Sex differences in behaviour and cognition

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UNITED KINGDOM · CHINA · MALAYSIA

Outline

First part:

- **General concepts & sex differences of the body**
- **Introduction to sex differences in behaviour and the relevant neurobiological substrates**

Second part:

Sex differences in behaviour and relevant neurobiological substrates:

- **Mating behaviour**
- **Other behavioural and cognitive functions**

General concepts and sex differences of the body

Comment is free...
John Crace: a sneak preview o
airport book guardian.co.uk/c

Gold medallist told to prove she is a woman

18-year-old athlete clocks year's fastest time

'She is female' insist South African officials

Anna Kessel Berlin

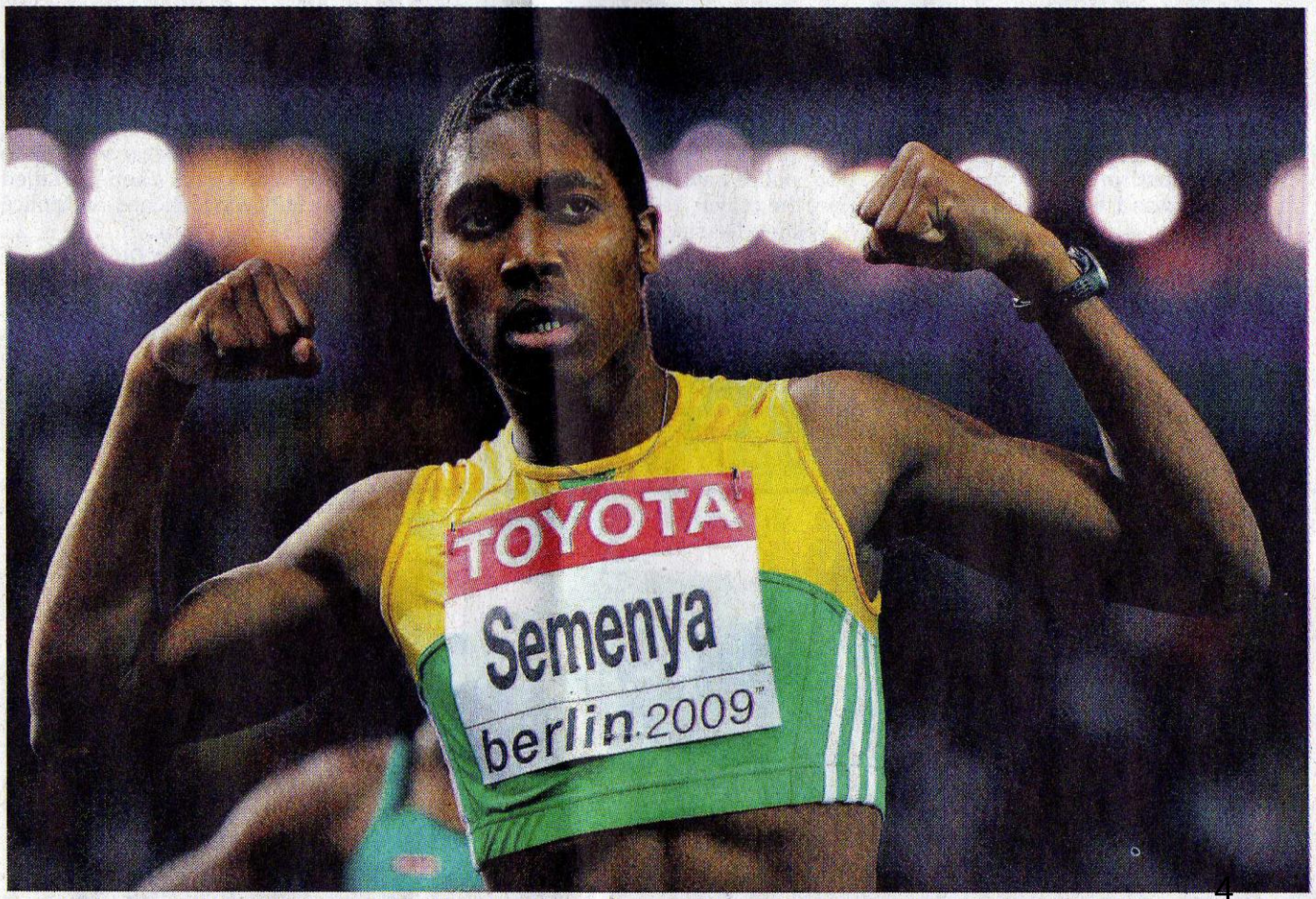
The world of athletics was hit by controversy last night after a female South African athlete who won the 800m final at the world championships was asked to take a gender verification test to prove she is a woman.

Caster Semenya, an 18-year-old who had never competed outside of Africa, before this week aroused suspicions when she posted the fastest 800m time in the world this year, winning gold at the African junior championships.

Last night she won the gold medal in Berlin in 1 minute 55.45 seconds, the best in the world this year, beating Janeth Jepkosgei, the defending champion, by 2.45 seconds. The British runner Jenny Meadows won the bronze medal.

Semanya, from Polokwane, Limpopo province, possesses an unusually developed muscular frame and a deep voice and has clocked times which belie her youth - last night's winning time is more than three-quarters of a second faster than Kelly Holmes's career best.

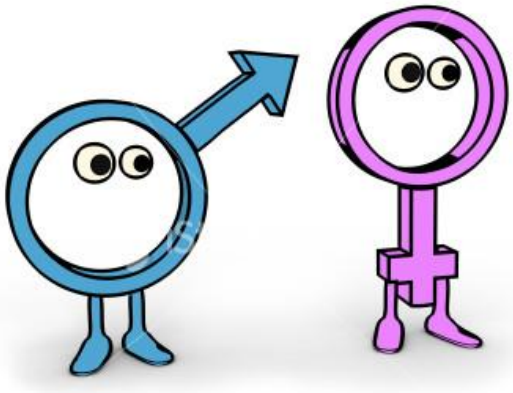
Nick Davies, a spokesman for the Inter-

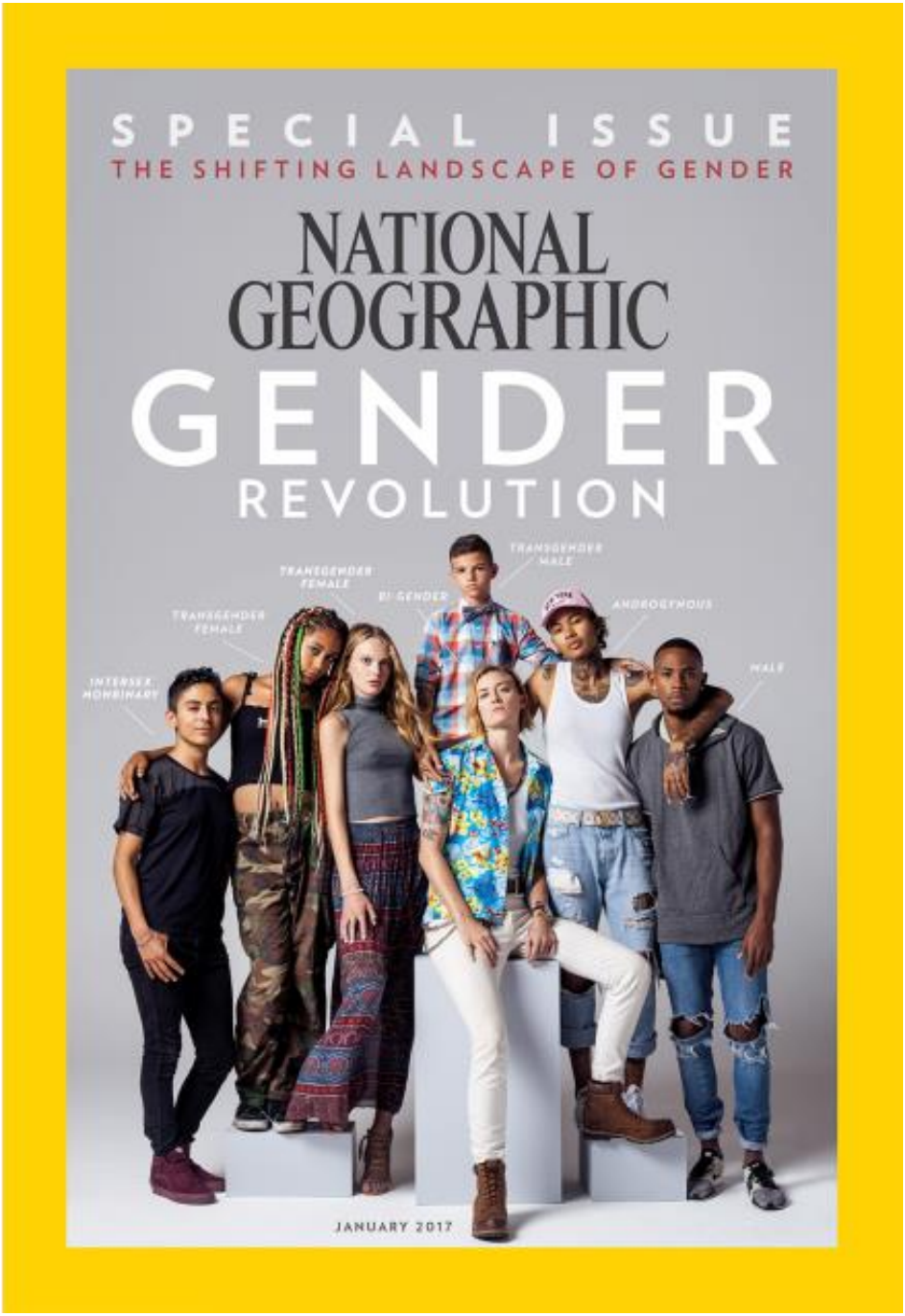


Caster Semenya celebrates victory in Berlin last night where she decimated her 800m rivals Photograph: Stu Forster/Getty

TYPES OF SEX DIFFERENCE

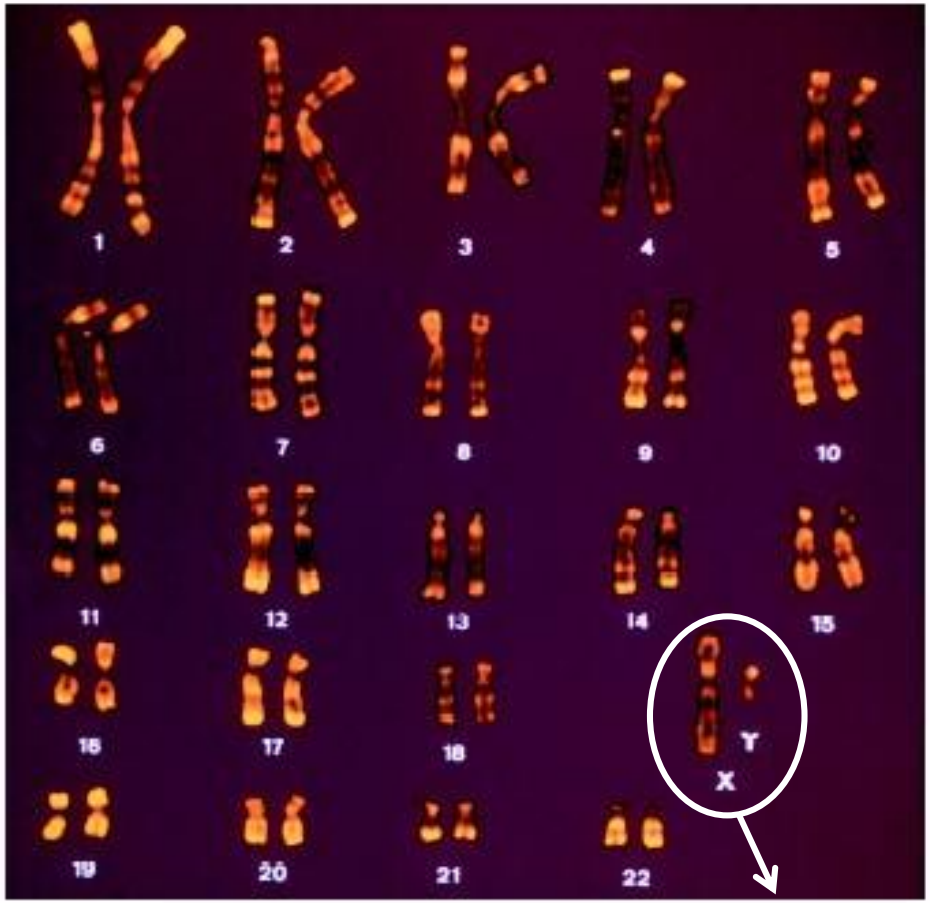
- Genetic or chromosomal sex
- Gonadal sex
- Internal reproductive system
- External reproductive system
- Pubertal sex changes
- Hormonal sex
- Brain sex
- Behavioural and ‘cognitive’ sex
- Sexual identity



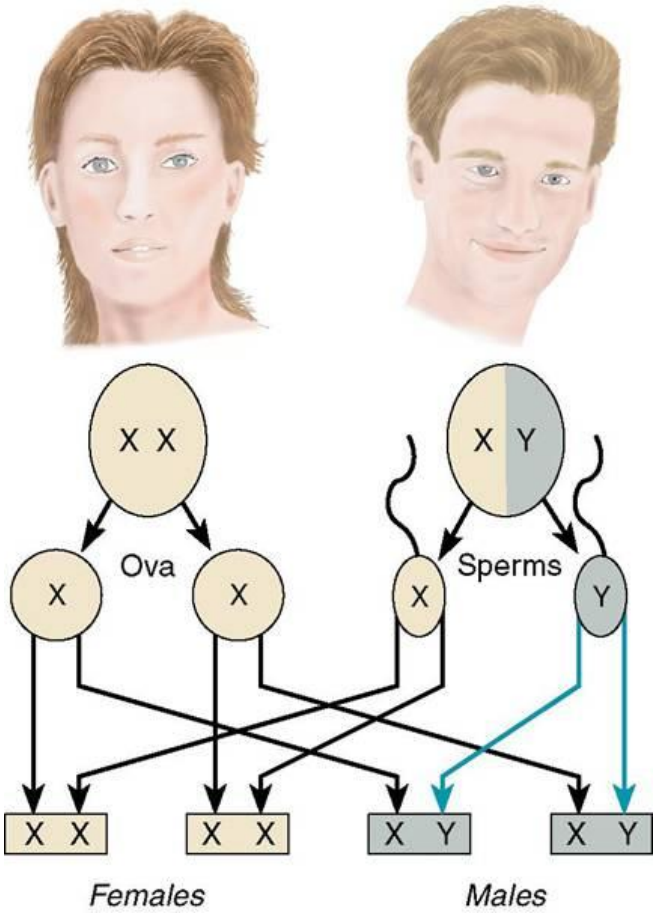


http://www.nationalgeographic.com/magazine/2017/01/

Genetic or chromosomal sex

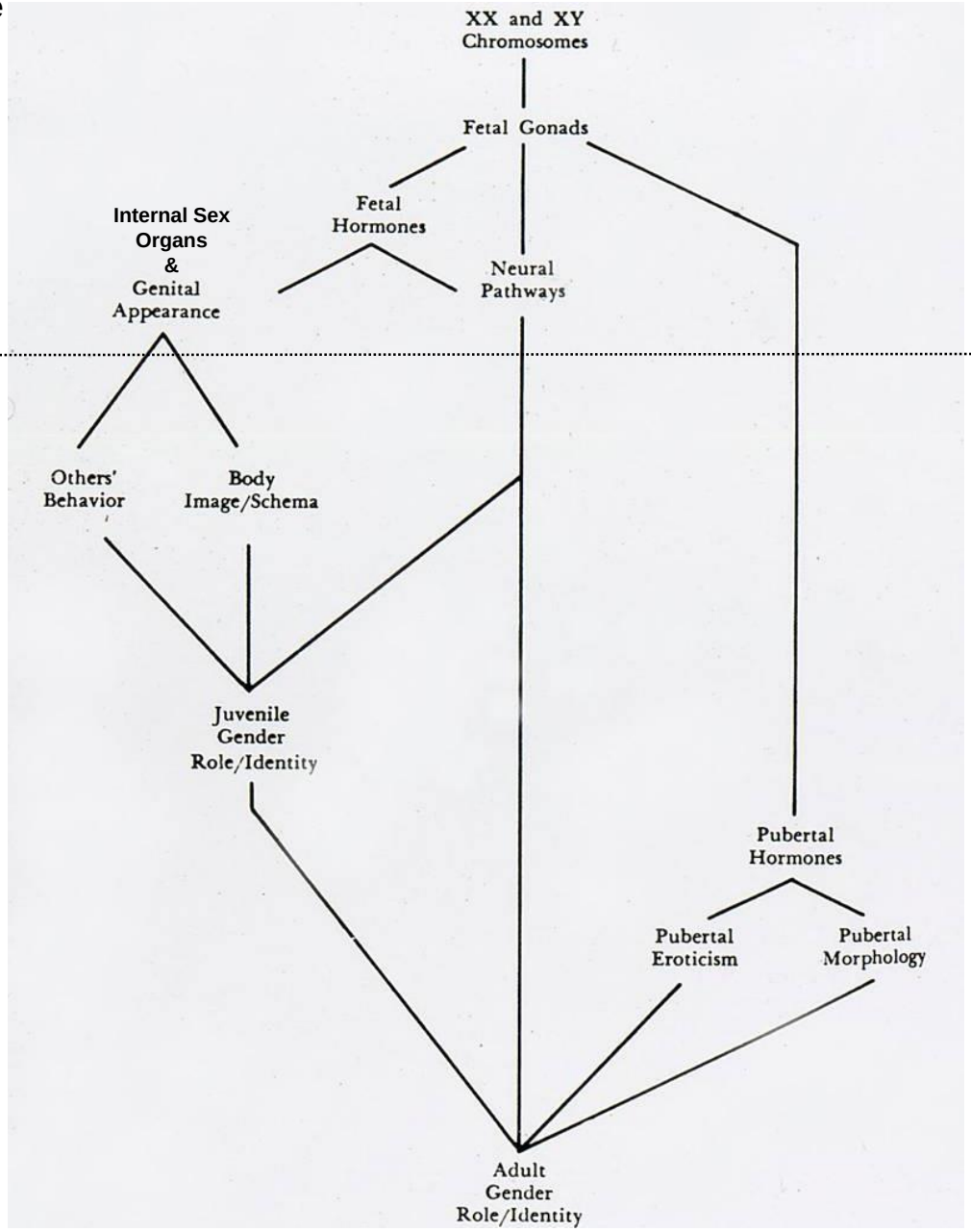


Sex chromosomes



Sexual differentiation: overview

Before birth



After birth

Organisational effects of sex hormones produced by fetal gonads

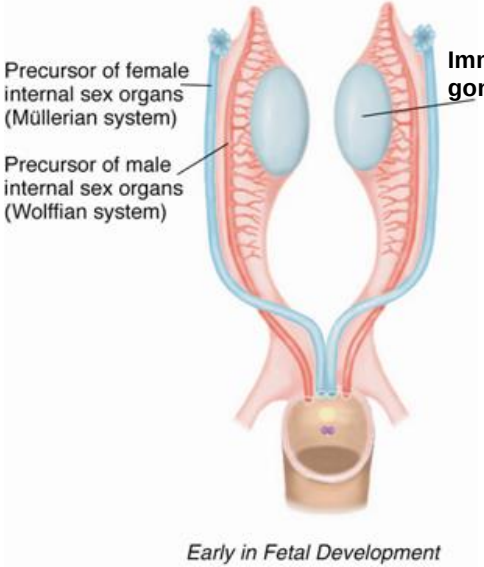
Permanent alterations in body or CNS induced by a hormone at a 'critical' period in development

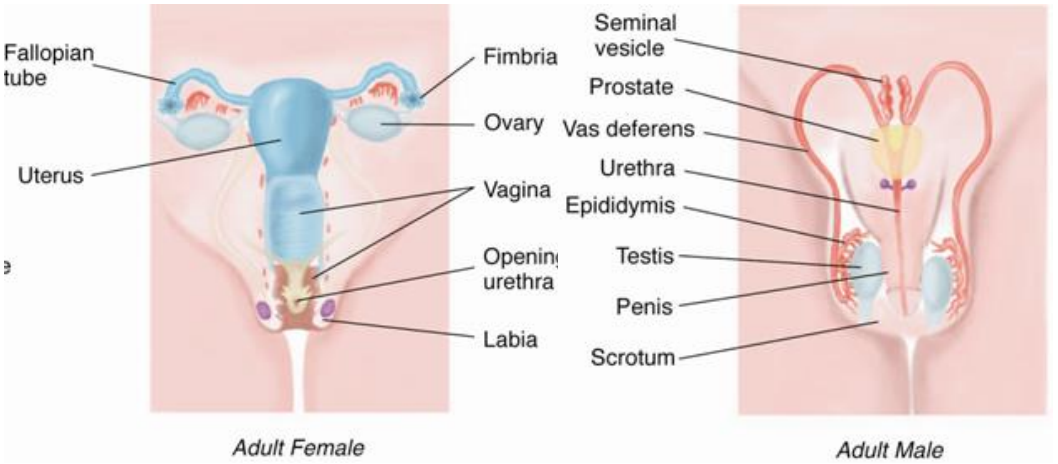
Activational effects of sex hormones produced by gonads

Hormon effects that occur in the fully developed organism; depend on previous organisational effects

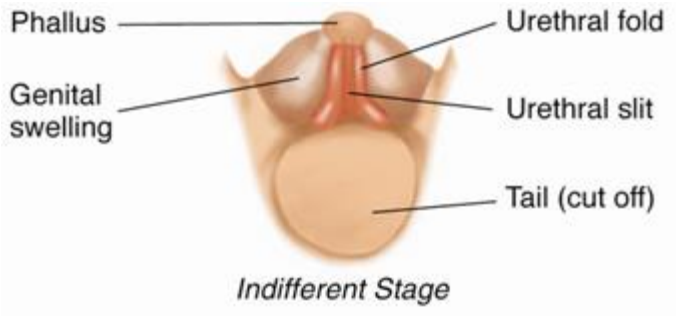
Development of sex organs

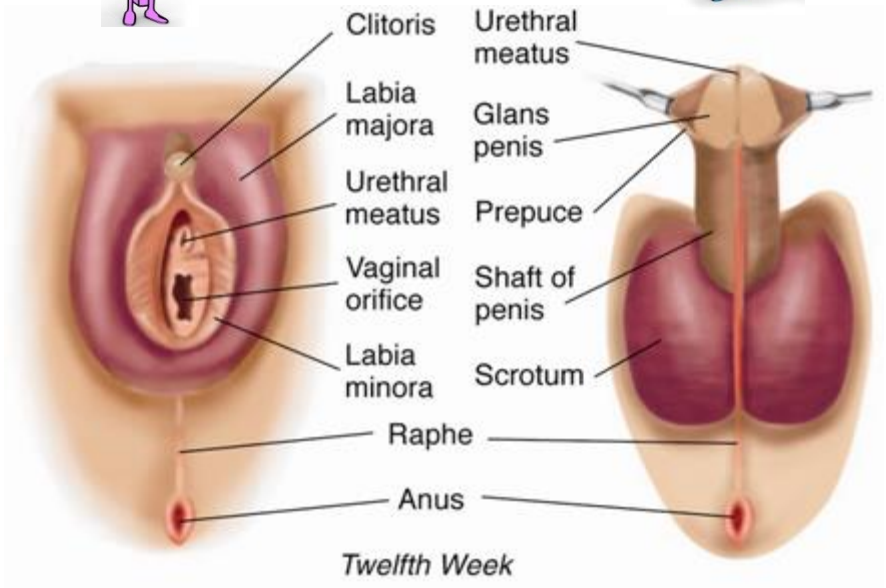
Gonads (ovaries or testes) and internal sex organs



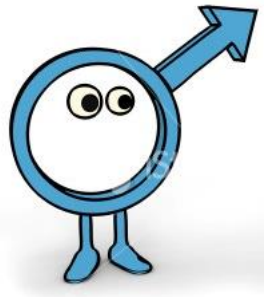


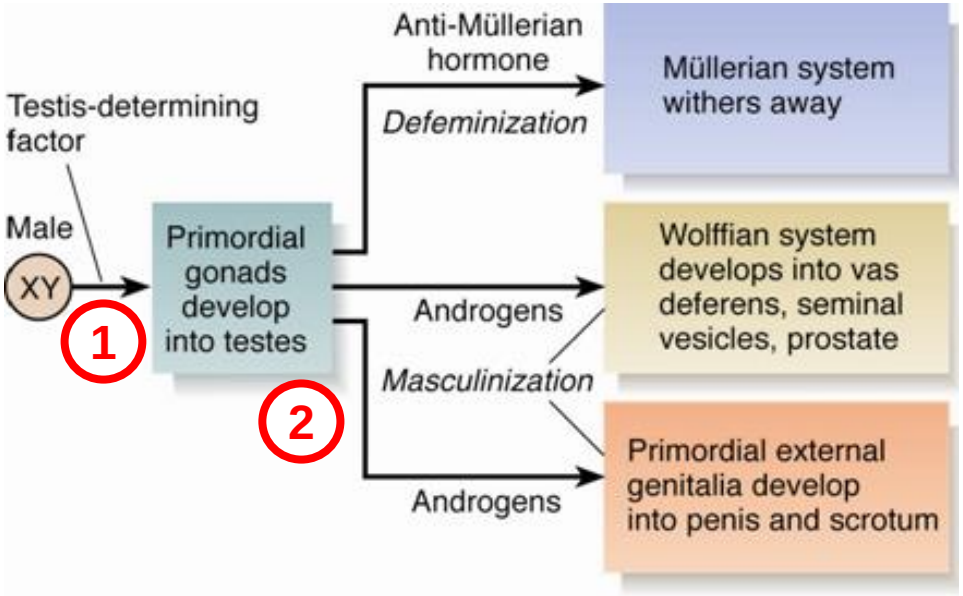
External sex organs





Factors determining the development of male sex organs

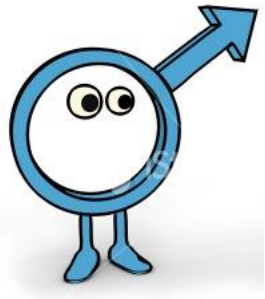




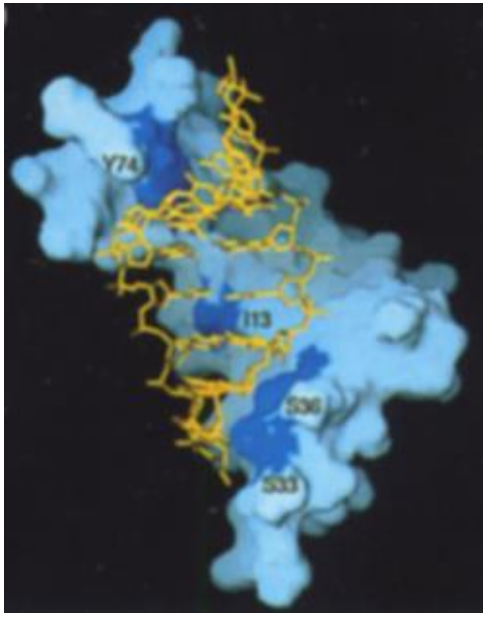
1 SRY region on Y chromosome codes for testis-determining factor (a transcription factor) that binds to DNA in cells of undifferentiated gonads and causes them to become testes.

2 Testes produce hormones that have defeminising (anti-Mullerian hormone) and masculinising (androgens) effects.

Factors determing the development of male sex organs



Testis-determining factor



Werner et al (1995) *Cell* 81 :705

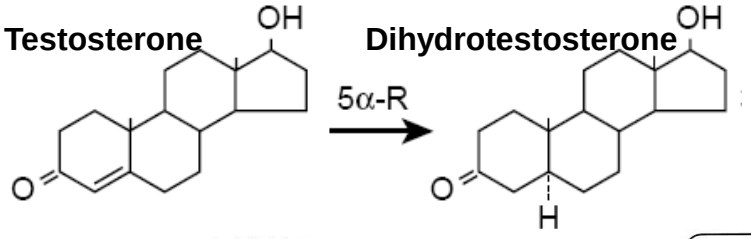
•230 amino-acid long protein coded for by SRY region of Y chromosome.
•Transcription factor binding DNA and, thereby, inducing conformational changes that enable transcription.
•Point mutations can prevent development of testes (and hence of internal and external male sex organs) in XY individuals.

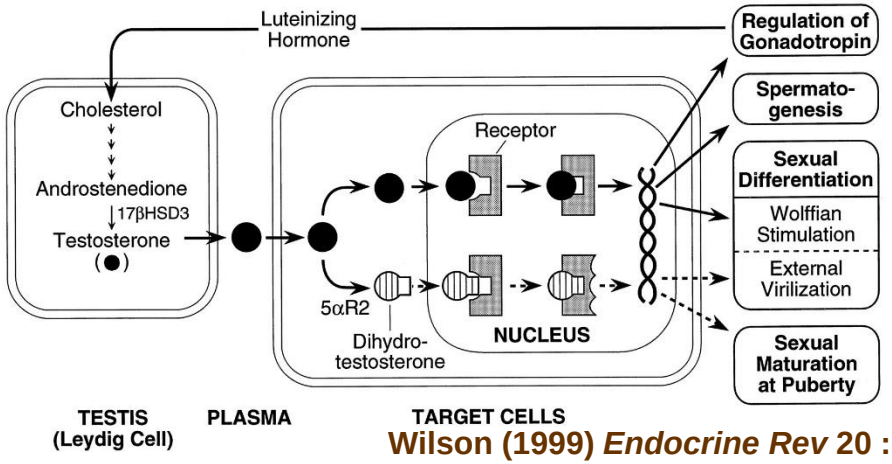
Anti-Mullerian hormone

A peptide secreted by the fetal testes that has defeminising effects, i.e. inhibits the development of the Mullerian system (precursor of female internal sex organs), by acting on anti-Mullerian hormone receptors in cells of that system.

Androgens: testosterone and dihydrotestosterone

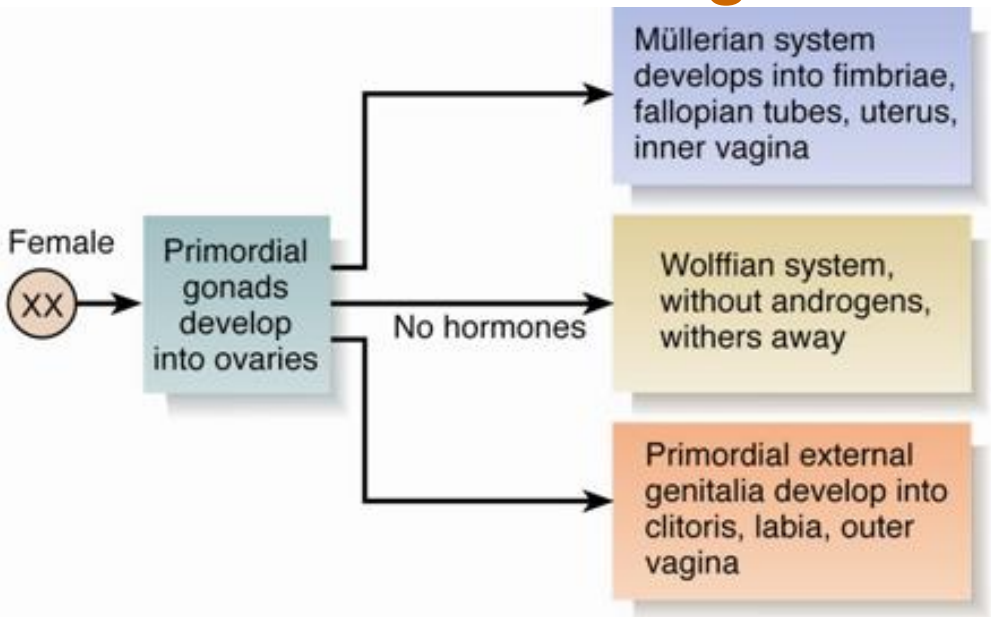
Two androgens are the primary causes of masculinisation during early development:
• Testosterone acts on androgen receptors in cells of the Wolffian system and stimulates its development into male internal sex organs.
•Dihydrotestosterone, produced from testosterone by 5alpha reductase, acts on androgen receptors in the primordial external genitals (with higher affinity than testosterone) and is critical to stimulate their development into male genitals.

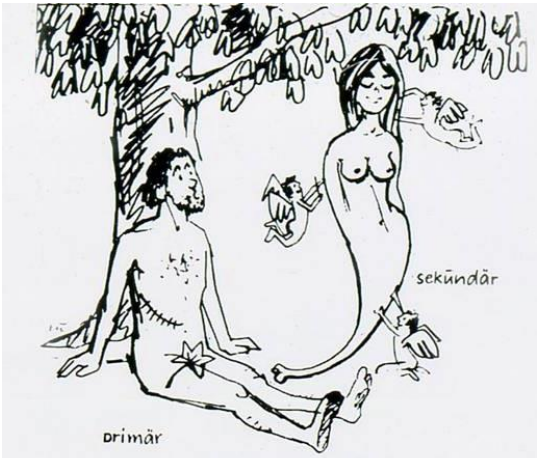




Wilson (1999) *Endocrine Rev* 20 :726

Factors determining the development of female sex organs





By default, primordial sex organs develop into female sex organs:

- In the absence of testis-determining factor primordial gonads develop into ovaries.
- In the absence of androgens produced by testes, internal and external sex organs develop into female organs (without any other hormonal influences necessary).

Note: Recent discovery suggests that Wolffian system regression requires COUP-TFII, a nuclear receptor, so is not a passive process (A Swain, 2017, Science 357:648).

The genetic sex of a human fetus is determined by:

a) A single factor on the X chromosome.

b) The father's sperm.

c) The gonads, i.e. sex hormones.

d) None of the above.

The prenatal development of female internal sex organs requires:

a) A Y chromosome.

b) Estrogen.

c) No hormones at all.

d) None of the above.

Abnormal development of sex organs

Many of the factors controlling sexual development were discovered in animal models, but various developmental anomalies in humans revealed similar principles.

XY sex reversal:
Point mutations in the SRY region of the Y chromosome result in female sex organs in XY individuals (see Werner et al, 1995, *Cell* 81 :705).

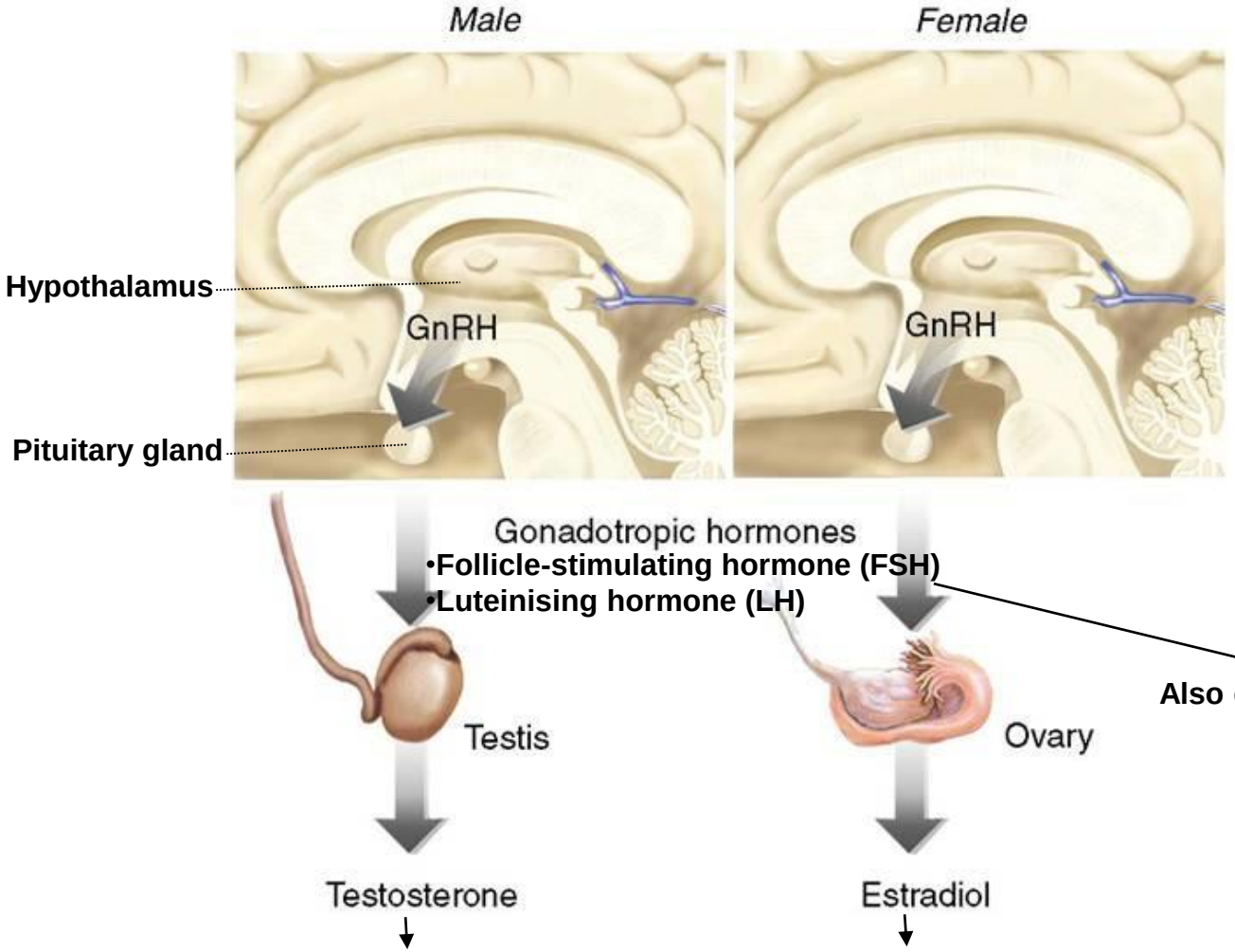
Androgen insensitivity syndrome:
A condition caused by congenital lack of functioning androgen receptors; in a person with XY sex chromosomes, causes development of a female with testes but no internal sex organs.

Turner's syndrome:
The presence of only one sex chromosome (an X chromosome) results in lack of ovaries but otherwise normal female sex organs and genitalia.

Persistent Mullerian duct syndrome:
Congenital lack of anti-Mullerian hormone causes the development of both male and female internal sex organs in an XY individual.

Sexual maturation (puberty)

While primary sex characteristics (gonads, internal and external sex organs) are present at birth, secondary sex characteristics (enlarged breasts, widened hip, facial hair, deep voice) and sexual maturity are not developed until puberty. Puberty is triggered by hypothalamic secretion of gonadotropin-releasing hormone (GnRH).



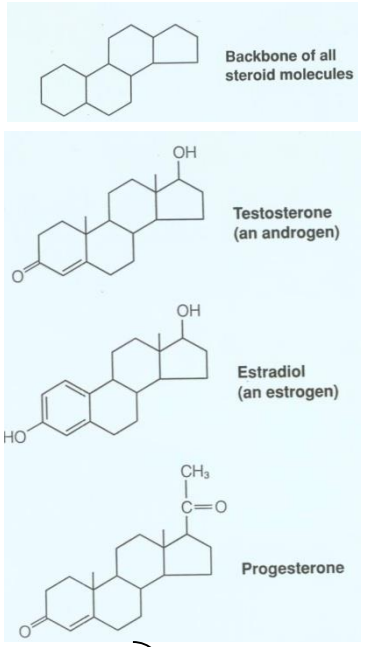
Secondary sex characteristics, control of reproductive functions and sexual behaviour (and other behaviours)

(Axillary and pubic hair in females are stimulated by testosterone produced by cortex of adrenal glands.)

Sex hormones overview

Class	Principal hormone in humans (where produced)	Examples of effects
Androgens	Testosterone (testes)	Development of Wolffian system; production of sperms; growth of facial, pubic, and axillary hair; muscular development; enlargement of larynx; inhibition of bone growth; sex drive in men (and women?)
	Dihydrotestosterone (produced from testosterone by action of 5α reductase)	Maturation of male external genitalia
	Androstenedione (adrenal glands)	In women, growth of pubic and axillary hair; less important than testosterone and dihydrotestosterone in men
Estrogens	Estradiol (ovaries)	Maturation of female genitalia; growth of breasts; alterations in fat deposits; growth of uterine lining; inhibition of bone growth; sex drive in women (?)
Gestagens	Progesterone (ovaries)	Maintenance of uterine lining
Hypothalamic hormones	Gonadotropin-releasing hormone (hypothalamus)	Secretion of gonadotropins
Gonadotropins	Follicle-stimulating hormone (anterior pituitary)	Development of ovarian follicle
Other hormones	Luteinizing hormone (anterior pituitary)	Ovulation: development of corpus luteum
	Prolactin (anterior pituitary)	Milk production; male refractory period (?)
	Oxytocin (posterior pituitary)	Milk ejection; orgasm

Steroids



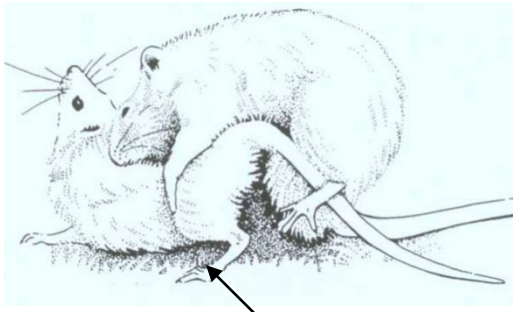
Also stimulate gonads to produce steroid sex hormones.

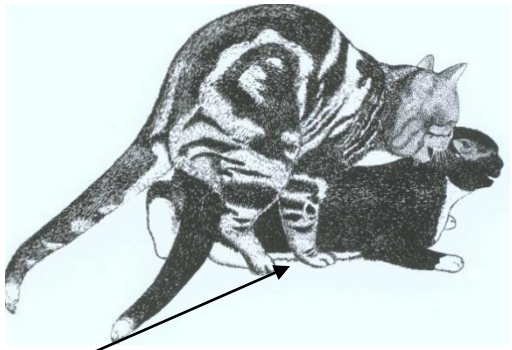
Peptides

Introduction to sex differences in behaviour and relevant neural substrates

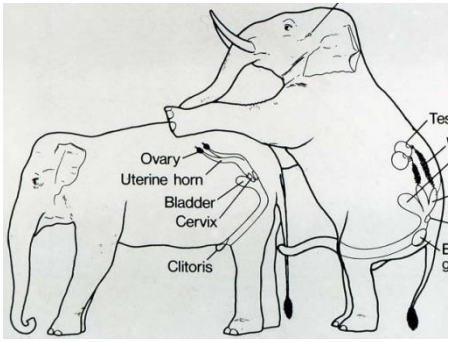
Sex differences in behaviour and cognition

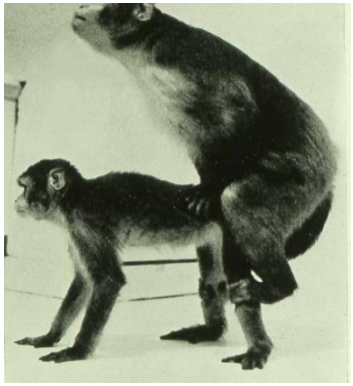
Sexual/copulatory behaviour





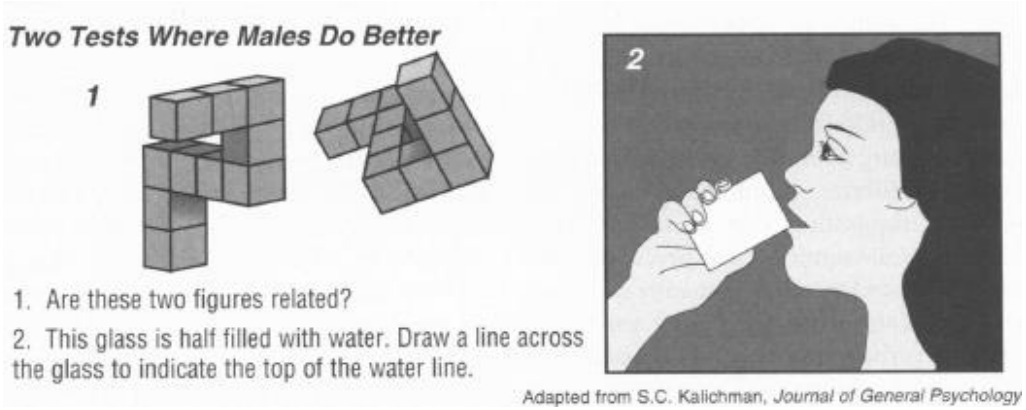
Lordosis response





Route learning and navigation?

Other cognitive and behavioural functions?



Taken from Holden (1991) *Science* 253 :959

Sex differences in brain and behaviour

Organisational hypothesis

Based on findings that exposing female rats and guinea pigs to androgen in utero during critical periods altered their adult sexual behaviour, William Young and colleagues proposed that early androgens, similar to their effects on sex organs, organise the developing CNS in a masculine way, so as to make female behaviours less likely (defeminisation) and male behaviours more likely (masculinisation) (Young et al, 1964, *Science* 143:212). (Without effects of androgens, the animals would behave in a female way – that is, as the sex organs, the animal's brain and behaviour would by default develop in a female way.)

Neural and behavioural sexual dimorphisms

•Since publication of the organisational hypothesis, many sex differences in the CNS – some subtle, some visible to the naked eye – have been reported in many vertebrates, including humans.

•In line with the organisational hypothesis many neural sexual dimorphisms in rodents have been demonstrated to depend on organising effects of androgens during critical developmental periods (in rodents, which are born relatively immature, these critical periods are shortly after birth).

•Other neural sexual dimorphisms have been demonstrated to depend on both organising and activating effects of androgens, and yet others only involve activating (and reversible) effects during adulthood.

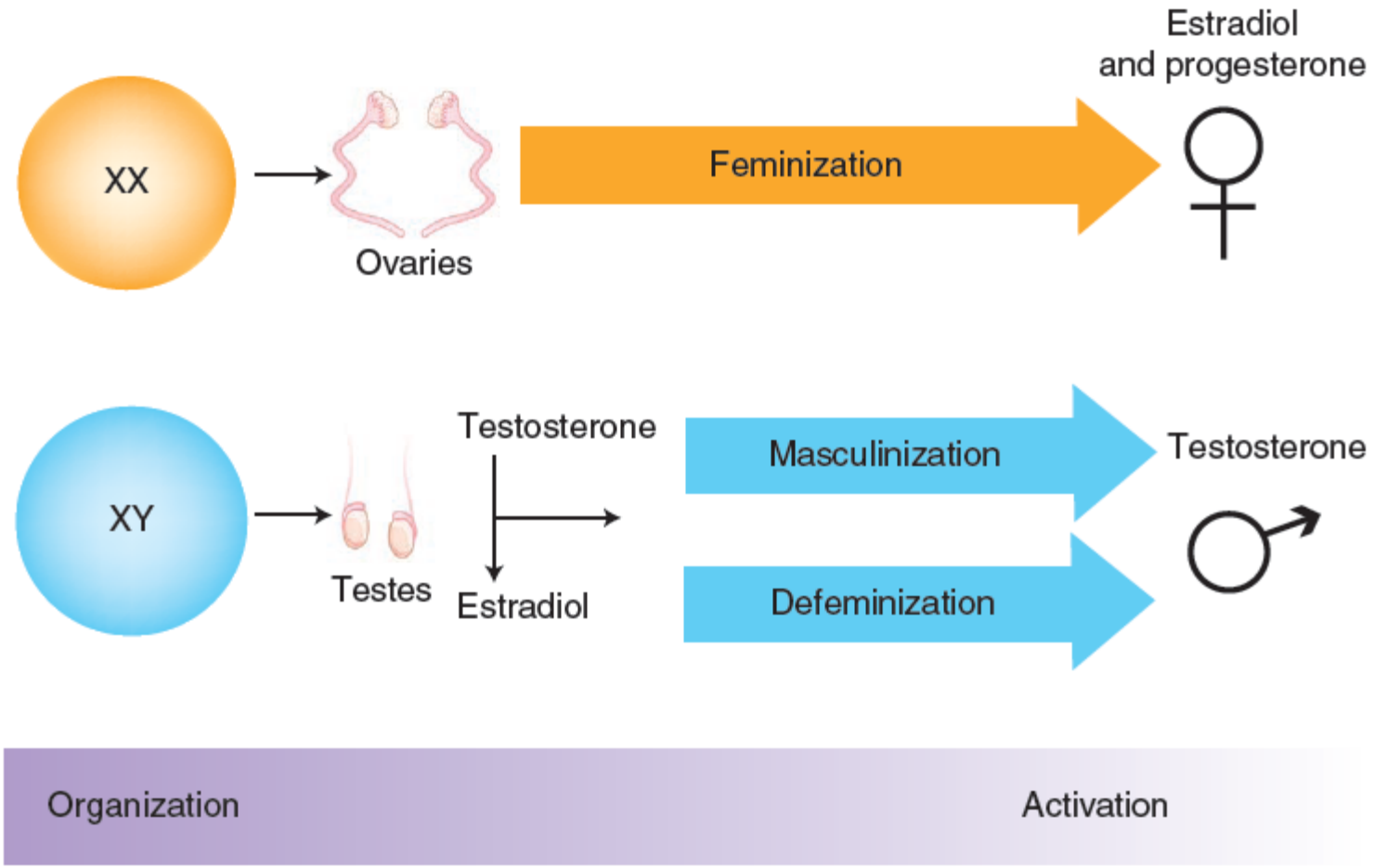
• There is evidence that neural sexual dimorphisms contribute substantially to sex differences in behaviour (especially reproductive behaviour), often in conjunction with activating effects of sex hormones on sexually dimorphic neural systems.

• There are also many instances of neural sexual dimorphisms described without obvious behavioural correlates and of behavioural sex differences (often produced by hormone effects) for which no clear neural substrates have yet been identified.

• There is also evidence for an interaction between environmental and hormonal influences on neural and behavioural sexual dimorphisms – so 'nature' and 'nurture' seem to interact.

Breedlove, 1994, Ann Rev Psychol 45:389; Morris, Jordan & Breedlove, 2004, Nature Neurosci 7:1034; Arnold, 2009, Horm Behav 55:570.

Sex differences in brain and behaviour – organisational/activational theory



Taken from McCarthy & Arnold(2011)
NatureNeurosci 14:677

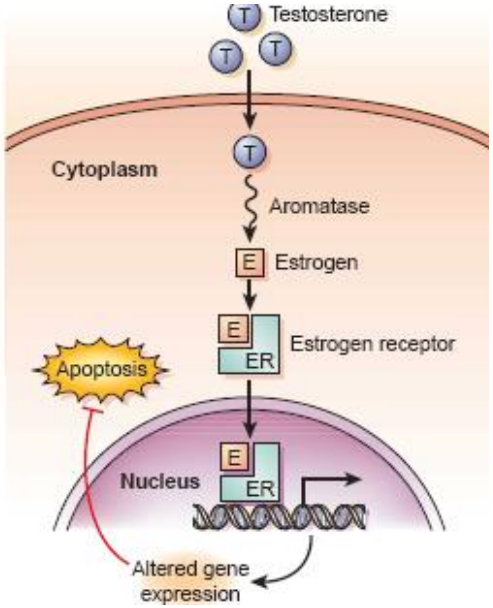
Excellent overview in: Arnold (2009) The organizational-activational hypothesis as the foundation of for a unified theory of sexual differentiation of all mammalian tissues. *Horm Behav* 55:570-578.

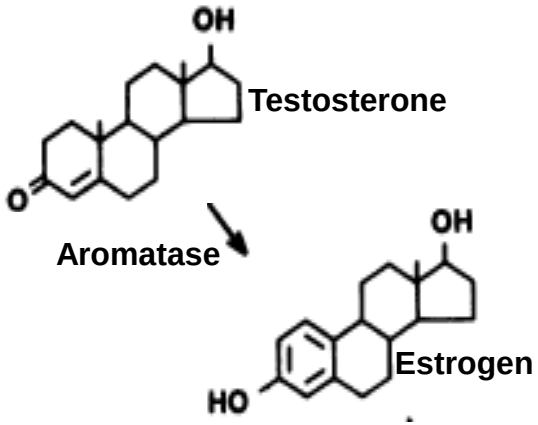
Masculinising effects of estrogen on brain and behaviour

Curiously, it was found in many cases that estrogens are as effective as testosterone in masculinising brain and behaviour in rodents. Moreover, many masculinising effects of testosterone were mediated by estrogen receptors.

Aromatisation hypothesis

Based on these findings it was suggested that in some CNS cells testosterone is converted to estrogen by an enzyme called aromatase before it acts on estrogen receptors to exert masculinising effects.





Protection hypothesis

The brains of developing rodents are 'protected' from the indiscriminate masculinising action of estrogen by an estrogen-binding protein, alpha-fetoprotein, in the blood. Testosterone is not bound by the protein, so can enter CNS cells where it can be converted to estrogen and then exert its masculinising effects.

Hypothesis is strongly supported by finding that alpha-fetoprotein mutant mice show masculinised brains and behaviour (Bakker et al., 2006, Nature Neurosci 9:220).

There is definitive experimental evidence that aromatisation plays a role in masculinising effects of testosterone in rodents. However, if aromatisation also plays a role in other species is not known.

Reviewed in Breedlove, 1994, Ann Rev Psychol 45:389 and Morris, Jordan & Breedlove, 2004, Nature Neurosci 7:1034.

Sex differences I: General concepts, sex differences of the body, introduction to sex differences in brain and behaviour – selected reading

***Textbook chapter*:**

Carlson NR (any recent edition) The physiology of behavior. Chapter 10.

***Review articles*:**

Arnold (2009) The organizational-activational hypothesis as the foundation for a unified theory of sexual differentiation of all mammalian tissues. *Horm Behav* 55:570-578.

Breedlove (1994) Sexual differentiation of the human nervous system. *Ann Rev Psychol* 45:389-418.

Sex differences I: general concepts and sex differences of the body, introduction to sex differences in behaivour and relevant neural substrates – Some questions for revision

- What type of sex differences are there?

- What is the relation between different types of sex differences?

- How do gonadal sex hormones contribute to sexual differentiation before and after birth?

- Why could the tests necessary to determine the sex of an athlete be an extremely complicated procedure, perhaps one with an ambiguous outcome?