Physiol. Res. 49: 323-330, 2000

Baroreflex Control of Heart Rate in Young and Adult Salt Hypertensive Inbred Dahl Rats

J. NEDVÍDEK, J. ZICHA

Institute of Physiology, Academy of Sciences of the Czech Republic, Prague, Czech Republic

Received February 21, 2000
Accepted March 27, 2000

Summary

Baroreflex control of heart rate was studied in inbred salt-sensitive (SS/Jr) and salt-resistant (SR/Jr) Dahl rats that were subjected to chronic dietary sodium chloride loading (for 4 weeks) either in youth or only in adulthood, i.e. from the age of 4 or 12 weeks. Using phenylephrine administration to pentobarbital-anesthetized male rats we have demonstrated the decreased baroreflex sensitivity (lower slope for reflex bradycardia) in young prehypertensive SS/Jr rats fed a low-salt diet as compared to age-matched SR/Jr animals. High salt intake further suppressed baroreflex sensitivity in young SS/Jr but not in SR/Jr rats. Baroreflex sensitivity decreased with age in SR/Jr rats, whereas it increased in SS/Jr rats fed a low-salt diet. Thus at the age of 16 weeks baroreflex sensitivity was much higher in SS/Jr than in SR/Jr animals. High salt intake lowered baroreflex sensitivity even in adult SS/Jr rats without affecting it in adult SR/Jr rats. Nevertheless, baroreflex sensitivity was significantly lower in young SS/Jr rats with a severe salt hypertension than in adult ones with a moderate blood pressure elevation. It is concluded that the alterations of baroreflex sensitivity in young inbred SS/Jr rats (including the response to high salt intake) are similar to those described earlier for outbred salt-sensitive Dahl rats. We have, however, disclosed contrasting age-dependent changes of baroreflex sensitivity in both inbred substrains of Dahl rats.

Key words

Baroreflex sensitivity • Heart rate • Blood pressure • Age • Salt intake • Phenylephrine • Inbred Dahl rats

Introduction

Impaired baroreflex control of heart rate and peripheral vascular resistance has been observed in various forms of salt-dependent hypertension in both humans and experimental animals. Miyajima and Bunag (1985) demonstrated in Sprague-Dawley rats that dietary salt loading considerably reduced reflex bradycardia elicited by phenylephrine injection. Surgical denervation of arterial baroreceptors increased salt sensitivity of Wistar-Kyoto rats in which blood pressure is relatively resistant to dietary salt intake (Howe *et al.* 1985). Sabra salt-resistant rats subjected to baroreceptor denervation became susceptible to hypertensive effects of DOCA-salt treatment (Weinstock *et al.* 1984). Not only rats (Gordon *et al.* 1981, Schorer-Apelbaum *et al.* 1984) but also rabbits (Weinstock and Schorer-Apelbaum 1985, Weinstock and Borosh 1993) with lower baroreflex sensitivity are prone to develop salt hypertension. Increased salt intake was also reported to depress baroreflex sensitivity in normotensive humans (Creager *et al.* 1991). Nevertheless, other authors observed that

Fax+4202 24920590
E-mail: physres@biomed.cas.cz http://www.lf2.cuni.cz/physiolres/physiolres.htm

baroreflex sensitivity was augmented by high salt intake in salt-resistant but not in salt-sensitive hypertensive patients (Sakaguchi *et al.* 1988, Trimarco *et al.* 1991, Piccirillo *et al.* 1996).

Reduced baroreflex sensitivity was also found in young Dahl and Sabra salt-sensitive rats kept on a low or normal salt intake, i.e. prior to the development of salt hypertension (Gordon *et al.* 1981, Miyajima and Bunag 1986, Weinstock *et al.* 1984). Attenuated baroreflex control of heart rate, sympathetic nerve activity and vascular resistance in prehypertensive outbred Dahl salt-sensitive (DS) animals is characterized by reduced arterial baroreceptor discharge without changes in aortic arch distensibility compared to outbred salt-resistant (DR) rats (Gordon and Mark 1983, 1984). High salt intake augments these strain differences in baroreflex control, although the underlying mechanisms are still not completely clear. According to Ferrari and Mark (1987) high salt intake sensitizes arterial baroreceptors in DR but not in DS animals. In contrast, other investigators reported reduced baroreflex sensitivity in DS rats subjected to chronic salt loading but no significant changes in similarly treated DR animals (Brown *et al.* 1989, Miyajima and Bunag 1987). Andresen (1989) demonstrated that high salt intake increased baroreceptor pressure threshold (without changes in baroreflex sensitivity) in Dahl rats of both genotypes so that the pressure threshold values were substantially higher in DS than in DR rats fed a high-salt diet. On the other hand, Weinstock *et al.* (1984) reported that high salt intake (accompanied by mineralocorticoid administration) did not alter baroreflex sensitivity in rats of hypertensive or normotensive Sabra strains.

Some years ago, Nedvídek and Zicha (1993) demonstrated that baroreflex sensitivity is also altered in inbred salt-sensitive (SS/Jr) Dahl rats, the impairment being similar to that described in outbred Dahl salt-sensitive (DS) animals (Gordon *et al.* 1981, Miyajima and Bunag 1987). Our observation was confirmed by Murphy and McCarty (1995) who studied baroreflex control of heart rate in SS/Jr rats fed a standard laboratory chow containing 0.7% NaCl.

The present study is focused on i) the influence of high salt intake on the baroreflex sensitivity in young inbred SS/Jr and SR/Jr Dahl rats, ii) the development of baroreflex sensitivity in SS/Jr and SR/Jr Dahl rats under the conditions of low salt intake, and iii) the changes of baroreflex control of heart rate induced by high salt intake in adult SS/Jr and SR/Jr rats. It should be pointed out that blood pressure response of adult Dahl rats to chronic excess salt intake is diminished as compared to that of immature animals. This is true for both outbred (Dahl *et al.* 1968) and inbred (Zicha *et al.* 1987, Dobešová *et al.* 1995) Dahl salt-sensitive rats.

Methods

The experiments were performed in 78 inbred male salt-sensitive (SS/Jr) and salt-resistant (SR/Jr) Dahl rats that were obtained from our breeding colony established due to the courtesy of Dr. John P. Rapp (Toledo, Ohio). The animals were weaned at the age of 4 weeks and fed either a low-salt (0.3% NaCl) or high-salt (8% NaCl) natural ingredient diets. Young and adult animals were subjected to high-salt diet feeding from the age of 4 and 12 weeks, respectively. All rats drank tap water *ad libitum*.

At the age of 8 weeks (young) or 16 weeks (adult) the rats were anesthetized with sodium pentobarbital (Spofa, Prague, 40 mg/kg). PE catheters filled with heparinized saline were implanted into carotid artery (PE 50) and jugular vein (PE 10). The core body temperature was maintained at 37 °C by placing the animals on an infra-red heated table the operation of which was controlled according to core body temperature measured by rectal thermistor. Baroreflex control of heart rate was studied in Dahl rats under pentobarbital anesthesia because its impairment was seen not only in conscious DS rats (Brown *et al.* 1989, Gordon *et al.* 1981, Miyajima and Bunag 1986) but also in DS animals anesthetized with urethane (Ferrari and Mark 1987, Gordon and Mark 1984), chloralose (Miyajima and Bunag 1986, 1987) or pentobarbital (Andresen 1989, Andresen *et al.* 1989).

Graded doses of phenylephrine (0.5-5 μg/kg, Sigma, St. Louis) or angiotensin II (2-20 μg/kg, Hypertensin, Ciba, Basel) were given intravenously as bolus injections in a volume of 50 μl/100 g b.w. The order in which these two agents were given was randomized. Drug injections were not repeated until blood pressure and heart rate returned close to baseline values. Saline injections (50 μl/100 g b.w.) had no effects on blood pressure or heart rate.

Stabilized baseline values of blood pressure (BP) and heart rate (HR) as well as pressor responses and associated heart rate changes were recorded for 1 min before and for 5 min after each drug administration. Phasic arterial pressure was registered using MP-15

transducers (Micron Instruments, Los Angeles, Ca) and Hewlett-Packard 7702B recorder. Obtained pressure signal was sampled at 100 Hz frequency by means of 12-bit A/D converter (PCL-718, Advantech Ltd., Taiwan) before further data processing.

Baroreflex sensitivity was evaluated from the slope (gain) of the baroreflex heart rate control during reflex bradycardia elicited by increasing BP with phenylephrine or angiotensin II. We determined peak pressor responses and associated peak reflex changes in pulse interval which occurred in the first 30 or 60 s after phenylephrine and angiotensin II injection, respectively. In each rat the baroreflex slope was obtained by fitting a linear regression line through particular points (Δ pulse interval vs. Δ mean arterial pressure) over a wide range of pharmacologically-induced BP changes.

Data expressed as means ± S.E.M. were evaluated by one-way-analysis of variance with the calculation of least significant differences and by factorial analysis (Snedecor and Cochran 1968). $P<0.05$ was considered as significant.

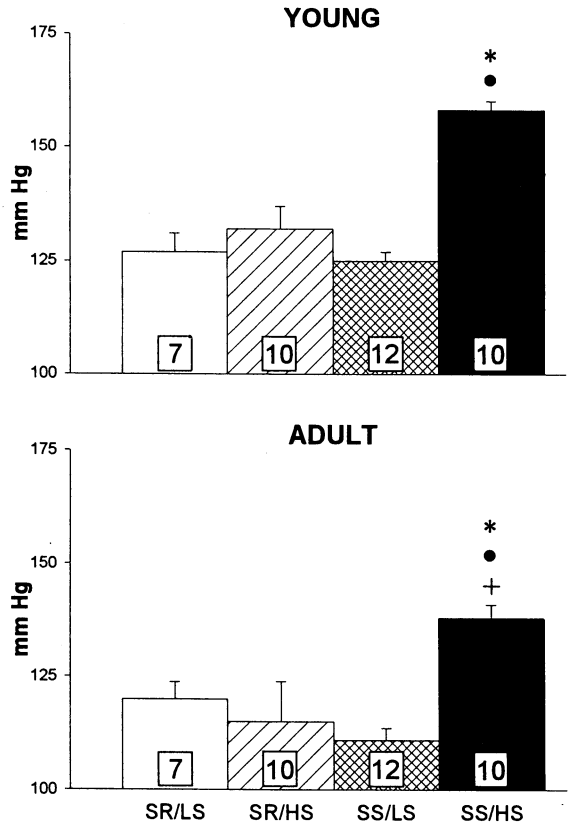

Fig. 1. *Mean arterial pressure in young (8-week-old, upper panel) and adult (16-week-old, lower panel) Dahl SR/Jr and SS/Jr rats that were fed either a low-salt diet (LS) or a high-salt diet (HS) feeding for 4 weeks. Data are means ± SEM. The number of animals is given at the bottom of the columns. Significant differences ($p<0.05$): asterisks from the animals fed LS diet, dots from SR/Jr rats and crosses from the respective young group.*

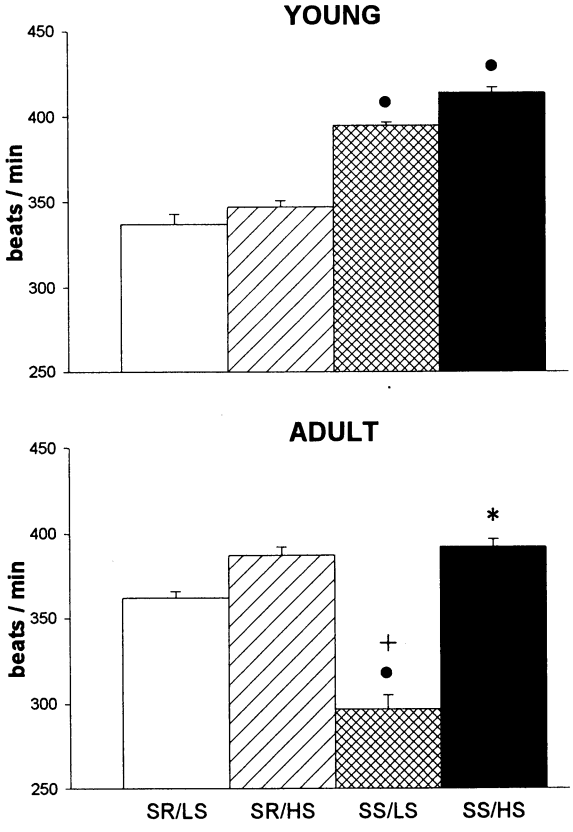

Fig. 2. *Heart rate in young (8-week-old, upper panel) and adult (16-week-old, lower panel) Dahl SR/Jr and SS/Jr rats that were fed either a low-salt diet (LS) or a high-salt diet (HS) feeding for 4 weeks. For other legend see Figure 1.*

Results

Blood pressure was elevated by high-salt diet in both young and adult SS/Jr rats but this increase was more pronounced in young animals (Fig. 1). No significant blood pressure changes occurred in SR/Jr animals. Heart rate was higher in young SS/Jr than in SR/Jr rats irrespective of the diet. On the other hand, significantly lower heart rate was observed in adult SS/Jr rats fed a low-salt diet (Fig. 2).

The relationship between phenylephrine-induced changes in mean arterial pressure and pulse interval was linear up to 5 μg phenylephrine/kg b.w. in most of experimental groups. This relationship was shifted to the right in both young and adult salt hypertensive SS/Jr rats compared to animals fed a low-salt diet (Fig. 3).

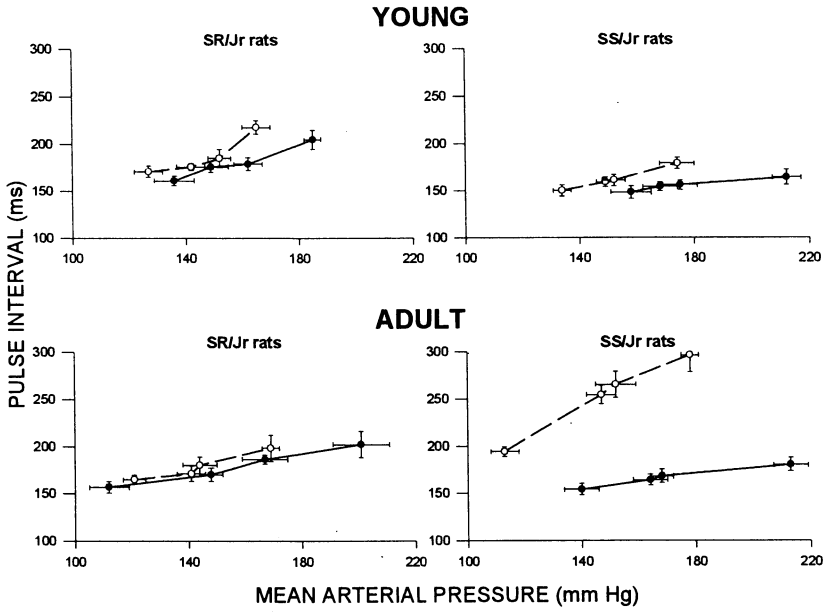

Fig. 3. *Initial values of pulse interval and mean arterial pressure as well as peak values of both parameters induced by phenylephrine administration (0.5, 1.0 and 5.0 μg/kg b.w.) in young (8-week-old, upper panels) and adult (16-week-old, lower panels) Dahl SR/Jr (circles) and SS/Jr (squares) rats that were fed either low-salt (open symbols) or high-salt diet (full symbols) for 4 weeks. Data are means ± SEM.*

Table 1. Factorial analysis of phenylephrine-induced changes in mean arterial pressure and pulse interval: the effects of salt intake, genotype and age of animals.

Phenylephrine dose	**Salt (HS vs. LS)**	**Genotype (SS/Jr vs. SR/Jr)**	**Age (young vs. adult)**
	Mean arterial pressure		
0.5 μg/kg	–1.7±4.5	+0.6±4.5	–9.3±4.5*
1.0 μg/kg	–4.6±4.7	–1.6±4.7	–14.0±4.7*
5.0 μg/kg	+7.4±4.7	+6.6±4.7	–1.9±4.7
	Pulse interval		
0.5 μg/kg	–8.9±3.4*	+7.8±3.4*	– 9.7±3.4
1.0 μg/kg	–15.7±4.3*	+7.9±4.3	–14.6±4.3*
5.0 μg/kg	–25.7±6.8*	–3.0±6.8	–10.1±6.8

Analysis is based upon pressor and bradycardic responses shown in Figure 4. Data are factorial effect means ± S.E.M. Asterisks indicate significant effects ($p<0.05$).

Pressor responses to phenylephrine were generally smaller in young rats as compared to the respective adult groups (Table 1). Phenylephrine-induced bradycardia was greater in rats fed a low-salt diet. When young rats were analyzed separately, pressor responses were greater in SS/Jr than in SR/Jr rats, but the reverse was true for phenylephrine-induced pulse interval changes (5 μg/kg: +16.9±2.8 mm Hg and –27.3±6.3 ms, $p<0.02$).

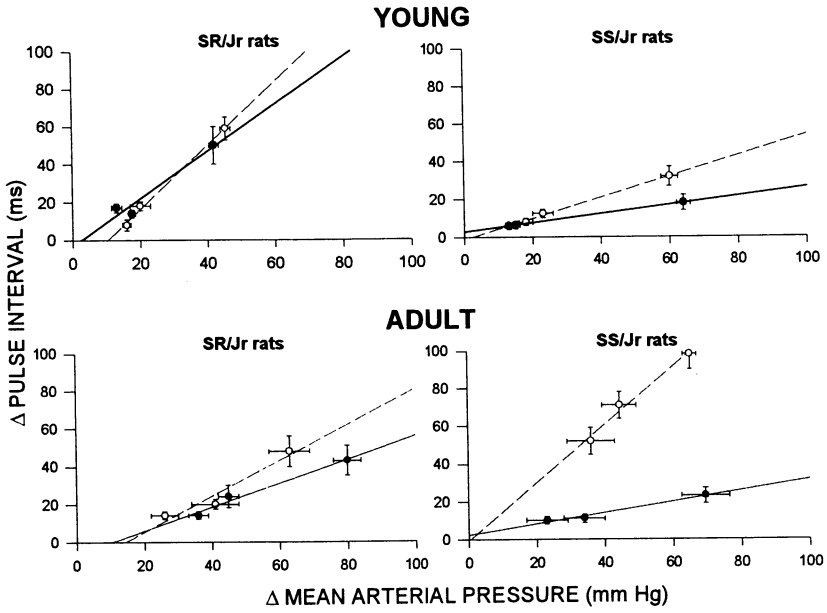

Fig. 4. *Phenylephrine baroreflex slopes calculated from peak changes of pulse interval and mean arterial pressure in young (8-week-old, upper panels) and adult (16-week-old, lower panels) Dahl SR/Jr (circles) and SS/Jr (squares) rats that were fed either a low-salt (open symbols, broken lines) or a high-salt diet (full symbols, full lines) for 4 weeks. Data (means ± SEM) correspond to pressor and bradycardic responses induced by phenylephrine (0.5, 1.0 and 5.0 μg/kg b.w.).*

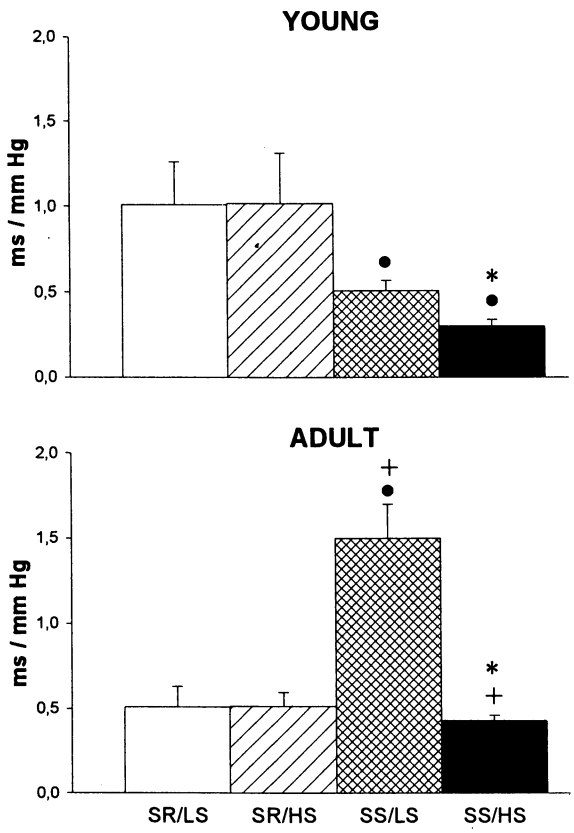

Fig. 5. *Phenylephrine baroreflex slope in young (8-week-old, upper panel) and adult (16-week-old, lower panel) Dahl SR/Jr and SS/Jr rats fed either a low-salt (LS) or high-salt (HS) diet for 4 weeks. For other legend see Figure 1.*

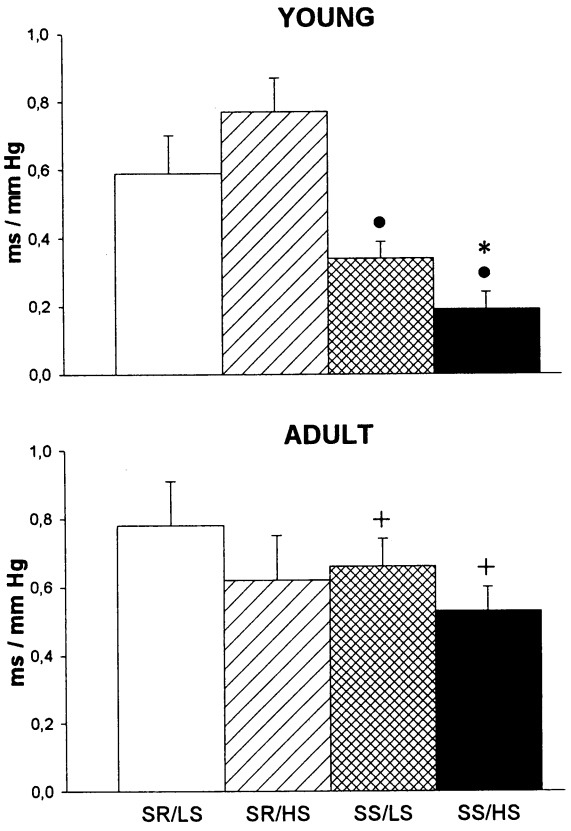

Fig. 6. *Baroreflex slope (calculated from the responses to angiotensin II administration) in young (8-week-old, upper panel) and adult (16-week-old, lower panel) Dahl SR/Jr and SS/Jr rats fed either a low-salt (LS) or high-salt (HS) diet for 4 weeks. For other legend see Figure 1.*

Baroreflex sensitivity (calculated on the basis of the relationship between peak changes in pulse interval and mean arterial pressure) was dependent on the genotype, age and salt intake of animals (Figs 4 and 5). It is evident that the baroreflex slope was greater in SR/Jr than in SS/Jr rats aged 8 weeks. This was found not only in young animals fed a low-salt diet, but the difference was even augmented in rats subjected to dietary salt loading in youth. It is important to note that under the conditions of low salt intake the baroreflex sensitivity decreases with age in SR/Jr rats but increases in SS/Jr animals. Consequently, in adult animals aged 16 weeks baroreflex slope was much greater in adult SS/Jr than in SR/Jr rats fed a low-salt diet. High salt intake lowered baroreflex slope in both age groups of SS/Jr rats but never significantly affected the slope in SR/Jr animals (Fig. 4). However, SS/Jr rats in which high salt intake began at weaning, had significantly lower baroreflex slope than SS/Jr animals fed a high-salt diet only in adulthood which developed less pronounced salt hypertension compared to the younger group (Fig. 5).

Obtained values of baroreflex slope correlated better with initial heart rate (HR) ($r = -0.485$, $p<0.001$, $n = 78$) than with initial values of mean arterial pressure (MAP) ($r = -0.305$, $p<0.01$). This was true in both age groups (young animals, HR: $r = -0.552$, $p<0.001$, MAP: $r = -0.471$, $p<0.001$, $n = 40$; adult animals, HR: $r = -0.467$, $p<0.01$, MAP: $r = -0.183$, n.s., $n = 38$).

Baroreflex sensitivity was also evaluated using the slope calculated from the data obtained after angiotensin II administration (Fig. 6). Though the absolute values were somewhat different than those derived from phenylephrine data, it was again demonstrated in young Dahl rats that the baroreflex sensitivity was significantly lower in SS/Jr rats in which it was further decreased by a high-salt diet. We have also confirmed that baroreflex slopes in adult SS/Jr animals were significantly greater than in corresponding young groups (Fig. 6). Nevertheless, the values of baroreflex slope seen in SS/Jr rats fed a low-salt diet did not surpass those of other experimental groups as it was after phenylephrine administration. Furthermore, using angiotensin II administration we did not reveal the age-dependent decrease in baroreflex sensitivity in SR/Jr rats.

Discussion

The present study confirmed that inbred salt-sensitive (SS/Jr) Dahl rats possess a similar abnormality in the baroreflex control of heart rate as it was earlier described in outbred salt-sensitive (DS) animals (Gordon *et al.* 1981, Miyajima and Bunag 1986, 1987, Brown *et al.* 1989). There was a lower baroreflex slope in young 8-week-old male SS/Jr Dahl rats fed a low-salt diet compared to age-matched SR/Jr animals. High salt intake, which started at weaning, further augmented this difference because it lowered baroreflex sensitivity in young SS/Jr rats without affecting baroreflex slope in SR/Jr animals. Recently, Huang and Leenen (1998) reported that both brain angiotensin II and endogenous ouabain contribute to the impairment (desensitization) of baroreflex, decreased sympathoinhibition and increased sympathoexcitation in salt hypertensive Dahl rats. It should be mentioned that the impairment of the baroreflex control of heart rate is usually accompanied by altered baroreflex control of sympathetic nervous activity which is decisive for peripheral vascular resistance and BP level (Gordon and Mark 1983, 1984, Miyajima and Bunag 1986, 1987, Huang and Leenen 1995, 1998).

The age-dependent changes in the baroreflex control of heart rate seen in rats of both genotypes fed a low-salt diet were the most surprising finding of our study. Baroreflex sensitivity decreased with age in SR/Jr rats, whereas the opposite was true in the SS/Jr strain. Consequently, at the age of 16 weeks baroreflex slope was higher in SS/Jr than in SR/Jr rats, although the reverse difference was found in 8-week-old animals. These unexpected observations are in a good agreement with the fact that the suprathreshold pressure sensitivity was similar in aged outbred DS and DR rats but significantly lower in younger DS than in DR rats (Andresen 1989, Andresen *et al.* 1989). A comparison of both Andresen's papers indicated the rise of suprathreshold sensitivity in DS rats with aging. Thus the developmental changes of baroreflex function in Dahl rats are completely different from those described earlier in spontaneously hypertensive rats (SHR). Baroreflex sensitivity was reported to increase during postnatal life in normotensive Wistar-Kyoto rats, while no significant changes occurred in SHR between 5 and 30 weeks of age (Andresen *et al.* 1980, Struyker-Boudier *et al.* 1982).

The failure of angiotensin II administration to reveal the age-dependent changes in baroreflex sensitivity of Dahl rats fed a low-salt diet might be explained either by slower blood pressure rise after angiotensin II (compared to phenylephrine) or by the interference of angiotensin II with baroreflex mechanisms. It should, however, be noted that the values of baroreflex slope obtained after angiotensin II administration fully confirmed the age-dependent influence of high salt intake

on baroreflex sensitivity in SS/Jr rats. The phenylephrine-based method, which is generally accepted as a "golden standard" for the evaluation of baroreflex sensitivity, seems to be a more sensitive tool than other approaches. This has also been indicated by the comparison of baroreflex sensitivity determined by means of phenylephrine and sodium nitroprusside in DS rats fed a low-salt diet in which only phenylephrine-based method disclosed the impairment of baroreflex sensitivity (Miyajima and Bunag 1986). On the other hand, the defect of baroreflex sensitivity in salt hypertensive DS rats was robust enough to be disclosed even after sodium nitroprusside administration (Miyajima and Bunag 1987).

High salt intake lowered the sensitivity of baroreflex control of heart rate in both age groups of SS/Jr rats, but baroreflex sensitivity in adult SS/Jr rats fed a high-salt diet was still higher than that found in the corresponding group of young SS/Jr animals. There was a pronounced strain difference in baroreflex sensitivity between salt-loaded SS/Jr and SR/Jr young rats, whereas we only observed a borderline difference between the respective adult groups. At present we cannot decide whether this is a consequence or a cause of the different salt-induced hypertensive response which is generally higher in younger rats (Zicha *et al.* 1986, Zicha and Kuneš 1999). This age-dependent difference in BP response to high salt intake was indeed reported in both outbred DS (Dahl *et al.* 1968) and inbred SS/Jr Dahl rats (Zicha *et al.* 1987, Zicha and Duhm 1990, Huang and Leenen 1998).

It can be concluded that baroreflex abnormality disclosed in inbred Dahl salt-sensitive (SS/Jr) rats is similar to that described in outbred DS animals. High salt intake lowered baroreflex sensitivity in both young and adult SS/Jr rats, but the resulting baroreflex slope was inversely proportional to the severity of salt hypertension in both age groups. If such an age-dependent impairment of baroreflex sensitivity would also influence the sympathetic control of vascular resistance, this might be a highly important mechanism in the pathogenesis of the age-dependent BP response to chronic excess salt intake.

Acknowledgements

Partially supported by the research grants 71117 of the Czechoslovak Academy of Sciences and A7011805 of the Grant Agency of AS CR.

References

ANDRESEN MC: High-salt diet elevates baroreceptor pressure thresholds in normal and Dahl rats. *Circ Res* **64:** 695-702, 1989.

ANDRESEN MC, KURAOKA S, BROWN AM: Baroreceptor function and changes in strain sensitivity in normotensive and spontaneously hypertensive rats. *Circ Res* **47:** 821-828, 1980.

ANDRESEN MC, RUDIS SK, BEE DE: Aberrant baroreceptor mechanotransduction in adult Dahl rats on low-salt diet. *Am J Physiol* **256:** H446-H454, 1989.

BROWN DR, MORGAN DA, PEULER JD, THOREN P: 24-hour blood pressure recordings in Dahl rats on high- and low-salt diets. *Am J Physiol* **257:** R1225-R1231, 1989.

CREAGER MA, RODDY MA, HOLLAND KM, HIRSCH AT, DZAU VJ: Sodium depresses arterial baroreceptor reflex function in normotensive humans. *Hypertension* **17:** 989-996, 1991.

DAHL LK, KNUDSEN KD, HEINE MA, LEITL GJ: Effects of chronic excess salt ingestion. Modification of experimental hypertension in the rat by variations in the diet. *Circ Res* **22:** 11-18, 1968.

DOBEŠOVÁ Z, KUNEŠ J, ZICHA J: Body fluid alterations and organ hypertrophy in age-dependent salt hypertension of Dahl rats. *Physiol Res* **44:** 377-387, 1995.

FERRARI AU, MARK AL: Sensitization of aortic baroreceptors by high salt diet in Dahl salt-resistant rats. *Hypertension* **10:** 55-60, 1987.

GORDON FJ, MARK AL: Impaired baroreflex control of vascular resistance in prehypertensive Dahl S rats. *Am J Physiol* **245:** H210-H217, 1983.

GORDON FJ, MARK AL: Mechanism of impaired baroreflex control in prehypertensive Dahl salt-sensitive rats. *Circ Res* **54:** 378-387, 1984.

GORDON FJ, MATSUGUCHI H, MARK AL: Abnormal baroreflex control of heart rate in prehypertensive and hypertensive Dahl genetically salt-sensitive rats. *Hypertension* **3** (Suppl I): I135-I141, 1981.

HOWE PR, ROGERS PF, MINSON JB: Influence of dietary sodium on blood pressure in baroreceptor-denervated rats. *J Hypertens* **3:** 457-460, 1985.

HUANG BS, LEENEN FH: Brain 'ouabain' and desensitization of arterial baroreflex by high sodium in Dahl salt-sensitive rats. *Hypertension* **25:** 372-376, 1995.

HUANG BS, LEENEN FH: Both brain angiotensin II and "ouabain" contribute to sympathoexcitation and hypertension in Dahl S rats on high salt intake. *Hypertension* **32:** 1028-1033, 1998.

MIYAJIMA E, BUNAG RD: Dietary salt loading produces baroreflex impairment and mild hypertension in rats. *Am J Physiol* **249:** H278-H284, 1985.

MIYAJIMA E, BUNAG RD: Impaired sympathetic baroreflexes in prehypertensive Dahl hypertension-sensitive rats. *Clin Exp Hypertens A* **8:** 1049-1061, 1986.

MIYAJIMA E, BUNAG RD: Exacerbation of central baroreflex impairment in Dahl rats by high-salt diets. *Am J Physiol* **252:** H402-H409, 1987.

MURPHY CA, McCARTY R: Baroreflex control of heart rate in Dahl hypertensive (SS/Jr) and normotensive (SR/Jr) rats. *J Hypertens* **13:** 1145-1151, 1995.

NEDVÍDEK J, ZICHA J: Age-dependent changes of baroreflex efficiency in Dahl rats: effects of high salt intake. *Physiol Res* **42:** 209-212, 1993.

PICCIRILLO G, BUCCA C, DURANTE M, SANTAGADA E, MUNIZZI MR, CACCIAFESTA M, MARIGLIANO V: Heart rate and blood pressure variabilities in salt-sensitive hypertension. *Hypertension* **28:** 944-952, 1996.

SAKAGUCHI A, SAITO T, YAMAMOTO K, IWATA J, TONOOKA M, INAGAKI Y: Sodium sensitivity of blood pressure and baroreceptor reflex function in patients with essential hypertension. *J Hypertens* **6** (Suppl 4): S209-S212, 1988.

SCHORER-APELBAUM D, WEINSTOCK M, BEN-ISHAY D: Sympathetic component of baroreflex control of heart rate is impaired in hypertension-prone (SBH) Sabra rats. *J Hypertens* **2:** 257-260, 1984.

SNEDECOR GW, COCHRAN WG: *Statistical Methods.* Iowa State University Press, Ames, IA, 1968, pp 258-298.

STRUYKER-BOUDIER HA, EVENWEL RT, SMITS JF, VAN ESSEN H: Baroreflex sensitivity during the development of spontaneous hypertension in rats. *Clin Sci* **62:** 589-594, 1982.

TRIMARCO B, LEMBO G, RICCIARDELLI B, DE LUCA N, RENDINA V, CONDORELLI G, VOLPE M: Salt-induced plasticity in cardiopulmonary baroreceptor reflexes in salt-resistant hypertensive patients. *Hypertension* **18:** 483-493, 1991.

WEINSTOCK M, BOROSH M: Low baroreflex sensitivity predisposes to salt-sensitive hypertension in the rabbit. *Am J Physiol* **264:** H505-H511, 1993.

WEINSTOCK M, SCHORER-APELBAUM D: Impaired baroreflex sensitivity in the aetiology of salt hypertension in the rabbit. *Clin Sci* **68:** 489-493, 1985.

WEINSTOCK M, SCHORER-APELBAUM D, BEN-ISHAY D: Baroreflex sensitivity and susceptibility to systolic hypertension induced by DOCA-salt in the Sabra rat. *Am J Physiol* **246:** H448-H452, 1984.

ZICHA J, DUHM J: Kinetics of Na^+ and K^+ transport in red blood cells of Dahl rats. Effects of age and salt. *Hypertension* **15:** 612-627, 1990.

ZICHA J, KUNEŠ J: Ontogenetic aspects of hypertension development: analysis in the rat. *Physiol Rev* **79:** 1227-1282, 1999.

ZICHA J, KUNEŠ J, JELÍNEK J: Experimental hypertension in young and adult animals. *Hypertension* **8:** 1096-1104, 1986.

ZICHA J, BYŠKOVÁ E, KUNEŠ J, POHLOVÁ I, JELÍNEK J: Sodium pump activity in young and adult salt hypertensive Dahl rats. *Klin Wochenschr* **65** (Suppl 8): 76-81, 1987.

Reprint requests

Dr. Josef Zicha, Institute of Physiology, Academy of Sciences of the Czech Republic, Videnska 1083, CZ-142 20 Prague 4, Czech Republic. e-mail zicha@biomed.cas.cz.