Angiotensin II in paraventricular nucleus contributes to sympathoexcitation in renal ischemia–reperfusion injury by AT1 receptor and oxidative stress

Behjat Seifi, PhD,a,* Mehri Kadkhodaee, PhD,a Enayatollah Bakhshi, PhD, b Mina Ranjbaran, a Maryam Zahmatkesh, PhD, c Zahra Sedaghat, PhD, d Parisa Ahghari, e and Parvaneh Esmaeili, BSc f

a Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran
b Department of Biostatistics, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran
c Department of Neurosciences and Addiction, School of Advanced in Medicine, Tehran University of Medical Sciences, Tehran, Iran
d Department of Physiology and Pharmacology, Medical School, Bushehr University of Medical Sciences, Bushehr, Iran
e Department of Physiology, International Campus, Tehran University of Medical Sciences, Tehran, Iran
f Research Department, Eqlim Danesh Co. Ltd, Tehran, Iran

ARTICLE INFO
Article history:
Received 24 December 2013
Received in revised form 15 April 2014
Accepted 24 June 2014
Available online 5 July 2014

Keywords:
Renal ischemia–reperfusion
Paraventricular nucleus
Ang II
Sympathetic nerve activity

ABSTRACT
Background: To investigate the effect of angiotensin II (Ang II) in the hypothalamic paraventricular nucleus (PVN) on renal ischemia–reperfusion (IR) injury and to assay the role of renal sympathetic nerve activity (RSNA).
Methods: A cannula was inserted into the right side PVN in Sprague–Dawley rats for microinjection of Ang II (3, 30, and 300 ng); Ang II AT1 receptor antagonist, losartan (0.3 mg); and the superoxide dismutase (SOD) mimetic, tempol (20 nmol) before right side nephrectomy. After 1 wk, renal IR injury was induced by clamping the left renal artery for 45 min, and then reperfusion for 3 or 24 h. The extent of renal damage was determined by evaluation of renal functional indices. RSNA was recorded in all groups. Oxidative stress indices (SOD activity and malondialdehyde levels) were assayed in the PVN.
Results: Microinjection of pharmacologic doses of Ang II into the PVN exaggerated renal IR injury, increased RSNA and oxidative stress in the PVN dose dependently. The effects of Ang II (3 ng) was prevented by pretreatment with losartan into the PVN. Furthermore, the deleterious effects of Ang II on renal IR injury, RSNA, and oxidative stress were abolished by pretreatment with tempol.
Conclusions: These results indicate that the PVN is a responsive site for central Ang II increment damage in renal ischemia–reperfusion injury. We suggested the central effects of Ang II in the PVN on renal IR injury are mediated by AT1 receptors and oxidative stress in the PVN, and the peripheral effects by a sympathetic pathway.

© 2015 Elsevier Inc. All rights reserved.

This company is not employed by the government. They are working by own and in relationship with ADInstrument company.
* Corresponding author. Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran 14155 6447, Iran.
Tel.: +98 2164053288; fax: +98 2166419484.
E-mail address: b-seifi@tums.ac.ir (B. Seifi).
0022-4804/$ – see front matter © 2015 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jss.2014.06.042