Sex: Hormonal and Neural Basis (Ch 12) II

- Sexual Development and Differentiation
  - Development of the **Body** (when things go a different way)
  - Development of the **Brain (Organizational Effects)**
  - Hormonal influences of development of male and female sexual behaviour, brain differences

When Sexual Development Goes a Different Way (I)

- **Androgen Insensitivity Syndrome**
  - Genetic defect: no functional androgen receptors
  - No effect of T during development:
  - Testis form (SRY from Y chromosome), but remain internalized
  - Mullerian duct atrophy (AMH from testes) but Wolffian ducts DO NOT develop
  - Female external genitals develop
  - During puberty, secondary sex characteristics develop from estrogens released from adrenal glands and testes
  - Look and behave like XX genetic women on the outside, but no menstruation, no body hair.

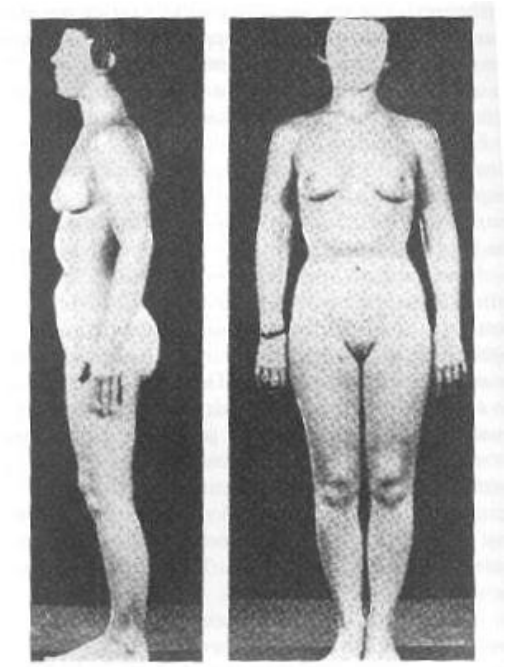
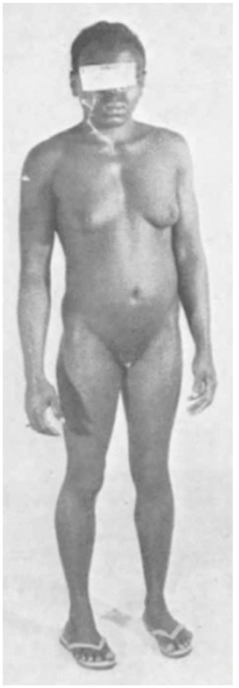


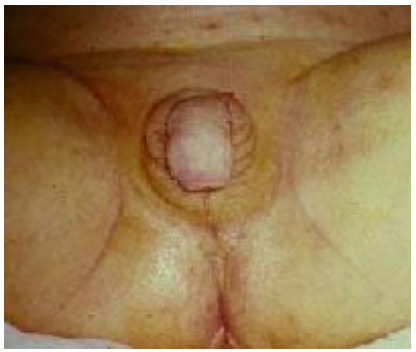
Figure 11.10 A woman with an XY chromosome pattern but insensitivity to androgens
Two undescended testes produce testosterone and other androgens, to which the body is insensitive. The testes and adrenal glands also produce estrogens that are responsible for the pubertal changes. *(Source: Federman, 1967)*

When Sexual Development Goes a Different Way (II)

➢ **Androgenital Syndrome**

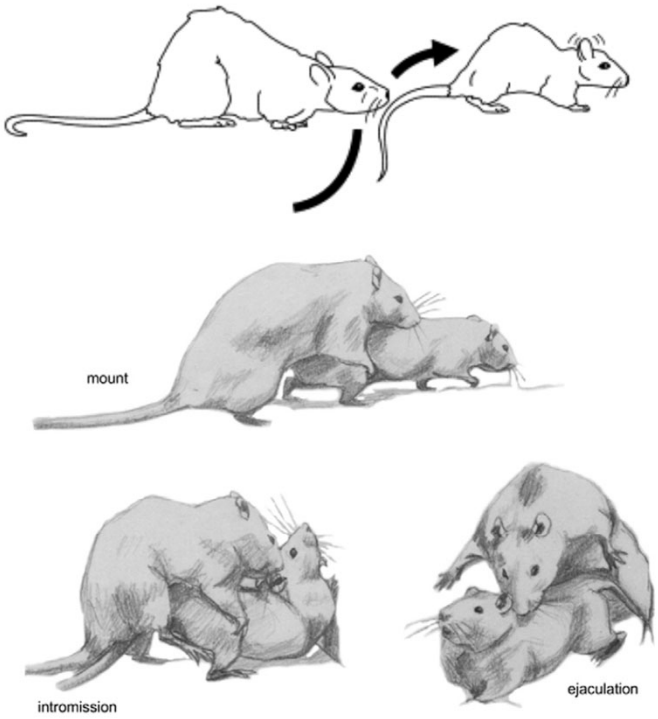
- Caused by congenital adrenal hyperplasia
  - Normally, fetal adrenals produce **cortisol**, inhibits T release from adrenal glands
  - Some fetuses don't produce enough cortisol = MORE THAN NORMAL TESTOSTERONE (T)
- T goes on to masculinize XX fetus
  - Primordial gonads still form ovaries
  - Both Wolffian AND Mullerian ducts grow
  - External genitalia are "intersex"
- Gender identity varies; some are raised as girls, but look like boys in puberty and vice versa





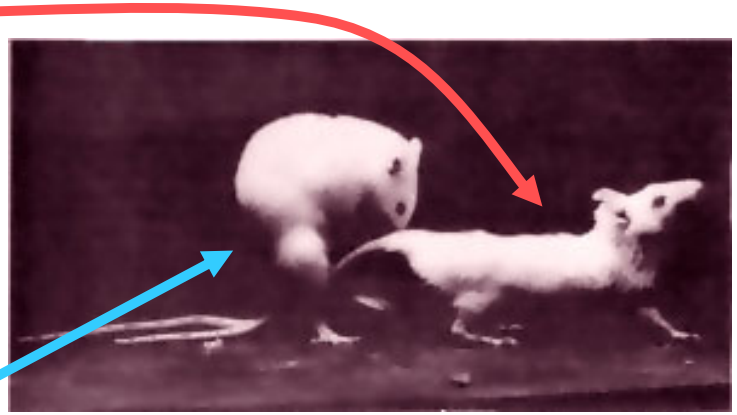
Rat sexual behaviour

- In rats, a sexual encounter starts with female (which ovulates every 4-5 days)
- **Step 1**: During ovulation, **female** displays **proceptive** behaviours
  - Darting, hopping, ear wigging in front of male
- **Step 2**: **male** begins to mount receptive female
- **Step 3**: **female** eventually arches her back, moves tail to one side (**lordosis)**
- **Step 4**: **male** then **intromits** (inserts penis) and thrusts
- **Step 5**: repeat steps 2-4 until male ejaculates



Sexually Stereotyped Behaviours

- **Females:** the lordosis, darting, hopping, and ear wiggling are stereotyped behaviours specific to normal female rodents in heat



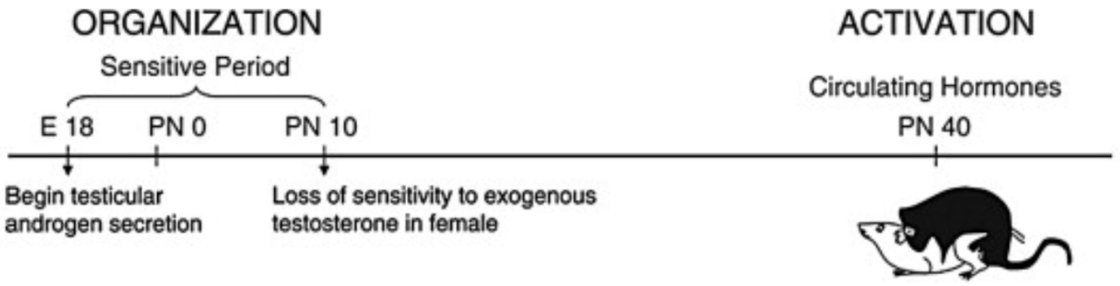
- **Males:** the mounting and intromissions are stereotyped behaviours specific to normal male rodents in response to a receptive female

- These behaviours index of changes in male/female sexual brain development

Hormonal regulation of sexual behaviour

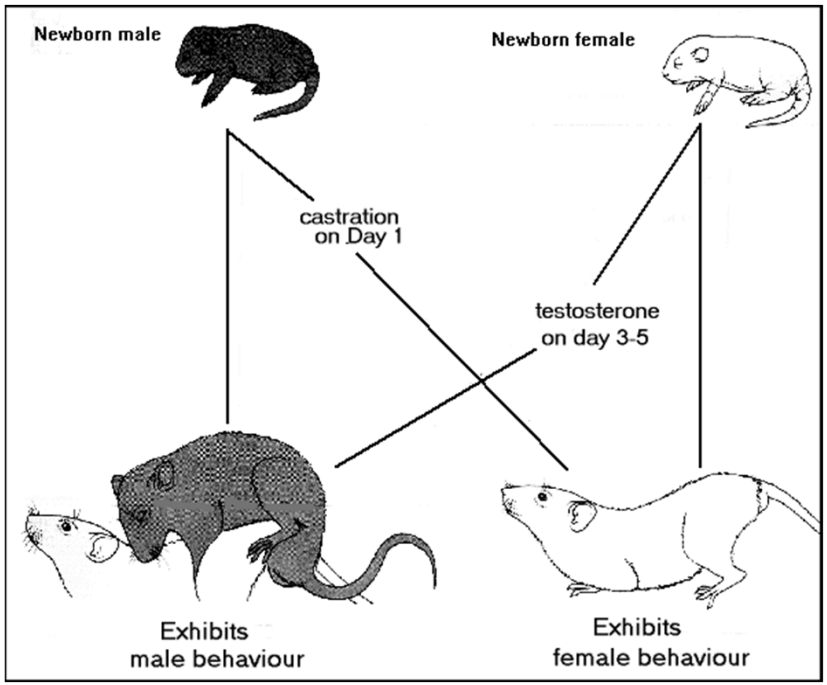
Sex hormones regulate sexual behaviour in ***TWO MAIN WAYS***:

- **Organizational Effects:** changes in body/brain occurring during development
  - Changes are permanent
  - Hormones exert these effects during **critical periods** of development (e.g. in utero and puberty for humans)
- **Activational effects:** on body/brain- behaviour after development
  - Typically occur after sexual maturity (puberty)
  - Transient effects that varies with amount of hormones in bloodstream

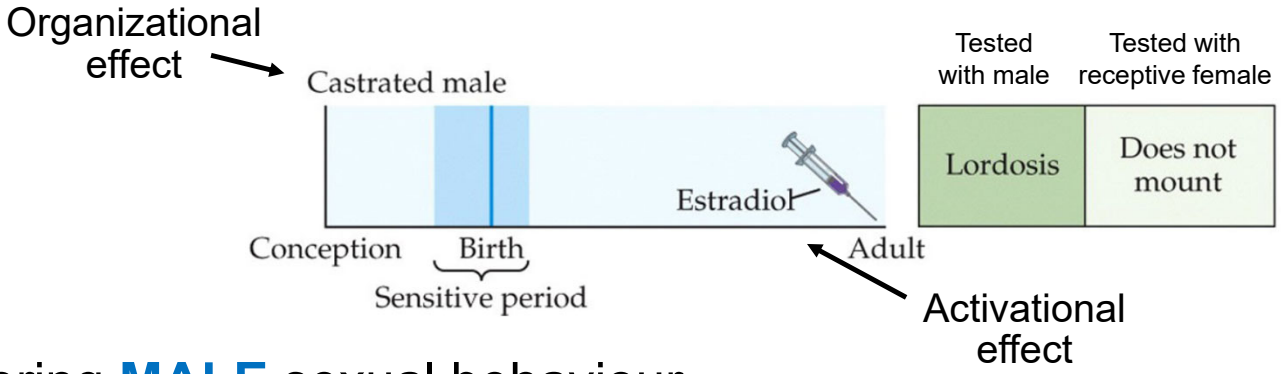


Neural Sexual Development (1)

- Development of parts of the rat brain responsible for male/female sexual behavior occurs for days ***after*** birth
  (unlike humans/primates)
- Like development of the body, sexual brain development is regulated by **presence or absence of testosterone (T)**
- **No androgens** during critical period **= female neural development by default**



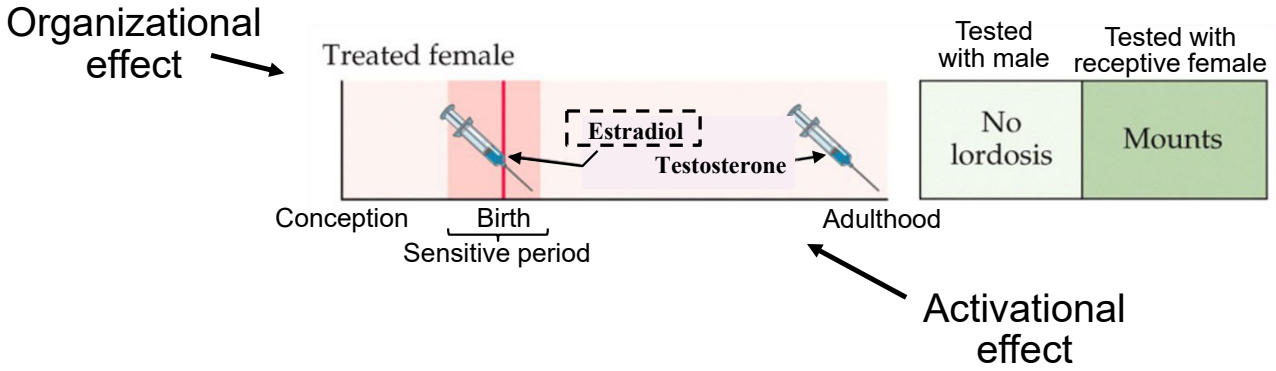
Neural Sexual Development (2)



Altering **MALE** sexual behaviour

- Castrate **males** *in 1st week after birth* = **de-masculinizes** and **feminizes** behaviour in adulthood
  - Males do not show sexually-stereotyped behaviours (mounting, intromitting)
  - Replacement T in adulthood, DOES NOT reinstate "male like" behaviours
  - **BUT:** Giving estrogens to adult *male* rats castrated neonatally can induce ***female*** behaviours (e.g: lordosis)
- This is **not** observed if rats are castrated ***after*** puberty

Neural Sexual Development (3)

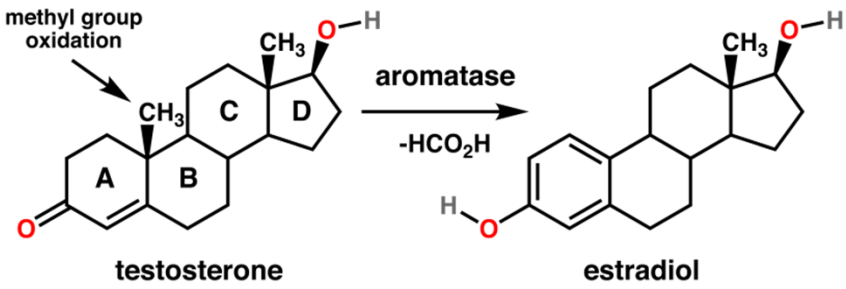


Altering **FEMALE** sexual behaviour

- Give T to **female** rat ~ 1st week after birth = **defeminizes** and **masculinizes** sexual behaviour in adulthood
  - Females do not show stereotyped (lordosis, proceptive) behaviours
  - T given to these females (in adulthood) induces "male" behaviours (mounting)
- These effects are **not** observed if T is given **after** puberty
- **HOWEVER:** give estrogens to a ***neonatal female*** can ALSO cause "male" patterns of behaviour in adulthood. HUH?

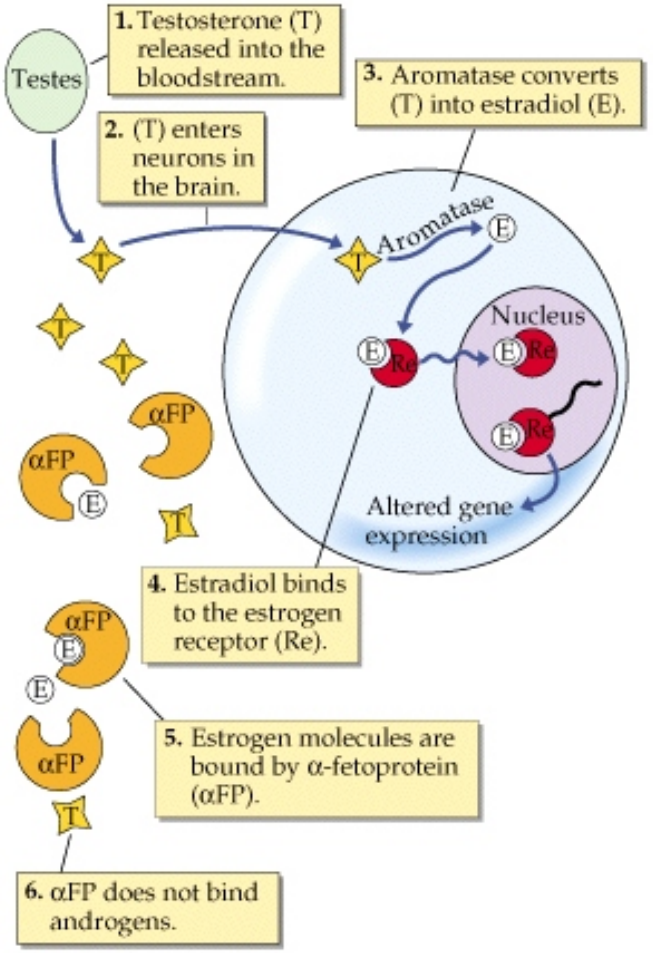
The Aromatization Hypothesis (1)

- Male rat fetuses/neonates release T testosterone (from testes)
- T gets into brain, and is **converted to *estradiol*** (IN THE BRAIN) by the enzyme **aromatase**



- Thus, early exposure to ***estradiol*** (not T) masculinizes rat brain
- **QUESTION:** Why doesn't mother's estrogens masculinize female fetuses?
- **α-Fetoprotein** is in blood of male and female neonates
  - **Binds to free floating estradiol, prevents its entry into brain**
  - **DOES NOT bind to androgens, T is allowed to enter brain and be converted to estradiol**

The Aromatization Hypothesis (2)



Evidence for Aromatization hypothesis:

1) Neonatal estradiol masculinizes behaviour (this saturates all α-fetoprotein molecules in bloodstream- extra estradiol can pass into brain)
2) Enzyme **aromatase** is present in neonates
3) Blocking aromatase or estrogen receptors disrupts masculinizing effects of T
4) Female α-Fetoprotein knockout mice show more male/less female like behavior
5) Dihydrotestosterone (DHT) **cannot be converted to estradiol,** has no masculinizing effects when given early in development in rats

Neural Sexual Development in Primates

•α-Fetoprotein is NOT responsible for protecting **primate/human** fetus from estrogens

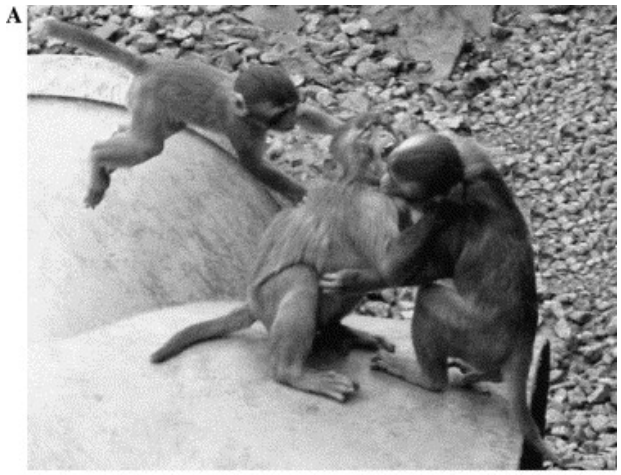
- •in humans, it does not bind estrogens well
- •unlike rats, development of primate sexual brain occurs primarily *in utero*

•**Sex Hormone Binding Globulin (SHBG)** protects fetal brain from estrogens

•However early treatment with either <u>estrogens ***OR***</u> <u>androgens</u> (eg, DHT) in pregnant primates can masculinize behaviour of female offspring (unlike rats)

- •Rough play, mounting

•Some synthetic estrogens (not blocked by SHBG) can also masculinize primate brain



Changes in Brain During Sexual Development

- **Preoptic Area (POA) of Hypothalamus**
  - Large lesions of entire area disrupt sexual behaviour
  - Sexually dimorphic nucleus (SDN) of the POA is larger in males than females
  - T injections in female neonates = **bigger nucleus**
  - Castration in male neonates = **smaller nucleus**
  - Selective lesions of **SDN-POA** do not have major impact on sexual behaviour