

Reno-renal and reno-adrenal reflexes in the rat

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Summary

1. Experiments were carried out to investigate whether the activation of renal chemoceptive receptors by natural stimuli might induce reflex alterations of efferent postganglionic activity to the ipsilateral kidney and preganglionic activity to the ipsilateral adrenal.

2. In anaesthetized rats with intact nervous system back-flow of urine and occlusion of the renal artery were accompanied by increments in efferent sympathetic activity both to the kidney and adrenal without concomitant changes in heart rate and blood pressure.

3. Greater excitatory responses in nerve activity to the same test stimuli were observed in rats with the spinal cord cut at C1.

4. These results indicate that the natural activation of renal chemoceptive receptors might induce reno-renal and reno-adrenal excitatory reflexes which are likely to be integrated at spinal and supraspinal levels.

Key words: renal chemoceptive receptors, renal nerves, reno-adrenal reflexes, reno-renal reflexes.

Introduction

In the renal nerves of the rat afferent nerve fibres exist whose activity is related to alterations in chemical composition of the renal interstitium. Two groups of renal chemoceptive receptors have been so far identified. The afferent fibres of the first group are 'silent' under control conditions, do not respond to back-flow of urine into the renal pelvis, and are activated by renal ischaemia produced by clamping of the renal artery, systemic hypotension, clamping of the renal vein and by the hypotension which accompanies systemic asphyxia (Recordati, Moss &

Wasselkov, 1978). The fibres of the second group have a resting discharge rate which is higher in non-diuretic than in diuretic conditions, are activated by renal ischaemia produced by clamping of the renal artery and respond markedly to back-flow of urine into the renal pelvis. This last response was found to depend on the chemical composition of the fluid to which sensory endings are exposed, and not to mechanical distension of the pelvis or increments in intrapelvic pressure (Recordati, Moss, Genovesi & Rogenes, 1980). These two groups of receptors have been respectively termed renal R1 and R2 chemoceptive receptors.

In the present series of experiments we investigated whether stimulation of renal chemoceptive receptors induces reflex alterations of efferent sympathetic activity to the ipsilateral kidney and adrenal and of arterial blood pressure and heart rate. Occlusion of the renal artery, which activates both R1 and R2 chemoceptive receptors, and back-flow of non-diuretic urine into the pelvis, which activates R2 receptors only, were used as test stimuli.

Methods

Male Sprague-Dawley rats (200-300 g) were anaesthetized by intraperitoneal injection of pentobarbital sodium (5 mg/100 g). Polyethylene catheters were inserted into (1) the left external jugular vein for continuous infusion of sodium chloride solution (154 mmol/l: saline) at 20 μ l/min, (2) the femoral artery to monitor arterial blood pressure and (3) the right ureter. The right kidney and adrenal and their nerve supply were exposed retroperitoneally through a para-vertebral incision. A short section of the right renal artery was carefully cleared of connective tissue to permit total occlusion with forceps. Small nerve bundles to the kidney and adrenal were dissected from surrounding tissues and positioned on bipolar hook electrodes for extracellular recordings. Efferent nerve activity from

small multifibre preparations was analysed with the aid of a neural spike analyser (Recordati, Lombardi, Bishop & Malliani, 1976) in terms of number of impulses every 1, 2 or 5 s. In all the experiments the right ureter was cannulated at the ureteropelvic junction with a catheter (PE 50) which allowed urine to flow freely while pelvic pressure was continuously monitored. Back-flow of urine into the pelvis was accomplished by elevating the free end of the catheter above the kidney level.

Four rats were artificially ventilated after bilateral vagotomy and section of the spinal cord at the C1 level. Arterial and ureteral pressures, nervous activity and ECG were recorded on a Polygraph recorder and stored on a magnetic tape. Heart rate was measured with an instantaneous frequency meter from ECG or blood pressure recording.

To determine whether the recorded efferent sympathetic activity was pre- or post-ganglionic at the end of each experiment a test dose of a ganglionic blocking agent (0.5–1.0 mg of trimetaphan; Arfonad, Roche) was injected intravenously.

Results

In rats with intact nervous system back-flow of non-diuretic urine into the pelvis of the right kidney produced an increase in efferent nerve activity to the ipsilateral kidney. Fig. 1 shows an example of such a response. The increase in

efferent nerve activity was almost simultaneous with the increase in pelvic pressure induced by back-flow of urine. After the release of the stimulus the nerve activity slowly subsided towards pre-stimulus levels. The time course of the response paralleled the excitation of R2 chemoreceptors induced by the same stimulus (Recordati *et al.*, 1980). In six experiments the mean increase in activity (impulses/s) was $24.2 \pm \text{SEM } 3.8\%$ with respect to control discharge and it was similar to the increments observed in efferent preganglionic activity to the ipsilateral adrenal (two experiments). In rats with intact nervous system, heart rate and arterial blood pressure were not consistently altered by back-flow of urine. Noxious stimuli, like pinching the tail, always elicited tachycardia, hypertension and a marked activation of nerve activity.

In rats with the spinal cord cut at C1, back-flow of urine caused a marked increase in efferent activity both to the ipsilateral kidney and adrenal. This increase was $49.3 \pm 12.9\%$ relative to control. In these rats slight increments in heart rate and arterial blood pressure were also observed. The occlusion of the renal artery, of 1 min duration, produced excitatory responses similar to those induced by back-flow of urine.

After ipsilateral renal denervation no reflex responses were observed to back-flow of urine or renal artery occlusion. Efferent sympathetic activity to the kidney ceased and that to the adrenal increased during the hypotension and bradycardia induced by the administration of a

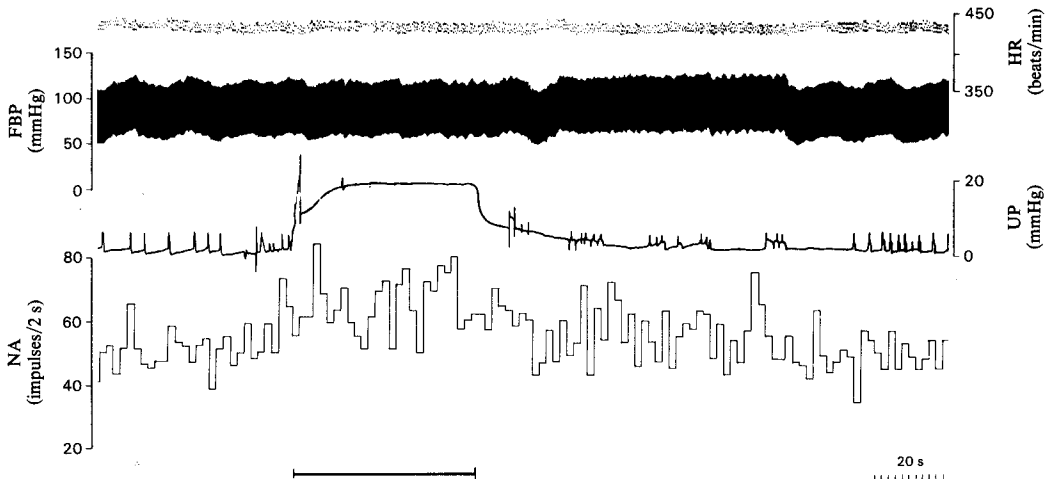


FIG. 1. Effects of back-flow of urine of 1 min duration (marked by a bar) into the pelvis of the right kidney on heart rate (HR), femoral blood pressure (FBP), ureteral pressure (UP) and efferent sympathetic activity to the ipsilateral kidney (NA). Nervous activity increased by 28% with respect to control discharge and slowly subsided towards prestimulus levels at the release of the stimulus.

ganglionic blocking agent. This indicates that multifibre preparations to the kidney were composed of postganglionic fibres and those to the adrenal of preganglionic fibres.

Discussion

These preliminary experiments indicate that in non-diuretic conditions the activation of renal chemoceptive receptors, either produced by back-flow of urine into the renal pelvis or by renal ischaemia, elicits nervous excitatory reflexes to the ipsilateral kidney and adrenal.

The reflex responses were excitatory both in rats with intact nervous system and in rats with the spinal cord cut at C1. This confirms that also at the lumbar spinal cord level sympathetic afferent nerve fibres mediate excitatory spinal reflexes (Franz, Evans & Perl, 1966; Malliani, Lombardi, Pagani, Recordati & Schwartz, 1975). The involvement of supraspinal pathways in the reflex response to electrical stimulation of afferent renal nerves has been recently demonstrated in rats (Brody & Johnson, 1980) and cats (Calaresu, Kim, Nakamura & Sato, 1978). It is reasonable to assume therefore that both spinal and supraspinal pathways are involved in reno-renal and reno-adrenal reflexes.

Electrical stimulation of afferent renal nerves produces hypotension in rabbits (Aars & Akre, 1970) and hypertension and tachycardia in cats (Calaresu, Stella & Zanchetti, 1976). In rats it induces a renal and mesenteric vasoconstriction and muscle vasodilatation without altering systemic blood pressure (Brody & Johnson, 1980), data that are consistent with those reported in the present paper. The opposite responses observed in different experimental animals are at present unexplainable.

R2 renal chemoceptive receptors are sensitive to urinary ions crossing the pelvic epithelium during back-flow of urine, have a resting discharge higher in the non-diuretic than in the diuretic state and are markedly activated by renal ischaemia (Recordati *et al.*, 1980). On the other hand efferent sympathetic activity to the kidney can modify renal vascular resistance, renin release (Zanchetti, Stella, Leonetti, Morganti & Terzoli, 1976; Thames & Di Bona, 1979) and sodium reabsorption at the tubular level (Di Bona, 1977; Gottschalk, 1979). Although speculative, the hypothesis can be made that excitatory reno-renal reflexes have a homeostatic function toward restoration of plasma volume

through an increase in sodium reabsorption and renin release. Moreover, in the light of the anatomical demonstration of an efferent sympathetic innervation of the adrenal cortex (Unsicker, 1971; Henry & Stephens, 1977) a similar function might be envisaged for reno-adrenal reflexes, i.e. a neural modulation of aldosterone secretion.

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