Gender and Sexual Diversity

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Declaration of interests

- None
Nature versus Nurture

Mother

"Nature" (Genotype)

Father

Environment “Nurture”

Final product (Phenotype)
A pup that is raised by an anxious, low-nurturing mother becomes an anxious adult.

A pup that is raised by a relaxed, high-nurturing mother becomes a relaxed adult.

http://learn.genetics.utah.edu/content/epigenetics/rats/
Epigenetics

- Unmethylated
- Methylated

CpG Island

Gene Expression

Gene Expression Repressed

Gene

http://missinglink.ucsf.edu/lm/genes_and_genomes/
Maternal licking and grooming

Low L/G
ccc M actccgggctgc
cattcattcagcgtcctg
cagaagcccagctgcc
gcgtctgccgggaggt

High L/G
cccggactccgggctgc
cattcattcagctgcctg
cagaagccccagctgcc
gcgtctgccggaggt

Adapted from Champagne et al. Frontiers in Neuroendocrinology 2008; 29: 386–397
Erasure of “Epi-marks”

Occurs in at least two phases of the life cycle of mammals:
• formation of gamete precursors in the embryo
• when gametes fuse to form the zygote
Determinants of gender and sexual diversity

- Biological sex (physical sex)
- Gender identity (psychological sex)
- Sexual orientation

Gender expression:
a manifestation of all of the above
Sequence of physical vs. psychological sex determination

- Gonads (ovary, testis)
  - Y chromosome (SRY gene) - male development

- Internal organs and external genitalia
  - Male development androgen dependent
  - Female development estrogen dependent

- Gender identity (psychological sex determination)
  - Testosterone = fetal brain masculinization
  - Absence of testosterone effect = fetal brain feminization
Steroid biosynthesis

Cholesterol side-chain cleavage enzyme

Progestagens (21 carbons)
- Cholesterol
- 17α-hydroxylase
- Progesterone
- 3β-hydroxysteroid dehydrogenase
- Androgens (19 carbons)
- Dehydroepiandrosterone
- 17β-HSD
- Androstenedione
- 5α-reductase
- Testosterone
- 5α-reductase
- Dihydrotestosterone

Mineralocorticoids (21 carbons)
- Aldosterone synthase
- Aldosterone
- Corticosterone
- 11β-hydroxylase
- 11-deoxycorticisol
- Cortisol

Glucocorticoids (21 carbons)

Cellular location of enzymes
- Mitochondria
- Smooth endoplasmic reticulum

Estrogens (19 carbons)
- Estrogen
- Estrone
- Estradiol
- Estriol

Wikipedia Commons
Development of external sexual organs

Grey's Anatomy and Wikipedia Commons
Intersex – “normalization surgery”

• Aim: to allow affected individuals to more easily “fit” into a socially accepted gender category
• Consequences include infertility, incontinence, scarring, loss of sexual pleasure, pain, mental suffering and depression
• Lack of concordance between physical and psychological sex
• Malta has recently passed a law that will ban normalization surgery on intersex infants
  – self-determination of gender identity
Gender identity (psychological sex determination)

• Hormonal effect on developing nerve cells in the sexually dimorphic preoptic area of the brain
  – Feminization is maintained by the active suppression of masculinization via DNA methylation
  – Testosterone decreases DNA methylation by reducing activity of DNA methyltransferase enzymes
  – This releases masculinizing genes from epigenetic repression

Transsexuality

Trans man

Trans woman
Consequences of gender dysphoria

• Social isolation
  – by choice or through ostracism
• Relationships with parents may be impaired
• Low self-esteem
• Anxiety, depression, suicidal ideation and suicide attempts
Sexual orientation

- Heterosexual
- Homosexual
- Bisexual
- Asexual
# The Kinsey scale

<table>
<thead>
<tr>
<th>Rating</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Exclusively heterosexual</td>
</tr>
<tr>
<td>1</td>
<td>Predominantly heterosexual, only incidentally homosexual</td>
</tr>
<tr>
<td>2</td>
<td>Predominantly heterosexual, but more than incidentally homosexual</td>
</tr>
<tr>
<td>3</td>
<td>Equally heterosexual and homosexual (bisexual)</td>
</tr>
<tr>
<td>4</td>
<td>Predominantly homosexual, but more than incidentally heterosexual</td>
</tr>
<tr>
<td>5</td>
<td>Predominantly homosexual, only incidentally heterosexual</td>
</tr>
<tr>
<td>6</td>
<td>Exclusively homosexual</td>
</tr>
<tr>
<td>X</td>
<td>No socio-sexual contacts or reactions (asexual)</td>
</tr>
</tbody>
</table>
Homosexuality – genetics

• Occurs in approx. 5% of individuals of both sexes in most populations
• Familial in both males and females
• Moderate level of concordance in twin studies
• Identification of potential loci
  – X-chromosome (Xq28) and chromosome 8 associated with development of homosexuality in males
  – does not imply that there are “mutations” in the “causative” genes in these regions
  – does not imply that homosexuality is a disorder
Take-home message

• Need to distinguish between
  – Biological sex (physical sex)
  – Gender identity (psychological sex)
  – Sexual orientation

• Gender expression is a manifestation of all of the above

• All possible permutations of these elements in combination are found in all societies and to varying degrees
When does a variant become a disorder or a disease?
Variants

• Disorder/disease variants
  – Distress/suffering
  – Significant impairment of personal, social, occupational or other important areas of life
  – Death

• Source of distress/impairment/death
  – Endogenous
  – Exogenous
Normal distribution and standard deviation
Body height and weight

Number of people

Height (cm)
Weight (kg)
Skin colour

Number of people

Pigmentation (skin colour)
Blood cholesterol levels

Number of people

Cholesterol
Thank you