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RAPID COMMUNICATION

The Lack of Cardiac Hypertrophy in Newborn Prague Hypertensive Rats

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Summary

Newborn rats of four different strains with spontaneous hypertension show heart enlargement mainly due to cardiac hyperplasia. To determine whether this anomaly is common in all genetically hypertensive rats, we have compared newborns of Prague hypertensive rats (PHR) with their respective normotensive controls (PNR). The heart ventricles, kidneys and livers of newborn animals were analyzed for their weight, protein and DNA content. The total heart weight and the heart/body weight ratio were significantly lower in PHR than in PNR. On the other hand, there were no differences in total or relative kidney weight and in total liver weight. The relative protein content was significantly lower in kidney and liver of PHR but there were no differences between hypertensive and normotensive animals in relative DNA content of all organs studied. Our results suggest a possible dissociation of genes which determine organ weights from those responsible for blood pressure determination.

Key words:
Heart – Kidney – Hyperplasia – Hypertrophy – DNA – Protein – Newborns – Prague hypertensive rat

Cardiac enlargement was well documented in newborn (Cutilletta *et al.* 1978) and prehypertensive spontaneously hypertensive rats (SHR) (Sen *et al.* 1976). Our previous studies (Hamet *et al.* 1982, Kuneš *et al.* 1987) revealed not only heart hyperplasia but also renal hyperplasia in newborn SHR. These results indicated that heart and kidney weights were disproportionally high in SHR despite their lower total body and liver weights as compared with Wistar-Kyoto (WKY) controls. Cardiac and renal hyperplasia in four different models of genetic hypertension contrasted with the absence of organ weight changes in experimental (DOCA-salt) hypertension (Pang *et al.* 1986). The present study was designed to determine whether this anomaly, common to all genetically hypertensive rats, is also present in the newborns of Prague hypertensive rats.

Newborn Prague hypertensive rats (PHR) and corresponding normotensive controls (PNR) were obtained from the colony maintained in the Institute for

Clinical and Experimental Medicine, Prague. The average systolic blood pressure of the parents of both sexes (measured by the puncture of carotid artery under light aether anaesthesia) was 208 ± 9 mm Hg for PHR and 151 ± 3 mm Hg for PNR, respectively. The newborn animals of both sexes were weighed and decapitated within 24 h after the delivery. Ventricles, kidneys (left and right kidney pooled) and livers were excised, weighed and stored at −70 °C until their protein and DNA contents were determined. Protein and DNA contents were assayed in homogenates by the method of Lowry *et al.* (1951) and Burton (1956), respectively. All data were evaluated by Walsh T-test and expressed as Means ± S.E.M.

Body weight was not significantly different between these two groups although it tended to be smaller in PHR. Total and relative heart weights were significantly lower in PHR than in PNR. The opposite was true for relative liver weight. On the other hand, there were no differences in both absolute and relative kidney weights or in absolute liver weight (Tab. 1).

Table 1
Body weight, absolute and relative organ weights of newborn rats

	PNR n = 33	PHR n = 33
Body weight (g)	5.49 ± 0.53	5.26 ± 0.10
Organ weight (mg)		
Heart	25.83 ± 0.60	23.59 ± 0.44*
Kidney	62.30 ± 1.78	61.82 ± 1.54
Liver	225.56 ± 7.71	238.41 ± 4.93
Organ: body weight ratio (mg/g)		
Heart	4.71 ± 0.05	4.49 ± 0.05*
Kidney	11.36 ± 0.21	11.72 ± 0.14
Liver	40.89 ± 0.71	45.53 ± 0.90*

PHR – Prague hypertensive rat, PNR – Prague normotensive rat,
** indicate significant differences between PHR and PNR at $p < 0.05$ level*

Total protein content was lower not only in heart but also in kidneys of PHR. Relative protein contents (Tab. 2) were significantly lower only in kidneys and livers of PHR. On the other hand, relative DNA contents that provide the information about the cellularity of particular organs. did not differ in all organs studied. Nevertheless, the DNA concentrations (in μg DNA/mg of protein) were higher in hearts and kidneys but not in livers of PHR (28.0 ± 0.7, 57.4 ± 1.2 and 25.2 ± 0.5, respectively) as compared to PNR rats (26.2 ± 0.6, 52.4 ± 0.8 and 24.2 ± 0.4, respectively).

Table 2
Protein and DNA content in organs from newborn PHR and PNR rats

	PNR n = 33	PHR n = 33
DNA (μg)		
Heart	84.03 ± 2.36	79.76 ± 2.25
Kidney	353.94 ± 10.43	352.33 ± 9.60
Liver	906.99 ± 30.32	932.33 ± 18.53
DNA: organ weight ratio (μg/100 mg)		
Heart	329.90 ± 7.19	340.96 ± 8.14
Kidney	573.99 ± 10.38	572.71 ± 11.19
Liver	406.03 ± 9.05	394.60 ± 9.11
Protein (mg)		
Heart	3.22 ± 0.07	2.91 ± 0.09*
Kidney	6.76 ± 0.17	6.19 ± 0.17*
Liver	37.35 ± 0.88	37.23 ± 0.76
Protein: organ weight ratio (mg/100 mg)		
Heart	12.68 ± 0.31	12.33 ± 0.29
Kidney	11.00 ± 0.20	10.03 ± 0.15*
Liver	16.82 ± 0.32	15.68 ± 0.25*

For legend see Table 1.

In the present study, we have tried to check the cardiac and renal hypertrophy and/or hyperplasia in a relatively new model of genetic hypertension originating from the same parental strain (Heller *et al.* 1990). It was well documented (Pang *et al.* 1986) that both cardiac and renal hyperplasia exist in newborns from four different strains with genetic hypertension. However, this was not true for Milan hypertensive strain (with a substantial renal pathogenetic component) and for induced DOCA-salt hypertension. Recently we have studied the genetic determination of heart and kidney weights in relation to blood pressure (Kuneš *et al.* 1990) using a set of recombinant inbred strains (Pravenec *et al.* 1989). In adult rats (15 weeks old) there was a positive correlation between systolic pressure and relative heart weight whereas a negative correlation between kidney weight and blood pressure was observed. The analysis of the degree of genetic determination revealed higher values for the relative kidney weight than for the relative heart weight (Kuneš *et al.* 1990).

Our present results support the suggestion that the genetic factors play a predominant role in the determination of organ weight. The lower absolute and relative heart weight in offsprings of Prague hypertensive rats is opposite to previous findings indicating that heart weight in SHR newborns is always greater than in WKY ones. These results could help to answer the question whether the hyperplasia of cardiomyocytes or vascular smooth muscle cells in genetic hypertension is a

primary event or a secondary response to the disease (Hamet *et al.* 1985). In spite of the lack of cardiac enlargement in newborn animals, PHR animals developed a severe hypertension within 3 months associated with a cardiac hypertrophy (Heller and Zicha, unpublished observations) suggesting that in this model of genetic hypertension the cardiac hypertrophy is secondary to high blood pressure.

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