The demonstration that the cerebral cortex of all mice is capable of some aromatization is noteworthy since other workers have failed to find such evidence in other rodents or mammals[4,5,7]. This inability to show aromatization may be due to low recoveries and/or age dependent changes in enzyme activity. That cortex can concentrate radiolabel from administered androgens has been demonstrated by several groups[15–18]. However, these authors did not determine whether any of the radioactivity concentrated in this brain region was derived from aromatization of accumulated androgen. Human fetal cortex has been shown to aromatize androgens[5] which is comparable to our observations on 30-day-old mouse cortex. In the present study no sex differences could be detected in cerebral cortex aromatization.

Mouse hypothalamic tissue[5] has been reported to aromatize androstenedione with a male:female ratio of 3. Since neither age of mice nor percentage conversions were given it was not possible to make direct comparisons with our results. Moreover, it was suggested that Tfm mice had aromatizing ability similar to that of normal males[5]. This is in contrast to the present data where the ability of both mutants was towards the female direction, and are consistent with data using liver tissue where it was demonstrated that in androgen insensitive rats steroid metabolism proceeds along female lines[19].

It is also of interest that there was a good conversion of testosterone to estrone in hypothalamic tissue of normal mice whereas in Tfm the major estrogen formed was estradiol-17β. Studies on further metabolism of testosterone in central tissues of genetic mutant mice are still in progress.

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Effects of handling normal and bulbectomized rats at adrenal and plasma corticosterone levels

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Summary. Normal and bulbectomized adult rats, male and female, handled daily for 4 weeks, show plasma and adrenal corticosterone values significantly lower than the non-handled ones.

In our previous investigations, we were able to study the effects of removal of olfactory bulbs on the corticoadrenal function in female rats[1,2]. The animals were handled during a predetermined period in order to avoid stress at the moment of decapitation. Bearing in mind that the activity of adrenal glands can be influenced by many factors, we wondered whether daily handling, in itself, would affect adrenocortical secretion. If this were the case, would it reveal itself in a similar manner in both normal and bulbectomized rats? The present study was undertaken to clarify this point.

Material and methods. 67 white adult rats bred in our institute were used: 34 females of between 160 and 270 g weight, and 33 males of between 230 and 360 g weight. All animals were kept under the same conditions, housed 8 per cage, with food and water available ad libitum. Animals of each sex were divided into 4 lots: a) non-handled normal rats; b) handled normal rats; c) non-handled rats with bilateral removal of olfactory bulbs; d) handled rats with bilateral removal of olfactory bulbs. Handling consisted in taking rats one at a time and holding them for a few seconds outside the cage, twice a day, for 5 days in the week. The cages of non-handled rats were only opened twice a day. After 4 weeks' handling, the rats were decapitated by means of a small animal guillotine at between 9 and 11 a.m., the time between

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	Corticosterone			
	Adrenal (μg/g)		Plasma (μg/100 ml)	
	Non-handled	Handled	Non-handled	Handled
Female				
Normal	20.9 ± 5.20* (8)	7.2 ± 1.19 (8)	35.1 ± 4.98 (8)	14.1 ± 1.26 (8)
Bulbectomized	10.0 ± 2.30 (7)	3.7 ± 0.55 (11)	19.9 ± 1.97 (7)	6.9 ± 1.10 (10)
Male				
Normal	10.5 ± 2.43 (9)	3.8 ± 0.71 (8)	19.8 ± 3.70 (9)	9.0 ± 1.48 (8)
Bulbectomized	11.2 ± 2.18 (9)	3.9 ± 0.59 (7)	20.2 ± 3.13 (9)	7.3 ± 2.07 (7)

*Mean ± SE. Number of animals is given in parentheses.

taking the animal out and its decapitation being not more than 5 sec. Trunk blood was collected and centrifuged. Individual samples of plasma were frozen and kept for subsequent determination of corticosterone.

Immediately after decapitation, the adrenal glands were dissected and weighed to an approximation of 0.1 mg, homogenized in a saline-alcohol solution and then frozen until corticosterone was determined. Bulbectomy was performed according to previously described technique[2]. Adrenal and plasma corticosterone was determined by means of the Rerup and Hedner method[3]. Results were evaluated by Student's t-test.

Results and discussion. Results obtained may be seen in the table. In the first instance, when comparing normal animals, handled with non-handled, it may be seen that adrenal and plasma corticosterone values are significantly less in handled rats, both male and female. In every case, the drop was over 50%. When considering bulbectomized animals, however, we have deemed it more convenient to make a separate analysis of results obtained in females and in males.

In bulbectomized females, handled animals reveal adrenal and plasma corticosterone values significantly lower than in non-handled. Furthermore, as may be seen in the table, the removal of olfactory bulbs produces a lowering in levels of both parameters in the handled and non-handled lots. Comparing bulbectomized with normal animals, it may be observed that the difference in adrenal corticosterone levels is statistically significant in the handled animal lot ($p < 0.010$). In non-handled animals, despite the drop of more than 50%, this does not become significant owing to the great dispersion of data. Respecting the plasma corticosterone, the differences with the normal animals are significant in both lots, i.e. handled ($p < 0.020$) and non-handled ($p < 0.005$).

Regarding males, the handled animals also show significantly lower values than non-handled (adrenal corticosterone, $p < 0.010$ and plasma corticosterone $p < 0.005$). On the other hand, the removal of olfactory bulbs in no way modifies the adrenal or plasma corticosterone either in handled or non-handled animals.

The effects of bulbectomy in females confirms previous findings in this laboratory[1,2,4] regarding relationship between olfactory bulbs and adrenal glands in rats. The fact has been confirmed by other investigators as being observed not only in rats[5,6] but also in dogs[7]. The fact that bulbectomy has no effect on the levels of corticosterone in males reveals a sexual difference in the effects of bulbectomy on adrenal activity. While studying other parameters in bulbectomized rats, we have, at the same time, been able to observe sexual differences in the results, together with insulin sensitivity test[8] and levels in serum free fatty acids[9].

These results indicate that handling reduces adrenal corticosterone synthesis in normal and bulbectomized rats. The exact nature of the mechanism, whereby handling produces diminishing corticoadrenal activity, we cannot explain at present. Perhaps variation in the levels of adrenal steroids produced by handling might cause alterations in sensitivity in hypothalamic areas which control the adrenal function, as Levine and Mullins[10] suggest when referring to rats handled during prepuberal age.

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'Adrenalectomy, ovarian HCG-binding and the onset of female puberty in the rat*

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Summary. The delay of puberty onset in female rats adrenalectomized before the 25th day of age is due neither to changes in the number of ovarian HCG-receptors nor to an altered hormone affinity of these receptors. It is assumed that glucocorticoids act on an intracellular level in the ovarian cells, possibly by alterations of cyclic AMP-dependent phosphodiesterase activity.

Involvement of the adrenal glands in the maturation and function of the reproductive system of the female rat has been implied in previous studies. Although adult rats without adrenal function maintain ovulatory cycles and can reproduce, some irregularities of the cycle have been noted[3]. According to Peppler and Jacobs[4], the adrenal glands are necessary for normal follicular development as well as for the normal complement of eggs to be shed. In the immature female rat, the adrenals play a definite role in determining the time of onset of puberty (for review see Ramaley[5]). Cory and Britton[6] induced precocious puberty with adrenocortical extracts. Bilateral adrenalectomy in rats younger than 25 days of age delays the normal appearance of vaginal opening and ovulation[7–9]. A restoration can be achieved by the administration of low doses of corticosterone[10], or by adrenal autotransplantation[8].

Adrenalectomy has been found to impair the sensitivity of immature female rats to gonadotrophins[11–13], with cortisone returning response to normal[11]. Hypophysectomized immature rats showed an impaired response to human chorionic gonadotrophin (HCG) unless adrenocorticotrophic hormone (ACTH) was also given[14]. Since the sensitivity of the ovary to gonadotrophins is dependent on the specific membrane-bound gonadotrophin receptors, one might speculate that the effects caused by adrenalectomy in female rats are due to the impairment of these receptors. In order to test this possibility, we studied the ovarian HCG-binding in adrenalectomized rats during sexual maturation.

Material and methods. Wistar female rats were received at 20 days of age and divided into control (N = 28) and experimental (N = 16) groups. Bilateral adrenalectomy was performed by an abdominal approach with the ani-