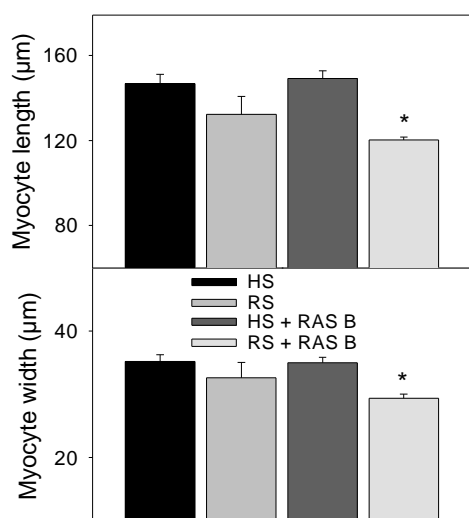


## REGRESSION OF CARDIAC HYPERTROPHY IN THE SHR BY RENIN-ANGIOTENSIN SYSTEM BLOCKADE AND DIETARY SODIUM RESTRICTION

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\* $P < 0.01$  vs HS + RAS-B

Combined angiotensin converting enzyme inhibition (ACEI) and angiotensin type-1 receptor ( $AT_1$ ) blockade offers new potential in the treatment of hypertension and cardiac hypertrophy. We previously demonstrated that combination treatment with losartan and perindopril caused pronounced hypotension and cardiac atrophy in normotensive Sprague-Dawley rats (Griffiths *et al.*, 1999). These effects were prevented in animals receiving a high sodium chloride (NaCl) diet suggesting that NaCl intake may be important during such treatment. In the present study we examined the effects of varied dietary NaCl intake and combined treatment with an ACEI together with the insurmountable  $AT_1$  blocker candesartan in spontaneously hypertensive rats (SHR) with established cardiac hypertrophy.

Adult male SHR (16-20 weeks) were fed high (4%) or reduced (0.2%) NaCl chow for 14 days. On days 7-14, i.p. injections of candesartan (3 mg/kg) and perindopril (6 mg/kg) were given (RAS-B). Diet only treated animals received vehicle injections. At day 14 tail-cuff blood pressures and body weights were measured. Animals were anaesthetized (pentobarbitone sodium, 60 mg/kg, i.p.) and hearts removed and weighed. Cardiac myocytes were isolated enzymatically and their dimensions were measured by widefield microscopy.

Treatment	Weight gain (g)	Heart weight (mg)	Cardiac Index (mg/g)
High NaCl	22 ± 5.1	1470 ± 15.2	3.88 ± 0.03
Reduced NaCl	34.2 ± 3.1	1452 ± 29.9	3.74 ± 0.08
High NaCl + RAS-B	26.6 ± 3.2	1372.6 ± 21.5	3.72 ± 0.10
Reduced NaCl + RAS-B	-21.6 ± 6.4*	1023.4 ± 40.2*	3.22 ± 0.04*

\* $P < 0.05$  vs all other groups ( $n=5$  animals each).

The Table shows the effect of the four treatments on body weight and cardiovascular parameters. Heart weight and cardiac index was decreased in the reduced NaCl + RAS-B group compared to all other groups, and these animals lost body weight (Table). A comparison of the myocyte dimensions among the treatment groups (Fig.) shows that cardiac myocytes from the reduced NaCl + RAS-B group were smaller in length and width, but that myocyte size was not affected in animals receiving high NaCl + RAS-B. The systolic blood pressure difference between these groups was significantly different (high NaCl + RAS-B,  $161 \pm 9$ ; reduced NaCl + RAS-B,  $100 \pm 8$ ;  $P < 0.01$ ).

These results indicate that combined RAS blockade with candesartan and perindopril is highly effective at regressing cardiac hypertrophy in hypertensive SHR on a reduced NaCl intake. The regression of hypertrophy reflects a reduction in cardiomyocyte dimensions. Hypertrophic regression was not observed when RAS blocker treatment was given in association with a high NaCl intake.

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