deviation

## Energy Expenditure

Oxygen consumption ( $\text{VO}_2$ ) and carbon dioxide production ( $\text{VCO}_2$ ) were measured via indirect calorimetry with the use of a mixing chamber with dilution technology [9]. A metabolic cart (SensorMedics Corp., Yorba Linda, CA) was used to measure indirect calorimetry by analyzing the exhaled air from the subject for fractions of mixed expired oxygen and carbon dioxide ( $\text{FEO}_2$  and  $\text{FECO}_2$ , respectively). Before each patient was tested, barometric pressure was measured and the metabolic cart calibrated. The dilution technique involves the use of a high-flow pump to draw air past the face of the subject through a loose-fitting mask [9]. As the subject breathed into this stream of air, the exhaled air was pulled into a 7 L mixing chamber. The total minute ventilation was set by the flow rate for the pump, which was governed by the fraction of carbon dioxide in the expired air. The ratio of room air to expired air was approximately 4:1; this ratio allowed for an  $\text{FECO}_2$  of 0.005 to 0.01 under normal resting breathing conditions. Although the pump was designed to adjust automatically for hyperventilation and hypoventilation, all subjects were rested for a minimum of 30 min and instructed to remain calm before and during data collection.

Basal energy expenditure (BEE), by our definition, was the energy expended by an individual when initially waking in the morning while lying supine in bed at normal body and ambient temperatures after at least a 12 h fast. Resting energy expenditure (REE) was defined as the energy expended by an individual when seated at least 4 h post-prandial at normal body and ambient temperatures. Predicted basal energy expenditure (pBEE) was determined by the Harris-Benedict equations [10]. The percentage of predicted energy expenditure (%pEE) was calculated as follows: %pEE = measured EE (mEE)/pEE  $\times$  100. All data were collected in a steady-state condition, defined as less than  $\pm 5$ -percent fluctuation in  $\text{VO}_2$  and  $\text{VCO}_2$  for 5 consecutive minutes. Equations for the following are as referenced: minute ventilation [11],  $\text{VO}_2$  (mL/min) [12],  $\text{VCO}_2$  (mL/min) [12], BEE (kcal/d) [13], REE (kcal/d) [13], pBEE (kcal/d) [10].

## Body Composition

Dual-energy x-ray absorptiometry (DXA) was used to determine fat-free mass (FFM) (kg), including bone. DXA was performed using a total-body scanner (model DPX, Lunar Radiation, Madison, WI) by standard methods [14–17]. The subjects were asked to lie on a table,

and whole-body scanning was performed with a congruent beam of stable dual-energy radiation at 40 and 70 keV. The radiation passed through the patient from below while the differential absorption was measured above. The ratio of absorption between the two x-rays of different energies was linearly related to the FFM tissue compartment. The procedure for scanning was about 30 min. DXA provides a three-compartment partition of the body: bone mineral, fat mass (FM), and FFM. The precision and accuracy of DXA for soft tissue has been reported to be 99 percent with  $<1$ -percent error [18].

Total body potassium (TBK) was determined by the use of a 4-Pi whole-body counting chamber [19]. Subjects were placed on a stretcher and inserted into the chamber for 9 min. The radioisotope  $^{40}\text{K}$  occurs naturally as a trace element mixed with  $^{39}\text{K}$ . Potassium, the predominant cation in the body cell mass (BCM), can be measured by the highly sensitive whole-body counting chamber. TBK (mEq) is almost exclusively in the BCM compartment (95 to 98%) and has been shown to be a useful indicator of the quality and quantity of the lean tissue mass [19]. The  $^{40}\text{K}/^{39}\text{K}$  ratio is constant and known at 0.0018, providing a marker for the TBK [20]. The measurement has a precision of  $\pm 4$  percent [19]. TBK includes the combined  $^{40}\text{K}$  contribution from skeletal muscle and viscera, and this measurement has been referred to as BCM.

## Statistical Analyses

The results are expressed as mean  $\pm$  standard deviation of the mean. Paired *t*-tests were performed to determine significant differences within the pairs. Intrapair difference (IPD) scores (paralyzed twin–able-bodied twin) were calculated within the twin pairs for BEE. Linear regression analyses were used to determine the relationship between energy expenditure (BEE or REE) with measures of FFM or TBK, as well as the relationship between BEE and duration of injury.

## RESULTS

The characteristics of the subjects for the SCI and able-bodied twin groups are shown in **Table 1**. Twins with SCI had a significantly lower body weight, body mass index, and body surface area than the able-bodied twins. FFM and TBK were lower in twins with SCI than in non-SCI co-twins (FFM:  $45.6 \pm 10.0$  vs.  $55.5 \pm 11.9$  kg,  $p < 0.0005$ ;

TBK:  $2,534 \pm 911$  vs.  $3,515 \pm 916$  mEq,  $p = 0.01$ ). Total FM was similar in the SCI and non-SCI twins ( $19.8 \pm 11.8$  vs.  $19.3 \pm 8.8$  kg), but because of the reduction in lean tissue, the ratios of FM to FFM and FM to TBK were lower in the SCI compared to the non-SCI twins ( $0.35 \pm 0.15$  vs.  $0.436 \pm 0.22$ ,  $p = 0.08$ , and  $8 \pm 4$  vs.  $6 \pm 2$  g/mEq,  $p = 0.01$ , respectively). After application of the Harris-Benedict equation for age, height, weight, and gender, the predicted basal energy expenditure was significantly reduced in the twins with SCI (Table 3) [10]. The twins with SCI had a significantly lower percentage of predicted BEE than the able-bodied twins ( $85 \pm 13$  vs.  $96 \pm 11\%$ ;  $p < 0.05$ ). The actual measured energy expenditure (BEE or REE) was significantly lower in the twins with SCI compared to the non-SCI twins. However, the energy expenditure per kilogram of body weight (BEE/kg or REE/kg) was not significantly different between the SCI and non-SCI groups (Table 3). There were significant linear correlations between FFM with BEE or REE (Figure 1) and TBK with BEE or REE (Figure 2). There was no significant difference in the increment of BEE or REE to either measure of lean tissue in the SCI compared with the able-bodied twins. An inverse trend was noted between the IPD scores for BEE and duration of injury ( $R = -0.44$ ,  $p < 0.14$ ).

## DISCUSSION

Persons with SCI have body compositional changes that are similar to those reported in the elderly, with loss

of lean tissue and relatively increased adiposity [21,22], although the anthropometrical distribution of muscle mass may differ. In an identical twin study, with one co-twin in each pair having SCI, Spungen et al. reported a loss of lower-limb muscle mass that was continuous and directly correlated with duration of injury [4]. Strong correlations between altered body composition and the level of SCI have been observed, with successively higher, more complete spinal cord lesions associated with decreased FFM and body cell mass [23]. In this study, the loss of lean body tissue in twins with SCI with similar absolute FM to their non-SCI co-twins results in a relative increase in the ratio of body fat to lean tissue in twins with SCI compared with non-SCI co-twins.

The dramatic muscle atrophy in patients with acute SCI is clearly related to the degree of paralysis and immobilization. The etiology for the apparent accelerated loss of muscle mass in those with chronic SCI is less certain. However, similar to that which occurs with advancing age, persons with SCI have shown a reduction in endogenous anabolic hormones, testosterone and growth hormone. Although the literature is conflicting concerning serum testosterone concentrations in persons with SCI [14,24–29], there are undoubtedly subsets of men with relative or absolute androgen deficiency, with several etiologies possible in the SCI population [30–35]. Blunted release of growth hormone to provocative stimulation has been reported in subjects with SCI [36]. The average plasma insulin-like growth factor-I (IGF-I) level,

**Table 3.**  
Energy expenditure measurements.

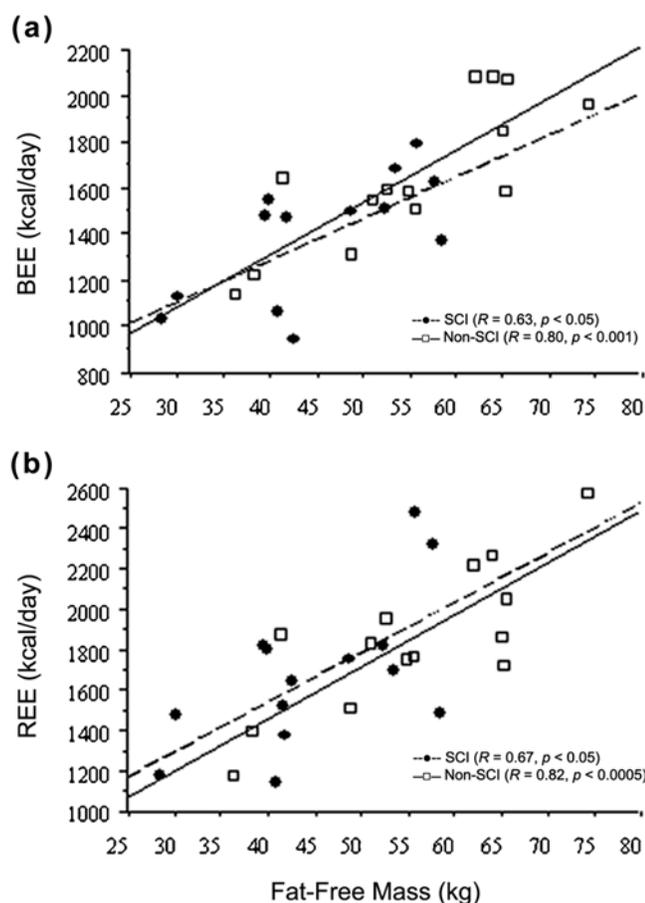
Measurements	SCI Twins ( <i>n</i> = 13)	Non-SCI Twins ( <i>n</i> = 13)	Paired <i>t</i> -test	<i>p</i> Value
pBEE (kcal/d)	$1634 \pm 290$	$1735 \pm 295$	-2.694	<0.05
BEE (kcal/d)	$1387 \pm 268$	$1660 \pm 324$	-3.455	<0.005
BEE/kg (kcal/kg)	$20.4 \pm 3.8$	$21.5 \pm 2.9$	-1.523	—
BEE (%pred)	$85 \pm 13$	$96 \pm 11$	-2.906	<0.05
REE (kcal/d)	$1682 \pm 388$	$1854 \pm 376$	-2.146	<0.05
REE/kg (kcal/kg)	$24.9 \pm 5.4$	$24.2 \pm 4.1$	0.796	—
REE (%pred)	$103 \pm 20$	$109 \pm 16$	-1.599	—

pBEE = predicted basal energy expenditure using the Harris-Benedict equations [Harris JA, Benedict FG. Biometric studies of basal metabolism in man. Washington, DC: Carnegie Institution of Washington; 1919. Publication No. 279.]

BEE = basal energy expenditure

%pred = percent predicted EE from the Harris-Benedict equations and is calculated as %pEE = measured EE (mEE)/pEE  $\times$  100.

REE = resting energy expenditure

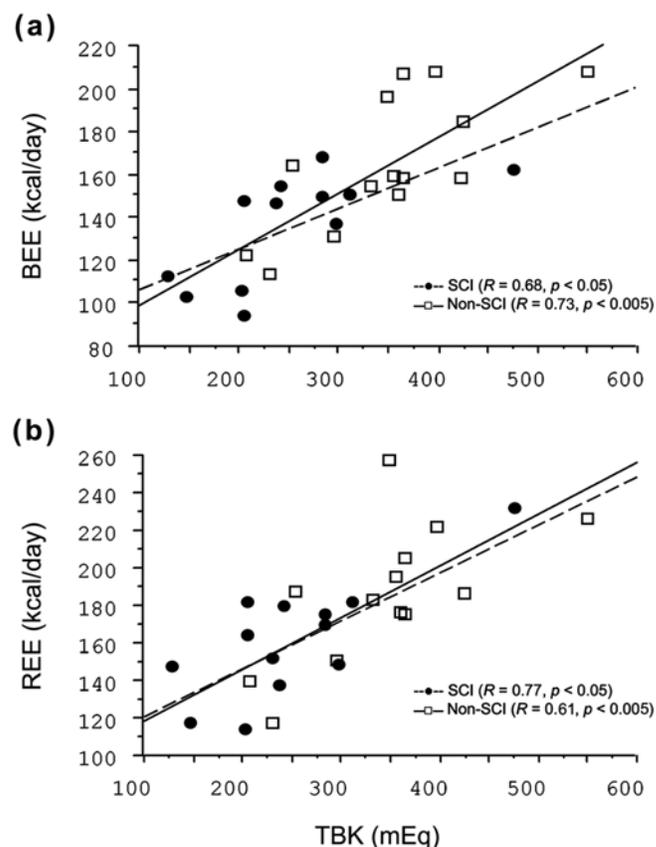


**Figure 1.**

Relationship between basal energy expenditure (BEE) and fat-free mass in SCI and able-bodied twins. REE = resting energy expenditure, SCI = spinal cord injury.

the second messenger of growth hormone, was significantly lower in younger individuals with SCI [36], a finding confirmed by others [37]. A low IGF-I level has been reported to have functional significance in persons with post poliomyelitis syndrome [38] and may be relevant to the activities of daily living in other disabled populations.

In a study of 241 monozygotic and 228 dizygotic twin pairs that examined the relationship between physical activity and total body or abdominal fat, physical activity predicted lower generalized and central adiposity in middle-aged women [39]. The influence of physical activity in those who were susceptible to adiposity also demonstrated a significant salutary effect of physical activity [39]. Behavioral factors were studied as predictors of weight gain in 12,669 adult Finns [40]. The prevalence of obesity was inversely associated with physical



**Figure 2.**

Relationship between resting energy expenditure (REE) and total body potassium in SCI and able-bodied twins. BEE = basal energy expenditure, SCI = spinal cord injury, TBK = total body potassium.

activity, as well as other sociodemographic factors. Parity and caloric intake predicted weight gain in women [40]. In another study in 436 female twins, no significant relationship was found between recent dietary fat consumption and total or abdominal adiposity, after controlling for genetic and some environmental factors [41].

Epidemiological studies have demonstrated that the incidence rates for diabetes mellitus decline as energy expenditure and regular exercise increase [42,43]. Leisure time activity was inversely correlated to the development of type 2 diabetes mellitus in 5,990 male alumni of the University of Pennsylvania [42]. Each 500 kcal increment in energy expenditure was associated with a 6-percent reduction in the age-adjusted risk of diabetes [42]. In a prospective study of 21,271 physicians who were participating in the Physicians' Health Study, exercise appeared to reduce the risk of developing diabetes mellitus, even after adjusting for body mass index [43]. Whether a

decrement in basal energy needs per se, as was the case in our study, will influence the risk for diabetes mellitus, has not been addressed in the literature. However, the obvious need to encourage increased activity-related energy expenditure in persons with disability who have a propensity for the development of diabetes is certainly supported by the above epidemiological studies [42,43]. Of note, the protective effect of physical activity was greatest in those who were at highest risk for the development of diabetes mellitus [42].

If appetite is not diminished and energy requirements are reduced, the result will inevitably be weight gain and obesity. We are not aware of any studies that specifically address satiety after an individual has sustained a SCI. Increased relative or absolute adiposity has certainly been reported for persons with chronic SCI, with unfavorable metabolic consequences [44,45]. Appetite regulation and measures of satiety remain necessary and provocative areas of future investigation in individuals with disability—including, but not limited to, those with SCI.

Related to these adverse body composition changes and reductions in energy requirements, individuals with SCI have a pattern of metabolic changes that is atherogenic. In persons with SCI, there have been reported adverse lipid changes [46,47], a reduction in metabolic rate [1], glucose intolerance, and insulin resistance [5,47,48]. The “multiple metabolic syndrome” has been well appreciated to increase risk of premature cardiovascular disease in the able-bodied population and would be expected to be at least equally deleterious in those with SCI [7,8,48–54].

## CONCLUSION

In this study of monozygotic twins who are discordant for SCI, a clear reduction in energy expenditure has been demonstrated after chronic paralysis. Without regard to injury status, the reduction in energy needs is directly related to lean tissue: the greater the reduction in lean tissue, the greater the reduction in energy expenditure. There appears to be an inverse relationship, albeit not reaching significance, between energy expenditure and duration of injury. Although this study was performed in twins discordant for SCI, our findings may be generalized to persons with various disabilities that limit mobility and/or reduce muscle mass, and who will be

expected to have similar reductions in energy requirements. Once again, if there is a reduction in energy needs, the appropriate exercise and dietary interventions should be considered.

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