Response to Role of Hyperleptinemia in the Regulation of Blood Pressure and Cardiac Function

We appreciate Dr Tsuda’s comments and observations on the involvement of nitric oxide in leptin-induced endothelial dysfunction and cardiac failure. We agree with Dr Tsuda that similar mechanisms might occur in neonatal leptin–treated rats. Because endothelial dysfunction represents an early form of vascular disease that precedes other cardiovascular complications, the role of neonatal leptin on endothelial function may provide valuable mechanistic insights.

Although we will be proposing to conduct these analyses, we will also investigate the role of the overactive sympathetic nervous system in the neonatal leptin–treated rats, which may influence vascular tone and cardiac function. Recent study by Wang et al demonstrates that endothelial dysfunction in leptin-induced mice is blocked by mesenteric sympathetic denervation. Interestingly, also superoxide scavenger TEMPOL (4-hydroxy-2,2,6,6-tetramethylpiperidin-1-oxy) treatment had similar therapeutic effects and suggests reactive oxygen species and sympathetic outflow as potential targets for leptin-induced endothelial dysfunction and hypertension.

Leptin has also shown a negative inotropic effect in the heart, which has been shown to be dependent on nitric oxide and STAT-3 (signal transducer and activator of transcription 3)–induced p38 mitogen–activated protein kinase activation. These mechanistic pathways will be considered in future work, as well as potential targets, which mediate the adverse cardiac effects secondary to neonatal hyperleptinemia.

Sources of Funding

This study was supported by the British Heart Foundation (FS/10/003/28163) and Biotechnology and Biological Sciences Research Council (BB/D521861).

Disclosures

None.

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*Hypertension*. 2014;63:e2; originally published online November 25, 2013; doi: 10.1161/HYPERTENSIONAHA.113.02399

*Hypertension* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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