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

To the Editor:

Sampson et al\textsuperscript{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\textsuperscript{1} argued the clinical justification for their study. It is, therefore, incumbent on the authors\textsuperscript{1} and the editorialists\textsuperscript{2} to address the clinical implications of these data\textsuperscript{1} 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.\textsuperscript{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.\textsuperscript{5} Is it possible that the mechanisms described by Sampson et al\textsuperscript{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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Duncan John Campbell

St Vincent’s Institute of Medical Research and Department of Medicine
University of Melbourne
St Vincent’s Hospital
Fitzroy, Victoria, Australia

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