Renin-Angiotensin and Sympathetic Nervous System Interactions in the Control of Blood Pressure in Fructose-Induced Metabolic Syndrome

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Editorial

Activation of the sympathetic nervous system (SNS) stimulates renin release from the juxtaglomerular cells of the kidneys that leads to the generation of angiotensin I, which is then converted to angiotensin II (Ang II), the major effector peptide of the renin-angiotensin system (RAS). The formed Ang II can facilitate noradrenaline release from the renal sympathetic nerve endings in addition to its effect in the anterior hypothalamus and rostral ventrolateral medulla (RVLM) [1,2]. At RVLM neurons, Ang II acts either postsynaptically, by decreasing K+ currents, or presynaptically by activating vasomotor sympathetic glutaemeric receptors resulting in an increase in sympathetic nerve activity and arterial blood pressure [3-5]. In the renal vasculature, Ang II enhances renal adrenergic function via a presynaptic site of action in anaesthetised dogs [6], while in anaesthetised rats Ang II facilitates noradrenergic control at epithelial neuroeffector junctions [7,8]. In conscious rats, Veelken et al. have shown that endogenous Ang II modulates the sympathetic nervous impact on the kidney [9]. On the other hand, it is also recognised that chronic activation of α1-adrenoceptors can result in the down regulation of AT1 receptors [10]. Ang II has been shown to induce transcription and expression of α1-adrenoceptors, mainly α1a, in rat cultured vascular smooth muscle cells, therefore, some actions of Ang II might be mediated via genomic mechanisms [11]. This mechanism is further illustrated by the finding that the stimulatory effect of Ang II on smooth muscle cell DNA synthesis can be blunted by treatment with the α1-adrenoceptor antagonist prazosin [12]. Therefore, Villalobos-Molina and Ibarra [13] have hypothesized that a long term action of Ang II, through the stimulation of expression and function of vascular α1a-adrenoceptors, may participate in the development of hypertension.

Thus, it becomes apparent that these two major regulatory systems can interact with each other and contribute to the genesis of many disorders. This interaction has been reported in hypertensive models characterized by insulin resistance an example of which is the spontaneously hypertensive rat [14] which has been described as a model of human insulin resistance syndrome due to reduced insulin-mediated glucose disposal and defective fatty acid metabolism [15,16]. A further example is the rat model of fructose-induced hypertension where the SNS and RAS both appear to play a major role [17,18], and can contribute importantly to the sustained hypertension in this model. This view is supported by the observation of increased renal sodium and fluid retention and elevated blood pressure due to hyperactivity of SNS and RAS [19-21]. Accordingly, a consensus has developed that blockade of RAS using ACE inhibitors or AT, receptor blockers (ARB) may have beneficial effects on insulin resistance in the rat [18,22,23] and in man [24,25]. The usefulness of ACE inhibitors or ARBs involves not only improving glucose metabolism and insulin sensitivity [26] but also restores vascular function. Moreover, it has been reported that the ACE inhibitor captopril blunted the vasoconstrictor responses to the α1-adrenoceptor agonist phenylephrine [27] while the ARB losartan enhanced the vascular responsiveness in 8-week fructose-fed rats [28].

Collectively, all these reports support the notion that Ang II importantly interacts with adrenergic neurotransmission in controlling vascular tone in normal and pathophysiological states. This interaction has been clearly shown in a large number of studies [14,29,30]. Recently, reports have highlighted this interaction between AT1 receptors and α1-adrenoceptors in playing an important role in modulating vascular tone in the fructose-fed rat model [31,32]. However, neither the exact mechanism of this interaction nor its importance has been clearly identified.

References


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