COGS17  Neurobiology of Cognition

Lecture 9: Sexual Development and Behavior

REMINDERS: Hypothalamus controls Endocrine (hormone) systems via effect on adjacent Pituitary Gland (the “Master Gland”)
- Produces Releasing Hormones that flow via blood vessels to Anterior Pituitary stimulating gland to release its own hormones
- Produces other Hormones (e.g. Oxytocin) sent (like NTs) via axons to Posterior Pituitary, then circulate in bloodstream

Reproductive Hormones have Organizing Effects (on anatomy in fetal delval & puberty) & Activating Effects (influence behavior)
- Both sexes have female (Estrogens) and male (Androgens) hormones, just in different proportions
- These Steroid Hormones are produced mainly in Ovaries/Testes, but also in Hypothalamus and Adrenal Glands
- NOTE: Typically, males have XY sex chromosomes, females have XX, but hormone activity is required to determine gender!

ORGANIZING EFFECTS

Fetal Development of Sexual Anatomy
- Every mammalian fetus has the anatomical precursors for BOTH sexes
  - e.g. Gonads, earliest sex structure to develop, same initial structure will become Testes or Ovaries
  - e.g. Genitalia, same initial structures in all fetuses, develop into male or female anatomy, depending on Androgens/Not
  - e.g. Each fetus has both Wolffian and Mullerian ducts; Their development depends on Androgens/Not
    - These become ether Vas Defens & Prostate or Fallopian Tubes & Uterus respectively; Other system degenerates
- The genes controlling male/female body & brain development are also present in BOTH sexes, EXCEPT…
  - The “switch” is on the male’s Y Chromosome; it signals production of the Testis-Determining Factor (TDF) Enzyme
  - Occurs during Critical Period of fetal development (TDF appears : 6th–8th week; Genitals developed by 4th month)

- If TDF is NOT present => Female
  - Ovaries differentiate, Mullerian system develops, Wolffian regresses, female genitalia develop – regardless of genotype!
    - If fetus is XY, but lacks specific gene for TDF (or other TDF deficit), will develop internally & externally as female
    - If fetus is XO (Turner’s Syndrome, no Y Chromosome) will develop internally & externally as female
      - Both non-XX above will be infertile, however, since two Xs required to produce ova (eggs)

- If TDF is present => Male
  - Testes differentiate, producing Androgens, including Testosterone => Wolffian ducts and male genitalia develop
    - Testes also produce Anti-Mullerian Hormone, inhibits development of Mullerian system
  - If XY fetus is Androgen-Insensitive, it’s testes still produce Androgens and Anti-Mullerian Hormone, but since its
    Wolffian system’s androgen receptors are absent, it not develop, and its Mullerian System is inhibited
    - So individual has no internal sex organs (& so is infertile) except rudimentary, internal testes
  - But external body develops as a female, although without androgen-stimulated pubic, or other secondary, hair
  - If XX fetus is exposed to Testosterone during critical period, develops male, or semi-male form, sometimes infertile
    - Some tendency for these individuals to be homosexual, tho per body, brain, and/or societal influences?!

-PLUS: Testosterone enters fetal cells, where it is converted (“aromatized”) into Estradiol (an Estrogen!) => Male development
  - So, why doesn’t Mom’s estradiol masculinize every fetus? Answer: Apha-Fetoprotein!
    - Apha-Fetoprotein in fetal/infant blood, binds with Estrogen, preventing it from entering fetal cells (later inactivated)
  - Excessive Estrogens (e.g. DES, synthetic estrogen to prevent miscarriage) can overwhelm safeguard, masculinize fetus

Secondary Sexual Characteristics at Adolescence
- In both sexes, Hypothalamus releases Gonadotropin-Releasing Hormones (GnRH), causing Anterior Pituitary to release the
  Gonadotropic Hormones: Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH)
- In Males, these hormones >> Testes produce sperm and Testosterone (and other Androgens, and low levels of Estrogens)
  - >> facial & other secondary hair growth (& later baldness), muscular development, enlargement of larynx, stop bone growth
  - In Females, these hormones >> Ovaries produce ova and Estradiol (and other Estrogens, and low levels of Androgens)
    - >>breast development, alteration of fat deposits, menstrual cycle of egg release & uterine build-up/decline, stop bone growth
      - Female secondary hair growth via Androstenedione (an Androgen) released by Adrenal Glands

Sexual Differences in Brain Development
- Presence/Absence of Testosterone during prenatal period and early infancy => differences in brain
  - Medial Preoptic Area (MPOA) of Hypothalamus, has Androgen receptor sites, is esp active during Male sexual behavior
    - This area includes the Sexually Dimorphic Nucleus (SDN) which is 2.5X larger in Males than Females
    - Early Testosterone is required for this delval, and w/o it adult Male will not respond normally to androgen activity
  - Vento-Medial Hypothalamus (VMH), has Estrogen receptor sites, is especially active during Female sexual behavior
    - Develops (esp sensitivity to estrogens) in absence of early Testosterone  (Area also implicated in control of eating)
- Other sexual dimorphisms in brain anatomy (may be related to early Testosterone levels, but insufficient data) include:
  - **Connectivity** patterns in cortex, per diffusion-based imaging
    - Males show more *intra*-(within)-hemispheric connections while females show more *inter*-(between)-hemispheric
    - Suggests males may better integrate perception & action, females better integrate analytic & intuitive processing
    - May help account (with Culture) for better spatial abilities in males, better communication abilities in females
  - **INAH3**, part of Sexually-Dimorphic Nucleus, larger in Heterosexual Males, smaller in Females and Homosexual Males
  - In homosexual males, not clear if such differences are *cause* or effect of behavior?

**ACTIVATING EFFECTS**

Neural and Hormonal Activation of Sexual Behavior - All depend on pre-established “Organizing Effects”

- **In Males:**
  - **Medial Preoptic Area (MPOA)** of Hypothalamus, including Sexually Dimorphic Nucleus, is critical for sexual behavior
    - Releases **GnRH** (Gonadotrophin Releasing Hormone) > Anterior Pituitary releases the Gonadotrophins LH & FSH
    - These Gonadotrophins travel through bloodstream > Testes release Testosterone
    - Testosterone feeds back to MPOA, escalating arousal
  - Circuit includes **VTA** (Ventral Tegmental Area) > **Nucleus Accumbens** (*Pleasure*) near Basal Forebrain
    - Releases **Dopamine** to Nucleus Accumbens in response to sexual stimulation
    - Area also implicated in addiction to amphetamines, cocaine, and chocolate; Rats will stimulate area to death
  - MPOA also stimulates **Basal Ganglia** which communicates with Spinal Nucleus of the Bulbocavernosus (SBN)
    - Motor neurons of SBN => rhythmic contractions for ejaculation
  - At orgasm, MPOA signals Pituitary to release **Oxytocin**
  - After ejaculation, Anterior Pituitary releases **Prolactin**, producing Refractory Period before male can respond again
  - MPOA also **responds** to input from **Medial Amygdala**, implicated in **Aggression** (see Emotion lecture)
    - Some correlation between high Testosterone and Aggression (as in violent crime, tho not nec sexual crime)
  - NOTE: Medial Amygdala also likely receives **Pheromone** input, as well as Somatosensory info from genitals
    - In rodents, smell can inhibit aggression toward females, increase aggression toward rival males
  - Also responds to input from **Cerebral Cortex** (Learning plays a greater role in human sexual activity than in nonhumans)
    - Includes Sensory (including visual identification), Memory, Prefrontal evaluation, and Motor organization
    - Can lead to idiosyncratic partner-, place- or object-specific sexual responses

- **In Females:**
  - **Androstenedione** (chemically like Testosterone), an **Androgen** produced by **adrenals**, for sexual motivation
    - Gets converted into Testosterone in bloodstream, activates MPOA
  - Then, just as in Males, MPOA > GnRH > LH & FSH > stimulates Ovaries and Adrenals (short-term positive feedback)
  - Estrogens from Ovaries stimulate **Ventro-Medial Hypothalamus (VMH)**,
    - This is region most activated during female sexual behavior
  - VMH and MPOA stimulate pleasure circuit: **VTA** releases **Dopamine** to **Nucleus Accumbens** for reinforcement
    - Basal Ganglia > SBN for rhythmic contractions, as in males
  - VMH also stimulates **Periaqueductal Gray Area** which produces **Endorphins**, in part to suppress Pain
  - Also signals Posterior Pituitary to release **Oxytocin** (at time of orgasm)
    - Oxytocin also linked to release of milk in lactating females, aids in bonding with offspring
  - After sex, females do not show same Prolactin release or Refractory Period
    - Note: Instead, **Prolactin** in pregnant females, stimulates milk production
  - **VMH also responds** to input from **Medial Amygdala** (Pheromones) and from **Cerebral Cortex** (Learning etc)

**Role of Pheromones in Mediating Sexual Behavior**

- **Pheromones** = Hormones released by one individual that affect behavior/physiology of conspecific; Found in sweat of humans
  - In most mammals, detected by **Vomeronasal Organ (VNO)** – specialized olfactory receptors, respond only to pheromones
  - Direct connections to Medial Amygdala and Medial Preoptic Area of Hypothalamus
  - VNO controversial in humans: Exist / Not? Vestigial / Functional?
  - However, humans DO appear to respond to pheromones (Pheromones *control* rat behavior, *influence* human behavior)
    - In Women: Sweat in alcohol swabbed on upper lip of other women (!) vs. placebo => *synchronized* menstrual cycles
    - In Men: Aftershave spiked with male pheromone vs. placebo => *increased* # of sexual interactions (inc’d attractiveness)