Letter to the Editor

Thyrotropin-Releasing Hormone Precursor Gene Knocking Down Impedes Melanocortin-Induced Hypertension in Rats

To the Editor:

Recently, da Silva et al\(^1\) reported that endogenous melanocortin may cause elevation of arterial blood pressure (ABP) in spontaneously hypertensive rats. We invite authors to consider that the hypothalamic thyrotropin-releasing hormone (TRH) system may be involved, because spontaneously hypertensive rats show an hyperactivity of this system,\(^2\) and intracerebroventricular (ICV) injections of a prepro-TRH antisense oligonucleotide (AS) decreases both elevated TRH content and ABP independent of thyroid status.\(^3\)

Leptin effects include increases in sympathetic activity and inhibition of the starvation-suppressed expression of thyroid hormones apparently by upregulating prepro-TRH gene expression. Then, leptin can increase the MC4R ligand (α-melanocyte-stimulating hormone) production to regulate TRH expression.\(^4\) Furthermore, we have shown that ICV leptin injections induce a pressor effect that is avoided by prepro-TRH AS pretreatment.\(^5\)

In conclusion, we show that the melanocortin 3 and 4 agonist induced hypertension only in the presence of an intact hypothalamic TRH system; thus, we propose that an activation of the axis leptin-melanocortin-TRH might explain increases of ABP in this genetic model of hypertension.

Sources of Funding

These studies were supported by grants from the Agencia Nacional De Investigaciones Científicas y Técnicas (ANPCyT): PICT-03-13862 and PICT-05-25920.

Disclosures

None.

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### Table. Effect of TRH Gene Knocking Down on Melanocortin-Induced Hypertension

<table>
<thead>
<tr>
<th>ICV 1</th>
<th>ICV 2</th>
<th>ABP Basal, mm Hg</th>
<th>ABP 24 Hours, mm Hg</th>
<th>ABP 48 Hours, mm Hg</th>
<th>TRH, pg/mg of Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>V</td>
<td>V</td>
<td>109.7 ± 3.3</td>
<td>107.3 ± 6.3</td>
<td>109 ± 3.6</td>
<td>1161.4 ± 212</td>
</tr>
<tr>
<td>V</td>
<td>MTII</td>
<td>105.1 ± 2.0</td>
<td>106.5 ± 2.8</td>
<td>113.8 ± 7.3†</td>
<td>1926.8 ± 454.3‡</td>
</tr>
<tr>
<td>AS</td>
<td>MTII</td>
<td>105.7 ± 3.2</td>
<td>102.4 ± 2.4</td>
<td>93.9 ± 3.4†</td>
<td>1098.6 ± 253</td>
</tr>
<tr>
<td>Inv</td>
<td>MTII</td>
<td>106.7 ± 4.0</td>
<td>102.6 ± 8.5</td>
<td>109.8 ± 3.9*</td>
<td>1839.3 ± 297‡</td>
</tr>
</tbody>
</table>

Results are expressed as means ± SDs. Inv indicates inverted.

*P < 0.05 vs 24 hours.
†P < 0.05 vs basal.
‡P < 0.05 vs vehicle and AS + MTII (n = 4).

M.S.L. and S.I.G. contributed equally to this work. *(Hypertension, 2008;52:e8.)*

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*Hypertension* is available at http://hyper.ahajournals.org

DOI: 10.1161/HYPERTENSIONAHA.108.114686
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Melanocortin-Induced Hypertension in Rats
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Hypertension. 2008;52:e8; originally published online June 16, 2008;
doi: 10.1161/HYPERTENSIONAHA.108.114686

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