Effects of chronic spinal cord injury on body weight and body composition in rats fed a standard chow diet

Stefany D. Primeaux,1 Melissa Tong,2 and Gregory M. Holmes2

1Dietary Obesity Laboratory, Pennington Biomedical Research Center; and 2Neurotrauma and Nutrition Laboratory, Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, Louisiana

Submitted 2 April 2007; accepted in final form 10 July 2007

POSTINJURY WEIGHT LOSS is a common consequence of any surgical procedure or major accident, including spinal cord injury (SCI). The early stages of SCI are immediately marked by reduced energy expenditure, increased catabolic rate, and extensive nitrogen losses which may last from weeks to several months (29, 30, 43). Nitrogen losses following SCI are compounded by the sudden and complete disuse atrophy of muscles below the level of the injury, and these losses persist despite parenteral supplementation. Parenteral nutritional calculations in human acute SCI care are largely inadequate when based upon the commonly utilized Harris-Benedict equation (29, 43). In general, clinical reports indicate that SCI persons are at risk for a lifelong inability to maintain a neutral energy balance (e.g., Refs. 7, 29, 30, 47, 48). Nutritional deficits leading to an underweight body mass in SCI present a number of risk factors to the individual in both the acute and chronic phases of injury. Low body weight increases the risk of developing infection and prolongs the recovery process from major traumatic injury (13, 14). Furthermore, insufficient subcutaneous fat mass increases the risk of developing pressure ulcers (1, 45). The presentation of recurrent pressure ulcers, in turn, is a comorbidity that triggers proinflammatory cytokine release, which can exacerbate the cachexic state of the patient (8).

Our aim was to test fat and lean mass postinjury and the resulting risk for developing either excessive loss of fat mass (underweight) or the obesity-related metabolic syndrome due to excessive adiposity, in animals with chronic T3-level spinal cord transection. Specifically, we analyzed the whole body fat mass in vivo with NMR, for comparison with ex vivo fat pad weights and whole body weights after high thoracic spinal transection. In addition, we analyzed the daily caloric intake of chronic SCI animals, basal glucose, glucose tolerance, plasma insulin, and leptin, as well as post mortem levels of uncoupling protein-1 (UCP1) as a marker for thermogenesis within brown adipose tissue. This latter measure served as an indirect measure of thermogenesis in both groups of animals.

MATERIALS AND METHODS

All procedures were performed according to National Institutes of Health guidelines and were approved by the Institutional Animal Care and Use Committee at the Pennington Biomedical Research Center. Wistar female rats (n = 16; Harlan) were maintained in a temperature-controlled room on a 12:12-h light-dark cycle with unrestricted access to food and water. Animals were pair-housed until surgery, which occurred at 12 wk of age, after which animals were housed singly and observed daily. One group of rats was randomly assigned to receive a spinal cord transection centered at T2-T3 (n = 10), and the remaining rats (n = 6) were selected to serve as surgical controls. Body weights before surgery were recorded and tested to ensure that no significant weight difference existed between groups.

Surgical procedures and animal care. Anesthesia for all surgical procedures was Nembutal (60 mg/kg ip; Abbott Laboratories, Chicago, IL). Supplemental doses of all anesthetics were given as necessary to maintain areflexia. Before any surgical manipulation, the animal was administered ophthalmic ointment to both eyes, buprenorphine (0.1 mg/kg ip; Reckitt Benckiser Pharmaceuticals, Richmond, VA) to alleviate postoperative pain, and antibiotics (Baytril, 2.5 mg/ml concentration at 1 ml/kg sc; Bayer, Shawnee Mission, KS) to reduce postsurgical infection. The T2-T3 spinal cord was exposed

Address for reprint requests and other correspondence: G. M. Holmes, Pennington Biomedical Research Center, 6400 Perkins Rd., Baton Rouge, LA 70808 (e-mail: HolmesGM@pbrc.edu).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
through a midline incision over the vertebral column, after which the muscles were detached from the vertebrae. Subsequently, the T2 spinous process was removed with fine-tipped rongeurs to expose the T2-T3 spinal cord surface. The segment of the dorsal median vein that marked the boundaries of the lesion site was lightly cauterized, so as to limit bleeding, and the lesion site was irrigated with 2% lidocaine for 5 min. Spinal transection was performed at the rostral most T3 spinal segment with microscissors and subpial aspiration (T3 TX). Procedures for the sham animals were the same as for spinal injury, except that the spinal cord and surrounding dura mater were not disturbed after laminectomy. Once the surgical procedure was complete, the muscle tissue overlying the lesion site was closed in anatomical layers with Dexon II suture, and the skin was closed with 9-mm wound clips. Animals were administered warmed supplemental fluids (5 ml lactated Ringer solution) and placed in an incubation chamber maintained at 37°C until the effects of anesthesia had subsided.

Chronic care of both sham and injured animals used procedures described previously (6). Postoperatively, animals were kept in a warm environment and received subcutaneous supplementary fluids (5–10 cc lactated Ringer), analgesics (carprofen, 5 mg/kg ip; Pfizer Animal Health, Lititz, PA) once daily for 3 days and antibiotics (Baytril, 2.5 mg/kg) twice daily for 5 days after surgery. Body weights and the remaining Chow weight were recorded each morning for all animals, and bladder expression and cleaning of the hindquarters were performed at least twice daily in animals with transection SCI until the return of spontaneous voiding. The ventrum of sham animals was inspected daily without need for manual compression of the bladder. Once spontaneous voiding returned in rats with SCI, all animals were inspected only once daily after weighing. When necessary, animals were administered additional analgesics to minimize pain and discomfort and antibiotics for 5 days following the indication of a bladder infection. Two rats that received a spinal cord transection were removed from the study after developing chronic dermatitis.

Glucose tolerance testing and blood collection. An intraperitoneal glucose tolerance test (IPGTT) was administered to 24-h fasted animals. Each animal (n = 16) received a 2 g/kg body mass dose of 5% glucose solution intraperitoneally. Blood samples (0.5 ml) were collected from the tail of lightly restrained animals and analyzed with a commercially available glucose meter (Therasense Freestyle, Abbott Laboratories). Samples were drawn 10 min before injection of glucose (fasted baseline, FB) and at 15-min intervals for 75 min after injection. The area under the glucose tolerance test curve was calculated for IPGTT using the trapezium method.

Insulin assay. During blood collection at FB, 15, 45, and 75 min after glucose, an additional 100-µl sample was taken and stored on ice in 600-µl microcentrifuge tubes. Coagulated samples were centrifuged at 4°C (5 min at 2,100 g), blood serum was collected into fresh microcentrifuge tubes, stored (−20°C), and later analyzed for serum insulin concentration at each time point using ELISA (Ultrasonic sensitive rat/mouse insulin ELISA kit, Crystal Chem, Downers Grove, IL).

In vivo body composition analysis. Awake, unfasted rats were placed into the restraint tube of a Bruker minispec LF90 time domain NMR spectrometer (Bruker Optics, Billerica, MA). The restraint tube was adjusted to minimize movement by the animal without impairing respiration. The tube was placed, with the animal on a horizontally oriented axis, into the LF90, and fat mass, fat-free mass, and fluid were analyzed in triplicate. The entire length of the triplicate analysis took 4 min, after which the rat was removed from the restraint tube and returned to the home cage.

Basso, Beattie, Bresnahan locomotor rating. Locomotor performance was assessed by open field locomotion using the standard Basso, Beattie, Bresnahan (BBB) locomotor rating scale (5). Tests were administered at 72 h after surgery, and at once-a-week intervals for the duration of the experiment.

Post mortem tissue analysis and real-time PCR. Animals were rapidly euthanized by decapitation. The intercapacular brown adipose tissue (IBAT), and bilateral retroperitoneal and genital fat pads were removed and weighed. The IBAT was immediately placed into a polyethylene centrifuge tube, frozen on dry ice, stored (−80°C), and later analyzed for UCP1 mRNA using real-time-PCR.

RNA was isolated using Tri-Reagent (Molecular Research Center; Cincinnati, OH) and RNeasy Minikit procedures (Qiagen, Valencia, CA) and based on Primeaux et al. (42). Briefly, fresh tissue was homogenized in Tri-Reagent using a motorized tissue homogenizer, chloroform was added to lystate, and the mixture was centrifuged in phase-lock tubes to separate RNA. Ethanol was added to the upper aqueous phase, which was filtered by centrifugation. After several washes, the samples were subjected to an elution step using RNAase-free water. Reverse transcription (RT) was conducted using the high-capacity cDNA archive kit (Applied Biosystems, Foster City, CA). For RT, 2 µg of RNA from each sample was added to random primers (10×), dNTP (25×), MultiScibe reverse transcriptase (50 U/µl) and RT buffer (10×) and incubated in a thermal cycler (PTC-100, MJ Research, Watertown, MA) for 10 min at 27°C, then for 120 min at 42°C. Primers for UCP1 were taken from White et al. (49).

Primers for cyclophilin were designed using Primer Express (Applied Biosystems). The following primers were used for UCP1: 5'-GGACCTCAAAATGCCTTACAGGTTACG-3' and 5'-TCCGCTCTTTC-CACAGTGTG-3' and for cyclophilin: 5'-CCCCACCGTGTTCTTC-GACAT-3' and 5'-CTGTCGTGGTTGAACTTGTGCG-3'. For real-time PCR, SYBR Green 2× Master Mix (Applied Biosystems), forward and reverse primers (10 M), and RT product (10 ng) were added to a 384-well plate. The cycling parameters consisted of an initial 2-min incubation at 50°C, followed by 10 min at 95°C, then 15 s at 95°C and a 1-min annealing step at 60°C (40 cycles). A dissociation step (15 s at 95°C) was added following 40 cycles to determine specificity of primers. In this assay, the dissociation step confirmed the absence of nonspecific amplifications. Quantity of UCP1 mRNA was based on a standard curve and normalized to cyclophilin RNA (ABI Prism 7900 Sequence Detection System, Applied Biosystems).

Statistical analysis was performed using SPSS (SPSS Inc, Chicago, IL). Data for body weight change between groups and over time were analyzed by two-way ANOVA. Data for BBB were analyzed by one-way repeated-measures ANOVA, followed by Tukey post hoc test. Caloric intake, basal fasted blood glucose, insulin, glucose tolerance curves, NMR body composition, fat pad, brown adipose tissue, and UCP1 expression were analyzed by t-test. Significance was set at P < 0.05.

RESULTS

Assessment of successful spinal cord transection procedure. The BBB locomotor score of the control animals was not impaired following surgery and remained at the maximum possible score of 21 (Fig. 1). In the T3 TX rats, hindlimb function was limited to single hindlimb joint movement immediately after surgery. At day 63 postinjury, the locomotor score for these rats reached a plateau of 5.5 ± 0.9, which represents extensive range of movement in two joints and slight movement in a third. The difference in locomotor score was significantly different between sham and T3 TX groups for all test days [F(1,12) = 205.475, P < 0.05].

SCI changes ability to maintain body weight. Daily body weights from all experimental animals are plotted in weekly intervals, as change in weight from preoperative weight (Fig. 2). Surgical control rats receiving only a laminectomy (n = 6) displayed a significant decrease [F(18,240) = 7.546, P < 0.05] in weight of −6.0 ± 4.86 g 1 day after surgery. Control rats returned to preoperative levels by day 14 (2.16 ± 4.79 g difference from preoperation, P < 0.05) and had significant

AJP-Regul Integr Comp Physiol • VOL 293 • SEPTEMBER 2007 • www.ajpregu.org
weight gains thereafter. The body weight of T3 TX rats \((n=8)\) decreased below preoperative levels in the 1st wk after surgery to a difference from preoperative levels of \(-30.33 \pm 2.44 \text{ g}\) and remained below preoperative levels until stabilizing at preoperative levels at week 5 [not significant (NS), \(P>0.05\)]. After surgery, the body weight of T3 TX animals remained significantly lower than sham animals for the duration of the experiment \([F(1,12)=21.026, P<0.05]\).

Caloric intake is elevated in chronic SCI animals. During weeks 16–18, when body weights had stabilized, the daily caloric intake of standard laboratory chow was measured (Fig. 2, gray-shaded region). At the end of the 2-wk monitoring period, the cumulative caloric intake (Fig. 3A) was significantly greater in the T3 TX group \((t=2.254, df=12, P<0.05)\). Over the 2-wk monitoring period, this amounted to T3 TX rats consuming 19.4% more calories than sham animals, but without a significant increase in body weight \((P>0.05)\).

The mean energy intake (MEI) represents the daily average of kilocalories consumed per 100 g of body weight for each week that food intake was measured. The MEI for control animals was 20.69 \pm 1.0 kcal \(\text{day}^{-1}\text{100 g}^{-1}\) compared with T3 TX animals, which was 30.94 \pm 0.91 kcal \(\text{day}^{-1}\text{100 g}^{-1}\) for week 1. For week 2, the MEI was 20.26 \pm 0.90 and 29.65 \pm 1.60 for controls and T3 TX animals, respectively. As seen in Fig. 3B, the MEI of T3 TX animals was significantly higher for both week 1 \((t=5.64, df=12, P<0.05)\) and week 2 \((t=3.65, df=12, P<0.05)\).

Glucose tolerance and insulin sensitivity in chronic SCI. Basal blood glucose levels measured 4 h into the light cycle at 1 wk preoperatively and postoperative weeks 1 and 16 showed no significant difference in blood glucose between groups for any time point (Table 1, \(P>0.05\)). Presurgical blood glucose levels during IPGTT were not significantly different between animals assigned to either surgical group (data not shown). At 1 wk after surgery, there was no difference between groups in

---

**Fig. 1.** The mean BBB locomotor rating scores ± SE of rats tested before surgery (denoted as week 0) through 18 wk after surgery. Locomotor scores were significantly lower in the spinal cord injury (SCI) group (*\(P<0.05\)).

**Fig. 2.** Change in body weight after SCI expressed as the difference from preinjury weight. Control animals (Sham) did not lose weight after surgery, while spinal cord-transected rats (T3 TX) displayed a significant weight reduction immediately after surgery and did not return to preoperative weight until 5 wk after surgery (*\(P<0.05\)). The weekly difference in weight between groups was significantly different throughout the entire course of the study. Gray-shaded region denotes the period during which nightly food consumption was measured.

**Fig. 3.** Effect of chronic injury on the caloric intake of standard laboratory chow (Purina #5001). A: animals with T3 TX consumed a greater nightly number of calories. This difference in caloric intake was significantly different from control animals by day 14 (*\(P<0.05\)). B: daily mean energy intake, calculated as kilocalories consumed per day per 100 grams body weight for each week that food intake was measured, is significantly higher in long-term SCI rats compared with controls (*\(P<0.05\)).
blood glucose (Fig. 4A) or in the area under the curve (AUC) of the IPGTT (Fig. 4C, \( P > 0.05 \)). During the IPGTT test administered at 16 wk after surgery, the T3 TX rats displayed a lower blood glucose level by the 30-min time point that remained lower throughout the remainder of the testing period (Fig. 4B). Subsequently, the AUC was significantly lower in the T3 TX rats (\( t = 2.55 \), \( df = 12 \), \( P < 0.05 \); Fig. 4C). Basal insulin levels did not differ in the T3 TX rats compared with sham rats (\( t = 1.94 \), \( df = 12 \), \( P > 0.05 \)). The insulin response to IPGTT was lower at all time points in the T3 TX rats (Fig. 5A), and the insulin AUC for the entire sampling period was significantly lower (\( t = 3.13 \), \( df = 12 \), \( P < 0.05 \); Fig. 5B).

**Body composition and UCP1 RNA expression after SCI.** The in vivo measurement of lean tissue mass was significantly lower in T3 TX rats as measured by NMR at the conclusion of monitoring food intake (\( t = 5.54 \), \( df = 12 \), \( P < 0.05 \); Fig. 6A). When calculated as the percentage of the whole body weight, lean mass in T3 TX animals (68.01 ± 1.63\%) was not different from control animals (67.00 ± 1.28\%, \( P > 0.05 \)). The corresponding ratio of fat mass to lean tissue was even further reduced in T3 TX animals compared with controls (\( t = 4.40 \), \( df = 12 \), \( P < 0.05 \); Fig. 6B). Upon death, animals with T3 TX had significantly lower retroperitoneal-fat pad (\( t = 3.82 \), \( df = 12 \), \( P < 0.05 \)) and gonadal fat pad (\( t = 3.34 \), \( df = 12 \), \( P < 0.05 \)) weights (Fig. 6C), while IBAT weight remained unchanged (\( P > 0.05 \)). Lastly, the expression level of UCP1 mRNA in the IBAT from rats in the T3 TX group (0.55 ± 0.06, means ± SE, AU) was significantly lower than that of surgical controls (1.09 ± 0.08, means ± SE, AU; \( t = 5.91 \), \( df = 12 \), \( P < 0.05 \)).

**DISCUSSION**

In the present study, we demonstrate that 1) chronic low body weight, as is seen in a subset of the human SCI population, occurs in a rodent model of chronic SCI; 2) despite an increase in cumulative caloric intake in chronic SCI, low body weight persists in injured animals; 3) white adipose fat mass is lower in SCI; 4) basal glucose levels are unchanged, yet glucose tolerance is significantly enhanced in chronic T3 SCI animals; 5) basal insulin levels are lower in chronic T3 SCI animals; and 6) thermogenesis, as measured by UCP1 RNA, was lower in SCI animals. These data provide the first direct evidence that high thoracic SCI triggered a prolonged postinjury loss of body weight, including fat mass, which is not due to hypophagia or an increase in sympathetically mediated thermogenesis but exists despite significant hyperphagia by injured animals.

Our conclusions are based upon the following observations. Animals in our injury model received a spinal transection at the third thoracic spinal segment (T3 TX) and were maintained for

---

**Table 1. Basal fasted glucose in control and spinally transected rats**

<table>
<thead>
<tr>
<th></th>
<th>Sham</th>
<th>T3 TX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative glucose</td>
<td>61.0±4.4</td>
<td>63.8±2.4</td>
</tr>
<tr>
<td>1 wk postop glucose</td>
<td>90.4±9.2</td>
<td>91.0±2.9</td>
</tr>
<tr>
<td>16 wk postop glucose</td>
<td>78.0±4.7</td>
<td>75.9±2.9</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SE. Basal fasted glucose values are given in milligrams per deciliter.

---

Fig. 4. Effect of chronic injury on the IPGTT serum glucose levels at baseline (B) immediately before glucose injection (2 mg/kg ip) and at 15-min intervals after injection. A: at 1 wk post-SCI, animals with T3 TX did not show any difference in glucose tolerance compared with control animals (\( P < 0.05 \)); B: at 16 wk post-SCI, glucose clearance was more rapid in the T3 TX animals. C: glucose clearance was significantly enhanced (\( *P < 0.05 \)) in T3 TX animals as measured by area under the curve (AUC) for the entire glucose tolerance test.
18 wk postinjury. Transection at spinal T3 produced a permanent paraplegia in laboratory rats and segmentally mediated locomotor reflexes were consistently observed. Although locomotor recovery was not the focus of the present experiment, locomotor scores were collected as a measure of spontaneous muscle activity and movement below the level of the lesion and as a measure of lesion completeness. The BBB scores provide a common index of motor paralysis for comparison, despite the inherent complexity of assessing locomotor function following SCI, which has recently been addressed (36). In the present group of transected rats, BBB score was greater than in previously published data, which centered transection at lower thoracic levels (6, 35). However, the animals with T3-level injury displayed qualitatively greater trunk instability and diminished forelimb ambulation than that which is typically observed in the more common T9-level injury. Though incapable of weight support, extensive movement of all three hindlimb joints was observed in our animals. The residual motor activity in the hindlimbs of T3-transected animals may be sufficient enough to merit consideration in future experiments regarding the, albeit diminished, metabolic requirements of the muscle mass below the lesion.

Our weekly body weight data demonstrate that the weight disparity between SCI and non-SCI rats continued to increase throughout the experiment. This reflected the rate of increase in the non-SCI control animals, as the SCI body weights were not significantly different from preinjury levels beginning 5 wk postoperatively. Our observations suggest that SCI rats defend a set body weight. Specifically, we observed that SCI rats that were fasted overnight for basal glucose testing returned to prefasted body weight at the same rate as similarly fasted sham controls. Thus, while SCI rats maintained a lower body weight, they were capable of rapidly compensating for reduced energy intake imposed by fasting. This effect is consistent with previous reports that fasting-induced weight losses in neurally intact animals are quickly reversed once feeding is reestablished (26).

Evidence from our data plotting the cumulative caloric intake of T3 TX and control animals over a 2-wk period indicates that the long-term injured animals were consuming a greater number of calories than controls. Postinjury muscle atrophy demonstrated previously (20, 24, 34, 44) and confirmed in our own NMR data, which is coupled with a reduction in energy expenditure (31), would predict a commensurate reduction in ad libitum feeding; however, during our monitoring of feeding, we observed the opposite. This increased caloric consumption was more clearly evident in the mean energy intake, as long-term injured animals were consuming more calories despite a lower body weight. In separate animal studies from our laboratory monitoring acute-SCI rats, the caloric intake from ad libitum feeding in T3-transected rats returns to levels comparable to surgical shams within 1 wk after surgery. As with our present data, body weight in these acute SCI animals remained below preinjury levels through the end of the 3-wk observation period and was 20% below the cohort of surgical controls (G. M. Holmes, unpublished observations).

In the present experiment, we were unable to determine whether the observed cumulative caloric intake reflected a continuing attempt to replenish diminished energy stores, or the defense of a new body weight set point that resulted from prolonged hypermetabolism. The repeated application of core temperature recording and indirect calorimetry to monitor the metabolic status of animals during the postinjury period would resolve questions about a prolonged hypermetabolic state. However, clinical evidence from the SCI population (29, 30, 43) does not favor the hypothesis of hypermetabolism for any time point over the course of this study. Furthermore, changes in core body and surface temperature have been recorded in a rat T4 transection model of SCI (32), in which core tempera-
tured dropped the day after surgery and stabilized within 3 days at a lower basal level. Those authors concluded that the resolution of spinal shock, coupled with increased IBAT thermogenesis, led to the partial restoration of core temperature. The elevation in tail surface temperature was a likely cause of the reduced core temperature since blood flow to the tail is a major thermoregulatory mechanism in the rat (17, 39). Loss of supraspinal control over sympathetic vasoconstriction (see Ref. 19 for a review) is the likely mechanism for the chronic elevation in peripheral temperatures following spinal transection (32) and not thermogenesis.

The compensatory role of IBAT thermogenesis proposed by Laird and colleagues (32) in their study remains plausible since the sympathetic preganglionic innervation of the stellate ganglion, which innervates the IBAT, is located within the mid- to upper-thoracic spinal cord (11). The injury model in that study (32) may have spared a sufficient number of preganglionic neurons to permit compensatory IBAT activation. However, without some measure of activation of IBAT tissue, the conclusions of compensatory IBAT thermogenesis following any model of mid- to upper-thoracic SCI remains speculative. One such measure involves UCP1 expression in IBAT tissue since UCP1 is the mechanism responsible for thermogenesis in IBAT (reviewed in Ref. 2). Our observed reduction in IBAT UCP1 expression after chronic SCI suggests that IBAT-mediated thermogenesis was severely compromised, most likely occurring from the moment of injury, as most sympathetic preganglionic neurons were at, or below, the level of our T3 injury. It should be noted that IBAT ablation in otherwise neurally intact animals induces obesity due to decreased thermogenesis (25). Ultimately, the proposed changes in sympathetic outflow to IBAT after acute and chronic SCI require confirmation through direct electrophysiological testing of sympathetic neural activity.

Our measures of glucose tolerance and insulin sensitivity suggest highly efficient carbohydrate homeostasis, which would be expected from lean subjects (18, 23). Our analysis of both in vivo body composition at 16 wk after surgery and post mortem weights of gonadal and retroperitoneal fat pads indicated that the fat mass of chronic SCI rats was significantly reduced. When available carbohydrates do not meet energy demand, triglycerides stored within the white adipose tissue are converted to free fatty acids, and fat mass can rapidly be depleted during an imposed fasting period (4). Surprisingly, our observed reduction in the fat mass of SCI rats occurred despite a higher cumulative caloric intake. In neurally intact animals, lipid mobilization in white adipose tissue is mediated by the sympathetic innervation of white fat (3), while denervation of white fat diminishes fat mobilization (21, 46). Fasting increases both norepinephrine turnover (37) and noradrenergic innervation of white adipose tissue (22). Because sympathetic outflow to white fat would presumably be diminished after SCI, it would be expected that white adipose tissue would increase in size after injury, but such was not the case.

Accidental trauma, including neurotrauma, and surgical procedures are considered clinically significant stress events. Both short- and long-term effects of single or repeated restraint stress on food intake, body weight, and body composition have been reported in rodents (27, 28), whereby adult rats exposed to repeated restraint stress show a transient reduction in food intake, coupled with a prolonged reduction in body weight (28). The stress-related neuropeptide, CRF, has been shown to centrally influence in vivo gastrointestinal function (33, 38), which prompted Harris and coworkers to suggest that CRF-mediated reduction in gastrointestinal motility and activation of the hypothalamic-pituitary-adenal axis initiated the short-term hypophagia following restraint stress. Other studies suggest that repeated restraint stress leads to an increase in the intake of highly palatable foods or “comfort foods” and an increase in circulating corticosterone (15, 16, 40). In rats with SCI, serum corticosterone levels are increased over a 28-day period (41), which may explain, at least in part, why rats with SCI exhibit a long-term increase in food consumption. However, the consumption of “comfort foods” in our paradigm was not directly examined. We believe that the post-SCI effect of chronic stress hormones on the complex interplay between body composition, gastric reflex function, and feeding behavior may be important to our observations and remains to be systematically investigated.

In the chronic stages of SCI, muscle atrophy inherent in long-term immobility leads to a maintained reduction in resting energy expenditure (7, 9, 10). Although the injured animals became quite well adapted to forelimb locomotion, they clearly exhibited disuse atrophy of the musculature innervated...
below the T3 lesion and are very likely to have experienced a concomitant reduction in resting energy expenditure. This reduction in resting energy expenditure is considered a causative factor in the prevalence of increased adiposity in a majority of the human SCI population (47, 48) and requires further investigation in our model. Given the broad variability in the human cafeteria-style diet, compared with the strict standard chow diet of the typical laboratory animal, it is very likely that dietary composition is responsible for the contrasting alterations in body composition seen clinically and experimentally. Although adjustments in postinjury dietary intake are often prescribed for the clinical SCI population that are at risk for obesity (12), the form and the magnitude of these adjustments are often based upon guidelines for the able-bodied population. Potential changes in alimentary absorption of nutrients, as well as physiological responses to macronutrients may necessitate dietary guidelines that are specific to the SCI population. Without fully developed animal models, translational research leading to appropriate health and nutritional management strategies remains underdeveloped for the SCI population.

ACKNOWLEDGMENTS

The authors wish to thank G. A. Bray in the Dietary Obesity Laboratory for commentary on the preparation of this report and for access to the RT-PCR resources within his laboratory. C. Morrison for valuable suggestions and advice. We thank Dr. Barry Robert, Cynthia Kloster and Hsin (Frank) Hsu for their technical assistance.

GRANTS

This work was supported by NINDS 49177 (GMH), S. Primeaux and the Dietary Obesity Laboratory are supported by NIDDK 32089 (awarded to GA Bray) and the Pennington Medical Foundation.

REFERENCES