Repeated Thermal Therapy Diminishes Appetite Loss and Subjective Complaints in Mildly Depressed Patients

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Objective: We observed that repeated thermal therapy improved appetite loss and general well-being in patients with chronic heart failure. The purpose of this study is to clarify the effects of repeated thermal therapy in mildly depressed patients with appetite loss and subjective complaints. **Methods:** Twenty-eight mildly depressed inpatients with general fatigue, appetite loss, and somatic and mental complaints were randomly assigned to thermal therapy group ($n = 14$) or nonthermal therapy group ($n = 14$). Patients in the thermal therapy group were treated with 60°C far-infrared ray dry sauna for 15 minutes and were then kept at bed rest with a blanket for 30 minutes once a day, 5 days a week for a total of 20 sessions in 4 weeks. **Results:** Four weeks after admission, somatic complaints, hunger, and relaxation scores significantly improved ($p < .001$, $p < .0001$, $p < .0001$, respectively) and mental complaints slightly improved ($p = .054$) in the thermal therapy group compared with the nonthermal therapy group. Furthermore, the plasma ghrelin concentrations and daily caloric intake in the thermal therapy group significantly increased compared with the nonthermal therapy group ($p < .05$). **Conclusions:** These findings suggest that repeated thermal therapy may be useful for mildly depressed patients with appetite loss and subjective complaints. **Key words:** depressed patients, repeated thermal therapy, far-infrared ray dry sauna, appetite loss, subjective complaints, plasma ghrelin concentrations.

ICD = International Classification of Disease; **BMI** = body mass index; **CMI** = Cornell Medical Index; **SDS** = Self-Rating Depression Scale; **VAS** = visual analog scale.

INTRODUCTION

We observed that repeated thermal therapy using far-infrared ray dry sauna improved the quality of life by permitting an increase in daily activities, enhancing appetite, and improving the general well-being in patients with chronic heart failure (1). A chronic exposure to far-infrared ray radiation caused an increased weight gain in growing rats (2). However, there is no published human controlled study that investigated the relationships between repeated thermal therapy and improvement of appetite loss.

Ghrelin, a novel growth hormone-releasing peptide isolated from human and rat stomachs, stimulates food intake, body weight gain, and growth hormone secretion when administered centrally or peripherally (3–5). We found that repeated thermal therapy using far-infrared ray dry sauna increased plasma ghrelin concentrations and daily caloric intake in normal healthy people (6). We hypothesized that 1) repeated thermal therapy may be effective in mildly depressed patients with appetite loss and subjective complaints, and 2) the plasma ghrelin may be associated with the improvement of appetite loss.

METHODS

Subjects

Thirty-eight patients with general fatigue, appetite loss, and somatic and mental complaints consulted the outpatient clinic of our department between March 2002 and June 2004. Thirty-two agreed to our treatment protocol. Four patients who had a body mass index (BMI) of 26 kg/m^2 or greater were excluded, and the remaining 28 were entered into this study. Laboratory examinations, chest radiograph, abdominal ultrasound and computed tomography, and gastrofiberscope examination revealed no abnormal findings. They met the criteria of mild depressive episode with somatic symptoms according to the International Classification of Disease, 10th Revision (ICD-10) (7). The patients were randomly assigned to groups with the constraint that thermal therapy group ($n = 14$) or nonthermal therapy group ($n = 14$) were comparable in age, body weight, and illness characteristics. There were no significant differences in age, BMI, gender, or duration of illness between the two groups (Table 1). Furthermore, there were no significant differences in median and quartile of BMI (thermal therapy group, 21.9 and 6.9 kg/m^2; nonthermal therapy group, 21.6 and 4.3 kg/m^2). They were not taking medication at initial consultation and were not medicated during this study. Written informed consent was obtained from all patients. The Ethics Committee of the Faculty of Medicine, Kagoshima University approved the experimental protocol.

Thermal Therapy

A far-infrared ray dry sauna system (Olympia Co., Miyazaki, Japan) was used for thermal therapy (1,8,9). An approximately 15-m^3 sauna room was heated with a far-infrared ray device to maintain the surface temperature of the bed in the room at 60°C.

The patients, wearing a gown and underwear, were placed in a supine position on a bed for 15 minutes, then moved into a room maintained at 28°C and kept warm for 30 minutes wrapped in a blanket. Patients were weighed before entry into the sauna room and after postsauna warming. Body weight loss after thermal therapy was regarded as equal to the amount of perspiration, and this was replenished with water to prevent dehydration.

Study Protocols

All patients were admitted to our hospital and fed identical meals of 2000 calories a day during this study. Thermal therapy was performed once a day, 5 days a week on Monday through Friday for a total of 20 sessions during 4 weeks. The therapy was performed between 2:00 PM and 5:00 PM, and the schedule for individual patients was adjusted in a systematic way during these hours. During this study, the patients in the nonthermal therapy group were placed in a supine position on a bed in a temperature-controlled (24°C) room for 45 minutes once a day in the afternoon. The patients in the thermal therapy group took a shower 1 hour after thermal therapy and those in nonthermal therapy group also took a shower between 5:00 PM and 6:00 PM, and Japanese-type baths were off limits during this study. The patients participated in the same rehabilitation programs, including physical therapy and occupational therapy, once a day in the morning 5 days a week for 4 weeks.

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TABLE 1. Characteristics of Subjects

	Nonthermal Therapy Group (n = 14)	Thermal Therapy Group (n = 14)
Male/female	6/8	6/8
Age	38.6 ± 12.3	38.2 ± 14.8
Duration of illness (month)	8.7 ± 7.0	9.7 ± 7.8
BMI (Kg/m^2)	21.5 ± 3.3	20.9 ± 3.7

Mean ± standard deviation are presented. There were no significant differences in all parameters between the two groups.

Assessment of Subjective Symptoms

Somatic and mental complaints and depressive mood were evaluated by Japanese versions of the Cornell Medical Index (CMI (10)) and the Zung Self-Rating Depression Scale (SDS (11)), respectively. The CMI and SDS are frequently used in the field of Japanese psychosomatic medicine. The CMI test consists of 144 questions regarding ocular/otic, respiratory, cardiovascular, digestive, muscular/skeletal, nervous, urogenital, and dermal symptoms; fatigue, frequency of disease, medical history, and habits as somatic complaints; and of 51 questions regarding maladjustment, depression, anxiety, hypersensitivity, anger, and tension as mental complaints. Visual analog scale (VAS), using a marked 10-cm line extending from "no hunger" to "strong hunger" was used to score the patients' feeling of hunger. Another VAS, using a marked 10-cm line extending from "I can't relax at all" to "I can relax very well" was used to score the degree of relaxation.

Measurement Protocols

Plasma ghrelin concentrations were measured using radioimmunoassay (RIA) as previously reported (12,13). Intra- and interassay coefficients of variation (CV) were below 3.0% and 8.3%, respectively. Plasma glucose was measured by the glucose oxidase method. Plasma catecholamine (norepinephrine, epinephrine) concentrations were measured with high-performance liquid chromatography in seven patients of each group. Blood samples were taken from the antecubital vein at 7 AM after an overnight fast. Daily caloric intake was calculated by weighing meals before and after eating.

Somatic and mental complaints in CMI, SDS, daily caloric intake, plasma ghrelin and catecholamine concentrations, and plasma glucose were examined on admission and 4 weeks after admission. VAS for hunger and relaxation were investigated on admission and 1, 2, 3, and 4 weeks after admission. Hunger and relaxation scores were checked daily before bedtime and the mean values for each week were calculated.

Statistical Analysis

All data are expressed as mean ± standard deviation. Between-group comparisons were performed by the Student two-tailed group t test. To evaluate the effects and interactions of a group factor and repeated measures, the data on hunger and relaxation scores during treatment were assessed using two-way analysis of variance (ANOVA). In addition, one-way ANOVA followed by Bonferroni test was used to compare on admission and 1, 2, 3, and 4 weeks after admission. The relationships between the increase of daily caloric intake and the improvement of hunger and relaxation scores in the thermal therapy group were evaluated using Spearman's correlation coefficient by rank. p value of less than .05 was considered statistically significant.

RESULTS

The Changes of Subjective Symptoms

On admission, there were no significant differences in all parameters between the two groups. Four weeks after admission, somatic complaints were significantly smaller ($t = 4.84$, $p < .001$) and mental complaints were slightly smaller ($t = 2.02$, $p = .054$) in the thermal therapy group than those in the nonthermal therapy group. SDS did not change in either group 4 weeks after admission (Table 2).

There were significant effects of group and time course on hunger and relaxation scores (hunger scores: group effects, $F(1,130) = 38.3$, $p < .0001$, time effects, $F(4,130) = 39.3$, $p < .0001$: relaxation scores: group effects, $F(1,130) = 74.2$, $p < .0001$, time effects, $F(4,130) = 31.1$, $p < .0001$, Fig. 1). Significant interactions between group and time course for both hunger and relaxation scores were detected (hunger scores: $F(4,130) = 9.8$, $p < .0001$; relaxation scores: $F(4,130) = 10.2$, $p < .0001$). In the thermal therapy group, hunger and relaxation scores significantly increased from 2 weeks after admission compared with on admission (hunger scores: $F(4,65) = 33.0$; relaxation scores: $F(4,65 = 43.4)$. Both hunger and relaxation scores 2, 3, and 4 weeks after admission were higher in the thermal therapy than those in the nonthermal therapy group (hunger scores: $t = -2.55$, $p < .05$, $t = -5.98$, $p < .0001$, $t = -4.81$, $p < .0001$, respectively; relaxation scores: $t = -5.04$, $p < .0001$, $t = -5.69$, $p < .0001$, $t = -7.37$, $p < .0001$, respectively). In the nonthermal therapy group, hunger score significantly increased 4 weeks after admission ($F(4,65) = 8.5$, $p < .001$), but there were no changes in relaxation scores.

In the thermal therapy group, there was a positive correlation between the improvement in hunger score and the increase of daily caloric intake ($r = 0.65$, $p < .05$, data not

TABLE 2. The Changes of Parameters on Admission and 4 Weeks After Admission

	Nonthermal Therapy Group (n = 14)		Thermal Therapy Group (n = 14)		p
	On Admission	4 Weeks After Admission	On Admission	4 Weeks After Admission	
CMI					
Somatic complaints	39.9 ± 7.3	36.8 ± 7.0	39.4 ± 8.6	23.0 ± 8.0	<.001
Mental complaints	17.4 ± 5.9	14.9 ± 5.6	16.4 ± 5.4	10.9 ± 5.0	.054
SDS	51.4 ± 7.7	46.2 ± 5.3	52.6 ± 6.3	43.3 ± 5.0	.15
Plasma glucose (mg/dl)	93 ± 19	95 ± 14	98 ± 16	94 ± 13	.85
BMI (Kg/m^2)	21.5 ± 3.3	21.6 ± 3.1	20.9 ± 3.7	21.5 ± 3.3	.93

CMI = Cornell Medical Index; SDS = Self-Rating Depression Scale.
Mean ± standard deviation are presented. p = Comparisons of values 4 weeks after admission between the two groups.
Four weeks after admission, somatic complaints were significantly smaller ($p < .001$) and mental complaints were slightly smaller ($p = .054$) in the thermal therapy group than those in the nonthermal therapy group.

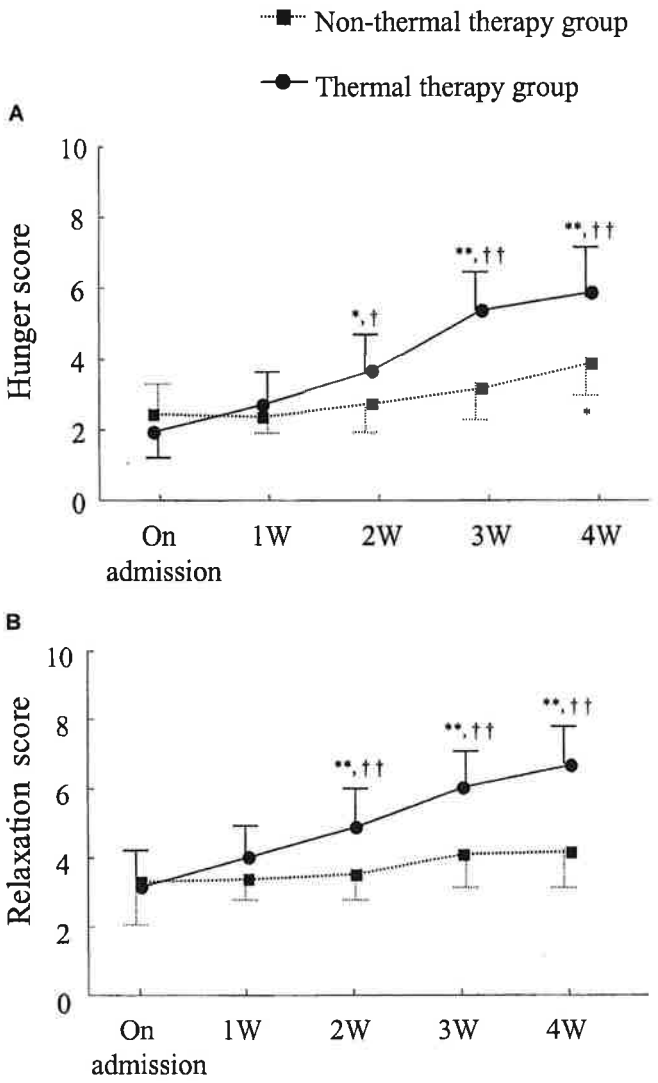

Figure 1. Hunger (**A**) and relaxation scores (**B**) on admission and 1, 2, 3, and 4 weeks after admission. Error bars represent standard deviation. Hunger and relaxation scores; time effect ($p < .0001$, respectively), group effect ($p < .0001$, respectively), time × group ($p < .0001$, respectively). *$p < .001$, **$p < .0001$ compared with on admission. +$p < .05$, ++$p < .0001$ compared with the nonthermal therapy group.

shown) but no correlation between the improvement of relaxation scores and increase of daily caloric intake.

The Changes of Plasma Ghrelin and Catecholamine, Glucose, Daily Caloric Intake, and Body Mass Index

The plasma ghrelin concentrations and daily caloric intake were significantly higher in the thermal therapy group than those in nonthermal therapy group 4 weeks after admission ($t = -2.32$, $p < .05$; $t = -2.65$, $p < .05$, respectively) (Fig. 2). The plasma norepinephrine concentrations 4 weeks after admission were slightly lower in the thermal therapy group than those in the nonthermal therapy group ($t = -2.07$, $p = .060$) (Table 3). Fasting plasma glucose, plasma epinephrine, and BMI did not change in either group 4 weeks after admission (Tables 2 and 3).

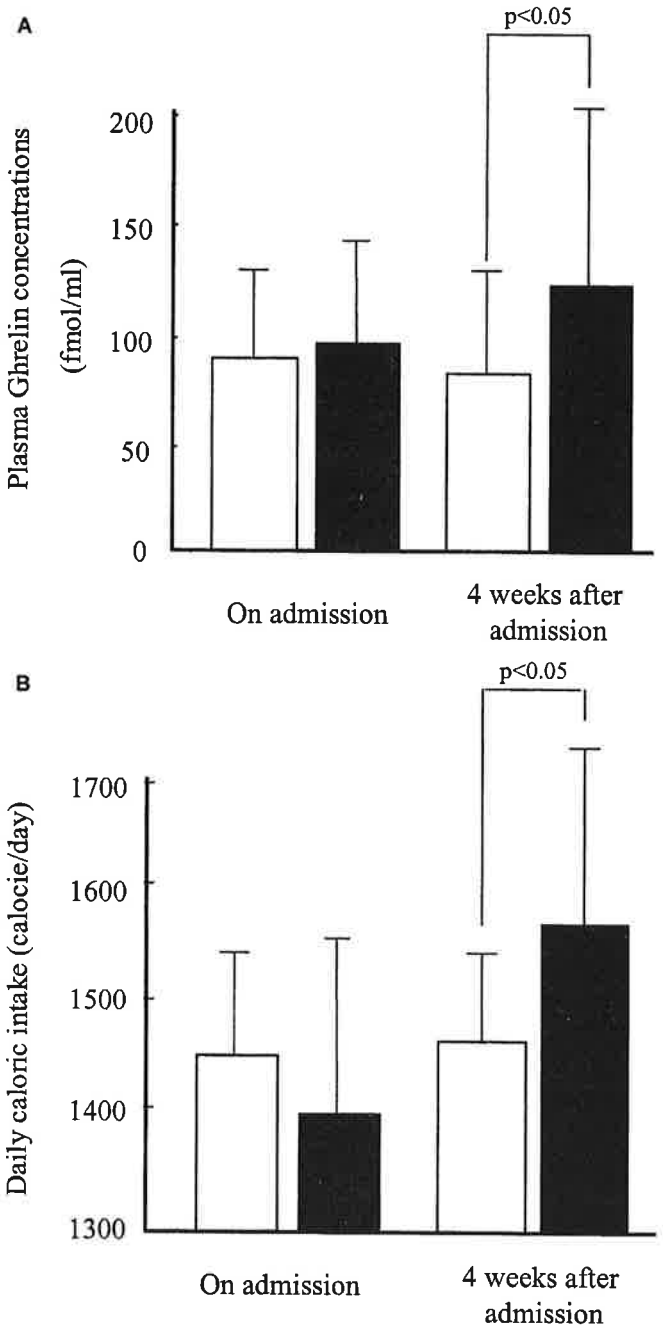

Figure 2. The plasma ghrelin concentrations and daily caloric intake on admission and 4 weeks after admission. The plasma ghrelin concentrations and daily caloric intake were higher in the thermal therapy group than those in the nonthermal therapy group 4 weeks after admission ($p < .05$, $p < .05$, respectively).

DISCUSSION

In mildly depressed patients, somatic and mental complaints decreased and a relaxation effect was obtained after repeated thermal therapy. Furthermore, we found that feeling of hunger occurred and the plasma ghrelin concentrations and daily caloric intake increased after repeated thermal therapy.

A far-infrared ray is an electromagnetic wave with a wavelength of more than 4 μm. The far-infrared ray of 8 to 14 μm that we are currently using is not easily absorbed by air and is

TABLE 3. The Changes of Plasma Catecholamines on Admission and 4 Weeks After Admission

	Nonthermal Therapy Group (n = 7)		Thermal Therapy Group (n = 7)		p
	On Admission	4 Weeks After Admission	On Admission	4 Weeks After Admission	
Norepinephrine (pg/ml)	522 ± 149	500 ± 93	527 ± 108	415 ± 55	.060
Epinephrine (pg/ml)	29 ± 10	22 ± 9	28 ± 11	20 ± 8	.67

Mean ± standard deviation are presented. p = Comparisons of values 4 weeks after admission between the two groups.
Plasma norepinephrine concentrations 4 weeks after admission were slightly lower in the thermal therapy group than those in the nonthermal therapy group (p = .060).

capable of directly heating the human body without markedly raising the temperature of the room air. Absorption of far-infrared ray does not depend on the human body site; this radiation has low skin permeability and it is mostly absorbed in the superficial layer of the skin. It can be perceived as heat by specialized nerve endings known as thermoreceptors in the skin, and stimulates the corium, blood capillaries, and sweat glands. When far-infrared ray is used for sauna bathing, skin temperature and blood flow increase and a sufficient volume of sweat is achieved at a relatively low temperature (40–60°C) without causing apnea, rush of blood to the head, damaged hair, or stress to the heart. Sweating begins quickly with an average total secretion of 300 to 500 g using a sauna (14–16).

We found that a single far-infrared ray dry sauna session at 60°C elevates core body temperature by 1.2°C (1). Increased blood temperature excites the warm neurons of the heat regulatory center in the hypothalamus and inhibits cold neurons. In addition, these neurons are projected to the neurons of the sympathetic/parasympathetic centers in the hypothalamus, influencing the autonomic nervous system. In this study, plasma norepinephrine concentrations 4 weeks after admission were slightly smaller in the thermal therapy group than those in the nonthermal therapy group. Furthermore, another study of ours using patients with cardiovascular disease showed significantly decreased plasma norepinephrine levels and increased coefficient of variance of R-R interval (CVR-R) on electrocardiogram after 20 sessions of similar thermal therapy (unpublished data). These findings suggest that the use of comfortable temperature and repeated sauna/postsauna warming may inhibit the sympathetic nerves, making the parasympathetic nerves predominant.

Mild warming of the whole body exhibits sedative effects through the sensory nerve ending (17). Thermal therapy using a hot spring increased the frequency of α waves on electroencephalograms (18) and sauna enhanced secretion of β-endorphin (19). We recently reported that repeated thermal therapy using far-infrared ray dry sauna improved fatigue, headache, and myalgia in patients with chronic fatigue syndrome (20). In this study, a relaxation effect was obtained after 10 sessions of thermal therapy, and somatic complaints significantly decreased and mental complaints slightly decreased after 20 sessions of thermal therapy. These findings suggest that repeated thermal therapy decreases the frequency of somatic and mental complaints by exhibiting psychosomatic relaxation and sedative effects.

A 10°C rise in temperature enhanced metabolism two- or threefold and increased energy consumption (21). Furthermore, warm-water bathing at 42°C for 10 minutes led to 40- to 70-Kcal energy consumption (22). Both warm-water bathing at 41°C for 10 minutes and 60°C sauna for 15 minutes increased core body temperature by 1.2°C (1), suggesting that thermal therapy with sauna elicits similar energy consumption. These findings suggest that the increase in core body and dermal temperatures enhances metabolism and increases energy consumption and that repeated thermal therapy may induce hunger.

Plasma ghrelin concentrations and daily caloric intake increased after repeated thermal therapy. A number of mechanisms may contribute to the increase of plasma ghrelin concentrations in the thermal therapy group, although we cannot specifically support any of these based on the current data. Ghrelin increased hunger score and stimulated appetite and food intake potently in people (23). There was positive correlation between the increase of daily caloric intake and improvement of hunger in this study. Therefore, repeated thermal therapy may stimulate appetite by inducing hunger and increasing plasma ghrelin concentrations, consequently resulting in the improvement of daily caloric intake.

This study has the following limitations: 1) In the nonthermal therapy group, the patients were rested on a bed not in the sauna room but in the ward; and 2) this study did not investigate the involvement of the autonomic nerves in appetite; however, this issue should be investigated in the future.

We have not observed symptomatic deterioration among patients during and after the thermal therapy using this method. In conclusion, repeated thermal therapy with far-infrared ray dry sauna may be useful for treatment of mildly depressed patients with appetite loss and subjective complaints.

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