Mechanisms maintaining kidney tissue oxygenation during renal ischaemia in anaesthetised rabbits

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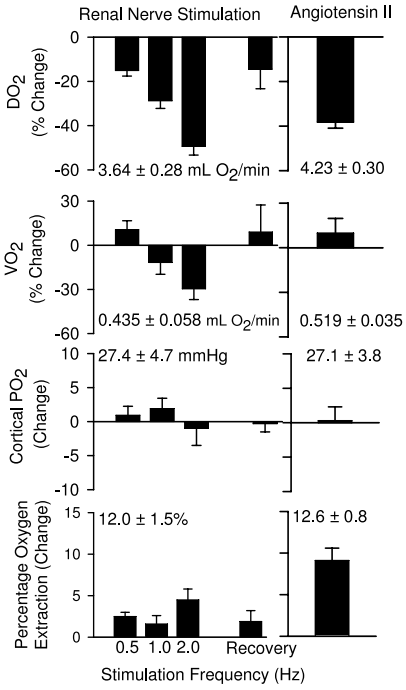
We have recently shown that the kidney has a remarkable ability to maintain stable tissue oxygen tension (PO_2) in the face of changes in renal blood flow (RBF) within the physiological range (O'Connor *et al.*, 2006; Leong *et al.*, 2007). According to the conventional view of kidney oxygenation, maintenance of homeostasis of kidney oxygenation is thought to be achieved almost exclusively through the 'flow limited' nature of kidney oxygen consumption (VO_2). That is, because most oxygen consumption by kidney tissue is attributable to sodium reabsorption, which in turn also drives reabsorption of other solutes, renal VO_2 often varies in proportion with glomerular filtration rate and thus RBF. However, this mechanism could only completely maintain homeostasis of kidney oxygenation if there is no mis-match between changes in renal oxygen delivery (DO_2) and VO_2. Therefore, we investigated the potential for percentage oxygen extraction by the kidney to increase during renal ischaemia, even in the absence of reduced tissue PO_2.

Rabbits were anaesthetised with pentobarbitone (90-150 mg plus 30-50 mg/h) and artificially ventilated. Catheters were placed in the ear arteries and renal vein and a transit-time ultrasound flow probe was placed around the renal artery. DO_2 and VO_2 were calculated from the oxygen content of renal venous and/or arterial blood and RBF. Cortical tissue PO_2 was determined by fluorescence optode. Urine was collected from the catheterized ureter. For electrical stimulation of the renal nerves (RNS, n = 15), the renal nerves were sectioned cranially and placed on stimulating electrodes (O'Connor *et al.*, 2006). For renal arterial infusion of angiotensin II (n = 12), a catheter was placed in the renal artery (Leong *et al.*, 2007).



The figure shows responses to RNS and angiotensin II infusion. Baseline values are within each panel. RNS caused frequency-dependent reductions in RBF (-44 ± 4% at 2 Hz) and DO_2 (-49 ± 4%), but a smaller reduction in VO_2 (-30 ± 7%). Angiotensin II reduced RBF (-37 ± 3%) and DO_2 (-38 ± 3%), but not VO_2 (+10 ± 10%). Despite mis-matched changes in DO_2 and VO_2, cortical tissue PO_2 did not fall. Percentage oxygen extraction increased 1.4-fold during 2 Hz RNS and 1.8-fold during angiotensin II. Renal venous PO_2 fell by -5.7 ± 1.7 mmHg during 2 Hz RNS and by -11.2 ± 2.0 mmHg during angiotensin II infusion. Neither renal venous blood PCO_2 nor pH changed in response to these ischaemic stimuli.

We conclude that during mild renal ischaemia, induced by RNS or angiotensin II infusion, reductions in DO_2 are not matched by reductions in VO_2. But tissue hypoxia does not occur, because the kidney extracts a greater proportion of DO_2, even in the absence of an increase in the PO_2 gradient between arterial blood and tissue. We speculate that increased percentage oxygen extraction could be driven by changes in the counter-current exchange of oxygen and/or carbon dioxide between renal arteries and veins. For example, diffusional shunting of carbon dioxide from intrarenal veins to arteries may *increase* during ischemia, reducing the pH of blood in peritubular capillaries. This should reduce the affinity of haemoglobin for oxygen (the Bohr effect) within renal peritubular capillaries, so increasing delivery of oxygen to tissue. There is also a theoretical basis for diffusional shunting of oxygen to *decrease* during renal ischemia (Evans *et al.*, 2008), which should increase delivery of oxygen to tissue.

Evans RG, Gardiner BS, Smith DW, O'Connor PM. (2008) *American Journal of Physiology – Renal Physiology* doi:10.1152/ajprenal.90230.2008

Leong C-L, Anderson WP, O'Connor PM, Evans RG. (2007) *American Journal of Physiology – Renal Physiology* **292:** F1726-33.

O'Connor PM, Kett MM, Anderson WP, Evans RG. (2006) *American Journal of Physiology – Renal Physiology* **290:** F688-94.