FH NE % max. attenuation 25 ± 4 vs. untreated FH 3 ± 1, p < 0.05; A-II % max attenuation 33 ± 6 vs. untreated FH 4 ± 3, p < 0.05). These data indicate, for the first time, that treating insulin resistance with metformin restores the vaso-dilatory actions of insulin in IR FH rats. Restoration of insulin’s vascular effects may serve to decrease peripheral vascular resistance and attenuate BP.

Key Words: Insulin resistance, fructose-induced hypertension, metformin, insulin-induced vasodilation, rats

E021

RELATIONSHIP BETWEEN INSULIN RESISTANCE AND LEFT VENTRICULAR ADAPTATION TO HYPERTENSION
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Objective: This study was designed to elucidate the association between left ventricular geometric adaptation and insulin resistance in essential hypertension.

Design and Methods: 73 untreated hypertensive patients were subdivided into 4 groups based on left ventricular mass index (LVMI) and relative wall thickness (RWT). With respect to insulin resistance, homeostasis model assessment (HOMA) was performed. HOMA-R = Fasting blood sugar (mmol/L) x Immunoreactive insulin (µU/ml)/22.5.

Results: 1) Among hypertensive patients, LVMI and RWT were normal in 29 patients (NG), whereas 9 patients had increased RWT with normal LVMI (CR), 12 patients had concentric hypertrophy (CH, increase both LVMI and RWT) and 23 patients had increased LVMI and normal in RWT (EH). 2) There were no significant differences in office blood pressure and body mass index (BMI) among 4 groups. 3) HOMA-R was 1.8 ± 1.2 in NG, 1.4 ± 0.9 in CR, 2.1 ± 0.8 in EH and 4.2 ± 1.8 in CH (p < 0.001 vs other 3 groups). In multiple regression analyses, there was a strongly significant correlation between the degree of LVMI and the severity of insulin resistance independent of office blood pressure and BMI.

Conclusion: Pattern of left ventricular geometric adaptation to hypertension is closely related to the severity of insulin resistance.

Key Words: Hypertension, insulin resistance, HOMA-R, left ventricular hypertrophy

E022

INCREASED INSULIN RESISTANCE IN SALT-SENSITIVE ESSENTIAL HYPERTENSION
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The aim of the present study was to evaluate the relationship between salt sensitivity and insulin resistance in essential hypertension, using gold standard techniques. We studied 17 essential hypertensive patients (35% women) aged 51.6 ± 9.4 years, with baseline systolic and diastolic blood pressure: 148.6 ± 14.6 mmHg and 94.4 ± 5.3 mmHg. All participants had body mass index <30 kg/m² and a normal oral glucose tolerance test. Insulin sensitivity index (M) and fasting insulin resistance index (FIRI) were calculated using the euglycemic hyperinsulinemic clamp technique. Baseline fasting glucose and insulin, as well as lipid profile, were determined using standard methods. Furthermore, salt-sensitivity was defined as a significant increase (p < 0.05) in 24-hour mean blood pressure, by ABPM, from 7 days of low salt (20 mmol/day) to 7 days of high salt (260 mmol/day) intake. Salt-sensitive hypertensive patients (SS; n = 6) showed a significant decreased insulin sensitivity index, compared to salt-resistant hypertensives (SR; n = 11). Moreover, we found a significant inverse correlation between the insulin sensitivity index and the blood pressure response to high-salt intake (r: −0.573; p = 0.016). SS patients also tended to have higher values of HbA1c, fasting plasma insulin, and serum cholesterol and triglyc-erides.

<table>
<thead>
<tr>
<th>SS (n = 6)</th>
<th>SR (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M (mg/Kg/min)</td>
<td>3.7 ± 0.5</td>
</tr>
<tr>
<td>FIRI</td>
<td>2.5 ± 0.8</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>4.9 ± 0.2</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>90.3 ± 2.7</td>
</tr>
<tr>
<td>Insulin (mg/dL)</td>
<td>9.6 ± 2.2</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>227 ± 11</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>132 ± 17</td>
</tr>
</tbody>
</table>

Values are mean ± s.e.m. • : p = 0.0009

In conclusion, these results confirm the existence of a relationship between salt sensitivity and insulin resistance in essential hypertension.

Key Words: Insulin resistance, dietary salt, salt sensitivity

E023

PLC-γ1 ACTIVITY IS REQUIRED FOR INSULIN-STIMULATED MITOGENESIS—IMPORTANT ROLE FOR SH2/SH3 DOMAINS
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In the Framingham Study, insulin resistance, hyperinsulinemia, hypertension, obesity, hypertriglyceridemia, and low HDL cholesterol have been shown to coexist with accelerated atherogenesis. The IRAS study has shown that insulin resistance is an independent risk factor for atherosclerosis. The mechanism linking hyperinsulinemia, insulin resistance and atherosclerosis remains poorly understood. Evidence is mounting that the vasculature is an important insulin-sensitive tissue. Cell proliferation and migration are important features of the atherogenic process. We studied the role of PLC-γ1 for insulin-stimulated DNA synthesis in HIRcB cells, and it’s effect on the Ras/Raf/MAP kinase pathway, which is intimately involved in cellular proliferation in many cell types. Here, we report for the first time that the PLC inhibitor U73122 significantly inhibited insulin-stimulated DNA synthesis, measured by 3(H)thymidine incorporation. Inhibition occurred in a dose dependent manner with an EC50 of 2 µM, while the control compound U73343 had no significant effect. Addition of increasing concentrations of a syn-