Differential neural control of glomerular ultrafiltration

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Homer Smith dismissed the renal nerves in his landmark book The Physiology of the Kidney (1937). Following the first kidney transplantations, the apparent lack of long-term effects on body fluid balance were taken as confirmation of the independence from nervous system control of renal vascular and tubular function. It is now appreciated that transplanted kidneys rapidly re-innervate and that changes in renal nerve activity are implicated in many clinical conditions (Dibona & Kopp, 1997).

The resurgence of interest in the neural control of renal function followed the first comprehensive anatomic study of the renal innervation (Barajas, 1978), demonstrating that all the major structural elements of the kidney were innervated. Although the glomerular afferent and efferent arterioles are densely innervated, the prevailing view today is that tubular innervation is of greater importance for body fluid homeostasis. Reviewing the literature, Dibona & Kopp (1997) argued that the evidence supports the hypothesis that changes in renal nerve activity around resting levels affect renin secretion and tubular function but not blood vessel tone. However, the majority of studies utilised electrical stimulation of the renal nerves, which does not resemble the normal nerve discharge pattern. Our studies suggest a very different situation.

Performing a detailed analysis of the renal innervation, we demonstrated that there are two distinct nerve types, that are differentially distributed to afferent and efferent arterioles (Luff *et al.*, 1992). Type I nerves almost exclusively innervate the afferent arteriole (Luff *et al.*, 1992). Type II nerves, are NPY positive (Anderson *et al.*, 2001) and evenly distributed on both arterioles (Luff *et al.*, 1992). We hypothesised that the different patterns of sympathetic outflow to the kidney may evoke selective changes in glomerular ultrafiltration.

We examined the effects of physiologically induced increases in renal sympathetic nerve activity (RSNA) in response to graded hypoxia on renal pre and postglomerular vascular resistances in anaesthetised rabbits (pentobarbitone, 90-150 mg plus 30-50 mg/h) (Denton *et al.*, 2002b). We demonstrated that 10% oxygen (O_2) caused neurally mediated increases in both pre and postglomerular resistance as reflected by the decrease in both renal blood flow (RBF) and glomerular filtration rate (GFR). However, 14% O_2 which induced a lesser increase in RSNA caused a predominant increase in postglomerular resistance and maintenance of GFR at a time when renal blood flow fell. These results provide evidence that different levels of reflexly induced increases in RSNA may differentially control pre- and post- glomerular vascular resistances, compatible with selective activation of Type I and II renal sympathetic nerves. A caveat to this conclusion was that, though in response to 14% O_2 plasma renin activity was not increased, intrarenal actions of neurally stimulated ANG II may have been responsible for the increase in postglomerular resistance in response to 14% O_2.

This question was investigated in rabbits receiving an ANG II clamp infusion (Denton *et al.*, 2002a). Measurements were made before (room air) and after 14% O_2. As seen in the previous study RSNA increased in response to 14% O_2 and decreased RBF without effecting GFR or arterial pressure. However, glomerular capillary pressure increased in both the vehicle and ANG II clamp groups during 14% O_2, indicating that ANG II was not responsible for the increase in glomerular pressure following RSNA. These results are compatible with our hypothesis that different populations of renal nerves selectively control pre and postglomerular resistance and hence glomerular pressure and ultrafiltration.

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