The interaction between intestinal fatty acid–binding protein 2 polymorphism and delta-6 desaturase activity in obese children

Dear Sir:

In a study recently reported in the Journal, Morcillo et al (1) examined the interaction between intestinal fatty acid–binding protein 2 (FABP2) polymorphism and the intake of dietary fats; they determined that the FABP2 Thr54 polymorphism was associated with insulin resistance in subjects with a high intake of sunflower oil. Weiss et al (2) confirmed that, among sedentary nondiabetic persons following a low-fat diet, FABP2 Thr54 carriers have lower glucose tolerance, lower insulin action, and higher lipid oxidation rates than do Ala54Ala carriers. These results were very interesting to our group, which had studied the effect of FABP2 polymorphism on delta-6 desaturase (D6D) activity in obese children (3).

In our study of 32 obese children with a mean (±SD) age of 12.0 ± 3.0 y, the allele frequencies were 0.66 and 0.34 for the FABP2 Ala54 and Thr54 polymorphisms, respectively. Among the FABP2 genotypes, no significant difference in age, body mass index, fasting glucose, insulin, or serum lipoproteins was observed. The content of arachidonic acid (AA) in fasting plasma was significantly lower in Thr54Thr carriers (x ±SD: 4.15 ± 0.94% wt/wt) than in Ala54Thr (5.24 ± 0.87) or Ala54Ala (5.24 ± 0.86) carriers (P = 0.0342, Kruskal-Wallis test). The index of D6D activity, estimated by the (18:3 + 20:3)/18:2 ratio, was significantly (P = 0.0091) lower in Thr54Thr carriers (0.05 ± 0.02) than in Thr54Ala (0.07 ± 0.02) or Ala54Ala (0.08 ± 0.02) carriers.

Recently, the linkage between D6D activity and obesity was investigated by Warenjsø et al (4). This study found that the risk of being overweight was increased by ≈60% for each 1-SD increase in D6D activity, which was estimated by the fatty acid profile of serum cholesteryl esters. Our group also studied D6D activity in children and found that the D6D was activated in obesity (5). The hypothetical mechanism proposed in rodent animal models is that the increased oxidation of AA must be met by compensatory activation of D6D (6). However, the activities of D6D and delta-5 desaturase are not modified in insulin-resistant animals, even though insulin is a strong activator of these enzymes (7, 8).

In an earlier study (5), our group found that ≈25% of obese children had low plasma AA content (>1 SD below the mean) and a low ratio of AA to linoleic acid, probably because of an impaired compensatory production of AA. In addition, the obese children with low AA content had higher insulin concentrations, although their percentage body fat, waist circumference, and leptin concentrations were similar to those in obese children with normal AA content. AA itself affects the insulin sensitivity of adipocytes because AA can act as a ligand for peroxisome proliferator–activated receptor-γ (9). Our results are compatible with the suggestion by Das (10) that impaired D6D activity is associated with insulin resistance, and they may partly explain the metabolic heterogeneity of obesity. Furthermore, our recent study of FABP2 polymorphism suggests that Thr54Thr may be a predisposing factor for the impaired D6D activation in obesity. We speculate that the modulation of the absorbed fatty acid composition by FABP2 genotype may affect D6D activity and AA content and, thereby, insulin sensitivity.

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Tomoo Okada
Noriko Sato-Furuhashi
Fujihiko Iwata
Hideo Mugishima

Department of Pediatrics
Nihon University School of Medicine
30-1, Oyaguchi-kamimachi, Itabashi-ku
Tokyo 173-8610
Japan
E-mail: tomo@med.email.ne.jp

REFERENCES
TABLE 1
Plasma phospholipid fatty acid composition (%) according to the Ala54Thr polymorphism of the FABP2 gene

<table>
<thead>
<tr>
<th>Ala54Thr polymorphism of the FABP2 gene</th>
<th>Ala54Ala (n = 417)</th>
<th>Thr54Ala (n = 322)</th>
<th>Thr54Thr (n = 66)</th>
<th>p²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated fatty acids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n−6 fatty acids</td>
<td>46.2 ± 6.67²</td>
<td>46.09 ± 6.62</td>
<td>46.12 ± 6.70</td>
<td>NS</td>
</tr>
<tr>
<td>n−3 fatty acids</td>
<td>52.8 ± 6.56</td>
<td>53.46 ± 5.34</td>
<td>53.87 ± 6.55</td>
<td>NS</td>
</tr>
<tr>
<td>MUFA</td>
<td>11.92 ± 2.75</td>
<td>12.06 ± 2.70</td>
<td>12.73 ± 3.05</td>
<td>0.02</td>
</tr>
<tr>
<td>D9D</td>
<td>0.83 ± 0.25</td>
<td>0.84 ± 0.23</td>
<td>0.90 ± 0.29</td>
<td>0.01</td>
</tr>
<tr>
<td>D6D</td>
<td>0.48 ± 0.13</td>
<td>0.49 ± 0.13</td>
<td>0.47 ± 0.13</td>
<td>NS</td>
</tr>
</tbody>
</table>

¹ FG, fasting glucose; IGT, impaired glucose tolerance; DM2, type 2 diabetes; MUFA, monounsaturated fatty acid; D9D, delta-9 desaturase; D6D, delta-6 desaturase; AA, arachidonic acid.
² Adjusted for age (y), sex, carbohydrate metabolism disorders (FG, IGT, DM2), obesity (BMI ≥ 30), and type of dietary oil (olive or sunflower oil).
³ x ± SD (all such values).
⁴ D9D activity estimated by the 18:0/18:1 ratio.
⁵ D6D activity estimated by the AA/18:2 ratio.

REFERENCES