Response to “Reducing Oxidative Stress in the Rostral Ventrolateral Medulla in Renovascular Hypertension by Peripheral Administration of Losartan: How and Where?”

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To the Editor: We thank Dr Braga for the letter, “Reducing Oxidative Stress in the Rostral Ventrolateral Medulla in Renovascular Hypertension by Peripheral Administration of Losartan: How and Where?”,1 and thoughtful comments regarding our article, “Losartan Reduces Oxidative Stress Within the Rostral Ventrolateral Medulla of Rats With Renovascular Hypertension.”2 Our article showed that chronic treatment with losartan decreases oxidative stress preferentially within the rostral ventrolateral medulla (RVLM) compared with other brainstem regions. In our interpretation, this is an important mechanism involved in the hypertensive and sympathoinhibitory response to chronic losartan administration in experimental renovascular hypertension. The point raised by Braga is important; one of the possible sources for AT1 angiotensin II (Ang II) receptor (AT1R) activation in the RVLM is Ang II acting in the subfornical organ (SFO), leading to activation of the paraventricular nucleus of the hypothalamus (PVN) and, subsequently, the rostral ventrolateral—the well known SFO-PVN-RVLM pathway.3 In fact, previous studies showed that the hypertension and sympathoexcitation induced by Ang II can be prevented or attenuated by selective blocking of AT1R or oxidative stress formation in this pathway.3–5 Thus, we cannot exclude that losartan is acting in the SFO-PVN-RVLM pathway by reducing oxidative stress formation within the RVLM. However, besides this pathway, other brain regions such as the area postrema (AP) may also play an important role in the central actions of Ang II. In fact, lesion of the AP prevents the chronic hypertension induced by Ang II, and the depressor effect of losartan treatment was significantly reduced in AP lesioned rats.6 Finally, because Ang II does not cross the blood–brain barrier, local production of Ang II may play an important role in the central actions of Ang II. In fact, lesion of the AP prevents the chronic hypertension induced by Ang II, and the depressor effect of losartan treatment was significantly reduced in AP lesioned rats.6

Our study describes that chronic losartan treatment reduces oxidative stress preferentially within the RVLM but not in other brainstem regions; this was accompanied by improvement of arterial baroreceptor function sensitivity and reduction of sympathoexcitation and hypertension. Thus, although the major focus of our article was the RVLM, the possibility that losartan is acting in other brain regions involved with cardiovascular regulation, such as the SFO-PVN or AP, leading to a reduction of oxidative stress within the RVLM, is possible. Again, the major focus of our article was the RVLM.

REFERENCES