To the Editor: We read with interest the article, “Losartan Reduces Oxidative Stress Within the Rostral Ventrolateral Medulla of Rats With Renovascular Hypertension,” by Nishi et al., which reported that peripheral angiotensin II type 1 (AT1) receptor blockade using losartan reduces oxidative stress within the rostral ventrolateral medulla (RVLM) in renovascular hypertension. Renovascular hypertension in rodents is a well-known model of experimental hypertension characterized by increased levels of angiotensin II. How circulating angiotensin II signals reach cardiovascular regulatory areas within the brain, such as the RVLM, to induce oxidative stress, considering that angiotensin II is not capable of crossing the blood brain barrier (BBB), has been a topic of extensive discussion among scientists. The most accepted hypothesis is that angiotensin II signals reach those areas by activating AT1 receptors in circumventricular organs, which partially lack the BBB.

The subfornical organ (SFO) is one of several circumventricular organs that lie outside the BBB and thus have access to circulating angiotensin II. Sakai et al. have reported that once activated by angiotensin II, neurons and glia in the SFO can locally produce de novo angiotensin II. Therefore, local production of angiotensin II and downstream NADPH oxidase–derived superoxide production in other brain areas, such as the paraventricular nucleus of the hypothalamus (PVN) and RVLM, may be triggered by activation of the SFO. This may shed some light on the paper by Nishi et al., which does not make it clear to the readers how peripheral administration of losartan reduces oxidative stress in the RVLM.

In addition, the authors mentioned that inhibition of oxidative stress in the PVN does not decrease blood pressure in spontaneously hypertensive rats. This concept was used to support their focus on the RVLM. Although that information is true based on the report by Nishihara et al., in renovascular hypertension, the PVN plays a crucial role in the maintenance of elevated blood pressure. Indeed, Burmeister et al. reported that viral delivery of Copper Zinc Superoxide Desmutase (CuZnSOD) to the PVN not only prevented the elevation in superoxide but also abolished renovascular hypertension. Furthermore, Burmeister et al. reported that renovascular hypertension caused a surge in activator protein - 1 (AP-1) activity in the PVN, which paralleled the rise in superoxide production in this brain region, and this was prevented by treatment with Adenovirus expressing Copper Zinc Superoxide Desmutase (AdCuZnSOD). Finally, they reported that adenovirus-mediated expression of a dominant-negative inhibitor of AP-1 activity in the PVN prevented renovascular hypertension. Therefore, the crucial role of the PVN in renovascular hypertension and its connections to the RVLM cannot be neglected.

DISCLOSURE

The author declared no conflict of interest.

REFERENCES