Reversible renal nerve denervation in the cat: effects on haemodynamic and excretory functions of the ipsilateral and contralateral kidneys

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Summary
1. In anaesthetized cats, reversible renal nerve denervation (cooling of the renal nerves on one side at 4°C for 16 min) was performed and its effects on haemodynamic and excretory functions of the ipsilateral and the contralateral kidneys were studied.

2. Renal nerve cooling did not cause any change in arterial pressure. Slight increase in blood flow, no change in glomerular filtration rate and a large increase in water and sodium excretion occurred in the ipsilateral kidney; simultaneously, no change in blood flow, a slight and transient decrease in glomerular filtration rate, and a significant decrease in diuresis and natriuresis were observed in the contralateral kidney.

3. Ipsilateral and contralateral renal changes were equally evident in the early (minutes 0 to 8) and late phases (minutes 8 to 16) of the cooling period.

4. When renal nerve cooling was repeated after surgical denervation of the contralateral kidney all contralateral effects were abolished.

Key words: denervation, haemodynamics, kidney, renal nerve, sodium.

Introduction
The role of renal nerves in the regulation of renal functions is still unclear. It has been reported that efferent renal nerve fibres can directly influence the proximal tubular reabsorption of sodium and water [1, 2], and that afferent renal nerve fibres can be activated either by baroceptive [3, 4] or by chemoceptive stimuli [5]. The recent electrophysiological demonstration of reno-renal reflexes [6] strongly supports the suggestion that changes in contralateral kidney functions after section of a renal nerve are neurally mediated [7, 8].

More definite information on the existence and the significance of these reno-renal reflexes has been sought by developing a model of reversible and hence repeatable renal denervation. In this way the dependence of the responses of the contralateral kidney on its innervation can be more convincingly shown by repeating renal nerve cooling, first when the contralateral kidney is normally innervated and then after it has been surgically denervated. Furthermore, monitoring of the ipsilateral and contralateral kidney responses to renal nerve cooling was performed to clarify whether the contralateral effects were simultaneous with or followed the well-known increase in diuresis and natriuresis from the denervated kidney.

Methods
The experiments were performed on seven cats anaesthetized with sodium pentobarbital. Polyethylene catheters were placed: (i) in a femoral artery to measure arterial pressure (Statham P23De pressure transducer) and to draw blood samples; (ii) in a femoral vein to infuse creatinine and sodium chloride solution (154 mmol/l: saline) at constant rate; (iii) in both ureters to collect urine separately from the two kidneys. Blood flow to both kidneys was recorded by Statham electromagnetic flow probes on a Grass polygraph, together with arterial pressure and heart rate. Sodium (flame photometer), creatinine (colorimetric method), and osmotic concentration (Osmette A osmometer) were analysed in urine and plasma. The clearance of exogenous creatinine was used as a measure of glomerular filtration rate.
The nerves of the left kidney were carefully isolated and placed on a metal tube connected with a refrigerator pump and, at due time, the temperature necessary for a cold block (about 4°C) was reached in a few seconds.

After surgery, at least 1 h of equilibration was allowed. After a control clearance period of 8 min, the left renal nerves were cooled, during which two consecutive 8 min clearance studies were performed; a subsequent 8 min clearance period followed rewarming of the left renal nerves (recovery). A second trial of left renal nerve cooling was repeated half an hour after the surgical denervation of the contralateral right kidney. The effectiveness of surgical denervation and cold block, and the integrity of the innervation before and after the cooling period, were tested by brief electrical stimulation of the pontine vasomotor centre [9].

Results were statistically assessed by analysis of variance with double classification [10], the comparison being between values in the control period and in the cooling period, and between values in the ipsilateral and the contralateral kidney.

Results

As shown in Fig. 1, cooling of the left renal nerves did not affect arterial pressure, but ipsilaterally caused a significant increase in renal blood flow and vascular conductance (18% and 21% respectively), with no change in glomerular filtration rate, and a significant and marked increase in water (109%) and sodium excretion (91%). Contralaterally, renal blood flow and vascular conductance were substantially unaffected by renal nerve cooling, and glomerular

![Fig. 1. Means and SEM of percentage changes in arterial pressure (AP), renal blood flow (RBF), renal vascular conductance (RC), glomerular filtration rate (GFR), urine volume (V) and sodium excretion (U_sodium) caused by renal nerve cooling in the ipsilateral (open histograms) and contralateral kidney (hatched histograms) before and after contralateral surgical denervation. *Statistical significance of difference between percentage changes (P < 0.05).]
filtration rate slightly decreased (-12%). Water and sodium excretion from the contralateral innervated kidney were affected in the opposite way to the pattern of the ipsilateral kidney, showing a definite and significant decrease (-26% and -27% respectively). Ipsilateral and contralateral renal responses were prompt and of equal size during the two consecutive clearance periods during cooling. Only a slight decrease in contralateral glomerular filtration rate occurred in the first clearance period, and was not seen in the second.

Repetition of left renal nerve cooling after surgical denervation of the right kidney gave the same ipsilateral responses, whereas the contralateral responses were entirely abolished. In fact, in the contralateral denervated kidney there were very slight and insignificant increases in renal blood flow (3%), in vascular conductance (7%) and in glomerular filtration rate (3%), with insignificant decreases in water (-7%) and sodium excretion (-3%).

Discussion

The transient block of renal nerve activity induced prompt excretory changes in the contralateral kidney, which were opposite to those observed in the ipsilateral one. The contralateral effects were shown to disappear after surgical denervation of the contralateral kidney and, therefore, are neurally mediated. The prompt occurrence of the contralateral reduction in diuresis and natriuresis rules out that it is secondary to the loss of fluid and sodium from the temporarily denervated kidney. Our observations therefore substantiate the hypothesis that there are tonic reno–renal reflexes inhibiting sympathetic activity of the contralateral kidney.

Our experiments indicate that denervation diuresis may partly be due to concomitant renal vasodilatation, whereas the contralateral antidiuresis and antinatriuresis seem to be independent of any haemodynamic changes, as only a slight and transient decrease in glomerular filtration rate has been measured.

Therefore it is likely that the sympathetic activity involved in the reno–renal reflexes we have described is that directly controlling proximal tubular reabsorption.

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References