Relationship between the Baroreceptor Reflex and the Variability of Arterial Pressure and of the Heart Beat Period in Rats with Arterial Hypertension

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The relationship between depression of the cardiochronotropic component of the baroreceptor reflex and arterial pressure and heart beat variabilities was investigated in normotensive rats and rats with renal hypertension (one kidney - one clamp). In the hypertensive rats, the arterial pressure and heart rate were both increased and more variable, while the cardiochronotropic component of the baroreceptor reflex was depressed. No cause-effect relationship between baroreceptor reflex attenuation and increased variability of hemodynamic parameters was found in this rat model of arterial hypertension.

Key Words: *arterial pressure; heart beat period; renal hypertension; arterial pressure variability*

Mean arterial pressure (AP) shows both rhythmic and aperiodic oscillations of varying amplitude, even in the resting state [9]. Spontaneously hypertensive rats have been reported to show increased AP variability combined with increased or decreased variability of the cardiac rhythm [5,7,14]. Heightened AP variability has also been observed after deafferentation of the major mechanoreceptor zones in the heart and major vessels [10]. Attenuation of the baroreceptor reflex (BRR) in arterial hypertension [1] suggests the existence of a cause-effect relationship between BRR attenuation and AP variability. Experimental verification of this hypothesis is only possible through computerized monitoring and analysis of vast arrays of current AP values for each systole.

The present study was undertaken to establish, using the technique we had devised for analyzing instantaneous AP values [2], how the magnitude of the BRR would relate to the variabilities of AP and of the heart beat period (HBP) in rats with renal arterial hypertension under conditions of a prolonged experiment.

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MATERIALS AND METHODS

The study was conducted on 19 male rats (body weight 200-250 g) in the awake state. In 9 of the rats renal arterial hypertension was produced by compressing, under general anesthesia, the left renal artery with a stainless steel clamp that ensured a standard inner diameter of the artery; the right kidney was removed. The remaining 10 rats served as normotensive controls. The experiment was started 13-17 weeks after the operation; 2-3 days before the experiment, polyethylene catheters (diameter 0.5-0.6 mm) filled with a 10% heparin solution were implanted into the aorta (via the femoral artery) and the femoral vein in all 19 rats under combined anesthesia (Nembutal 10 mg/kg and sodium oxybutyrate 1 g/kg, intraperitoneally). The distal ends of the catheters were brought out subcutaneously to the interscapulum using a long metal needle and were fixed there with a purse-string suture.

AP and HBP data were recorded using an automated device [2,3]. Information from the AP

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Table 1. Mean Values and Variability of AP and the HBP and Mean Magnitude of the BRR in Hypertensive and Control (Normotensive) Rats

Parameter	Control rats (n=10)	Hypertensive rats (n=9)
Mean AP, mm Hg	86.1±1.0	141.4±2.0***
AP variability, mm Hg	3.1±0.2	3.9±0.1**
HBP, msec	178.1±2.9	161.7±6.1*
Variability of the HBP, msec	4.9±0.4	12.1±0.5***
BRR magnitude, msec/mm Hg	1.49±0.20	0.94±0.09*

Note. *p<0.02, **p<0.005, ***p<0.001 in comparison with the control rats.

sensor of the device was transmitted through one of its channels to an H338 self-recorder for visual monitoring and record keeping; its other channel was used to deliver the signal, after amplification, via an analog-digital converter to a computer for subsequent mathematical processing [3].

Each test was divided into a day session (between 11:00 and 14:00 hours) and an evening one (between 17:00 and 20:00 hours), each session consisting of ten 1.5-minute periods separated by a 5-minute interval. In each period, the baseline AP was recorded for 1 min, after which the cardiochronotropic component of the BRR was tested [13]. Because the HBP response to an artificial rise in AP is delayed in rats, the magnitude of the BRR was calculated taking into account this phase shift [14].

A Statgraphics 2.1 software package was used for statistical processing of the data by Student's and Wilcoxon's tests and univariate and multivariate linear regression analyses.

RESULTS

As shown in Table 1, the hypertensive rats differed significantly from the normotensive controls in all five parameters. Thus, their mean AP was 64.2% higher and their HBP was 9.2% shorter, the AP and HBP variabilities (i.e., standard deviations [11]) were greater by 25.8% and 146.9%, respectively, and the BRR was depressed by 36.9%.

Comparison of the data obtained for the two parts of the day revealed a significant fall in AP and a significant increase in the BRR and in the HBP variability (p<0.01) in the hypertensive rats, but not in their normotensive counterparts, in which the only parameter that showed a significant difference (p<0.05) between the two parts of the day was the heart rate - there was a relative bradycardia in the later part (17:00-20:00 hours).

Comparison of the mathematical models obtained by the method of multivariate linear regression showed that the AP variability correlated only with the mean AP and HBP variability in the normotensive controls and, in addition, with the mean HBP and BRR magnitude in the hypertensive rats, and that only a decrease in the HBP could result in increased AP variability (because of the negative association - Table 2). On the other hand, the existence of a relationship between a depressed BRR and heightened AP variability in hypertensive rats was not confirmed, as there was a positive association between these parameters.

A positive correlation between HBP variability and BRR magnitude in hypertensive rats (r=0.623) was evident even when the method of linear regression was used. It follows from this that decreased size of the cardiochronotropic component of the BRR in experimental renal hypertension and, as a consequence, reduced tonus of the vagus nerve are not causes of HBP variability. HBP variability has been shown to be decreased in rats by transection

Table 2. Parameters of Multivariate Linear Regression Equations of the Type $y=b_1x_1+b_2x_2+ \ldots +b_nx_n$ Describing AP Variability as a Function of Other Factors in Control (Normotensive) and Hypertensive Rats

Parameter	Regression coefficients (b)	
	Control rats	Hypertensive rats
AP	0.03***	0.03***
HBP	–	−0.01**
Variability of the HBP	0.24***	0.06*
BRR magnitude	–	0.26*
Predictive value of the model, r^2×100%	80.8%	94.3%

Note. *p<0.05, **p<0.01, ***p<0.001 in comparison with the control rats.

of sinus and aortic nerves as well as by propranolol [4,6]. This suggests that the cause of severe HBP destabilization is activation of the sympathetic nervous system as a result of renal hypertension [12].

The results of this study warrant the conclusion that the development of experimental renal hypertension is accompanied by increases in both the level and variability of AP, by tachycardia with a sharp increase in the lability of the cardiac rhythm, and by weakening of the cardiochronotropic component of the BRR. No cause-effect relationship was found between changes in AP and the HBP, on the one hand, and BRR depression on the other.

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