Neural control of renal medullary perfusion

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Over the last decade, evidence has accumulated that the renal medullary circulation plays a key role in regulating arterial pressure in the long-term (Mattson, 2003). A favoured hypothesis rests on the notion of relatively poor autoregulation of medullary blood flow (MBF), allowing changes in MBF in response to changes in arterial pressure to initiate compensatory alterations in tubular sodium reabsorption. Indeed, alterations in MBF have been proposed as the chief mediator of pressure diuresis/natriuresis (Mattson, 2003). We have set out to elucidate the mechanisms that regulate MBF under physiological conditions. A key finding from our studies using laser Doppler flowmetry in anaesthetized (pentobarbitone, 90-150 mg plus 30-50 mg/h) and conscious rabbits, has been that vasoactive hormones can differentially affect MBF and cortical blood flow (CBF) (Evans *et al.*, 2000). This likely represents an important mechanism underlying hormonal control of blood pressure.

Until recently, our understanding of the impact of the renal sympathetic nerves on MBF has been rudimentary. Our recent findings show that MBF is less sensitive than CBF, to electrical stimulation of the renal nerves, particularly at low frequencies of stimulation (Leonard *et al.*, 2000). The responses of MBF to renal nerve stimulation appear to be similar in the outer and inner medulla (Guild *et al.*, 2002). We have also obtained evidence that the medullary circulation is normally insensitive to increases in endogenous renal sympathetic nerve activity within the physiological range, in that increases in renal sympathetic nerve activity of ~80% induced by hypoxia reduce CBF (by ~14%) but not MBF (Leonard *et al.*, 2001).

Our attention has now turned to elucidating the mechanisms underlying the relative insensitivity of MBF to renal nerve activation. Failure of these mechanisms would promote reductions in MBF in response to physiological activation of renal sympathetic nerve activity, which could in turn lead to salt and water retention and hypertension. We have preliminary evidence for a paradoxical role of angiotensin II in selectively blunting responses of MBF to activation of the renal sympathetic nerves. The renal medulla is unique in that, under certain conditions, angiotensin II can induce vasodilatation through release of nitric oxide and/or prostaglandins (Duke *et al.*, 2003). In anaesthetised rabbits, renal arterial infusion of angiotensin II at a dose that reduced basal CBF but not MBF, abolished reductions in MBF induced by renal nerve stimulation (Guild *et al.*, 2003). Ongoing studies are also investigating the roles of nitric oxide, prostaglandins, adrenoceptor subtypes, and sympathetic co-transmitters in the neural regulation of MBF.

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