

## **The role of renal sympathetic nerve activity in the hypertension induced by chronic nitric oxide blockade**

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Chronic blockade of nitric oxide leads to an increase in blood pressure that is maintained over the period of the blockade in baroreceptor intact animals (Scrogin *et al.*, 1998). In addition to the vascular actions of endothelium-derived nitric oxide, indirect evidence supports a role for the sympathetic nervous system in maintaining the hypertension. The decrease in blood pressure with ganglionic blockade is exaggerated with blockade of nitric oxide suggesting an increase in sympathetic tone (Liu *et al.*, 1998; Scrogin *et al.*, 1998). Guanethidine-induced sympathetectomy also attenuates the hypertension induced by chronic nitric oxide blockade (Sander *et al.*, 1997).

In order to test this possible interaction between nitric oxide and sympathetic nerve activity directly, we measured arterial pressure and renal sympathetic nerve activity before, during and after nitric oxide blockade using L-NAME (50mg/kg/day *via* drinking water) over 7 days, in baroreceptor intact and sino-aortic denervated (SAD) conscious rabbits.

In the baroreceptor intact animals, blockade of nitric oxide led to a significant increase in mean arterial pressure (from  $75 \pm 2$  to  $84 \pm 3$  mmHg) and decrease in heart rate (from  $233 \pm 8$  to  $195 \pm 8$  bpm) that was sustained over the 7 days of nitric oxide blockade. In all SAD animals, an initial increase in arterial pressure ( $82 \pm 3$  mmHg on the second day) was seen but was not sustained and recovered back to pre L-NAME levels. Direct recordings of renal sympathetic nerve activity suggest the increase in blood pressure in the baroreceptor intact animals is not accompanied by a change in renal sympathetic tone ( $9 \pm 3$  normalised units during control *v/s*  $10 \pm 4$  normalised units at day 7 of L-NAME treatment). There is evidence of resetting of the blood pressure- renal sympathetic nerve activity baroreflex curve such that blood pressure is maintained at a hypertensive level.

In summary, our results do not support a role for increased renal sympathetic nerve activity in maintaining the hypertension with nitric oxide blockade in baroreceptor intact animals. The lack of a sustained increase in pressure in the SAD animals suggests an important role for baroreflexes in the long-term control of arterial pressure.

Liu, Y., Tsuchihashi, T., Kagiya, S., Matsumura, K., Abe, I. & Fujishima, M. (1998) *Journal of Hypertension*, 16, 1165-1173.

Sander, M., Hansen, J. & Victor, R.G. (1997) *Hypertension*, 30, 64-70.

Scrogin, K.E., Hatton, D.C., Chi, Y. & Luft, F.C. (1998) *American Journal of Physiology*, 274, R367-R374.

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Supported by the Auckland Medical Research Foundation, the Health Research Council, the Maurice and Phyllis Paykel Trust and the University of Auckland.