Abstract—Controversy surrounds the pathogenetic mechanisms of the relationship between hyperdynamic circulation and insulin resistance. Two hundred eight children and young adults (mean age, 17.2±3.0 years; range, 11 to 26 years) from the Tecumseh Offspring Study whose parents had been assessed with Doppler echocardiography at the age of 34 years during the previous Tecumseh Blood Pressure Study were considered for this analysis. Offspring data were stratified according to tertiles of parental cardiac index. Parents in the top cardiac index tertile had increased heart rate ($P=0.001$), stroke volume ($P=0.0001$), left ventricular fractional shortening ($P=0.02$), and plasma epinephrine ($P=0.02$) compared with parents in the other tertiles. Body mass index (BMI) and blood pressure were similar in all groups. Offspring of parents with a high cardiac index had greater BMI ($P=0.001$), skinfold thickness ($P=0.008$), and waist/hip ratio ($P=0.02$), higher diastolic blood pressure ($P=0.02$) and plasma insulin level ($P=0.001$), and higher heart rate during Stroop’s color test ($P=0.02$) than offspring of parents with a lower cardiac index. In a multivariate regression analysis, offspring BMI was predicted by parental BMI and cardiac index ($P=0.0001$ and 0.003, respectively). The mother–child relationship explained most of the cardiac index–BMI association. In summary, parental hyperdynamic circulation was an important predictor of overweight, abnormal fat distribution, increased blood pressure, and hyperinsulinemia in offspring. Our results illustrate the complexity of interaction between a genetic tendency and its phenotypic expression. We speculate that the degree of β-adrenergic responsiveness may be a major determinant of the phenotypic differences between the parents and offspring found in this study. (Hypertension. 1999;33:769-774.)

Key Words: sympathetic tone ■ insulin ■ obesity ■ heart rate ■ hemodynamics ■ hypertension

A n association between sympathetic overactivity, overweight, and insulin resistance has been reported to occur in a large proportion of patients with hypertension. However, it is not known which of these factors is the key element in the observed association. A scenario in which eating behavior leads to weight gain, which causes oversecretion of insulin and insulin resistance, which then increase sympathetic tone, has been proposed by some investigators. According to others, insulin resistance is the primary phenomenon, and increased plasma insulin level causes sympathetic overactivity, hypertension, and dyslipidemias.3 The Ann Arbor group postulated the primacy of the enhanced sympathetic drive for the causation of both insulin resistance and hypertension. Although each of the proposed schemes is supported by data from studies performed in humans, most results were obtained from cross-sectional analyses in populations, making it difficult to distinguish cause and effect.

Studying these associations in siblings may help us to better understand the pathophysiological mechanisms of this condition. Recently, we had the opportunity to study the offspring of subjects previously enrolled in the Tecumseh Blood Pressure Study. The aim of the present study was to investigate the hemodynamic, neurohumoral, and metabolic features in offspring of parents who had a hypersympathetic-hyperdynamic circulation characterized by increased heart rate, elevated stroke volume, and enhanced cardiac contractility.

Methods

The aims, nature, and methods of the Tecumseh Blood Pressure Study have been extensively reported elsewhere. The Tecumseh Offspring Study was initiated in 1995. Two hundred fifty-one subjects aged 11 to 26 years whose parents had been studied between 1987 and 1990 were enrolled. Data from 347 parents were available from the previous Tecumseh data set. A complete set of hemodynamic and biochemical measurements was available for 290 parents (Table 1). For 96 children, we had data from both mothers and fathers; for 69 children, only the data from the mothers were available, and for 86 children, only the data from the fathers were available. All variables were similar in the 3 groups except for body...
mass index (BMI), which was slightly greater in the children for whom only data from the fathers were available ($P=0.02$).

**Offspring**

Two hundred eight children aged 11 to 26 years for whom parents' echocardiographic data were available were included in this analysis. Their clinical characteristics by gender are reported in Table 1. The children were examined at the same field office in Tecumseh, Mich, in which their parents had been examined.6,12 A battery of psycho-social, anthropometric, hemodynamic, and biochemical measures was obtained in each subject. All subjects read and signed an informed consent form, and the study was approved by the Institutional Ethics Review Board of the University of Michigan.

**Measurements**

Procedures used for clinical heart rate, blood pressure, cardiac index, and left ventricular fractional shortening measurements, anthropometric data collection, and blood sample processing in the children were the same as those used for parents in the Tecumseh Blood Pressure Study.12 Heart rate was also measured during Stroop’s color test, a computerized conflict-evoking test.9 Skinfold thickness was measured in triplicate at the triceps, biceps, and subscapular and suprailiac areas with a manual caliper, and the average of the 12 measurements was defined as skinfold thickness.

The method used to measure cardiac output in parents and children has been reported previously.12 In brief, cardiac output was assessed by a 2D Doppler echocardiography technique using images of the aortic root. The diameter of the aortic root was measured at the level of aortic leaflets during mid-systole, and the aortic cross-sectional area was calculated. Aortic outflow was measured with a continuous Doppler transmitter from the suprasternal notch using previously described procedures.12

**Data Analysis**

Offspring data were analyzed according to their parents’ cardiac index. Determinants of cardiac index were assessed by linear regression analysis, with cardiac index as the dependent variable and age, gender, and BMI as independent variables. Cardiac index values

<table>
<thead>
<tr>
<th>Variable</th>
<th>Fathers (n=139)</th>
<th>Mothers (n=151)</th>
<th>Sons (n=104)</th>
<th>Daughters (n=104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>34.6±2.6</td>
<td>33.2±3.1</td>
<td>17.0±3.2</td>
<td>17.3±2.9</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.4±4.3</td>
<td>25.8±4.9</td>
<td>23.5±4.3</td>
<td>24.3±6.1</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>119.4±9.5</td>
<td>109.6±10.2</td>
<td>112.6±10.1</td>
<td>107±9.9</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>80.1±8.8</td>
<td>73.1±8.9</td>
<td>69.1±7.9</td>
<td>67.3±8</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>71.6±9.6</td>
<td>76.6±10.6</td>
<td>70.8±10.3</td>
<td>76.1±8.7</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>43.8±2.7</td>
<td>39.5±3.3</td>
<td>44.2±2.9</td>
<td>39.9±2.4</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.3±0.7</td>
<td>0.9±0.5</td>
<td>1.1±0.6</td>
<td>1.1±0.5</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>4.9±0.9</td>
<td>4.6±0.8</td>
<td>3.9±0.7</td>
<td>4.0±0.8</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>0.97±0.2</td>
<td>1.26±0.3</td>
<td>1.07±0.2</td>
<td>1.14±0.2</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>5.4±0.4</td>
<td>4.9±0.7</td>
<td>5.0±0.4</td>
<td>4.8±0.3</td>
</tr>
<tr>
<td>Insulin, pmol/L</td>
<td>111.2±44.5</td>
<td>100.4±42.3</td>
<td>126.3±67.4</td>
<td>137.0±68.9</td>
</tr>
</tbody>
</table>

Data are mean±SD.

**TABLE 1. Clinical Characteristics of Parents Classified According to Cardiac Index**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bottom Tertile†</th>
<th>Middle Tertile†</th>
<th>Top Tertile†</th>
<th>$P^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Father/mother/midparent</td>
<td>25/17/27</td>
<td>16/22/31</td>
<td>16/30/24</td>
<td>NS‡</td>
</tr>
<tr>
<td>Age, y</td>
<td>33.6±0.33</td>
<td>34.0±0.34</td>
<td>34.1±0.32</td>
<td>NS‡</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>78.5±1.4</td>
<td>76.4±1.5</td>
<td>73.8±1.4</td>
<td>NS</td>
</tr>
<tr>
<td>Height, cm</td>
<td>171.0±0.7</td>
<td>169.9±0.7</td>
<td>168.7±0.7</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.7±0.4</td>
<td>26.2±0.4</td>
<td>25.6±0.4</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>114.6±1.0</td>
<td>113.6±1.1</td>
<td>114.6±1.0</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>76.9±0.9</td>
<td>76.7±0.9</td>
<td>76.1±0.9</td>
<td>NS</td>
</tr>
<tr>
<td>Echocardiographic heart rate, bpm</td>
<td>59.6±0.8</td>
<td>63.3±0.8</td>
<td>66.2±0.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>Cardiac index, L/min per m²</td>
<td>2.3±0.02</td>
<td>2.8±0.03</td>
<td>3.3±0.02</td>
<td>0.0001</td>
</tr>
<tr>
<td>Left ventricular fractional shortening, %</td>
<td>37.2±0.8</td>
<td>36.9±0.8</td>
<td>39.7±0.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>41.3±0.5</td>
<td>41.5±0.6</td>
<td>41.3±0.5</td>
<td>NS</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>4.8±0.1</td>
<td>4.8±0.09</td>
<td>4.5±0.09</td>
<td>0.047</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.14±0.03</td>
<td>1.06±0.03</td>
<td>1.11±0.03</td>
<td>NS</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.0±0.09</td>
<td>1.1±0.09</td>
<td>1.2±0.08</td>
<td>NS</td>
</tr>
<tr>
<td>Plasma insulin, pmol/L</td>
<td>107.6±5.74</td>
<td>93.8±5.74</td>
<td>97.6±5.0</td>
<td>NS</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>5.1±0.09</td>
<td>5.2±0.1</td>
<td>5.1±0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Plasma norepinephrine, pmol/mL</td>
<td>1.27±0.08</td>
<td>1.41±0.08</td>
<td>1.41±0.09</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Adjusted for age and gender.
†Data are mean±SEM.
‡Unadjusted.
were adjusted for age, gender, and BMI by standard statistical methods. Parents were subsequently grouped into tertiles of adjusted cardiac index, and children were grouped according to whether their parents’ cardiac index was in the bottom, middle, or top tertile. When data from both parents were available, the average of the readings from mother and father (midparent) was used in the classification.13 Between-tertile differences were assessed using a general linear model procedure. Data were adjusted for possible confounders. The independent association of children’s BMI with parents’ clinical characteristics was studied with multiple forward regression analyses performed, first keeping the parents grouped together and then separating fathers from mothers, using parents’ age, BMI, cardiac index, clinical heart rate, systolic and diastolic blood pressures, and gender (where applicable) as independent variables. As expected, parental BMI was the strongest predictor of offspring BMI ($P=0.0001$), followed by parental cardiac index ($P=0.003$) and age ($P=0.05$). This association was mostly explained by the mother-child relationship ($P=0.009$ for cardiac index), whereas the cardiac index–BMI association did not reach statistical significance for the father-child relationship. Similar relationships with cardiac index were found when children’s plasma insulin level was considered as the dependent variable ($P=0.003$ for parents taken together, 0.01 for mothers, and NS for fathers).

**Results**

Echocardiographically measured cardiac index was available for 290 parents. Cardiac index was similar in fathers and mothers (mean±SD=2.7±0.5 and 2.9±0.5 L/min per m², respectively; $P=0.5$). Data of parents classified according to their cardiac index are reported in Table 2. No significant differences in gender distribution was found between the 3 groups. Parents in the top tertile had a slightly smaller BMI than those in the other tertiles. Blood pressure was similar in all groups. Resting heart rate, measured at the visit and during echocardiographic assessment, was elevated in parents in the top tertile, as were stroke volume and left ventricular fractional shortening (Figure 1 and Table 2). Plasma epinephrine level was also higher in parents with a high cardiac index (Figure 1), whereas among the metabolic parameters, only triglycerides were slightly increased in the top tertile. However, the between-tertile differences did not attain the level of statistical significance.

Offspring of parents with a high cardiac index were heavier, had an increased degree of adiposity, and had a greater waist/hip ratio than offspring of parents with an intermediate or low cardiac index (Table 3 and Figure 2). Blood pressure was higher in offspring of parents in the top tertile, a difference that was significant for diastolic blood pressure (Table 3). Child’s heart rate tended to increase with increasing level of parents’ cardiac index, especially when measured during the Stroop test. Insulin and insulin/glucose ratio were both elevated in offspring of parents with hyperdynamic circulation (Figure 2 and Table 3); these children also had higher levels of triglycerides. Children’s cardiac index and left ventricular fractional shortening did not differ between the 3 groups (Table 3).

To determine which parental clinical variables influenced children’s BMI and plasma insulin level, a series of multiple linear regression analyses was performed, first keeping the parents grouped together and then separating fathers from mothers, using parents’ age, BMI, cardiac index, clinical heart rate, systolic and diastolic blood pressures, and gender (where applicable) as independent variables. As expected, parental BMI was the strongest predictor of offspring BMI ($P=0.0001$), followed by parental cardiac index ($P=0.003$) and age ($P=0.05$). This association was mostly explained by the mother-child relationship ($P=0.009$ for cardiac index), whereas the cardiac index-BMI association did not reach statistical significance for the father-child relationship. Similar relationships with cardiac index were found when children’s plasma insulin level was considered as the dependent variable ($P=0.003$ for parents taken together, 0.01 for mothers, and NS for fathers).

**Discussion**

In the past few years, our understanding of the pathophysiological correlates of insulin resistance syndrome has increased greatly. A number of studies suggest that people who have hyperdynamic circulation tend to display many of the features of insulin resistance syndrome, including obesity, unfavorable fat distribution, hyperinsulinemia, and metabolic disturbances.1–11 In contrast, however, the mechanisms of initiation and development of insulin resistance remain controversial. Furthermore, there is still considerable dispute about the most probable genetic mechanism that leads to the observed familial clustering of the features of insulin resistance syndrome.

In this study, parents with hyperdynamic circulation did not differ from other parents in body weight or metabolic variables. Nevertheless, the results show that offspring of parents with hyperdynamic circulation have a genetic predisposition to development of overweight and other features of insulin resistance syndrome. In fact, offspring of parents in the top tertile of cardiac index had an increased BMI and degree of adiposity, abnormal fat distribution, higher diastolic blood pressure, hyperinsulinemia, and slightly elevated triglyceride levels. After adjustment for BMI, most of these differences disappeared. The latter finding is in agreement...
long-standing sympathetic overdrive) has been described in

the classification of parents. A substantial downregulation of

fascinating association of parental circulatory abnormalities

in parents and offspring are so different. However, the

pressure.

overweight, elevated plasma insulin level, and higher blood

response to the Stroop test), but the leading features were

still detect some evidence of enhanced sympathetic tone

in the top cardiac index tertile. In the offspring, we could

parents, documenting the existence of increased sympathetic

and plasma epinephrine level between the 3 groups of

large differences in heart rate, left ventricular contractility,

other investigators.14

As a result of the cardiac index stratification, there were

with hyperdynamic circulation, in whom an attenuation of the

relationship between hyperkinetic state and features of insulin

resistance syndrome was found when BMI was accounted for.

The importance of the relationship between parental hyper-
dynamic circulation and the features of insulin resistance is

explained by mother-child relationship. Parental BMI was a

strong predictor of children’s BMI, confirming the results of

other investigators.14

with the results of Stern et al2 obtained in subjects with

hyperdynamic circulation, in whom a attenuation of the

relationship between hyperkinetic state and features of insulin

resistance syndrome was found when BMI was accounted for.

As a result of the cardiac index stratification, there were

large differences in heart rate, left ventricular contractility,

and plasma epinephrine level between the 3 groups of

parents, documenting the existence of increased sympathetic
tone in the top cardiac index tertile. In the offspring, we could

still detect some evidence of enhanced sympathetic tone

(faster resting heart rate and excessive tachycardia in re-
sponse to the Stroop test), but the leading features were

overweight, elevated plasma insulin level, and higher blood

pressure.

At first glance, it is difficult to explain why the phenotypes

in parents and offspring are so different. However, the

fascinating association of parental circulatory abnormalities

with metabolic abnormalities in offspring may in part reflect

the classification of parents. A substantial downregulation of

β-adrenergic responsiveness (presumably in response to a

long-standing sympathetic overdrive) has been described in

patients with “normokinetic” borderline hypertension15 and

with hypertension in general.16–18 Along the line of our

interest in the hyperkinetic state9,12,19 in this study, we

classified the parents according to tertiles of cardiac index. It

is likely that the top tertile consisted of individuals able to

respond to the sympathetic overdrive with high cardiac

output, increased stroke volume, fast heart rate, and enhanced

cardiac contractility. Generally, cardiac output and heart rate
decrease with age,20 and in the top cardiac index tertile, we

declared cardiac output and cardiac contractility in normotensive

hypertension patients with “normokinetic” borderline hyperten-
sion.20–21 If both circulatory and metabolic

β-adrenergic responsiveness had been preserved. In a series

of experiments, Landsberg and Kreiger14 documented that

enhanced sympathetic tone increases feeding-induced facul-
tative thermogenesis. This increase in metabolic rate is

viewed as an essential compensatory mechanism to ward off

future increases in body weight. Importantly, the thermogenic

effect of sympathetic stimulation is mediated through

β-adrenergic receptors.21,22 If both circulatory and metabolic

β-adrenergic responsiveness had been preserved in parents in

the present study, metabolic β-adrenergic responsiveness

may have prevented them from gaining weight. In fact, in a

previous report of the Tecumseh study, we noted that patients

with hyperkinetic hypertension (whose β-adrenergic responsiv-
eseness was similarly preserved as in normotensive hyper-
dynamic individuals in the present report) were not obese.10

The fact that children of hyperkinetic parents had no increase

in cardiac index and left ventricular ejective function suggests

that their β-adrenergic responsiveness did not differ from that

to their peers. If the sympathetic overactivity of parents in the

present study has been passed on to children but the offspring

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bottom Tertile†</th>
<th>Middle Tertile‡</th>
<th>Top Tertile†</th>
<th>P*</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, male/female</td>
<td>40/29</td>
<td>33/36</td>
<td>31/39</td>
<td>NS</td>
<td>§</td>
</tr>
<tr>
<td>Age, years</td>
<td>16.8±0.4</td>
<td>17.6±0.4</td>
<td>17.0±0.4</td>
<td>NS</td>
<td>§</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>63.0±1.9</td>
<td>66.1±2.1</td>
<td>72.1±1.9</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Height, cm</td>
<td>167.1±0.9</td>
<td>167.1±0.9</td>
<td>167.5±0.9</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>48.8±1.1</td>
<td>49.9±1.1</td>
<td>53.1±1.1</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>108.2±1.2</td>
<td>108.9±1.3</td>
<td>110.9±1.2</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>66.2±0.9</td>
<td>66.2±0.9</td>
<td>69.7±0.8</td>
<td>0.02</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>72.1±1.5</td>
<td>72.8±1.5</td>
<td>75.2±1.4</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate during Stroop’s test, bpm</td>
<td>76.5±1.4</td>
<td>82.3±1.5</td>
<td>82.2±1.4</td>
<td>0.02</td>
<td>0.006</td>
</tr>
<tr>
<td>Cardiac index, L/min per m²</td>
<td>3.1±0.09</td>
<td>2.8±0.06</td>
<td>2.9±0.09</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Left ventricular fractional shortening, %</td>
<td>41.7±0.7</td>
<td>41.3±0.7</td>
<td>41.0±0.7</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.1±0.07</td>
<td>1.0±0.07</td>
<td>1.2±0.07</td>
<td>0.05</td>
<td>NS</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>4±0.09</td>
<td>3.8±0.09</td>
<td>4±0.09</td>
<td>0.04</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.15±0.03</td>
<td>1.05±0.03</td>
<td>1.09±0.03</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>42.0±0.3</td>
<td>41.8±0.3</td>
<td>42.3±0.3</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Insulin, pmol/L</td>
<td>108.3±7.9</td>
<td>135.6±8.6</td>
<td>143.5±7.9</td>
<td>0.001</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine, μmol/L</td>
<td>72.2±0.9</td>
<td>74.2±0.9</td>
<td>75.1±0.9</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Adjusted for age and gender. †Data are mean±SEM. §Adjusted for age, gender, and BMI. 

"Hyperdynamic Circulation and Insulin Resistance"
did not share the parents resistance to downregulation of β-adrenergic responsiveness, they may have responded to sympathetic stimulation with insulin resistance, dyslipidemia, and increased body weight. The mechanism by which sympathetic stimulation causes insulin resistance and dyslipidemia has been discussed elsewhere.23 Our data suggest that in the future, it may well be worth testing the hypothesis that downregulation of β-adrenergoreceptor responsiveness, against a background of enhanced sympathetic tone, leads to overweight. The recent observation that markedly obese children have increased baseline plasma epinephrine levels and have a diminished lipolytic response to infusions of physiological doses of adrenaline24 adds further credence to the hypothesis. Decreased mobilization of triglycerides in these children may be mediated by α, β1, or β3 adrenoreceptors.

A body of evidence suggests that elevated heart rate is a risk factor for future hypertension and development of atherosclerotic lesions.25–27 This seems to be due to the coaggregation of fast heart rate with high blood pressure, overweight, increased plasma insulin level, and dyslipidemias.28 Sympathetic overactivity underlying tachycardia is the likely explanation for this association, even though other factors can interact to promote this clinical condition, as recently postulated by some investigators.29 The results of the present study suggest that this coaggregation can be genetically transmitted, even though the expression of the genetic defect may differ among siblings. As indicated above, we believe that β-adrenergic responsiveness may affect the phenotypic expression of the underlying sympathetic overactivity in parents and offspring. The nature of these modifiers of the phenotype is not understood. It is conceivable that other genetic factors affect β-adrenergic responsiveness, but environmental factors could also play a role. Diet may have an influence on offspring modifying the phenotypic manifestations of the syndrome. It has been reported that sodium intake affects β-adrenergic responsiveness.30–32 It is also possible that the education and socioeconomic status of the offspring differed from those of the parents and that these environmental differences had some other unknown effect on the phenotype.

In summary, we found that parental hyperdynamic circulation was an important predictor of the child’s overweight, abnormal fat distribution, increased blood pressure, and hyperinsulinemia. The mother-child relationship accounted for most of this association. These data suggest that sympathetic overactivity underlying hyperdynamic circulation is a key factor in the development of obesity and insulin resistance. The clinical traits related to insulin resistance syndrome are a complex coaggregation of factors in which the clinically defined phenotype can arise through a wide array of pathophysiological mechanisms. Nongenetic or genetic factors affecting β-adrenergic responsiveness may play a role in modulating expression of the genetic defect.

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Parental Hyperdynamic Circulation Predicts Insulin Resistance in Offspring: The Tecumseh Offspring Study
Paolo Palatini, Olga Vriz, Shawna Nesbitt, John Amerena, Silja Majahalme, Mariaconsuelo Valentini and Stevo Julius

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