SYMPATHETIC ACTIVITY IS LOWER IN RATS FED A HIGH FAT DIET THAN IN RATS FED A HIGH CARBOHYDRATE DIET UNDER PAIR-FEEDING CONDITION

Tatsuhiro MATSUO

ABSTRACT

Effects of a high fat diet compared with a high carbohydrate diet on sympathetic activity and body fat accumulation were studied in rats. Rats were meal-fed an isoenergetic diet based on either fat or carbohydrate for 8 weeks. Body weight gain, abdominal adipose tissue weight and carcass fat content were significantly greater (p<0.05) in the high fat diet group than in the high carbohydrate diet group. Basal norepinephrine content in interscapular brown adipose tissue was significantly lower (p<0.05) in the high fat diet group than in the high carbohydrate diet group, but contents in heart and pancreas were almost the same between the two dietary groups. Norepinephrine turnover rates in the high fat diet group were significantly lower (~<0.05) in interscapular brown adipose tissue, heart, and pancreas as compared with rates in the high carbohydrate diet group. These results suggest that the high fat diet promotes body fat accumulation by reducing sympathetic activity as compared with intake of the high carbohydrate diet.

Key words: high fat diet, high carbohydrate diet, body fat, sympathetic activity, brown adipose tissue, pancreas, rat

Previous studies have demonstrated that dietary intake exerts an important effect on sympathetic activity in the rat (1-3). Norepinephrine (NE) turnover techniques have shown that fasting suppresses sympathetic activity (4), whereas overfeeding sucrose has been shown to stimulate sympathetic activity in heart (5) and other tissues of the rat (6). An important role for carbohydrates in the relationship between dietary intake and sympathetic activity has been inferred from data indicating that hypoglycemia (4, 5) and 2-deoxy-D-glucose administration (6) suppress sympathetic activity, whereas hyperinsulinemia, in the absence hypoglycemia, has a stimulatory effect (7, 8).

On the other hand, the effects of noncarbohydrate nutrients on sympathetic activity have been studied about dietary fat. The demonstration that overfeeding mixed high-energy diets with substantial fat content alters sympathetic activity (9, 10) suggested that nutrients other than sucrose influence the sympathetic activity as well. However, in the many previous reports, animals were not fed the same energy of a high fat diet or a control diet. The study described in this report was undertaken to assess the effect of a high fat (FAT) diet on sympathetic activity compared with a high carbohydrate (CHO) diet under pair-feeding condition in the rat.

Sympathetic nervous system regulates diet-induced thermogenesis (DIT) and insulin secretion from pancreatic β cells. DIT occurs mainly in brown adipose tissue (BAT), and a decrease in sympathetic activity in BAT reduces DIT (11-13). In the pancreas, a decrease in sympathetic activity causes an increase in insulin secretion (14, 15). Furthermore, in studies of animal models of obesity, it was demonstrated that genetically and hypothalamically obese animals have decreased sympathetic activities, which are responsible for decreased DIT and increased insulin secretion (16).

Many studies have been performed on the role of dietary fats in the development of dietary obesity. The amount of fat in the diet is suggested to be a direct factor affecting body fat accumulation (17). It is hypothesized that sympathetic activities are lower in animals fed FAT diet than in those fed CHO diet under pair-feeding condition, resulting in greater body fat accumulation in the former. In the present study, sympathetic activity was investigated in interscapular BAT, heart and pancreas of rats fed FAT diet or CHO diet for 8 weeks by measuring NE turnover rate as an index of sympathetic activity.
MATERIALS AND METHODS

Animals and diets.
Fifty male Sprague-Dawley rats (4 weeks old) were obtained from CLEA (Tokyo, Japan). Half of the animals were fed FAT diet, and the other half were fed CHO diet. The compositions of both diets have been described previously \(^{19}\). The FAT diet provided 35%, 40%, and 25% of energy as carbohydrate, fat, and protein, respectively, the CHO diet provided 70%, 5%, and 25%, respectively.

Experimental design.
The animals were individually caged at 22 ± 2 °C, with lights on from 7 am to 7 pm. Each group of rats was meal-fed the diet at 8 to 9 am and 8 to 9 pm and given free access to water for 8 weeks. Both groups of rats were offered the appropriate diet in amounts such that the two groups consumed equal energy during the experimental period. The meal-feeding method was used to adjust the energy intake between the two dietary groups. Under meal-feeding conditions, feeding one meal (within 2 hours) per day causes the food intake of the animals to decrease; however, feeding two meals per day minimized this effect of meal-feeding. On the final day, rats in each diet group were fed a meal at 8 to 9 am. Then, six rats in each diet group were injected with the tyrosine hydroxylase inhibitor \( \alpha \)-methyl-\( p \)-tyrosine (250 mg/kg intraperitoneally [IP]) at 0 hours (10 am) and again with 150 mg/kg IP at 3 hours, and decapitated at 7 hours. Twelve rats in each diet group were administered 250 mg/kg IP at 0 hours and decapitated at 1 or 3 hours, whereas seven rats in each diet group received saline as controls at 0 hours and were immediately killed by decapitation. Interscapular BAT, heart, and pancreas were quickly removed, weighed, and stored at −70 °C until analyses. Carcass samples were obtained by removing the head, liver, digestive tracts, lungs, kidneys, testes, and abdominal adipose tissues, and were stored at −20°C until analyses of carcass composition.

Analysis.
NE contents of BAT, heart, and pancreas were assayed by high-performance liquid chromatography with electrochemical detection as modified by Refshauge et al. \(^{19}\). Estimation of NE turnover was performed using the method reported previously \(^{18,20,22}\). Saline-treated rats were used for measurement of the basal organ levels of NE. Since there is a monoexponential decline of organ NE levels after \( \alpha \)-methyl-\( p \)-tyrosine treatment, these data were then subjected to a least-square linear regression analysis of log NE concentration versus time \(^{20}\). Turnover rate (slope/[0.434/initial NE concentration]) was estimated from these data.

Carcass fat was analyzed using the method reported by Mickelsen and Anderson \(^{22}\).

Statistical analysis.
Statistical differences in body weight, tissue weights, NE turnover rate, and carcass fat content were analyzed by Student's \( t \)-test.

RESULTS AND DISCUSSION

Body weight, body fat, and tissue weights.
Body weight gain and carcass fat content were significantly greater \((p<0.05)\) in FAT diet group than in CHO diet group (Table 1). The weights of epididymal and mesenteric adipose tissues were significantly greater \((p<0.05)\) in FAT diet group, whereas perirenal adipose tissue weight was not different between the two groups (Table 1). Interscapular BAT, heart, and pancreas weights were not different between two dietary groups (Table 2).

Table 1 Body weight, abdominal adipose tissue weight, and carcass composition

<table>
<thead>
<tr>
<th>Diet group</th>
<th>CHO</th>
<th>FAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial (g)</td>
<td>92±1</td>
<td>92±1</td>
</tr>
<tr>
<td>Final (g)</td>
<td>391±4</td>
<td>403±3*</td>
</tr>
<tr>
<td>Gain (g)</td>
<td>299±4</td>
<td>311±3*</td>
</tr>
<tr>
<td>Epididymal (g)</td>
<td>55±0.2</td>
<td>65±0.2*</td>
</tr>
<tr>
<td>Perirenal (g)</td>
<td>8.2±0.4</td>
<td>8.9±0.4</td>
</tr>
<tr>
<td>Mesenteric (g)</td>
<td>56±0.2</td>
<td>63±0.3*</td>
</tr>
<tr>
<td>Carcass fat (g)</td>
<td>115±7</td>
<td>143±8*</td>
</tr>
<tr>
<td>Abdominal adipose tissue weight (%): 42±3</td>
<td>53±3*</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SE for 25 rats.
*Statistically significant difference \((p<0.05)\) vs CHO diet group (Student's \( t \)-test).
Table 2 Tissue weights and norepinephrine turnover rates

<table>
<thead>
<tr>
<th>Diet group</th>
<th>CHO</th>
<th>FAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown adipose tissue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (mg)</td>
<td>527±43</td>
<td>503±22</td>
</tr>
<tr>
<td>NEo (ng)</td>
<td>971±37</td>
<td>735±43*</td>
</tr>
<tr>
<td>k (%/h)</td>
<td>16.4±3.1</td>
<td>10.2±3.6</td>
</tr>
<tr>
<td>NET (ng/tissue/h)</td>
<td>159±17</td>
<td>75±8 *</td>
</tr>
<tr>
<td>Heart</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (mg)</td>
<td>1045±15</td>
<td>1063±16</td>
</tr>
<tr>
<td>NEo (ng)</td>
<td>966±46</td>
<td>894±30</td>
</tr>
<tr>
<td>k (%/h)</td>
<td>13.2±1.2</td>
<td>8.7±2.3 *</td>
</tr>
<tr>
<td>NET (ng/tissue/h)</td>
<td>138±12</td>
<td>77±6 *</td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (mg)</td>
<td>958±45</td>
<td>974±46</td>
</tr>
<tr>
<td>NEo (ng)</td>
<td>634±6</td>
<td>622±20</td>
</tr>
<tr>
<td>k (%/h)</td>
<td>11.6±2.4</td>
<td>4.7±2.6 *</td>
</tr>
<tr>
<td>NET (ng/tissue/h)</td>
<td>71±9</td>
<td>27±4 *</td>
</tr>
</tbody>
</table>

Values are the means ± SE for 25 rats. k, fractional turnover; NET, turnover rate
* Statistically significant difference (p < 0.05) vs CHO diet group (Student's t-test).

diet group (Table 2, Fig 1).

The present study shows that intake of FAT diet promotes body fat accumulation as compared with intake of CHO diet in rats, and it is suggested that this effect of FAT diet is at least in part ascribed to decreased DIT (16). Since it has been reported that the thermogenic effect of food is mediated by the sympathetic nervous system (9, 12), NE turnover was analyzed in the present study. The results are clearly shown here that the NE turnover rate in interscapular BAT, a main thermogenic tissue in rats, was lower in FAT diet group than in CHO diet group. Because both groups of rats consumed diets with same energy throughout the experimental period, the difference in NE turnover rates between the two dietary groups was ascribed to the different dietary fat amount. NE turnover rate in heart was also lower in FAT diet group, and this might be related to the lower DIT in FAT group, because it has been suggested that tissues other than BAT are involved in thermogenesis (17, 24). The NE turnover rate in pancreas showed a great difference between the two dietary groups: the rate in the FAT diet group was approximately one third of that in the CHO diet group. A decrease in pancreatic sympathetic activity causes an increase in insulin secretion (31, 35). The higher blood insulin concentration might play a role in the decreased thermogenesis (25, 26).

When the fat content of the diet is increased, resistance to the development of obesity is associated with enhanced efferent signals that produce the following sequence of events (16). There is a reduction in food intake to offset the increased nutrient density of the food. There is an enhanced activity of the autonomic nervous system, both sympathetic and parasympathetic, which leads to a nearly normal partitioning of nutrients between fat and protein. When the dietary signals fail to activate these efferent systems via the controller, compensation for altered nutrient density (i.e., FAT diet) is inadequate, the sympathetic nervous system is not activated and the size
and relative composition of the nutrient stores shift towards more fat. It has been reported that sympathetic activity is reduced in most known forms of obesity, including hypothalamic and genetic forms, suggesting that the sympathetic nervous system plays an important role in the regulation of body fat accumulation. The present study demonstrated that dietary fats are modulators of sympathetic activity in relation to body fat accumulation, and suggests that long-term high fat diet promotes body fat accumulation by reducing sympathetic activity.

REFERENCES

ペア・フィーディング下におけるラットの交感神経活性は高炭水化物食に比べて
高脂肪食で低下する

松尾達博

高脂肪食が高炭水化物食に比べて交感神経活性と体脂肪蓄積に及ぼす影響をラットを用いて検討した。ラットに等エネルギー量の高脂肪食あるいは高炭水化物食を1日2食制のmeal-feeding下に与え、8週間飼育した。その結果、体重増加量、腹腔内脂肪組織重量および屠体脂肪含量は、高炭水化物食群に比べて高脂肪食群で有意に大きかった。肩甲骨周辺
色脂肪組織のノルエピネフリン含量は、高炭水化物食群に比べて高脂肪食群で有意に低かったが、心臓および腸管のノルエピネフリン含量には、2群間で差は見られなかった。ノルエピネフリン代謝回転速度は全ての組織において、高炭
水化物食群に比べて高脂肪食群で有意に低値を示した。これらの結果から、ペア・フィーディング下において、高脂肪
食は高炭水化物食に比べて交感神経活性を低下させ、体脂肪蓄積を増大させることが示唆された。