Can the Study of Female Rats Help Our Understanding of Women?

To the Editor:

Sampson et al.1 are to be congratulated for their important contribution to knowledge of the effects of gender on the effects of angiotensin peptides. Importantly, their study showed in rats that low-dose angiotensin II reduced blood pressure in females but not in males, and this blood pressure reduction was mediated by the angiotensin II type 2 receptor. Moreover, high-dose angiotensin II produced a lesser increase in blood pressure in female than in male rats.

These data have important and far-reaching clinical implications. First, therapies that reduce angiotensin II levels, such as angiotensin-converting enzyme inhibitors, renin inhibitors, and β-blockers, may be less effective in blood pressure reduction in women than in men and may even increase blood pressure in women by removing the angiotensin II–dependent, angiotensin II type 2 receptor–mediated depressor mechanism in women. Second, angiotensin receptor blocker therapies, by causing a reactive increase in angiotensin II levels, may increase angiotensin II type 2 receptor stimulation and thereby more effectively reduce blood pressure in women than in men.

In the introduction to their article, Sampson et al.1 argued the clinical justification for their study. It is, therefore, incumbent on the authors1 and the editorialists2 to address the clinical implications of these data1 and to suggest reasons why clinical studies failed to show differences between men and women in their blood pressure responses to angiotensin-converting enzyme inhibitor, β-blocker, and angiotensin receptor blocker therapies.3,4 Moreover, men and women showed similar changes in blood pressure, effective renal plasma flow, and renal vascular resistance, in response to angiotensin II infusion, although women showed a decrease in glomerular filtration rate not seen in men.5 Is it possible that the mechanisms described by Sampson et al.1 in rats do not apply to humans? If we want to understand the differences between men and women, would it not be more appropriate to study men and women?

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2. Sandberg K, Ji H. Why can’t a woman be more like a man? Is the angiotensin type 2 receptor to blame or to thank? Hypertension. 2008;52:615–617.
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