

## Depressed Baroreflex Sensitivity in Hypertensive Rats: A Role for Reactive Oxygen Species

Drielle D Guimaraes and Valdir A Braga\*

Biotechnology Center, Federal University of Paraiba, Joao Pessoa, PB, Brazil

Reactive oxygen species (ROS) play an important role in the development and maintenance of cardiovascular diseases including hypertension and heart failure. In special, the relationship between oxidative stress and hypertension has been demonstrated in several models of experimental hypertension. For instance, increased ROS formation precedes the development of hypertension in spontaneously hypertensive rats and in renovascular hypertensive mice [1-3].

One of the key mechanisms in controlling blood pressure in health and disease is the baroreflex. Baroreceptors located in the carotid sinuses and aortic arch detect changes in blood pressure and trigger reflex autonomic adjustments that buffer alterations in blood pressure. In pathological conditions such as hypertension, there is impairment in the autonomic control of blood pressure resulting in changes in baroreflex sensitivity [4-6]. Indeed, compelling evidence show that the baroreflex modulation of heart rate is impaired in spontaneously hypertensive rats and patients with primary hypertension [6,7]. We have recently demonstrated that acute antioxidant therapy improves baroreflex sensitivity in models of primary (essential) and secondary hypertension [5,6].

In a model of renovascular hypertension, the 2-kidney-1-clip (2K1C), we have shown that acute treatment with Vitamin C (150 mg/Kg, i.v.), a well-known antioxidant, restored the depressed baroreflex sensitivity in those hypertensive animals [5]. Furthermore, administration of apocynin (30 µg/Kg, i.v.), a NADPH oxidase inhibitor, improved baroreflex sensitivity in the 2K1C group. In the same study, autonomic blockade with either methylatropine or propranolol reduced the changes in heart rate to the same extent in normotensive and hypertensive groups suggesting that improved baroreflex sensitivity by antioxidants were mediated by improvement in autonomic function. Taken together, those data suggest that NADPH oxidase-derived reactive oxygen species are involved in the blunted baroreflex sensitivity in secondary hypertension and that acute scavenging of superoxide restores baroreflex sensitivity. Regarding primary hypertension, we have also demonstrated in spontaneously

hypertensive rats that acute scavenging of superoxide or inhibition of the NADPH oxidase, the main source of ROS in hypertension, improves impaired baroreflex sensitivity and reduces oxidative stress in those animals [6].

The precise site of action where acute antioxidant therapy produces its beneficial effects in order to ameliorate baroreflex sensitivity remains unknown. However, due to the ability of our antioxidant therapy to act beyond the blood brain barrier, it might involve both peripheral and central mechanisms. Those preliminary studies point out to a possible role to antioxidant therapy for improving baroreflex sensitivity in hypertensive patients. Although an interesting possibility, it still awaits further investigation.

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\*Corresponding author: Valdir A Braga, Director, Department of Biotechnology, Biotechnology Center, Federal University of Paraiba, Joao Pessoa, PB 58051-900, Brazil, Tel: 55 83 3216 7511; Fax: 55 83 3216 7511; E-mail: [valdir@cbiotec.ufpb.br](mailto:valdir@cbiotec.ufpb.br)

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