SHORT COMMUNICATION

Effect of age on hypertensive stimuli and the development of hypertension in Brattleboro rats

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Summary
1. In rats with inherited diabetes insipidus, unilateral nephrectomy plus drinking of 0.6% NaCl solution (saline) did not influence blood pressure in adult rats. However, when these factors applied before puberty, they produced hypertension.
2. We therefore analysed whether saline administration before puberty or unilateral nephrectomy before puberty was more important for this hypertensive response.
3. Saline drinking was found to be necessary for the response because hypertension was elicited by unilateral nephrectomy in adult rats only if saline consumption began before puberty.

Key words: age, diabetes insipidus, hypertension.

Introduction
The period preceding sexual maturity (up to age 60 days: Křeček, 1971) is critical for the response of Brattleboro rats with inherited diabetes insipidus to hypertensive stimuli (unilateral nephrectomy and the drinking of 0-6% NaCl solution) (Dlouhá, Křeček & Zicha, 1977). In order to establish whether one of these two components is of major importance for the hypertensive response of young rats, the hypertensive stimulus was divided in time so that one of its components was applied before sexual maturity and the other in adulthood.

Methods
Female rats with diabetes insipidus (i.e. animals with a daily fluid intake greater than 50% body weight) were weaned at 30 days and reared under standard conditions (diet containing 1% NaCl). Seven experimental groups were used, the periods of provision of 0-6% NaCl solution for drinking, and times of nephrectomy, being as shown:
- Group 1 (n = 11): from 4 weeks.
- Group 2 (n = 17): from 12 weeks.
- Group 3 (n = 16): from 4 weeks, unilateral nephrectomy at 4 weeks.
- Group 4 (n = 22): from 12 weeks, unilateral nephrectomy at 12 weeks.
- Group 5 (n = 14): from 4 weeks, unilateral nephrectomy at 12 weeks.
- Group 6 (n = 13): from 12 weeks, unilateral nephrectomy at 4 weeks.
- Group 7 (n = 10): from 12 weeks, unilateral nephrectomy at 19 weeks.

Unilateral nephrectomy was carried out by removing the left kidney. Intake of saline (0-6% NaCl solution) was measured in week 1 and week 14 of the experiment. Blood pressure was measured once a week by means of the ‘tail-cuff’ method (Dlouhá et al., 1977). Hydronephrosis was detected at an autopsy.

Statistical evaluation was done by Student’s t-test and χ² test.

Results
When both unilateral nephrectomy and the drinking of 0-6% NaCl solution were applied at the age of 4 weeks (group 3), there was a gradual increase in blood pressure up to the age of 10 weeks (157.7 ± 6.28 mmHg). After a transitory stabilization between week 10 and week 15, the blood pressure increased again and at the age of 17 weeks it was 175.4 ± 4.35 mmHg. The blood pressure values of
group 1 (saline consumption from age 4 weeks only, see Fig. 1) differed significantly from the values of the group 3 (saline and unilateral nephrectomy at 4 weeks) at age 16 weeks.

We further investigated whether the blood pressure would increase in rats when the onset of saline drinking was separated from unilateral nephrectomy. The blood pressure values of group 5 significantly surpassed the values of group 1 at age 15 weeks (Fig. 1). However, there was no difference between blood pressures of groups 3 and 5. No stabilized hypertension was observed during the 20 weeks of the experiment in rats that began to drink 0.6% solution in week 12 (group 2). This was also true for group 6 (animals drinking saline from week 12 with unilateral nephrectomy at 4 weeks), group 4 (animals drinking saline and unilaterally nephrectomized at week 12) and group 7 (animals drinking saline from week 12 with unilateral nephrectomy at week 19).

The mean intakes ± SEM of 0.6% NaCl solution at the beginning and at the end of the experiment (expressed in ml 24 h⁻¹ 100 g⁻¹) were as follows: group 1 196.9 ± 12.88 (n = 24) and 251.3 ± 12.49 (n = 6) respectively; group 3 171.4 ± 9.24 (n = 23) and 163.3 ± 8.32 (n = 6) respectively; group 2 221.5 ± 9.69 (n = 8) and 301.2 ± 19.19 (n = 17) respectively; group 4 181.9 ± 13.76 (n = 7) and 253.6 ± 19.90 (n = 7) respectively. Although no differences were found at the beginning of the experiment, at its conclusion both the unoperated and the unilaterally nephrectomized rats, drinking saline from age 12 weeks, consumed significantly more saline than rats drinking it from week 4.

Hydronephrosis occurred more frequently in unilaterally nephrectomized rats drinking saline from week 4 (27 out of 30 animals, groups 3 and 5) than in rats drinking it from age 12 weeks (11 out of 35 animals, groups 4, 6 and 7) ($\chi^2 = 22.8$, $P < 0.0001$). In general, rats with hydronephrosis had significantly higher blood pressures than rats without hydronephrosis. Nevertheless, among hydronephrotic animals, mean values of blood pressure were higher in rats drinking saline from week 4 than in those drinking saline from week 12 [173.1 ± 3.50 mmHg (n = 27) vs 152.8 ± 3.34 mmHg (n = 11), $P < 0.002$].

**Discussion**

The high salt intake in the period preceding sexual maturation seems to be a necessary prerequisite for establishing hypertension in rats with diabetes insipidus. Unilateral nephrectomy performed in adulthood caused hypertension in rats adapted to high salt intake before puberty, but it was ineffective in rats that had begun drinking saline when adult. Binet, Dejours & Lacaisse (1951) reported that albino rats adapted to an increased salt intake in a different way when reared on a high salt regimen from conception than if they were exposed to a high salt intake when mature. Gröllman & Gröllman (1962) presented data which suggest that this early adaptation of developing rats to high salt...
intake could be followed by hypertension in adulthood.

The longitudinal monitoring of blood pressure in rats with diabetes insipidus, that have been unilaterally nephrectomized and have drunk saline from before puberty, disclosed two phases in the development of hypertension: an early one and a late one. The transient 'early phase' of hypertension appears not only after the application of the whole hypertensive stimulus but also after saline drinking from before puberty. 'Late-phase' hypertension is produced only if both components of the hypertensive stimulus are applied.

Hydronephrosis accompanied by blood pressure elevation was present in both the hypertensive and non-hypertensive groups but its presence was a less important factor for the severity of hypertension than the saline consumption from before puberty.

References


