The Endocrine System

Endocrine glands secrete "hormones" directly into bloodstream.

In Chap 11 the Hypothalamus, Pituitary, Gonads, and Adrenal glands will play a role in sexuality.

From Our Neurotransmitter Chapter:

Neurotransmitters convey a message from the sending neuron to the receiving neuron(s). Hormones, on the other hand, "broadcast" a message throughout the body via the bloodstream, so are able to influence cells in many distant organs/tissues. But we'll hold off on hormones for the moment, because before there could be hormones, there had to be genes to develop the glands.

Sexual Differentiation in Mammals (Chap 11)

How do we become the sexual individuals we are?

What defines male or female?

Role of Sex Chromosomes

- Genetic sex (XX or XY) is determined by the sperm (X-bearing or Y-bearing) that fertilizes the egg.
- Early gonads have potential to be either ovaries or testes for ~6 weeks.
- Sex-determining region of the Y chromosome (SRY) is a gene producing a *protein causing the middle of baby gonads to become testes.
- If testes develop, they begin to produce androgens like testosterone.
- If SRY gene is not present, the outside of the early gonads turns into ovaries.

*sometimes called testis-determining factor
Organizational Effects

- After gonad development, the remainder of sexual development depends largely on hormone environment during critical or "sensitive" period.
- Normal sources of sex hormones:
  - Testes and ovaries
  - Adrenal cortex

Experimental Evidence

- Removal of SRY gene from Y → XY mouse develops as a female
- Add SRY gene to X → XX mouse develops as a male
- Injection of SRY's protein in genetic female develops testes
- Inject genetic male with drug that blocks the SRY's protein develops ovaries

Endocrine Glands

- Release hormones directly into bloodstream
- Although the pituitary is sometimes called the "master gland" in fact the hypothalamus is the "master" of the pituitary.
• We all begin with ducts, genitals & brains which can go either way (male or female).
• The "default" setting for development of the reproductive system is "female". This will occur in the absence of hormones. (Female differentiation of brain however IS affected by early estrogens)
• Prenatal differentiation of male ducts, genitals, & brain depends on action of androgens (testosterone & dihydrotestosterone (DHT)).
• In fact, in males, development of female ducts must be actively inhibited by release of another hormone from testes: Mullerian inhibiting hormone (MIH), usually in 2nd & 3rd month of gestation for humans.
• During development only, there is positive feedback (hormone levels in blood stimulate gonad growth and even more hormone production). When we are sexually mature there is negative feedback (hormone in blood is the signal NOT to release more).

• Masculinization of genitalia occurs primarily in response to dihydrotestosterone (DHT).

• Androgens also have defeminizing and masculinizing effects on developing brain.
• Example: Exposure to androgens "program" the hypothalamus for the fairly constant sex hormone secretions seen in males vs the cyclic hormone secretion of females. Exposure to androgens leads to growth of certain brain areas; their absence develops other regions.
• Masculinization of brain appears to occur later in gestation than masculinization of body.
• Early estrogens have some feminizing effects on the brain.
• Early hormone environment also leads to corresponding behavioral changes.
Sexually Dimorphic Nucleus (SDN) of Preoptic Region of Hypothalamus

Sex-Typical Behaviors

Early exposure to androgen → mounting & thrusting later in life

No early androgens → lordosis (female sexual posture) later in life

Another of Mother Nature's Jokes: The Aromatization Theory

- Masculinizing of the rat brain is not just due to testosterone
- Testosterone entering rat brain is turned into estradiol!
- Estradiol, in turn, triggers "masculinization" of the brain.
- Brain areas like the hypothalamus which show sex differences have high levels of aromatase enzyme that converts T → E during the sensitive period.
- If this enzyme is blocked then T does not masculinize brain!
- Maternal estrogens bind to alpha-fetoprotein & can't leave the bloodstream so don't masculinize brain.
- However, if excess synthetic estrogens are present, some do get into brain and can bias brain/behavior in a male direction in a variety of species including humans.
- * Now know this is not the only mechanism causing sex diffs in brain & that this does not seem to be the primary influence in humans. But unusual exposure to estrogens may have some impact.

Other examples of brain differences

- Females
  - More neurons in the planum temporale
  - Larger corpus callosum
  - More programmed cell death (apoptosis) during development
- Males
  - Larger cortex
  - Thicker right hemisphere cortex
  - Different cellular organization in several regions of cortex
Gender Differences in Behavior

• Females
  • Verbal fluency
  • Verbal memory
  • Perceptual matching
  • Fine motor skills
  • Preference for dolls

• Males
  • Mathematical reasoning
  • Spatial tasks
  • Large muscle skills
  • Higher in sensation seeking
  • Preference for “boy toys”
  • Higher in rough & tumble play, physical activity
  • Higher aggressiveness

• Parallels in animals
• Correlated with anatomical changes
• Anatomy changes with experimental hormone manipulation in animals

Data That Gender Diffs in Play Not All Due to Socialization

• Infants too young to yet display a behavioral preference show a gender difference in what toys they look at the most.
• Baby monkeys show the same gender diffs in toy preferences.
• Young female monkeys or female humans who had greater exposure to early T show increased male-typical play & toy pref
• Sons of women who tested high in phthalates (which decrease T) during pregnancy show less interest in boy toys and more interest in girl toys

Sexual Orientation

• ↓ mid-pregnancy testosterone in males OR testosterone treatment of females induces same sex preferences and changes in other sex-typical patterns of behavior in a wide range in species (rats, hamsters, ferrets, pigs, finches, dogs, sheep etc.).
• Data from both men and women shows a correlation between early hormone environment and later sexual orientation.
• Maternal stress & some drug used during pregnancy can decrease testosterone exposure; other drugs may act like androgens (e.g. diethylstilbestrol (DES))

Other Evidence for a Biological Basis of Sex Orientation

• Brothers both homosexual?
  • identical twins - 52% of time
  • fraternal twins - 12% of time
  • adopted brothers - 11% of time
• Sisters both lesbian?
  • identical twins - 48%
  • fraternal twins - 16%
  • nontwin sister – 14%
  • adopted sisters - 6%
• Pattern of results replicated in small representative sample from national twin study

60 Minutes segments

• [http://www.youtube.com/watch?v=cISvVOJX_nik](http://www.youtube.com/watch?v=cISvVOJX_nik)
• [http://www.youtube.com/watch?v=SSQYVe0mjY&feature=related](http://www.youtube.com/watch?v=SSQYVe0mjY&feature=related)

• National Geographic
  • [http://www.youtube.com/watch?v=sAOgF8XVWVA&feature=related](http://www.youtube.com/watch?v=sAOgF8XVWVA&feature=related)

• The more older brothers a male has, the greater the probability that he will be homosexual.
• Hypothesis – mother’s earlier pregnancies carrying a male fetus triggered future immune responses against testosterone or some related protein.
Sexual Orientation Brain Differences

• Simon LeVay- 3rd interstitial nucleus of the anterior hypothalamus (INAH3) in humans is larger in heterosexual males and smaller in females and gay males.

• Other areas of brain that differ with sexual orientation:
  • Anterior commissure
  • Suprachiasmatic nucleus
  • Both are larger in heterosexual women and gay men
  • These are not areas known to be related to sexual behavior, but the pattern does suggest the brains of gay men are more similar to female brains than heterosexual male brains.

Another M/F size difference:
Digit ratio

• Finger length distribution is sexually dimorphic – especially the 2nd (2D) and 4th (4D) fingers of the right hand

• Dimorphism results as male hormones, particularly testosterone, affect finger growth in utero

Digit ratio

Masculine
4D>2D

Digit ratio

Feminine
2D= or >4D

Lesbians have more masculine finger lengths, and gay males, more feminine as well as shorter arms and leg bones.

Summary

• Early in life hormones have an organizational effect on body and brain.

• Amount & timing of hormones will have a life-long effect on physiology & behavior.

• Alterations in hormones during critical periods of prenatal development are a likely causes of variations in sexual orientation & gender dissatisfactions.

• In utero biasing of brain may be more important to gender identity than sexual differentiation of the body.

• Later in life, hormones serve to activate sexual motivation & the functioning of those organs (e.g. menstrual cycle, make sperm & eggs)

• So is the androgen environment not just “masculinizing” body and brain, but actually influencing factors like motor programs for how one moves, vocal tone and inflection, and interests/preferences?

• There is also a growing body of research looking at early hormone environment, brain differences and genetic contributions related to transgender cases.
Androgen Insensitivity Syndrome

- X-linked recessive defective variant of the androgen receptor gene
- Androgen ineffective → small testes, no male ducts, female genitalia but no female ducts. Have female identity
- (supports a role for androgen receptors in some aspects of masculinization of human brain)
- At puberty don’t see pubic hair or darkening of nipples (normal androgen effects in females)
- If AIS is known to exist in a family, genetic testing can reveal whether a woman carries the recessive gene
- 1 in ~13,000 births have complete androgen insensitivity; in addition some are born with partial insensitivity (probably another mutation)

Congenital Adrenal Hyperplasia or Adrenogenital Syndrome

One cause of androgen exposure in females

- The effects of androgen exposure of a female fetus
- Degree of masculinization depends on amount of androgen and timing
- Also about 1 in 13,000 births

CAH is associated with

- Greater preference for boy toys and later for sports magazines, masculine sports, even male dominated professions like auto mechanic, truck driver
- Increased physical activity; increased aggression
- Low romantic interest in males at adolescence; less interest in infants
- Moderate increase in bisexuality or homosexuality, or continued low interest in sexual relationships
- Usually score intermediate between females and males and degree is correlated with androgen level
5-alpha-reductase deficiency →
“Guevedoces” (“eggs@12”)

Testosterone can’t be converted to
dihydrotestosterone which is most
important androgen for masculinizing
genitals before birth.

Testosterone surge at puberty does
stimulate growth of penis and scrotum.

Most easily transition to male gender
identity despite early upbringing

Organizational vs Activational Effects
Of Sex Hormones

<table>
<thead>
<tr>
<th>Organizational</th>
<th>Activational</th>
</tr>
</thead>
<tbody>
<tr>
<td>permanent effects</td>
<td>transitory effects</td>
</tr>
<tr>
<td>occur during early critical period</td>
<td>in puberty-adulthood</td>
</tr>
<tr>
<td>structural changes in body and brain</td>
<td>motivational/functional changes</td>
</tr>
</tbody>
</table>

Activational Effects

• Activating effects of hormones increase sensitivity to
  sexual stimuli and increase the activity of sex regions of
  the hypothalamus.

• Sexual receptivity of females of many species is totally
tied to their estrogen levels (primates seem less
dependent on estrogens)

• Castration decreases sexual motivation and activity but
doesn’t necessarily abolish sexual behavior in those
  with sexual experience.

• Studies of women not on hormonal birth control show
  a peak of sexual interest just before ovulation.

Hypothalamus secretes
“gonadotropin releasing hormone” to tell pituitary
what to do

In response, anterior
pituitary secretes
“gonadotropins” to tell the
gonads what to do

Without these hormonal
commands, gonads won’t
produce sex hormones or
sperm/eggs