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Relationships between thermic effect of food, insulin resistance and autonomic nervous activity

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Abstract : Background: The thermic effect of food (TEF) is higher in lean than in obese human subjects.
Objective:Relationships between TEF and insulin resistance during meals, from the point of view of autonomic nervous activity, were evaluated.
Methods : Autonomic nervous activity was evaluated in 20 young adults using the spectral analysis of heart rate variability from one hour before to two hours after a meal. Heart rate data were analyzed based on low frequency components (LF power, 0.04 - 0.15 Hz), high frequency components (HF power, 0.15-0.40 Hz), and LF/HF ratios. Energy expenditure and the TEF were measured 30 min after a meal. Homeostasis model of insulin resistance index (HOMA-IR) was also measured.
Results : The LF/HF ratio was significantly increased 30 min after a meal ($p<0.05$). No correlation between LF power and HF power with TEF was found, but the LF/HF ratio was significantly and positively correlated with TEF ($r=+0.56$, $p<0.05$). Moreover, a significant negative correlation was found between the HOMA-IR and TEF ($r=-0.601$, $p<0.05$).
Conclusions : The findings suggest that a reduction in insulin sensitivity induces a poor response of sympathetic nervous activity in the postprandial phase and a reduction in postprandial energy expenditure. J. Med. Invest. 53 : 153-158, February, 2006

Keywords **:** *thermic effect of food (TEF), insulin resistance, autonomic nervous activity, heart rate variability*

INTRODUCTION

A relationship between obesity and the thermic effect of food (TEF) has been reported, and it has also been suggested that decreased TEF is a growing factor in obesity, with a relationship to the autonomic nervous system. De Jonge and Bray (1) concluded that the reduction of TEF in obesity is related to the extent of insulin resistance, which may be influenced by a low level of sympathetic activity. In the present study, we evaluated the relationships between autonomic nervous activity, TEF and insulin resistance before and after a meal.

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SUBJECTS AND METHODS

Study population

Twenty young adults were recruited for the present study. All the subjects were healthy volunteers (9 men

and 11 women; mean age 21.3±2.3 years) and weight stable, untrained, nonsmokers. The subjects were defined having no history of cardiac disorders, no circulation system irregularities, no physical abnormalities, a systolic blood pressure of < 120 mmHg, a diastolic blood pressure of < 90 mmHg and normal ECG. Subjects with obesity (body mass index >25.0), hypertension, diabetes mellitus and who had been treated with autonomic nervous drugs within 1 month before the initiation of the study were excluded. Women recruited for this study are not in the menstrual status.

The total calories in the meal consumed were 600 K calories on the day of the examination. The meal was solid and composed of 55% carbohydrates, 30% fat and 15% protein. All subjects consumed the same diet at the same time and in the same surroundings. About 30 minutes was required to consume the meal. Written informed consent was given by all subjects before participation.

Experimental protocol

1) Assessment of insulin resistance

The homeostasis model of insulin resistance index (HOMA-IR) as an index of insulin resistance, autonomic nervous activity and the thermic effect of food were measured. The HOMA-IR was obtained using the following equation :

HOMA-IR=Fasting glucose (mg/dl)(fasting insulin (μU/ml)÷405

2) Spectral analysis of heart rate variability

Autonomic nervous activity was evaluated using a spectral analysis of heart rate variability from one hour before to two hours after a meal on the same day. Two-channel Holter's ECGs (CM5 and CC5 leads) were recorded in the supine position to avoid the influence of positional changes using a Holter ECG recorder (SM-50; Fukuda Denshi Co., Ltd., Tokyo, Japan). Holter ECGs, recorded on magnetic tapes were analyzed using a Holter ECG analyzer (DMW-9000H), and the data for ECG R-R intervals were input into a personal computer (Windows XP) via an RS232C cable and analyzed using time-series data-analysis software (Fukuda Denshi Co., Ltd., Tokyo, Japan).

Using the spectral analysis of heart rate variability, 256 heart rate data points were analyzed based on low frequency components (LF power, 0.04-0.15 Hz), high frequency components (HF power, 0.15-0.40 Hz), and the LF/HF ratio at the pre-and postprandial phases. Extra and missing beats were excluded from the analysis of the R-R intervals.

3) Expiratory gas analysis

Expiratory gas was measured before and after eating in order to evaluate the TEF. The TEF was measured by the breath-by-breath method (oxycon gamma, Fukuda Denshi, Tokyo, Japan) in which the rate of oxygen uptake and rate of carbon oxide output were calculated from the total flow rate, and the difference in the oxygen and carbon oxide concentrations between the outside air and mixed gas in the mask was calculated. Energy expenditure in kilocalories per minute was calculated using the Weir equation. TEF measurements and spectral heart rate variability were performed in the resting state and postprandial phases, 30 min and 60 min after the meal, respectively.

Statistical analysis

All values are expressed as the means±SD. Statistical analyses were performed using Student's *t*-test (two-tail), and values of $p<0.05$ were considered to indicate statistical significance. Data analyses were performed using the StatView statistical software (Stat View 5.0 ; SAS Institute, Inc., Cary, NC, USA).

RESULTS

1) Energy expenditure and spectral heart rate variability at the pre- and postprandial phases

Figure 1 shows the energy expenditure before and 30 min after the meal. The energy expenditure before and 30 min after the meal was 0.85±0.23 Kcal/min and 1.08±0.30 Kcal/min, respectively, and the energy expenditure was significantly increased after eating because of TEF ($p<0.05$).

Figure 2 shows a representative case of spectral heart rate variability before and after the meal. The LF power before the meal and 30 and 60 min after the

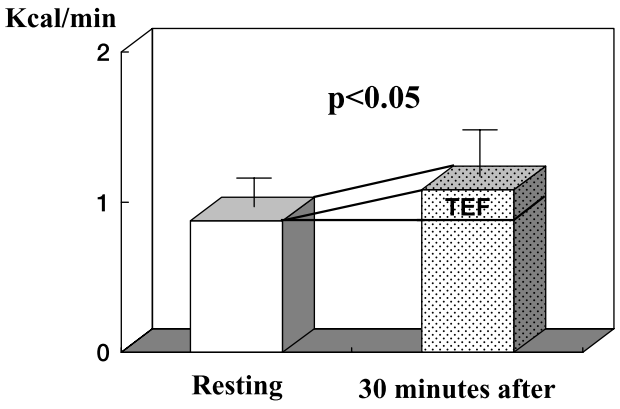

Figure 1. The thermic effect of food (TEF) before and 30 min after the meal. TEF was significantly increased 30 min after eating (p<0.05).

meal was 156 msec^2, 878 msec^2, and 244 msec^2, respectively. LF/HF ratios before the meal and 30 and 60 min after the meal were 1.2, 5.5 and 0.66, respectively. The HF power before the meal and 30 and 60 min after the meal was 127 msec^2, 159 msec^2 and 371 msec^2, respectively. That is, the LF power and LF/HF ratio, indicators of sympathetic nervous activity, were increased at 30 min after the meal. At sixty minutes after the meal, the HF power, an indicator of parasympathetic nervous activity, was increased and the LF/HF ratio was decreased.

Figure 3 shows the change in autonomic nervous activity in the postprandial phase by spectral analysis of heart rate variability. The LF power tended to decrease and the HF power tended to increase 45 min after the meal, but not to a statistically significant degree. However, the LF/HF ratio was significantly increased 30 min after the meal, but 45 min after the meal, it was decreased.

2) Relationship among HOMR-IR, autonomic nervous activity and TEF

Figure 4 shows the relationship between HOMA-IR and TEF. A significant negative correlation was found between HOMA-IR and TEF ($r=-0.601$, $p<0.05$).

Figure 5 shows the relationship between TEF and autonomic nervous system activity before and after a meal. No correlation was found between LF power and HF power with TEF, but the LF/HF ratio and TEF had a significant positive correlation ($r=+0.56$, $p<0.05$).

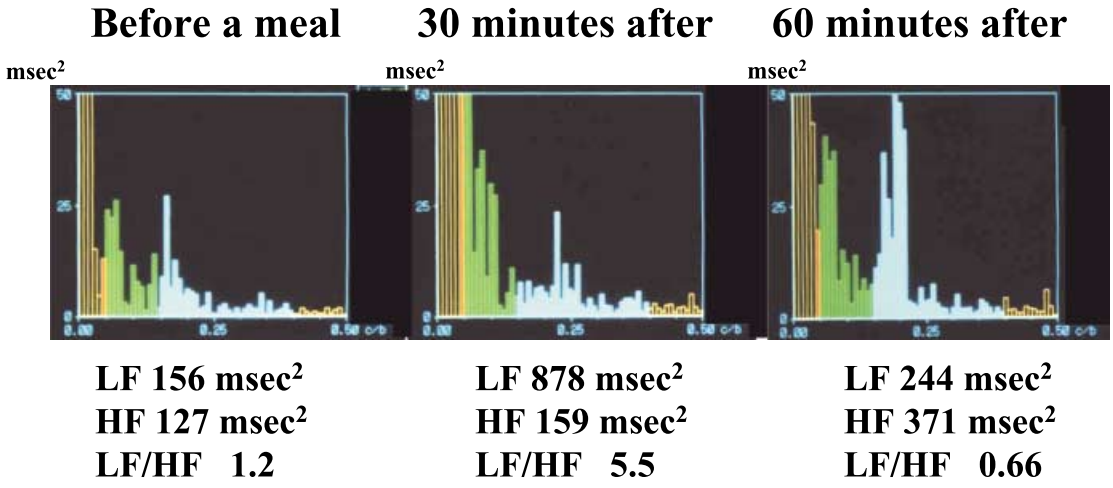

Figure 2. Representative case of spectral heart rate variability before and 30 and 60 min after the meal.
LF power and LF/HF ratios were increased 30 min after the meal. The HF power was increased and the LF/HF ratio was decreased 60 min after the meal

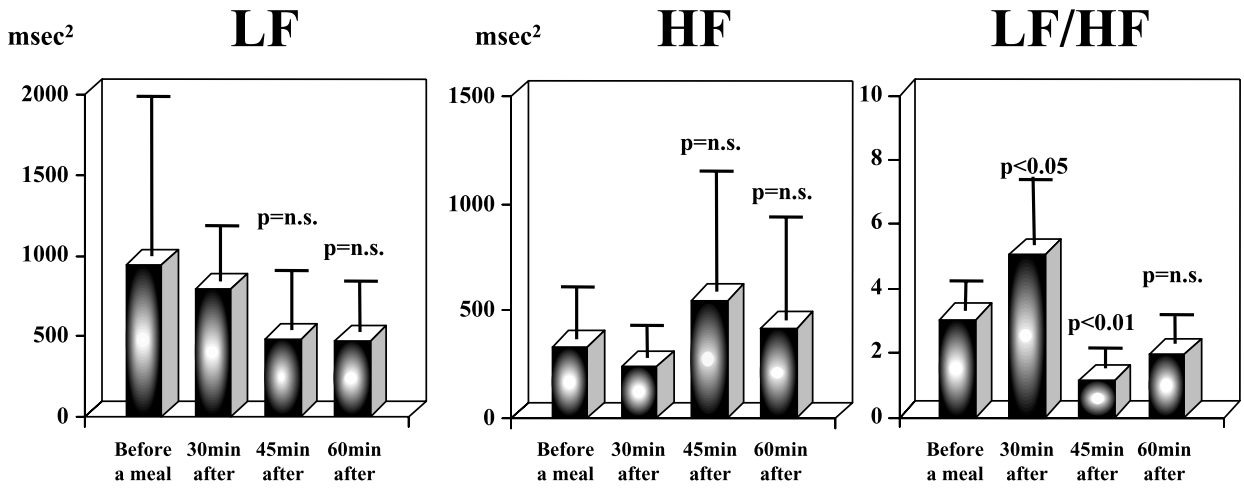

Figure 3. Change in autonomic nervous activity in the postprandial phase by a spectral analysis of heart rate variability.
Postprandial changes in LF power and the HF power were not significant, and the LF/HF ratio was significantly increased 30 min after the meal, but, 45 min after the meal, it was decreased.

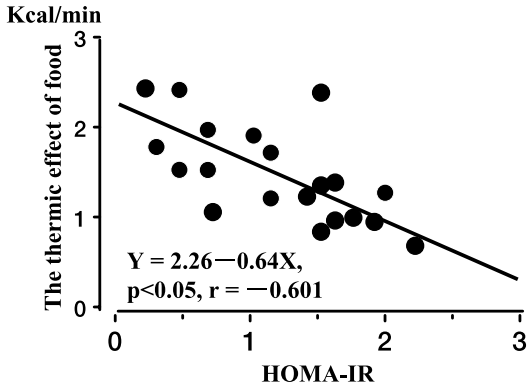

Figure 4. Relationship between HOMA-IR and TEF.
A significant negative correlation was found between HOMA-IR and TEF ($r = -0.601$, $p<0.05$).

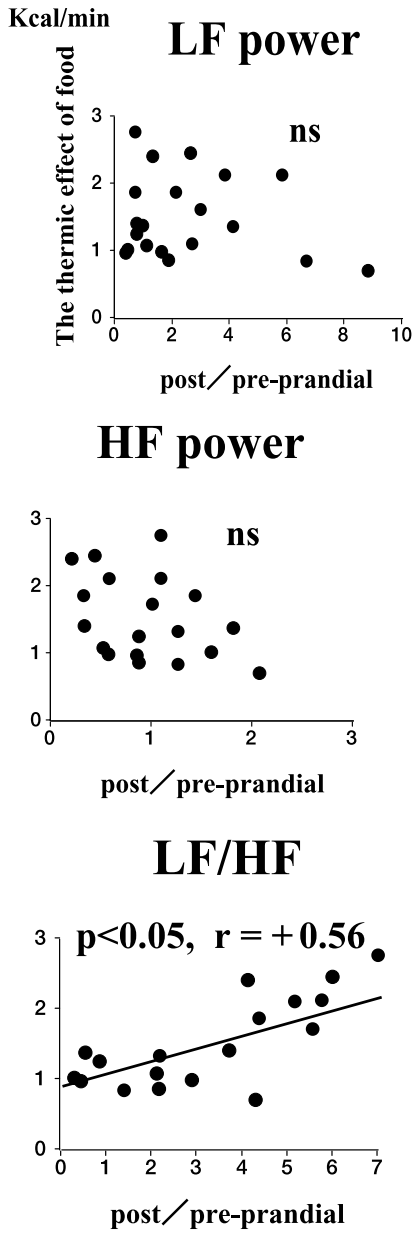

Figure 5. Relationship between TEF and autonomic nervous system activity before and after a meal.
A significant positive correlation was found between TEF and LF/HF ratios ($r = +0.56$, $p<0.05$).

DISCUSSION

Relationships among TEF, insulin resistance and autonomic nervous activity after a meal was examined. The results suggest that the depression in insulin activity causes a decrease in sympathetic nervous activity after a meal, and, as a result, a decrease in TEF. The results indicate that insulin resistance causes a depression in energy expenditure by food intake, and that energy is stored following the hypo-reactivity of the autonomic nervous function. Fat accumulation promotes insulin resistance, and therefore the worsening of insulin resistance contributes to a vicious circle of the aggravation of life-style related diseases.

1) Relationships between the thermic effect of food, autonomic nervous activity and insulin resistance

In previous reports concerning TEF, the measurement of the interval of energy expenditure was different than that used herein. Therefore, the most important factor appeared to be the duration used in the measurement for TEF. In the most studies, the measurement of TEF was not continued for more than 2.5 to 3 hours (1). However, measuring the TEF until oxygen consumption returns to its resting, postabsorptive status, provides more reliable data

TEF can be divided into the two main components. Obligatory thermogenesis is due to energy expended for digestion, absorption, transportation, and storage, and accounts for two-thirds of the total TEF. Facultative thermogenesis, which accounts for one-third of the TEF appears to have a cephalic phase and a postprandial phase.

In humans, the relevance of the facultative cephalic phase of TEF has been questioned, humans, but the facultative postprandial phase was assumed to depend on autonomic nervous activity (2-7).

In the present study, we evaluated relationships among TEF and insulin resistance, and autonomic nervous activity by a spectral analysis of heart rate variability. We found a positive correlation between TEF and LF/HF ratios associated with the sympathetic nervous activity. Moreover, a negative correlation was found between TEF and the insulin resistance measurement for HOMA-IR. These results suggest that a low insulin sensitivity induced a dysfunction in sympathetic nervous activity after the meal and energy storage.

2) Relationship between thermic effect of food and obesity

In previous reports (8 -14), the postprandial plasma

norepinephrine concentrations were reported to be higher than norepinephrine concentrations at the postabsorptive phase, indicating sympathetic nervous activation in the postprandial phase. Furthermore, it was reported that the only hyperinsulinemia without hyperglycemia also raises plasma norepinephrine concentrations (15, 16), and suggesting a possible association between hyperinsulinemia and postprandial activation of the sympathetic nervous system. In addition, it has been reported that clonidine, a β- and α-adrenergic antagonist, inhibits the postprandial activation of the sympathetic nervous system and reduces the thermic effect of food (17, 18). The results of these reports are consistent with the results of the present study, that is, the action of the postprandial sympathetic nervous system appears to be associated with TEF, especially in subjects with high plasma insulin levels. These results indicate that TEF is decreased when insulin sensitivity is lower, and that this reduction in TEF appears to play a role in the mechanism of developing obesity (19-27).

3) Obesity and autonomic nervous activity

Schwartz *et al.* (28) confirmed a relationship between a reduction in TEF and a decrease in sympathetic activity in elderly subjects. Moreover, previous studies (29) reported that a disturbance in the autonomic nervous system after a meal due to aging causes postprandial hypotension. Therefore, it is possible that high insulin resistance leads to a disturbance of postprandial energy expenditure, leading to postprandial hypotension. It was also reported, in an experimental study using rats, that the reduced sympathetic nervous activity is a result of obesity (30). However, there is little evidence to support this hypothesis in humans. It is difficult to evaluate whether impaired sympathetic nervous activity is the cause of or the result of obesity. In order to solve this hypothesis, it will be necessary to demonstrate whether sympathetic nervous activity and energy expenditure are disturbed in pre-obese subjects in the postprandial phase or not. Because it is not possible to predict whether normal weight subjects will become obesity in the future, it is difficult to demonstrate this hypothesis prospectively.

In the present study, no correlation was found between TEF, body mass index, and body fat rate. Therefore, we assumed that impaired sympathetic nervous activity is not only the result of obesity. Although the subjects recruited in the present study were not severely insulin resistant, we were able to detect a significant negative correlation between the HOMA-IR and TEF, as shown in Figure 4. The findings of present study suggest that a decreased in insulin sensitivity influenced the reduction in TEF and the poor response of the sympathetic nervous activity in the postprandial phase.

STUDY LIMITATION

In the present study, 11 of young female subjects were included in the study. It has been reported that the estrous cycle is related to insulin resistance and autonomic nervous activity because of the hormonal environment before and after ovulation. Moreover, subjects with a HOMA-IR value of more than 2.5 should be examined. In future studies, the HOMA-IR, TEF, and each parameter of autonomic nervous activity should be measured as a function of the estrous cycle, and subjects with increased insulin resistance should be enrolled in a study of the effects of obesity.

CONCLUSION

Relationships between TEF, insulin resistance and the variation in autonomic nervous activity after a meal were examined. The findings suggest that a reduction in insulin sensitivity induces the poor response of sympathetic nervous activity in the postprandial phase and a reduction in postprandial energy expenditure. Therefore, a high insulin resistance may induce a poor activation of the sympathetic nervous system in the postprandial phase and a reduction in energy expenditure, and more storage of energy leading to the exacerbation of insulin resistance.

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