Sex Differences in Salt Taste: 
The Effect of Testosterone

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KŘEČEK J. Sex differences in salt-taste: the effect of testosterone. PHYSIOL. BEHAV. 10(4) 683-688, 1973. - Free selection between water and 3% saline intake was studied in the rat as a function of sex. Administration of 1 mg testosterone propionate to rats aged 2 days suppressed the sex difference in saline intake. The same dose of this hormone injected at age 12 days was without action on the sex differences in saline intake. The neonatal action of testosterone was only in females, which changed over to a male pattern of fluid intake. The role of the hypothalamus in this effect is discussed.

RESULTS

The Effect of Neonatal Administration of Testosterone on the Intake of 3% Saline and Water

The neonatal action of testosterone was tested sepa-
rately in males and females. Seventy-two males and the same number of females were subdivided in groups of 4 into 18 cages and received 1 mg of testosterone subcutaneously the second day after birth. The same number of rats of both sexes received at the same age the same volume injection of olive oil which contained no steroid. In all females we followed the oestrous cycle after opening the vagina. Females which received only oil had a normal cycle lasting 4–5 days on the average. Females which received neonatal testosterone showed, in agreement with the literature [5,8], continual oestrus as a manifestation of suppression of the cyclic function of the hypothalamus.

Figure 1 shows the intake of water and 3% saline in males and females which received testosterone or oil alone neonatally. Control animals from age 45 days showed a higher water intake in males than in females. The sex difference in saline intake was obvious from the start of measurement at age 30 days, females drinking more than males. Neonatal testosterone decreased or completely eliminated the sex difference both in water intake and in saline intake.

Because of this different dependence of measured values on body weight, we expressed the intake of both fluids in such a way that the effect of body weight would be eliminated.

This expression is the concentration of NaCl in the total amount of water which was drunk by each animal under free choice conditions. These values are shown in Fig. 3. The apparent salt concentration of the intake of control females is higher than that in the males. This sex difference was systematically statistically significant from age 42 days. On the other hand animals which received neonatal testosterone showed a complete absence of this sex difference. If, on occasional days a sex difference did appear, the values were at some times higher in females, at other times, in males. In order to determine whether the disappearance of the sex difference is due to testosterone
FIG. 3. Dependence of sex difference in the apparent concentration of NaCl in the total water intake on neonatal administration of testosterone. Upper part of the graph (0) - oil injection alone; lower part of the graph [TP2] - testosterone administration. X axis - age in days; Y axis - apparent concentration of NaCl in meq/1. Full lines - females; dashed lines - males. Black points show parts of values which differ statistically (p<0.05).

FIG. 4. Dependence of the changes in concentration of NaCl in the total water intake induced by neonatal administration of testosterone on the sex of the animal. Upper part of the graph (0) - males; lower part of the graph (9) - females. X axis - age in days; Y axis - apparent concentration of NaCl in meq/1. Full line - rats with testosterone; dashed line - rats with oil. Black points show pairs of values with a statistical difference (p<0.05).

males or females, the apparent salt concentration of the total fluid intake is shown separately in Fig. 4 for each sex and values are compared between control and experimental groups. This comparison shows that testosterone was more effective in females than in males, whereas the action in females was manifest by a significant decrease in the concentration of NaCl to values near to those which usually occur in males.

The Effect of Administration of Testosterone at Age 12 Days on the Intake of 3% Saline and Water

It is known that testosterone is ineffective on the hypothalamus if given to rat females at age 12 days, because the sensitive period lasts only for 1 week [5,8]. For this reason in further experiments we compared the action of testosterone given to rats at age 2 days with the same dose given to rats at age 12 days. In agreement with the results of previous experiments testosterone given at age 2 days suppressed the sex differences in intake of water and saline (Fig. 5). On the other hand this difference was not removed by administration of testosterone to 12-day-old animals. The latter behaved in the same manner as rats which received only oil at age 2 days: males drank more water than females, the reverse being the case for saline intake.

Growth curves (Fig. 6) show that the sex difference in body weight was maintained after neonatal testosterone as well as after testosterone administered at age 12 days. Males and females which received testosterone at age 12 days were, however, lighter than animals of the same sex given testosterone neonatally.

We further calculated the apparent concentration of NaCl in the total daily water intake and showed (Fig. 7) that just as in previous experiments there was no sex difference in animals which had received testosterone neonatally, however in animals which received the same dosage at age 12 days females showed a higher apparent NaCl intake concentration than males, with statistical significance of this difference maintained from age 40-50 days.

In order to determine whether the observed differences are not dependent on the number of animals in a single cage, 16 randomly selected animals from each experimental group were transferred at age 100 days into separate cages. After 4 weeks we continued in the measurement of intake of both fluids. The results are shown in Fig. 8. In animals which received testosterone at age 12 days, the sex difference was markedly depressed. Suppression of the difference in salt intake was therefore present in rats maintained in groups of 4 in a single cage as well as in rats maintained individually in cages.
DISCUSSION

The data presented here show that the sex difference in salt intake becomes manifest in rats in the period of sexual maturation and can be suppressed by a single dose of testosterone given at age 2 days, whereas the same large dose of hormone is without effect if given at age 12 days. Disappearance of the sex difference in saline intake after neonatal testosterone is produced by a change of the female pattern of saline intake toward that of the male.

It is known that neonatal testosterone suppresses the cyclic character of hypothalamic activity in female rats, with a disappearance of the oestrous cycle and sterility. For this action of testosterone the critical period of sensitivity

lasts only several days after birth [5, 8, 9]. The action of neonatal administration of testosterone on saline intake therefore has a similar critical period in terms of age and duration.

The regulation of saline intake just like the reproductive function is associated with hypothalamic activity [1, 12, 15, 18]. An increase in saline intake with a two bottle free selection produces a rise in the content of RNA in hypothalamic cells of rat males, without any observable change in the females [10]. Neonatal administration of testosterone, however, increases RNA content in hypothalamic cells even in female rats showing an increase and removing scatter in relation to the oestrous cycle [13]. All these changes were observed in the nucleus paraventricularis. Thus far there was no evidence that this part of the hypothalamus plays a role in saline intake or in reproductive function. The action of neonatally administered testosterone on reproductive function is attributed to an effect on the area preoptica and the anterior hypothalamic area [5]. A report has already been presented on the regulation of saline intake from the anterior hypothalamus [1]. Other authors, however, localize this regulation to other portions of the same organ. At present, no definite statement can be made as to precise localisation of regulative function in the
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FIG. 7. Dependence of sex differences on the apparent concentration of NaCl in the total water intake per day in rats given 1 mg of testosterone at age 2 or 12 days. Upper part of the graph (TP 2) - TP given at age 2 days; lower part of the graph (TP 12) - TP given at age 12 days. For other details see Fig. 3.

FIG. 8. Dependence of sex differences in the apparent concentration of NaCl intake in the total water intake per day in relation to administration of 1 mg TP at age 2 or 12 days in animals maintained separately in individual cages. For details see Fig. 7.

hypothalamus in terms of reproductive function and saline intake. It cannot be excluded that the action of neonatal testosterone on saline preference is not based only on a modification of hypothalamic function. Increased saline intake does not influence, for example, only the RNA content of hypothalamic cells, but also hippocampal cells in rat males [10], whereas neonatal testosterone has no such effect on hippocampal RNA content [13]. The action of testosterone given neonatally also is not manifest only in terms of a changed brain function. For example, the female pattern of corticoid metabolism in the rat liver changes into a male pattern [2]. During masculinisation, processes regulating saline intake in females could be affected by an action of testosterone into metabolic processes occurring outside of the central nervous system, e.g. aldosterone.

REFERENCES