NO and α-adrenoceptor subtypes in regional renal vascular responses to renal nerve stimulation in rabbits

G.A. Eppel[1], L.L. Lee[1], K.M. Denton[1], S.C. Malpas[2] and R.G. Evans[1], [1]Department of Physiology, Building 13F, Monash University, VIC 3800, Australia and [2]Department of Physiology, University of Auckland, Auckland, New Zealand.

Introduction. Renal medullary blood flow (MBF) plays a critical role in long-term control of arterial pressure. Therefore understanding the mechanisms controlling MBF is important. When renal sympathetic drive is increased reflexively (Leonard *et al.*, 2001), or by electrical stimulation (RNS, Leonard *et al.*, 2000), MBF is reduced much less than cortical or total renal blood flow (CBF, RBF). Zou and Cowley (2000) have shown that MBF responses to noradrenaline infusion are blunted by α_2-adrenoceptor mediated NO release. We tested whether this mechanism blunts MBF responses to RNS in pentobarbitone anaesthetised rabbits (90-150mg + 30-50mg/h iv).

Methods. RBF was measured by transit-time ultrasound flowmetry, CBF and MBF were measured by laser-Doppler flowmetry. RNS was performed at a supramaximal voltage (2ms pulse duration) for 3min at each frequency (0.5,1,2,4 and 8Hz in random order). In Experiment 1, RNS was performed before and after prazosin (α_1-adrenoceptor antagonist; 0.2mg/kg + 0.2mg/kg/h iv; n=6), rauwolscine (α_2-adrenoceptor antagonist; 0.5mg/kg + 0.25mg/kg/h iv; n=6) or vehicle treatment (n=6). In Experiment 2, responses to RNS were measured under control conditions, after NO synthase blockade with N^G-nitro-L-arginine (L-NNA, 20mg/kg/min + 5mg/kg/h iv), and then during co-infusion of glyceryl trinitrate at a dose that restored arterial pressure and RBF to control levels (10-50 μg/kg/min iv). A second group (n=6) served as a time control, receiving only vehicle treatment.

Results. In all groups RBF, CBF and to a lesser extent MBF, were reduced by RNS in a stimulus-dependent manner. In Experiment 1, prazosin decreased baseline arterial pressure by −11±4% and CBF by −18±3%. Prazosin blunted RNS-induced responses of RBF and CBF but not MBF. For example at 4Hz, RBF, CBF and MBF were reduced by −85±3%, −89±2% and −20±12% respectively during the control period, and by −39±3%, −42±5% and −28±7% during prazosin treatment. Rauwolscine increased arterial pressure by 8±2% and decreased RBF by −25±2% and CBF by −14±3%. Rauwolscine increased CBF and MBF responses to RNS but only at frequencies ≤ 2Hz. For example RNS at 1Hz reduced CBF by −21±2% but not MBF (+9±9%) during the control period. During rauwolscine treatment, RNS at 1Hz reduced CBF by −30±6% and MBF by −12±8%. Baseline haemodynamic variables and responses to RNS were not significantly affected by vehicle treatment. In Experiment 2, L-NNA increased arterial pressure by 34±4% and decreased RBF and MBF by −16±2% and −52±5% respectively. L-NNA treatment enhanced responses to RNS, particularly MBF at the lower frequencies. For example, stimulation at 2Hz during the control period reduced RBF by −48±7% and CBF by −39±6% but not MBF (+1±18%). During L-NNA treatment the responses were −58±6%, −43±4% and −32±11% for RBF, CBF and MBF respectively. Glyceryl trinitrate infusion restored arterial pressure, RBF and MBF to control levels and also restored RBF, CBF and MBF responses to RNS to their control levels. Responses to RNS remained relatively stable in the time control group.

Conclusions. These data indicate that both α_2-adrenoceptor activation and NO blunt MBF responses to RNS at low frequencies, but also blunt CBF responses to some extent. Whether the impact of α_2-adrenoceptor activation is mediated by NO, remains to be determined. MBF remained less responsive to RNS than CBF during NO synthase and α_2-adrenoceptor blockade, indicating that other mechanisms also contribute to the differential impact of RNS on CBF and MBF. α_1-adrenoceptors make an important contribution to RNS-induced changes in CBF but seem to contribute less to RNS-induced changes in MBF.

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