INVESTIGATION IN FEMALE RATS OF THE EFFECTS OF ANDROGEN TREATMENT, DURING THE PRE- AND POSTNATAL PERIODS, ON GROWTH AND REPRODUCTIVE FUNCTION

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by

Elizabeth Mary Sommerville

In experiments investigating the perinatal period of sensitivity to androgen of hypothalamic functions, testosterone propionate (TP) was administered to female rats at different ages before and after birth and for varying time intervals.

Administration of TP was by subcutaneous injection in oil, or by subcutaneous polydimethylsiloxane (PDS) capsules. Plasma testosterone concentrations were measured by radioimmunoassay in adult female rats after insertion and removal 72h later, of 3 sizes of TP-filled capsule (5, 10 and 20mm crystal length); in 3 day old female neonates after insertion and removal 4h later of a TP-filled capsule (2.5mm crystal length), or after injection of TP (90μg in oil); and in growing female rats after neonatal implantation with a TP-filled capsule (2.5mm crystal length) which was not removed (chronic implantation). The plasma half-life of testosterone estimated after implantation with TP capsules was much shorter in adults (1h) than in neonates (8.6h). After TP injection to 3 day old rats the half-life was 48h and after chronic implantation of TP capsules was 69h.

Exposure of foetal rats to exogenous androgen, achieved by subcutaneous implantation of pregnant rats with TP capsules (3 sizes) for 24h or 72h at varying stages during gestation, did not alter ovarian function, feminine sexual behaviour or growth, despite abnormal development of the external vaginal opening in rats exposed to TP during the last 6 days of gestation.

Female rats aged 2, 3 or 5 days given brief periods of TP treatment by subcutaneous 2.5mm PDS TP-filled capsules, removed after 4, 8 or 24h, were compared with rats given 90μg TP by injection at the same ages. Control of gonadotrophin secretion, as indicated by ovarian morphology and cyclic changes in the vaginal epithelium, was sensitive to alteration by brief periods of exposure to TP. Treatment on days 2 or 3 with 4h implants produced anovulatory sterility at 90 days in at least 50% of animals. Feminine sexual behaviour, assessed by lordosis quotient, was depressed only by treatment longer than 24h at any of the 3 ages. Injection with TP prevented ovulation and depressed the lordosis quotient regardless of day of treatment. Although analysis of variance demonstrated an increased body weight from 14 weeks in rats injected with TP on days 2 or 5, regression analysis did not confirm an increased growth rate. The external vaginal orifice was altered by 4h TP implants given on days 2 or 3, but was unaffected by TP treatment of any duration given on day 5.

Testosterone propionate-filled capsules (2.5mm), implanted in female rats on days 2, 3 or 5 and not removed, prevented ovulation and abolished feminine sexual behaviour. Adult body weight was severely retarded by treatment commencing on day 2, but not altered by treatment beginning on days 3 or 5.

It can be concluded from this investigation that the hypothalamic control of gonadotrophin secretion in the female rat is insensitive to androgen prenatally, and is very sensitive 2 or 3 days after birth, when even brief (estimate of 28h exposure) periods of treatment are able to prevent ovulation. The control of feminine sexual behaviour is insensitive to prenatal TP. Depression of behaviour appears to require a longer neonatal period of exposure to TP (estimate of 48h minimum exposure) than that required to modify gonadotrophin secretion. Stimulation of growth appears to be a variable feature of the androgenized rat.

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