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Original Article

The thermic response to food intake in persons with thoracic spinal cord injury

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Abstract. [Purpose] To investigate the influence of the level of spinal cord injury on the thermic effect of food intake (TEF) in persons with thoracic spinal cord injury. [Subjects and Methods] Seven male subjects with spinal cord injury (SCI; age, 40 ± 6 years) and six able-bodied subjects (AB; age, 37 ± 8 years) volunteered to participate in the present study. The subjects consumed an identical test meal consisting of 7.9 kcal/kg of body weight. Energy expenditure and plasma norepinephrine concentrations were measured over a 3-hour period. [Results] The adjusted TEF at 60 min was almost the same among the three groups [AB, SCI with high thoracic cord (T5–6) injury (HSCI), and SCI with low thoracic cord (T9–12) injury (LSCI)]. Although the LSCI group had almost the same adjusted TEF at 120 min as the AB group, the adjusted TEF at 120 min of the HSCI group was significantly lower than that of the AB group. The changes in plasma norepinephrine concentration and heart rate in response to food intake were similar among the three groups. [Conclusion] SCI at the T5–6 level results in a lower TEF due to sympathetic decentralization.

Key words: Energy expenditure, Obesity, Sympathetic nervous system

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INTRODUCTION

Total daily energy expenditure consists of three factors: resting metabolic rate (RMR), thermic effect of food intake (TEF), and physical activity[1)]. In general, RMR is the most important component accounting for 60–75% of total daily energy expenditure. TEF is defined as the increase in energy expenditure in response to food intake and it accounts for 10% of total daily energy expenditure[1)]. It has been accepted that sympathetic nervous system activity (SNA) plays a role in regulation of energy expenditure after food intake, because the thermic response is reduced by β-adrenergic blockade[2, 3)]. Previous studies have shown that food intake increases energy expenditure, and is accompanied by an increase in whole body SNA (for example, skeletal muscle, abdominal tissue, adrenal medulla, and kidneys)[2, 4, 5)].

Preganglionic fibers of the sympathetic nervous system exit from the spinal cord between T1 and L2 and synapse with their respective ganglion, at which postganglionic neurons originate and eventually project to their target organs[6)]. The sympathetic nerves originating from T1 to T6 mainly innervate the organs of the head and upper thorax, such as the lungs and heart, while the sympathetic nerves originating below T7 mainly innervate the organs in the lower thorax, such as the kidneys and adrenal glands. Furthermore, the sympathetic nerves innervating the adrenal medulla originate between the T5 and T9 segments[7)]. Because supraspinal control of sympathetic preganglionic neurons is interrupted in persons with cervical and higher thoracic spinal cord injury (SCI), SCI often results in autonomic dysfunction as well as motor and sensory deficits in the upper and/or lower extremities. Several studies have reported that SNA is decreased in subjects with cervical and higher thoracic cord injury as compared to able bodied subjects (AB)[8–11)], and this decrease in SNA may blunt TEF, as reported in elderly persons[12)].

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Obese subjects usually have a lower TEF than lean subjects[13–15]. It is evident that subjects with SCI have a higher fat mass and a lower lean muscle mass than AB subjects, even though they have a normal body mass index (BMI) value[16]. Therefore, SCI patients may have a lower TEF due to reduction in lean muscle mass as well as autonomic dysfunction, which would increase their risk of developing obesity, and obesity-related disorders, such as type 2 diabetes, cardiovascular diseases, and dyslipidemia. However, little is known about TEF in subjects with higher thoracic SCI (HSCI) and lower thoracic SCI (LSCI). If SNA plays an important role in the regulation of TEF, subjects with HSCI would exhibit a greater decrease in TEF than LSCI and AB subjects. To test this hypothesis, we examined the time courses of the TEF among the three groups of subjects (AB, HSCI, and LSCI) and assessed the relative contribution of the level of spinal cord injury to the TEF.

SUBJECTS AND METHODS

Seven male subjects with SCI and six AB subjects (controls), who were age- and gender-matched, participated in this study. All the SCIs were of traumatic origin and the level of injury in the subjects with SCI was between T5 and T12 (Table 1). All the persons with paraplegia were examined clinically and neurologically to classify the extent of spinal cord injury according to the American Spinal Injury Association (ASIA) Impairment Scale grade (AIS). Six individuals were classified with a complete injury (AIS A), and one with an incomplete injury (AIS B). Neurological examinations were performed by an approved physical therapist working in the rehabilitation hospital. None of the subjects had cardiovascular or pulmonary diseases, or diabetes mellitus. The experimental procedures of this study were approved by the ethical committee of the Graduate School of Integrated Arts and Sciences, Hiroshima University, and the study was performed in accordance with the ethical principles of the Declaration of Helsinki. All the subjects gave their written, informed consent before participating in the present study.

All experiments were performed between 8:30 A.M. and 12:30 P.M. after an overnight fast of 12 hours. Subjects were instructed not to exercise and to refrain from alcohol, caffeine, and smoking for 24 hours preceding the experiments. Some of the subjects took medication to suppress involuntary muscle spasms. They were asked to refrain from taking their medication on the day to minimize possible confounding effects on energy expenditure. All the subjects were also instructed to empty their bladders prior to the experiments. BMI was calculated as body weight (kg) divided by height squared (m^2). Each subject sat on their own wheelchair or a prepared chair during the experiment in thermoneutral environment (temperature, 23–27 °C; relative humidity, approximately 60%). After 15 min of quiet rest, expiration gas was analyzed with a gas analyzer (AE-300s Minato Medical Science Co., Ltd, Japan) to measure oxygen consumption (VO_2) and carbon dioxide production (VCO_2). At the end of the resting period, a venous blood sample was taken from an antecubital vein to measure plasma catecholamine concentrations.

After meal consumption, indirect calorimetry was performed over 3 hours. Blood was sampled every hour. Plasma catecholamine concentrations were analyzed by a HPLC method (Fukuyama Medical Laboratory Co., Ltd, Japan). Heart rate (HR) was measured continuously both at rest and during the postprandial period with a heart rate monitor (Polar S610i, Japan).

Energy expenditure was calculated from VO_2 and VCO_2 using the formulas outlined by Frayn[17]. The TEF was calculated as the area under the curve above the baseline level for 3 hours after food intake and expressed as the absolute and adjusted values against body weight.

The test meal, which was consumed within 10 min by the subjects, consisted of portions of Calorie Mate BLOCK and one Calorie Mate CAN (Otsuka Pharmaceutical Co., Ltd, Japan). The test meal size and the number of BLOCKs were determined using subjects' body weights, to achieve the same consumption of 7.9 kcal/kg of body weight[18]. Therefore, total caloric content consumed varied from 435 kcal to 670 kcal, with an energy composition of 49–52% carbohydrate, 36–40% fat, and 11–12% protein.

The subjects with SCI were divided into the two groups [HSCI (T5–6) and LSCI (T9–12)] according to the level of spinal cord injury. The physiological characteristics (age, body weight, height, and BMI) were compared among the three groups (AB, HSCI, and LSCI) by one-way ANOVA and Dunnett's post hoc test. If either the normality or the equal variance test failed, the Kruskal-Wallis test was performed. The differences in the responses of TEF, plasma norepinephrine, and HR among the three groups were examined using two-way ANOVA with repeated measures (one factor of time repetition). If the main effect and interaction were significant, the mean values at a given time were compared using Dunnett's post hoc test. All statistical analyses were performed using SigmaPlot® version 12.5 (Systat Software, San Jose, CA, USA). Statistical significance was accepted for values of $p<0.05$ in all cases.

RESULTS

The anthropometric characteristics of the three groups (AB, HSCI, and LSCI) are shown in Table 1. There were no significant differences in age, body weight, height, and BMI among the three groups.

Table 2 shows the average data of the resting energy expenditure (REE, kcal/min), absolute and adjusted TEF over 2 hours, and meal size of the three groups. The adjusted TEF over 2 hours and TEF (%meal) were significantly smaller ($p<0.05$) in the HSCI subjects than in the AB subjects.

The time courses of the average changes in absolute and adjusted TEF following food intake were compared among the three groups (Table 3). Two-way ANOVA of absolute TEF indicated a significant main effect of time ($p<0.05$), but not of group. Two-way ANOVA of adjusted TEF indicated significant main effects of group and time. The group × time interaction was also significant. *Post hoc* analyses revealed that the adjusted TEF at 120 min was significantly smaller in the HSCI group than in the AB group, whereas the adjusted TEF was the same in both the AB and LSCI groups.

Table 1. Group averages of physiological characteristics

	AB (n=6)	HSCI (n=3)	LSCI (n=4)
Age (years)	37.2 ± 7.6	40.0 ± 8.5	39.8 ± 4.9
Weight (kg)	75.7 ± 9.6	62.7 ± 11.6	65.5 ± 7.3
Height (cm)	173.7 ± 7.3	173.0 ± 6.1	174.8 ± 5.1
BMI (kg/m^2)	25.0 ± 2.3	21.0 ± 4.3	21.5 ± 2.5

Values are mean ± SD.
AB: able-bodied subjects; SCI: spinal cord injury; HSCI: higher thoracic SCI subjects; LSCI: lower thoracic SCI subjects

Table 2. Resting energy expenditure, thermic effect of food, and meal size during the TEF study

	AB (n=6)	HSCI (n=3)	LSCI (n=4)
REE (kcal/min)	1.14 ± 0.07	0.96 ± 0.08	1.07 ± 0.05
Postprandial EE (kcal/min)	1.51 ± 0.09	1.15 ± 0.12	1.34 ± 0.05
TEF (kcal for 2h)	44.5 ± 4.9	23.2 ± 5.8	32.0 ± 0.3
Adjusted TEF against body weight	0.59 ± 0.05	0.36 ± 0.06 *	0.49 ± 0.04
TEF (%meal)	7.4 ± 0.06	4.6 ± 0.07 *	6.2 ± 0.04
Meal size (kcal)	602.5 ± 30.5	501.7 ± 55.3	521.3 ± 28.8
Meal size/REE	37.0 ± 1.5	36.9 ± 4.7	34.1 ± 2.1

Values are mean ± SEM. REE: resting energy expenditure; TEF: thermic effect of food intake; AB: able-bodied subjects; SCI: spinal cord injury; HSCI: higher thoracic SCI subjects; LSCI: lower thoracic SCI subjects
*Significantly lower ($p<0.05$) than AB

Table 3. The time courses of absolute TEF and adjusted TEF in the three groups

	Absolute TEF (kcal)			Adjusted TEF (kcal/kg)		
	60 min	120 min	180 min	60 min	120 min	180 min
AB (n=6)	19.1 ± 2.0	25.4 ± 3.0	17.8 ± 1.2	0.25 ± 0.03	0.33 ± 0.03	0.24 ± 0.02
HSCI (n=3)	13.0 ± 2.3	10.2 ± 4.5	11.7 ± 4.2	0.21 ± 0.05	0.15 ± 0.06 *	0.17 ± 0.05
LSCI (n=4)	13.7 ± 1.0	18.4 ± 1.1	14.3 ± 2.3	0.21 ± 0.01	0.29 ± 0.03	0.22 ± 0.03

Values are mean ± SEM.
AB: able-bodied subjects; SCI: spinal cord injury; HSCI: higher thoracic SCI subjects; LSCI: lower thoracic SCI subjects
Because the energy expenditure in one subject with HSCI involved an artifact at 180 min, we removed his TEF from pooled data at 180 min and did not perform statistical analysis for the absolute and adjusted TEF at 180 min.
*Significantly lower ($p<0.05$) than in AB (two-way ANOVA)

Table 4. The time courses of plasma norepinephrine concentration and HR in the three groups

	Norepinephrine concentration (ng/ml)				HR (bpm)			
	baseline	60 min	120 min	180 min	baseline	60 min	120 min	180 min
AB (n=6)	0.33 ± 0.05	0.43 ± 0.08	0.33 ± 0.05	0.47 ± 0.11	65.9 ± 3.3	70.2 ± 4.2 †	68.6 ± 2.8 †	65.9 ± 2.1
HSCI (n=3)	0.38 ± 0.16	0.46 ± 0.13	0.45 ± 0.15	0.43 ± 0.07	65.2 ± 2.5	75.7 ± 7.0 †	76.2 ± 8.1 †	70.2 ± 4.2
LSCI (n=4)	0.44 ± 0.02	0.54 ± 0.05	0.50 ± 0.02	0.45 ± 0.03	73.3 ± 6.6	77.3 ± 7.3 †	76.5 ± 8.0 †	72.3 ± 6.4

Data are shown in mean ± SEM. Baseline means the resting period.
AB: able-bodied subjects; SCI: spinal cord injury; HSCI: higher thoracic SCI subjects; LSCI: lower thoracic SCI subjects
†Significant differences from the resting value ($p<0.05$, two-way ANOVA)

Table 4 shows the time courses of the postprandial changes in plasma norepinephrine concentration and HR among the three groups. Two-way ANOVA of norepinephrine levels indicated no significant main effects of group or time. Two-way ANOVA of HR identified a significant main effect of time ($p<0.05$), but not of group. In all the three groups, HR had increased ($p<0.05$) at 60 min and 120 min, compared to rest, but had returned to the baseline level at 180 min.

DISCUSSION

The present study has examined whether the level of spinal cord injury affects the thermic response to food intake. The major findings of this study are that: 1) the adjusted TEF at 60 min was the same among the subjects, irrespective of the presence or the absence of SCI; 2) the adjusted TEF at 120 min was significantly smaller in the subjects with HSCI than AB subjects, but was not different between the LSCI and AB subjects. Taken together, it is likely that thoracic SCI at a lesion level T5–6 may decrease the thermic response to food intake.

Generally, it is known that TEF consists of obligatory and facultative components[3]. The obligatory component is the energy that is required for nutrient digestion, absorption, transport, and storage. It may be mainly modulated by parasympathetic nervous system activity[3, 19]. The facultative component, which occurs in several tissues especially in skeletal muscles, is the energy spent in excess of the obligatory requirements[2–4]. It may be mediated in part by sympathoadrenal system activity[2, 3]. The energy expenditure in skeletal muscles stimulated by an increase in muscle SNA contributes substantially to the whole-body TEF in humans[20, 21]. Despite a number of studies of the TEF, the time courses of the two components during the postprandial period remains to be established.

Based on the time courses of the TEF measured in this study, two possible conclusions can be drawn from the differences in the adjusted TEFs of the three groups (AB, HSCI, and LSCI). First, the adjusted TEF at 60 min was not different among the three groups, suggesting that the TEF at 60 min may be mainly attributable to the obligatory component. This conclusion seems reasonable, because these all of the subjects had an intact parasympathetic nervous system. It is additionally supported by a previous finding that the obligatory thermogenesis to food intake is not affected by the SCI[22]. Second, the adjusted TEF at 120 min was blunted in HSCI, compared to AB, suggesting that the TEF at 120 min may correspond to the facultative component, which is influenced by sympathetic nervous system. The adjusted TEF at 120 min was not significantly different between AB and LSCI. Thus, it is conceivable that the extent of the facultative component may depend on the level of injury. The decreased SNA due to the sympathetic decentralization may affect, at least partly, the facultative component of the subjects with HSCI.

Another possible explanation for the reduction in the facultative component of adjusted TEF may be a decrease in the lean muscle mass. Several studies have shown that TEF is higher in lean subjects than obese subjects, implying that skeletal muscle mass plays a role in increasing energy expenditure after meal consumption[13–15]. Furthermore, Astrup et al. suggested that the facultative TEF occurs mainly in skeletal muscles, while the contribution of fat tissues to facultative TEF is negligible[2, 21]. Based on these findings, it is likely that the amount of lean muscle mass is an important physiological determinant of facultative TEF. In SCI, body composition drastically changes with a loss of lean muscle mass as well as bone below the level of injury and an increase in the total fat mass[23, 24]. Therefore, it is likely that a decrease in lean muscle mass would result in a reduction in the facultative TEF.

Several limitations of this study should be mentioned. First, the sample size used in this study was small. Nevertheless, a significant difference was found in the changes in adjusted TEF, in addition, the present TEF values were approximately the same as those previously reported for SCI[25]. Second, the forearm venous norepinephrine concentration may be an inaccurate measure of the influence of the sympathetic decentralization of HSCI and LSCI on SNA below the level of injury. Forearm venous norepinephrine concentration may not reflect whole body SNA but suggest regional SNA[26]. Karlsson et al. found that leg norepinephrine levels were significantly lower in SCI subjects (C7–T4) than those in AB subjects, while arm norepinephrine levels were almost the same[27]. Third, we did not directly measure lean muscle mass, although the amount of lean muscle mass is one of the important physiological determinants of total TEF. Fourth, we did not measure core body temperature in the subjects with SCI. When drum temperature was measured in some AB subjects, drum temperature did not change after food intake, suggesting that food-intake thermogenesis may not affect core body temperature. Finally, we did not know whether all the six subjects with AIS A had autonomic complete dysfunction.

It is likely that thoracic SCI at a lesion level of T5–6 causes a lower thermic response to food intake due to sympathetic decentralization. It is known that measured RMR is lower in persons with tetraplegia and paraplegia than in AB subjects, probably due to decreased SNA[22]. Thus, in addition to lower RMR, reduced thermic response to food intake may also be a causative factor in the development of obesity in SCI, particular in HSCI.

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