Renal function and sympathetic activity during mental stress in spontaneously hypertensive rats

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Summary

1. The role of the renal sympathetic nerves in the urinary sodium excretion response to 'mental stress' in spontaneously hypertensive rats (SHR) and in Wistar–Kyoto normotensive (WKY) rats was examined. Urinary sodium excretion was measured during 'rest' and during a 20 min period of 'mental stress' in intact rats and in renal denervated rats. Under similar conditions renal sympathetic activity was also measured in a separate group of rats.

2. Urinary sodium excretion fell more during the stress period in SHR (−64 ± 5%) than in WKY rats (−34 ± 7%), despite a greater arterial pressure increase in SHR. This greater decrease in sodium excretion appeared to result from both a more pronounced reduction in GFR and a greater increase in tubular sodium reabsorption.

3. Renal sympathetic nerve activity, which was higher at rest in SHR than in WKY rats, increased much more in SHR than in WKY rats during stress. This may explain the greater reduction in sodium excretion in SHR during stress, because renal denervation almost abolished this latter response.

4. The neurogenically elicited renal response might contribute in an important way to the early development of SHR hypertension. Renal denervation, as well as attenuating sodium retention, also delays the pressure rise in the young SHR.

5. The initial tachycardia after mental stress gradually subsided towards the end of the stress period in SHR, whereas renal sympathetic activity remained elevated. This indicates that the increase in heart rate, if anything, may underestimate the true extent of sympathetic activation in for example the renal and splanchic regions during arousal.

Key words: mental stress, renal sympathetic nerve activity, sodium excretion.

Abbreviations: SHR, spontaneously hypertensive rats; WKY, Wistar–Kyoto rat strain; MAP, mean arterial pressure; HR, heart rate; GFR, glomerular filtration rate; RSNA, renal sympathetic nerve activity.

Introduction

Renal denervation delays the development of hypertension in young SHR [1, 2] and is associated with an increased excretion of sodium [3]. The renal sympathetic nerves might be particularly important during the early development of SHR hypertension, which is characterized by accentuated neurogenic cardiovascular reactions to alerting stimuli in terms of more marked pressor and heart rate responses [4].

The purpose of the present study was to investigate in conscious SHR whether intact renal nerves prevent the kidneys from increasing urinary sodium excretion during periods of mental stress, when arterial pressure increases considerably, which otherwise would lead to pressure diuresis. Measurements were also performed of renal sympathetic nerve activity in conscious rats, both during rest and during periods of mental stress. Furthermore, urinary sodium excretion was determined under the same conditions in rats subjected to renal denervation.

Methods

Male SHR (n = 11) and WKY rats (n = 11) 3–4 months old were used. They were equipped with catheters in the jugular vein, the tail artery and the urinary bladder [5]. A moderate diuresis was achieved by continuous intravenous infusion of 0.1 ml of sodium chloride solution (154 mmol/l:saline)/min, with the rats kept in Lucite
restraining cylinders. Initially some rats were uncomfortable in the cylinders but after 30–60 min they relaxed and showed stable values for mean arterial pressure (MAP) and heart rate (HR). In six rats of each group renal clearance measurements ($^{32}$Cr-labelled EDTA and sodium iodo[125$I$]hippurate) were performed to estimate glomerular filtration rate (GFR) and renal plasma flow. After a 3 h equilibration period renal function was determined by urine collections and arterial blood sampling for another 2 h before and 1 h after a 20 min stress period. The rats were then exposed to a jet of air, directed towards them, a procedure which is known to produce a typical defence reaction [6].

Urinary sodium excretion was also measured during rest and stress in a separate group of SHR ($n = 5$) and WKY rats ($n = 5$) subjected to bilateral renal denervation 5 days earlier [7]. Sodium concentration was measured in the urine and in some experiments also in the plasma by flame photometry. Changes in fractional urinary excretion (the renal sodium excretion expressed as a fraction of the filtered load of sodium at the glomerulus) could then be determined. Plasma and urine activity of $^{31}$Cr and $^{125}$I was measured in a Packard three channel liquid scintillation counter (model 5022, Packard Instruments Co.).

Renal sympathetic nerve activity (RSNA) was also measured in a third separate group of SHR ($n = 6$) and WKY rats ($n = 6$) rats. The left kidney, left renal artery and the abdominal aorta were exposed retroperitoneally via a flank incision during Brilval anaesthesia. A thin bipolar silver electrode was placed around a branch of the left renal nerve and it was isolated with silicone rubber [8]. The electrode cable was exteriorized at the neck.

The next day experiments were performed with the same protocol as above, except that only RSNA, HR and MAP were measured during rest and stress. The renal nerve signal was amplified (Grass P 511) and rectified and RSNA ($\mu V$) was recorded continuously on a Grass polygraph (model 7). After death renal nerve activity was recorded in all animals as a measure of the noise level.

The results are expressed as means ± SE. Student's $t$-test was used for the statistical evaluations. Statistical significance was taken as $P < 0.05$.

**Results**

MAP during the rest period was significantly higher ($151 \pm 4$ mmHg) in the SHR than in the WKY rats ($120 \pm 1$ mmHg) used for measurements of renal function. MAP increased considerably during the stress period in both SHR ($+15 \pm 2$ mmHg) and WKY rats ($+9 \pm 2$ mmHg, $P < 0.05$, SHR vs WKY). The immediate reaction to mental stress was a marked tachycardia in SHR ($+39 \pm 6$ beats/min), which, however, gradually diminished towards the end of the stress period. In contrast, six of 11 WKY rats responded with immediate bradycardia (average response for the whole group $+1 \pm 11$ beats/min, $P < 0.001$ compared with SHR), but then heart rate gradually increased during the stress period to reach a fairly stable level towards the end of the experiment, when it was even higher than in SHR ($425 \pm 9$ vs $391 \pm 7$ beats/min, $P < 0.01$).
Urinary sodium excretion (see Fig. 1) and GFR (0.907 ± 0.014 and 0.959 ± 0.029 ml min⁻¹ 100 g⁻¹ body wt., in SHR and WKY rats respectively) had similar values in both groups at rest. During the mental stress period, urinary sodium excretion was reduced by 64 ± 5% in SHR but only by 34 ± 7% in WKY rats (P < 0.005). This decrease in sodium excretion appears to be due to a decrease both in GFR (35 ± 10% in SHR and 25 ± 5% in WKY rats) and a decrease in fractional urinary sodium excretion (36 ± 8% in SHR and 15 ± 11% in WKY rats), although these particular differences between the two groups did not reach statistical significance.

Renal plasma flow was significantly higher during rest in SHR than in WKY rats (4.5 and 3.6 ± 0.1 ml min⁻¹ 100 g⁻¹ body wt. respectively). During stress it decreased by 56 ± 7% and 47 ± 5% in SHR and WKY rats respectively (not significant, SHR vs WKY). Renal denervated rats had a urinary sodium excretion at rest of 2.82 ± 0.67 and 3.71 ± 0.91 μmol min⁻¹ 100 g⁻¹ body wt. in SHR and WKY rats respectively. During the stress period it was largely unchanged (−7 ± 10%) in SHR although some reduction (22 ± 12%) was observed in renal denervated WKY rats.

Renal sympathetic nerve traffic was significantly higher in SHR than in WKY rats at rest (see Fig. 1). MAP, measured at rest before the 20 min stress period, was 154 ± 5 mmHg and 116 ± 3 mmHg respectively, in SHR and WKY rats. RSNA was even more increased during stress in SHR than in WKY rats. Sympathetic activity remained elevated in SHR throughout the stress period, in contrast to the initial tachycardia, which subsided towards the end of the stress period.

Discussion

These results on SHR and WKY rats show that urinary sodium excretion, renal plasma flow and GFR were all decreased during mental stress, despite marked increases in arterial pressure. The decrease in urinary sodium excretion during mental stress was significantly more pronounced in SHR than in WKY rats despite more pronounced arterial pressure increases in SHR, which, if only ‘pressure natriuresis’ is considered [9], would have been expected to cause an increase in urinary sodium excretion.

This marked decrease in urinary sodium excretion during stress can be explained by the clearly increased level of renal sympathetic activity during stress in SHR. Also in favour of this hypothesis is the clearly attenuated decrease in urinary sodium excretion during mental stress in SHR rats subjected to prior renal denervation. The increased renal sympathetic nerve activity acts both by reducing GFR and by increasing tubular sodium reabsorption, probably as a result of a direct effect upon the renal tubules [10].

During resting awake conditions, we observed a significantly higher renal sympathetic nerve activity in SHR than in WKY rats, as previously observed in anaesthetized SHR [11]. Although use of multifibre renal nerve activity recordings makes it difficult to compare actual discharge rate, because of marked dependence on electrode position as discussed by Coote & Sato [12], renal nerve traffic at rest was clearly higher in SHR than in WKY rats under similar experimental circumstances in the present study. Moreover, recordings of single fibre activity have revealed a definitely higher level of sympathetic activity to the kidney in anaesthetized SHR than in WKY rats [13].

The increased renal sympathetic discharge during stress was associated with a marked initial tachycardia in SHR, whereas many WKY rats responded with a bradycardia, in agreement with the results of Hallböck & Folkow [4]. However, during more long-lasting stress heart rate no longer truly reflected the level of renal sympathetic nerve activity in SHR, since the initial pronounced tachycardia diminished despite the fact that renal sympathetic nerve activity remained greatly elevated throughout the stress period. Thus the heart rate increases may sometimes underestimate the true extent of sympathetic activation to the visceral organs.

In this study renal plasma flow was higher in SHR than in WKY rats during rest, although no difference in this respect was observed by Beierwaltes & Arendshorst [14]. These differences may be due to the influence of the initial moderate diuresis upon renal plasma flow in the present study [15].

Both in early SHR and human hypertension there appears to be a hyper-reactivity to mental stress [4, 16], with a haemodynamic pattern of the nature of a mild defence reaction [6, 17]. The production of an increased renal vascular tone [18] and a further enhanced renal response to arousal may be of particular importance for the development of hypertension since renal denervation, besides attenuating the observed sodium retention of stress, also delays the pressure rise in young SHR [1, 2].

Acknowledgments

This investigation was supported by grants from
the Swedish Medical Research Council (no. 00016 and 4764) and from Magnus Bergvall's Foundation. Valuable advice given by Professor Gerald F. DiBona is gratefully acknowledged. Skilful technical assistance was given by Elisabeth Pollak.

References