OR-45
IS SYMPATHETIC NERVOUS SYSTEM IMPORTANT IN MEDIATING BLOOD PRESSURE LOWERING EFFECT OF WEIGHT LOSS?

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Reduction in sympathetic vasoconstrictor drive has been hypothesized to be a major mechanism explaining the blood pressure-lowering effects of dietary weight loss, but the evidence to support this notion is derived from strictly Caucasian cohorts. To determine if weight loss also leads to sympathoinhibition in African Americans (AA), the demographic group in the U.S. with the highest prevalence of hypertension, we measured sympathetic nerve activity (SNA) with microneurography in 11 normotensive (NT) young adult AA men and 6 NT young adult AA women before and after 16 weeks of a hypocaloric diet. In the women, 20 lb weight loss led to greater than 50% reduction in SNA (22 ± 3 to 10 ± 1 bursts/min) but 24-hour ambulatory blood pressure (BP) was unchanged (116 ± 2/68 ± 1 to 116 ± 3/70 ± 1 mmHg, p=ns). In the men however, 24 lb weight loss had no effect on SNA (26 ± 4 to 27 ± 3) but lowered the 24-hour ambulatory BP by 5/4 mm Hg (from 124 ± 2/74 ± 2 to 119 ± 3/70 ± 2 mmHg, P<0.05). To explore the mechanism of the blood pressure lowering effect of weight loss in these men, we measured 24-hour urinary sodium excretion and found that the 24-hour BP fell only in the men who had reduced their sodium intake along with the hypocaloric diet. In 6 men in whom urinary sodium excretion fell markedly from 165 ± 11 to 45 ± 17 meq/day, 24-hour BP fell by 8/6 mm Hg (from 123 ± 4/74 ± 5 to 115 ± 3/68 ± 3 mmHg) over the 16 week protocol, whereas in the 5 men in whom urinary sodium excretion did not fall, 24-hour BP remained unchanged despite comparable amounts of weight loss in both subgroups. Thus, in women, a substantial reduction in SNA with microneurography in 11 normotensive young adult AA men and women call in to question the importance of the sympathetic nervous system in producing the blood pressure lowering effect of dietary weight loss.

Key Words: Sympathetic Nervous System, Weight loss, Blood pressure

OR-46
ANGIOTENSIN II (Ang II) STIMULATES SYMPATHETIC NERVE (SNS) ACTIVITY THROUGH ACTIVATION OF OXIDATIVE STRESS

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There is substantial evidence that Ang II enhances SNS activity. The mechanisms of central SNS activation are not well established. We have shown that infusion of Ang II in the lateral ventricle (ICV) raises blood pressure (BP), renal SNS activity (RSNA), and norepinephrine (NE) secretion from the posterior hypothalamic nuclei (PH). Ang II also reduces the abundance of interleukin (IL-1β) and nNOS mRNA in the PH. Pretreatment with losartan, a (AT1) receptor antagonist, abolishes these effects of Ang II. These studies suggest that Ang II-induced decrease in NO expression may be responsible for SNS activation. In the current studies we have tested the hypothesis that the effects of Ang II on NO and SNS activity are mediated by increased oxidative stress. To test this hypothesis, we infused tempol, a superoxide dismutase mimetic, (50 mg/ Kg body weight/min, ICV) prior to Ang II (at the rate of 1.67 mg/ml/Kg/min x 60 min).

Ang II raised BP from 110 ±1.0 to 127 ±1.2 mmHg (P<0.01), NE secretion from the PH from 158 ±2.9 to 209 ±2.2 pg/ml (P<0.01), and RSNA by approximately 21 %, but reduced the abundance of IL-1β and nNOS in the PH.

Tempol completely abolished the effects of Ang II on BP and NE secretion from the PH, RSNA and IL-1β and nNOS expression. In conclusion, these studies support the hypothesis that the effects of Ang II on central SNS activation are mediated by increased oxidative stress in brain regions involved in the noradrenergic control of BP. This in turn results in down-regulation of nNOS and IL-1β, activation of the SNS and hypertension.

Key Words: Angiotensin II, Sympathetic nervous system, Oxidative stress

OR-47
EFFECT OF RAPID BLOOD PRESSURE DECREASES ON CORONARY FLOW RESERVE IN NORMAL CORONARY ARTERIES

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Background: Changes in blood pressure (MBP), heart rate (HR) and contractility are known to alter baseline and maximal coronary blood flow (CBF), but coronary flow reserve (CFR) may be a better functional measure. We evaluated the acute effects of 3 hypotensive medications (HMEDE) on CBF parameters in patients (pts) with angiographically normal (NL) coronary arteries (CA), under constant HR by atrial pacing.

Methods: We performed anatomic and CBF measurements via Doppler wire at rest (R) and during hyperemia (H), produced by intracoronary injection of 18 μg adenosine in pts with stable angina undergoing diagnostic coronary angiography: a) in the NL left circumflex CA (20 pts, age 59±8) pre- and post-IV infusion (INF) of 0.5 to 2 μg /kg/min nitroprusside sodium (NPR) and 10 to 90 μg/min nitroglycerin (NTG) titrated to reach a similar MBF decrease. After each INF (NPR first and then NTG) HR and MBP were allowed to return to baseline. b) in the NL LAD CA (19 pts age 58±9) pre- and 20 min post-INF of 150 μg clonidine (CLO) (50 μg 5 min). We measured CBF (systolic plus diastolic CBF), time-averaged peak velocity (APV, cm/s) and CFR (ratio of APV at H/APV at R).

Results: In NL CA lumen diameter increased following all HMEDE INF (from 2.2±0.4mm to 2.51±0.5mm after NPR, from 2.26±0.4mm to 2.67±0.5mm after NTG and from 3.28±0.6mm to 3.62±0.5mm after CLO, p<0.001). Hemodynamics at endpoint are shown in the table.

Conclusion: In angiographically NL CA, INF of 3 HMED to produce the same MBF decrease produces a different effect on CFR (increase with CLO, decrease with NPR and no change with NTG).

<table>
<thead>
<tr>
<th></th>
<th>MBP (mmHg)</th>
<th>CBF (ml/min)</th>
<th>CRF</th>
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<tbody>
<tr>
<td>PRE</td>
<td>104 ± 10</td>
<td>58.3 ± 18.6</td>
<td>2.73 ± 0.6</td>
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<tr>
<td>NPR</td>
<td>81 ± 9</td>
<td>66.5 ± 21.9</td>
<td>1.79 ± 0.5**</td>
</tr>
<tr>
<td>NTG</td>
<td>81 ± 9</td>
<td>60.6 ± 20.4</td>
<td>2.74 ± 0.4#</td>
</tr>
<tr>
<td>CLO</td>
<td>79 ± 8</td>
<td>66.5 ± 15.0</td>
<td>3.12 ± 0.7**</td>
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</tbody>
</table>

*p < 0.05, **p < 0.001 vs PRE, #p < 0.001 vs NPR

Key Words: Hypotension, Coronary Reserve, Clonidine