Reflex control of sympathetic nerve activity and heart rate from arterial baroreceptors in conscious spontaneously hypertensive rats

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Summary
1. Mean arterial pressure (MAP), heart rate (HR) and splanchnic sympathetic nerve activity were recorded in conscious, 4 months old, male spontaneously hypertensive rats (SHR; n = 9) and matched normotensive Wistar–Kyoto (WKY) rats (n = 8).

2. The reflex bradycardia and reflex inhibition of splanchnic sympathetic nerve activity were studied in each animal during baroreceptor activation. MAP was raised 30–50 mmHg above control with slow, intra-arterial infusion of noradrenaline (1 μg min⁻¹ kg⁻¹ body wt.). There was a significant negative linear correlation between MAP and splanchnic nerve activity and between MAP and HR in all experiments during noradrenaline infusion.

3. The baroreceptor sensitivity with respect to heart rate control was greatly reduced in SHR compared with WKY rats, being 1.5 ± 0.1 beats min⁻¹ mm⁻¹ Hg and 3.7 ± 0.4 beats min⁻¹ mm⁻¹ Hg respectively (P < 0.001).

4. However, baroreceptor sensitivity with respect to control of splanchnic nerve activity, defined as percentage nerve inhibition per mmHg of MAP rise, did not differ statistically between the two groups: 1.8 ± 0.2%/mmHg for SHR and 2.0 ± 0.3%/mmHg for WKY rats.

5. It is suggested that the baroreceptor control of sympathetic outflow is intact in conscious 4 months old SHR with early established hypertension.

6. It is also suggested that the impaired baroreceptor control of heart rate seen in SHR, and in human essential hypertension, is mainly due to an increased activity of the hypothalamic ‘defence area’, which can selectively block the efferent vagal component of the reflex bradycardia elicited from baroreceptor activation.

Key words: baroreceptor reflexes, heart rate, sympathetic nerve activity.

Abbreviations: HR, heart rate; MAP, mean arterial blood pressure.

Introduction
There are several reports demonstrating a reduced baroreceptor reflex influence on heart rate in established human essential hypertension [1, 2, 3], with less reflex bradycardia for a given pressure rise compared with normotensive subjects. Such a reduced baroreceptor ‘sensitivity’ with respect to heart rate control has also been shown in conscious adult spontaneously hypertensive rats (SHR) [4]. This has been attributed to a decreased distensibility of the arterial walls in the baroreceptor regions with less stretch of receptors per unit rise of blood pressure [1], a phenomenon known to occur in animals with experimental renal hypertension [5–8].

It is, however, possible that the decreased ability of the baroreceptors to control heart rate in established human essential hypertension and in SHR can be due also to central mechanisms. Stimulation of the hypothalamic defence area for instance can suppress especially the efferent vagal component of the reflex bradycardia upon baroreceptor activation, while reflex inhibition of the peripheral vasoconstrictor fibres produced by the same baroreceptor stimulation is largely unaffected by hypothalamic stimulation [9, 10, 11]. Mild defence reactions in man, evoked by mental arithmetic, can greatly decrease the
sensitivity of the baroreceptors in the control of heart rate [12].

It was therefore of interest to study in conscious SHR the ability of the baroreceptors to control both sympathetic nerve activity and heart rate simultaneously, since a haemodynamic pattern mimicking mild defence reactions is commonly seen both in early human essential hypertension [13] and in early SHR [14].

Methods

Nine spontaneously hypertensive rats weighing 335 ± 12 g were used in this study. Eight normotensive rats of the Wistar-Kyoto (WKY) strain were used as controls, weighing 342 ± 12 g. Both groups were 4 months old. During Nembutal anaesthesia the coeliac ganglion and the splanchnic nerves were identified via a left flank incision. A thin bipolar silver electrode was placed around a branch of the splanchnic nerve and isolated carefully with silicone rubber (Wacker Sil Gel 604). The animals were then allowed to recover for at least 36 h. Splanchnic nerve activity was recorded via a cable connected to an adaptor on the back of the animal. The nerve signal was amplified (Grass, p. 511) and rectified and the mean nerve activity was displayed on a Grass Polygraph (model 7). Arterial pressure and heart rate were continuously measured via a catheter placed in the caudal artery. In 11 of 17 experiments it was necessary to sedate the animals with diazepam (Valium; 50 μg intravenously) to obtain a stable control level of sympathetic nerve discharge. Though this dose of diazepam sedated the animals they could easily be wakened and aroused by trivial stimuli. The administration of diazepam did not change the basal level of sympathetic nerve discharge but decreased the emotionally elicited sympathetic excitations otherwise often noted in these awake animals.

The ability of the arterial baroreceptors to inhibit sympathetic activity and to decrease heart rate (HR) was tested in the following way. A slow intra-arterial infusion of noradrenaline (1 μg min⁻¹ kg⁻¹ body weight) was used to raise mean arterial pressure (MAP) 30–50 mmHg within 60 s. This caused reflex bradycardia and an inhibition of splanchnic sympathetic nerve activity in all experiments. There were no signs of tachycardia due to a possible β-receptor stimulation by noradrenaline. There was a significant negative linear correlation between MAP and splanchnic sympathetic nerve activity and between MAP and HR in all experiments during noradrenaline infusion. So-called baroreceptor sensitivity with respect to control of splanchnic sympathetic nerve activity was defined as percentage nerve inhibition from control per mmHg of MAP rise (%/mmHg) and with respect to control of HR as HR decrease per mmHg of MAP rise (beats min⁻¹ mm⁻¹ Hg).

Student’s t-test was used for the statistical evaluations. A P value <0.05 was considered as statistically significant.

Results

MAP before the intra-arterial infusions of noradrenaline was 136 ± 4 mmHg for SHR and 103 ±
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3 mmHg for WKY rats (P < 0.001), and the control values for HR were 450 ± 12 beats/min and 455 ± 23 beats/min for SHR and WKY rats respectively (N.S.). The values for percentage nerve activity inhibition per mmHg of MAP rise (baroreceptor sensitivity) did not differ statistically between SHR and WKY rats: the respective values were 1.8 ± 0.2%/mmHg and 2.0 ± 0.3%/mmHg (Fig. 1). The ability of the baroreceptors to decrease HR during increases of MAP was, however, greatly impaired in SHR. The baroreceptor sensitivity with respect to heart rate control was 1.5 ± 0.1 beats min⁻¹ mm⁻¹ Hg for SHR and 3.7 ± 0.4 beats min⁻¹ mm⁻¹ Hg for WKY rats (P < 0.001) (Fig. 1).

Discussion

This study confirms the report from Struyker-Boudier et al. [4] of a reduced baroreceptor control of heart rate in conscious 4–5 months old SHR. However, the baroreceptor control of sympathetic outflow seems to be normal in conscious SHR as compared with WKY rats. It is thus unlikely that the reduced ability of the baroreceptors to control heart rate is due only to a reduced distensibility of the arterial wall at the baroreceptor areas, because, if so, the sensitivity of the baroreceptors to control splanchnic sympathetic nerve activity would also have been greatly impaired in SHR. This dissociation of the efferent responses to a certain blood pressure change in conscious SHR could well be of central origin. It is known that stimulation of the hypothalamic defence area can, at the bulbar level, selectively block the efferent vagal component of the reflex bradycardia elicited by baroreceptor stimulation. On the other hand baroreceptor inhibition of sympathetic activity is largely unaffected by such hypothalamic stimulation [9, 10]. From direct recordings of renal sympathetic nerve activity in anaesthetized cats it has been shown that the slope of the linear curve relating MAP and reflex inhibition of sympathetic nerve traffic during noradrenaline infusion is normal but shifted to the right when the hypothalamic defence area is stimulated simultaneously [11]. Judy et al. [15] demonstrated in anaesthetized 4 months old SHR that increased baroreceptor stimulation effectively inhibited sympathetic nerve activity with the same sensitivity as found in normotensive control rats. However, with increasing age the ability of the baroreceptors to inhibit sympathetic activity was decreased in SHR, probably because of vascular wall changes at the receptor level, as shown by Sapru & Wang [16] and Sapru & Krieger [17].

It is suggested from this study that the baroreceptors in conscious 4 months old SHR with an early established hypertension respond normally to certain blood pressure changes, as reflected by a normal baroreceptor control of sympathetic activity. The decreased baroreceptor influence on heart rate in SHR at this age and also in early human essential hypertension is partly or perhaps mainly due to a central suppression of the baroreceptor control of heart rate, perhaps as a consequence of increased hypothalamic activity, which can fairly selectively block the efferent vagal component of the reflex bradycardia elicited by baroreceptor stimulation.

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References

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