Blockade of angiotensin type 1 (AT1) receptors in the rostral ventrolateral medulla increases renal sympathetic activity and arterial pressure under hypoxic conditions

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Administration of exogenous angiotensin II (AngII) into the rostral ventrolateral medulla (RVLM) increases sympathetic activity and blood pressure, indicating that it has an excitatory effect on presympathetic neurons in this region. Blockade of angiotensin type 1 (AT1) receptors in the RVLM under normal conditions results in little change in sympathetic activity, suggesting that under these conditions endogenous AngII has little tonic effect in the RVLM. Recently, however, it has been suggested that endogenous Ang II has a tonic action on both excitatory and inhibitory mechanisms in the RVLM, so that the ultimate effect on sympathetic activity depends upon the balance between the excitatory and inhibitory effects of endogenous AngII on presympathetic neurons (Hu *et al.*, 2002). If that is the case, then this balance could be altered under conditions in which the level of activity of excitatory or inhibitory synaptic inputs to RVLM neurons is altered. In this study we have tested this hypothesis by determining the effects of blockade of AT1 receptors in the RVLM under hypoxic conditions, which is known to enhance the excitatory glutamatergic inputs to RVLM presympathetic neurons. Rats were anaesthetised with urethane (I.P. 1.35g/kg) and arterial pressure, heart rate and renal sympathetic nerve activity were recorded. Unilateral microinjections of an AT1 receptor antagonist, candesartan (100pmol), into the RVLM during moderate hypoxia (PO_2 10%) resulted in an increase in arterial pressure and renal sympathetic nerve activity, whereas microinjections of the vehicle solution had little effect. The results indicate that, under hypoxic conditions, endogenous AngII has a net tonic sympathoinhibitory effect. Taken together with other recent findings, the results are consistent with the hypothesis that AT1 receptors can mediate both tonic excitatory and inhibitory effects on RVLM sympathoexcitatory neurons, and the balance of these effects is altered under different physiological conditions.

Hu, L., Zhu, D., Yu, Z., Wang, J.Q., Sun, Z. & Yao, T. (2002) *Journal of Applied Physiology,* 92, 2153-2161.