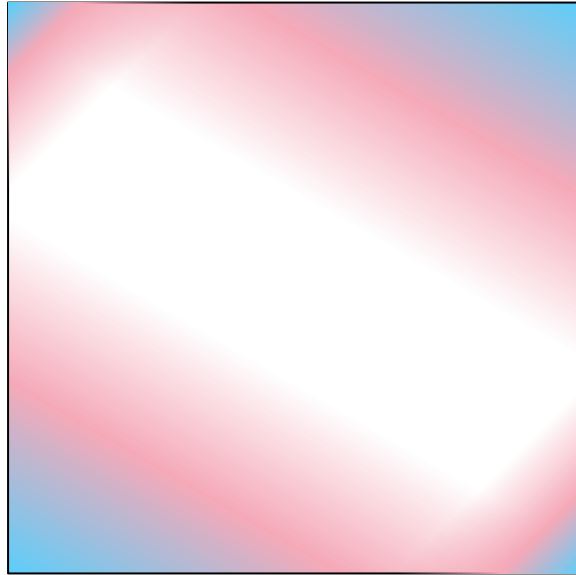


Genetics associated with Gender Dysphoria



August 2022 - A puzzle arrives



r/DrWillPowers · 2 yr. ago
Drwillpowers MOD



The Nonad of Trans? I continue to see more associated conditions with both MTF and FTM transgender people at rates far beyond what is plausible to be due to chance. Please help me out with this.

Post by Dr. Powers

Basically, here is the list. An overwhelming amount of my patients have these conditions, ranked in order of most common to least common, but nearly all patients have at least two.

1. Gender Dysphoria (pretty obvious why my patients would have this a lot)
2. A non-straight sexual orientation. Some flavor of the rainbow.
3. Autism Spectrum Disorder - Anywhere on the spectrum, often "eccentric" or "Asperger's" or "gifted and different", described that they were a "sensitive" child. Often dyslexic
4. ADHD or ADD - Associated with sleep disorders, particularly irregular sleep schedules and general problems with time regulation and insomnia.
5. Hypermobility - Ranging from severe to mild, hypermobile joints, loose skin, translucent skin, easy bruising. (I often see telangiectasia or "spider veins" on the upper central back, or in dermatomal patterns along the anterior abdomen. These are often coupled with nevus anemicus. These patients also often have unexplained striae (stretch marks) even if they are skinny and have never been overweight. (in fact the amount of "lanky" transgender women I have is astounding).
6. Postural orthopedic tachycardia syndrome / Dysautonomia- Low blood pressure, passes out when standing up

At the same time...

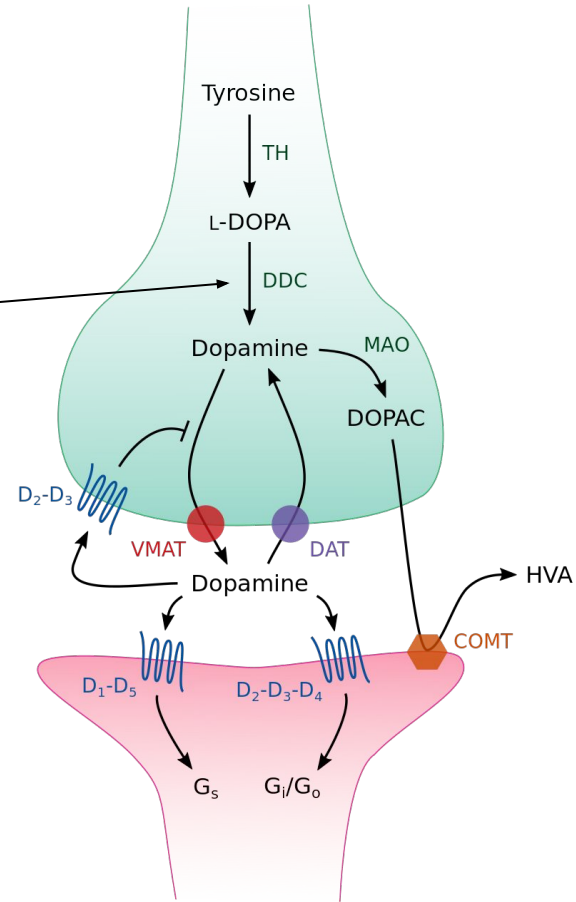
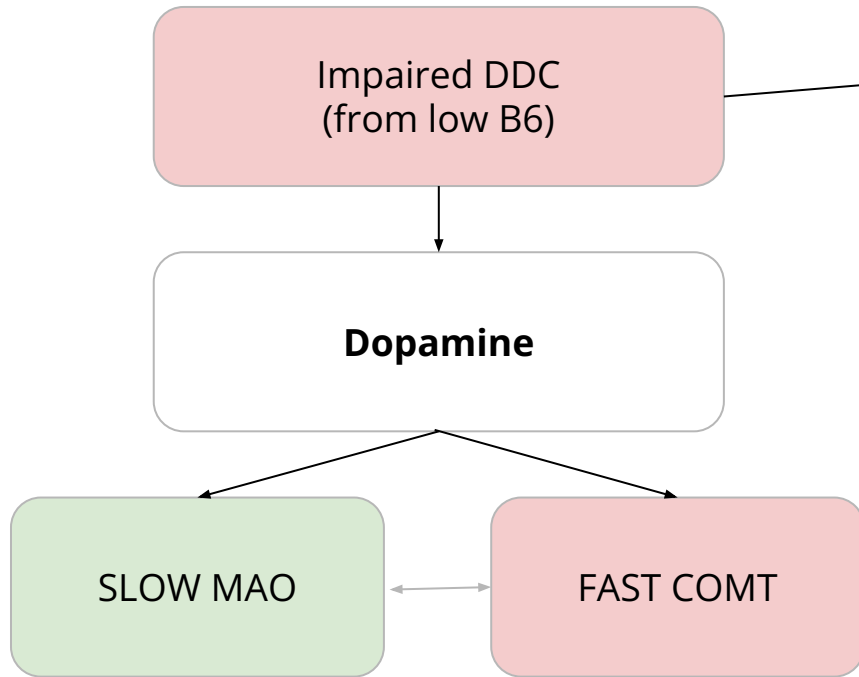
My ADHD meds were inconsistent...

I took a DNA test a few years ago...

I can debug this...



My ADHD



How are these related to gender dysphoria?

Primary adrenal insufficiency

- Congenital Adrenal Hyperplasia
- Ehlers-Danlos syndrome
- POTS
- Hypermobility
- Lean / Anorexia
- PCOS
- PTSD
- Spider veins
- MCAD/MCAS
- Hypothyroidism
- Low pain tolerance
- IBS

LGBT

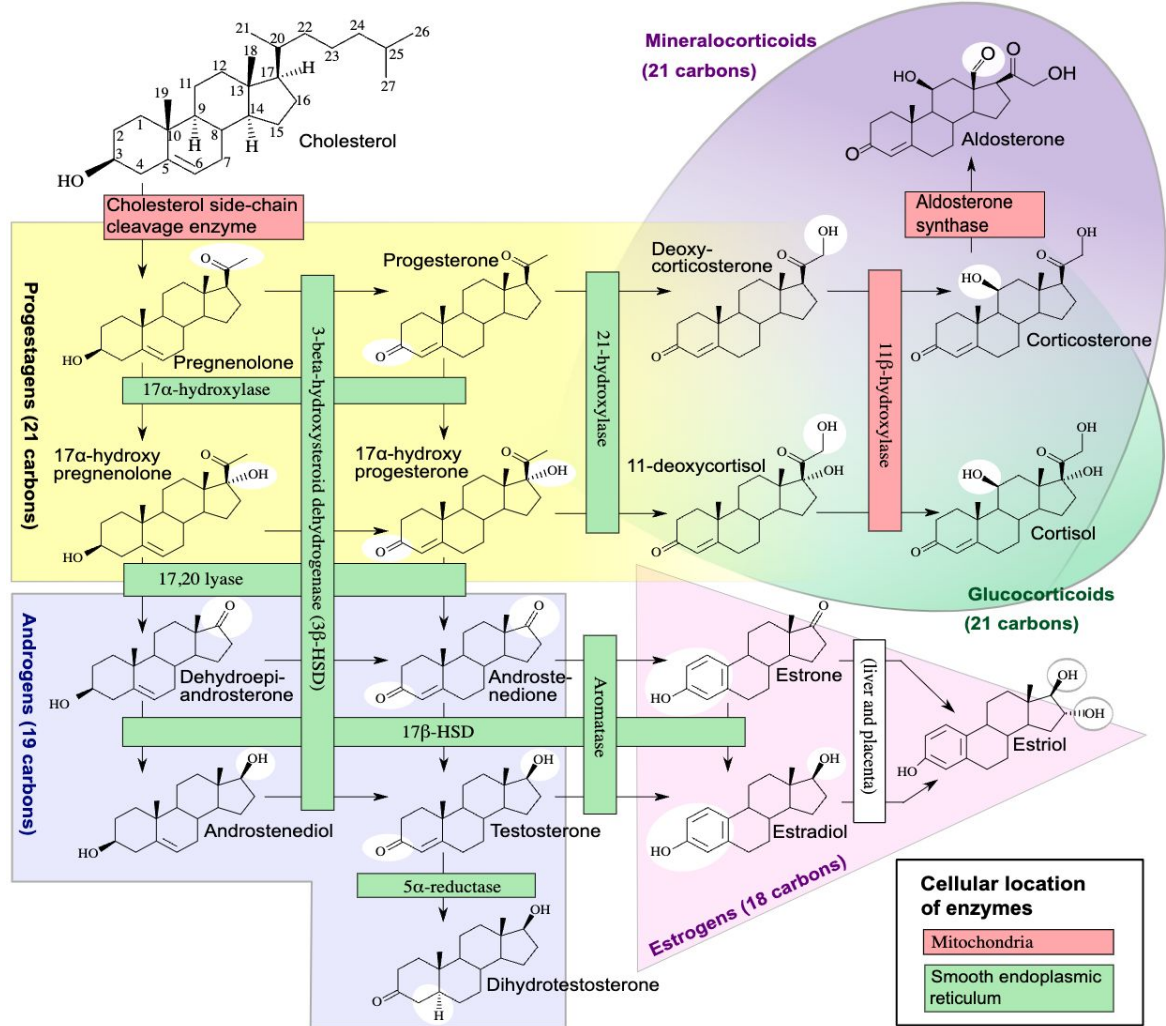
Androgen Signaling

- CAH
- Low Zinc
- AIS

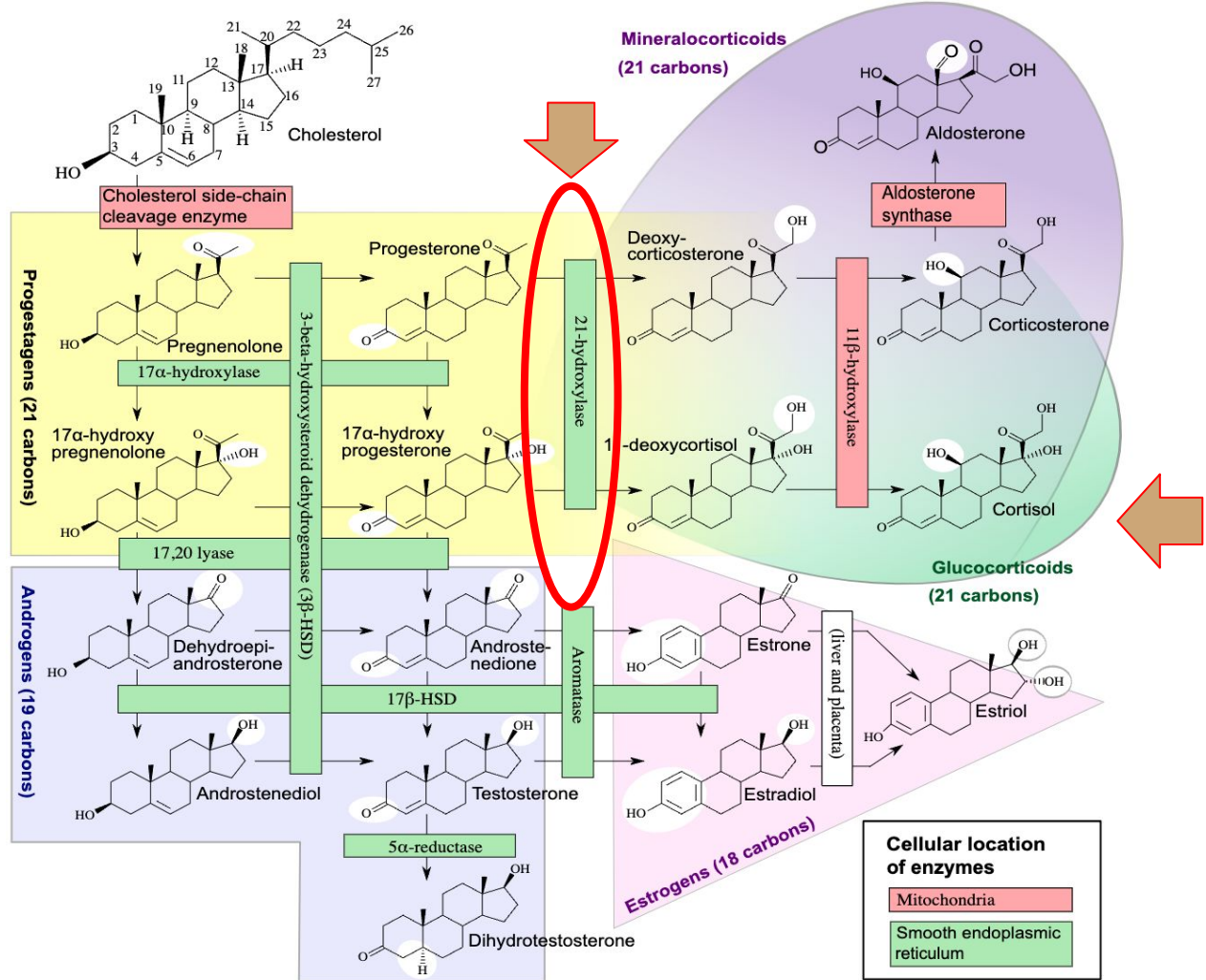
Estrogen Signaling

- Low Bone Density
- Hypospadias
- Brain Masculinization
- Autism / Dyslexia / Gifted / ADHD
- Alzheimer's
- ...

Steroidogenesis



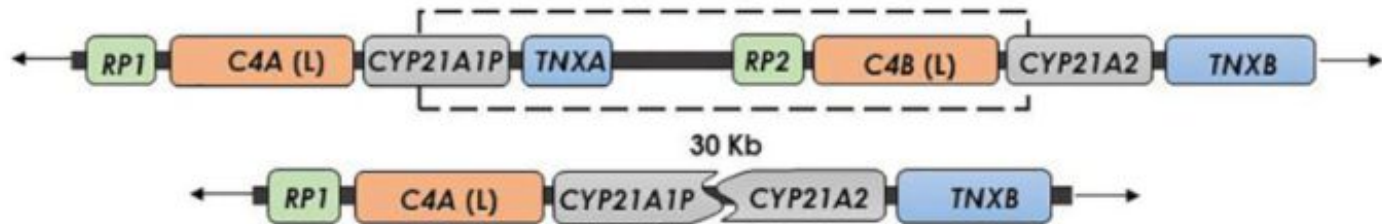
CAH



CYP21A2 and Ehlers-Danlos syndrome

A CAH

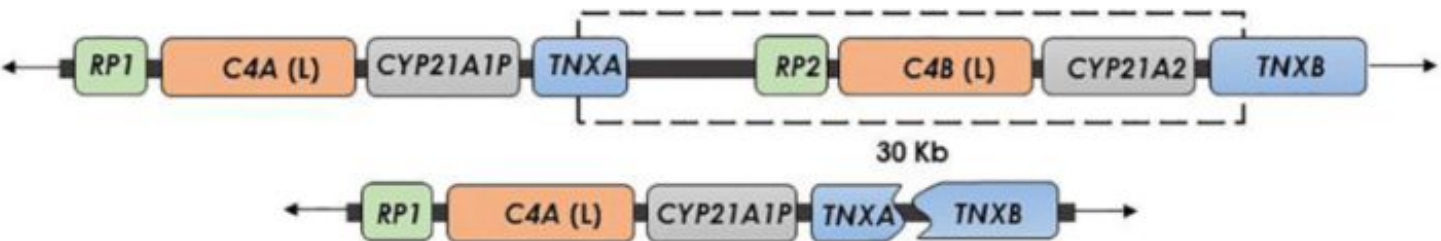
Genetic change:



Clinical presentation: CH4 and CH9 → NC CAH
CH1, CH2, CH3, CH5, CH7, CH8 → SW CAH

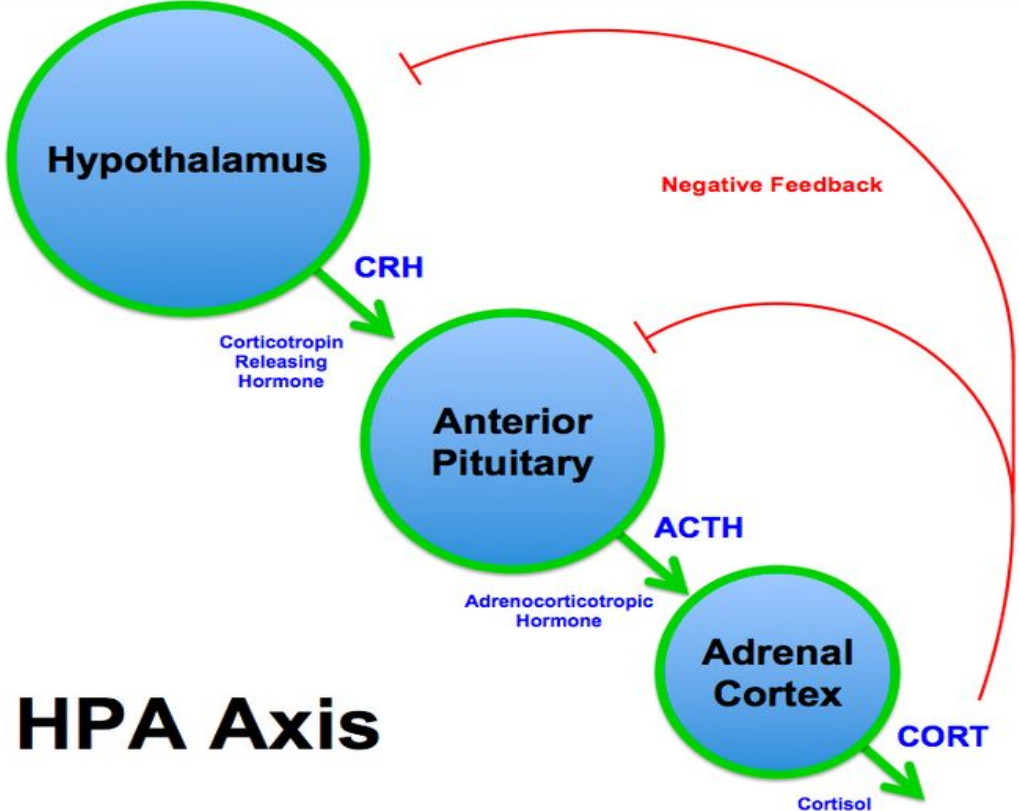
B CAH-X

Genetic change:

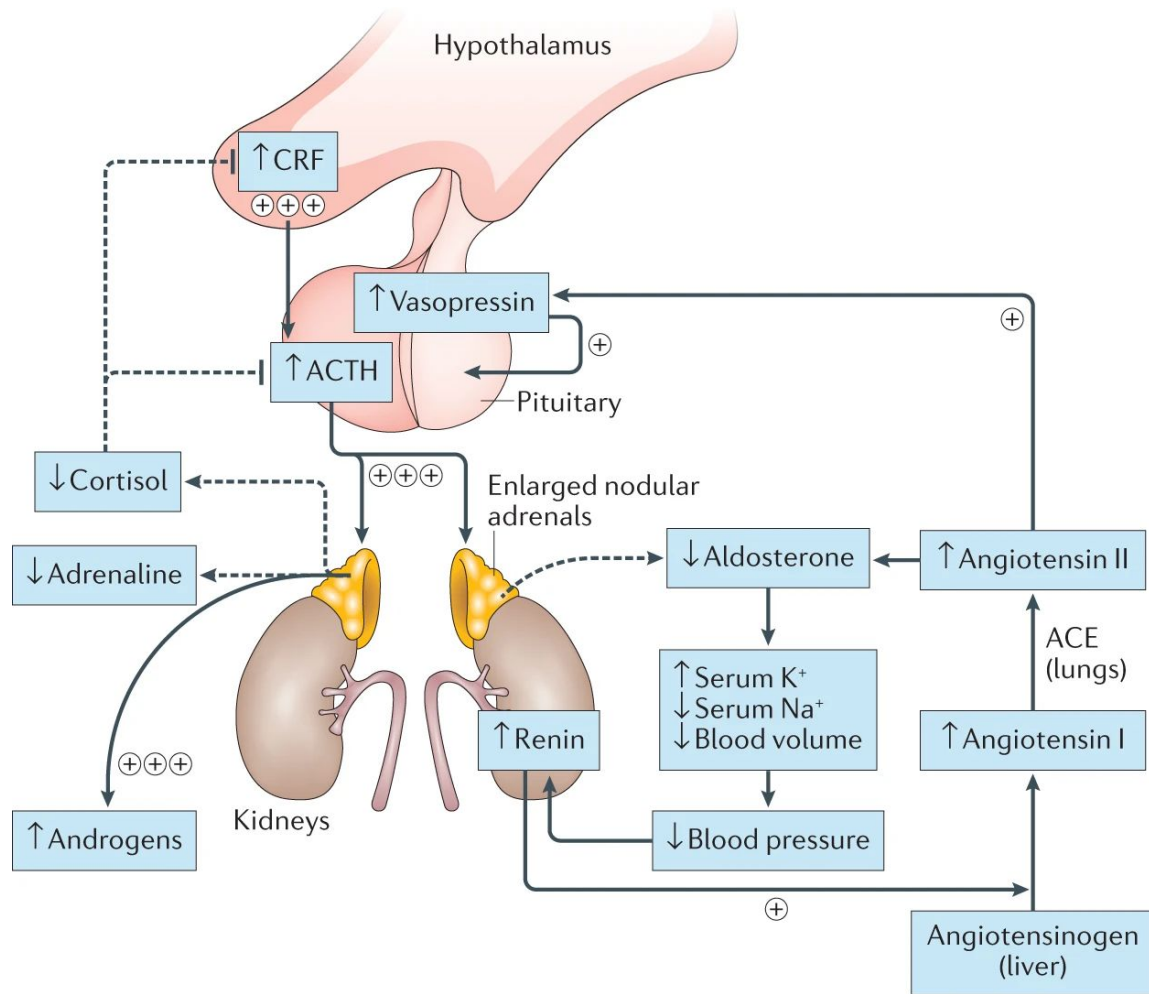


Clinical presentation: CAH-X Syndrome

CAH & HPA-Axis



HPA Axis



Hypothalamus

↑ CRF
⊕ ⊕ ⊕

↑ ACTH

↑ Vasopressin

Pituitary

↓ Cortisol

↓ Adrenaline

↑ Androgens

Enlarged nodular adrenals

↑ Renin

↓ Aldosterone

↑ Angiotensin II

↑ Serum K⁺
↓ Serum Na⁺
↓ Blood volume

↑ Angiotensin I

↓ Blood pressure

Angiotensinogen (liver)

ACE (lungs)

⊕ ⊕ ⊕

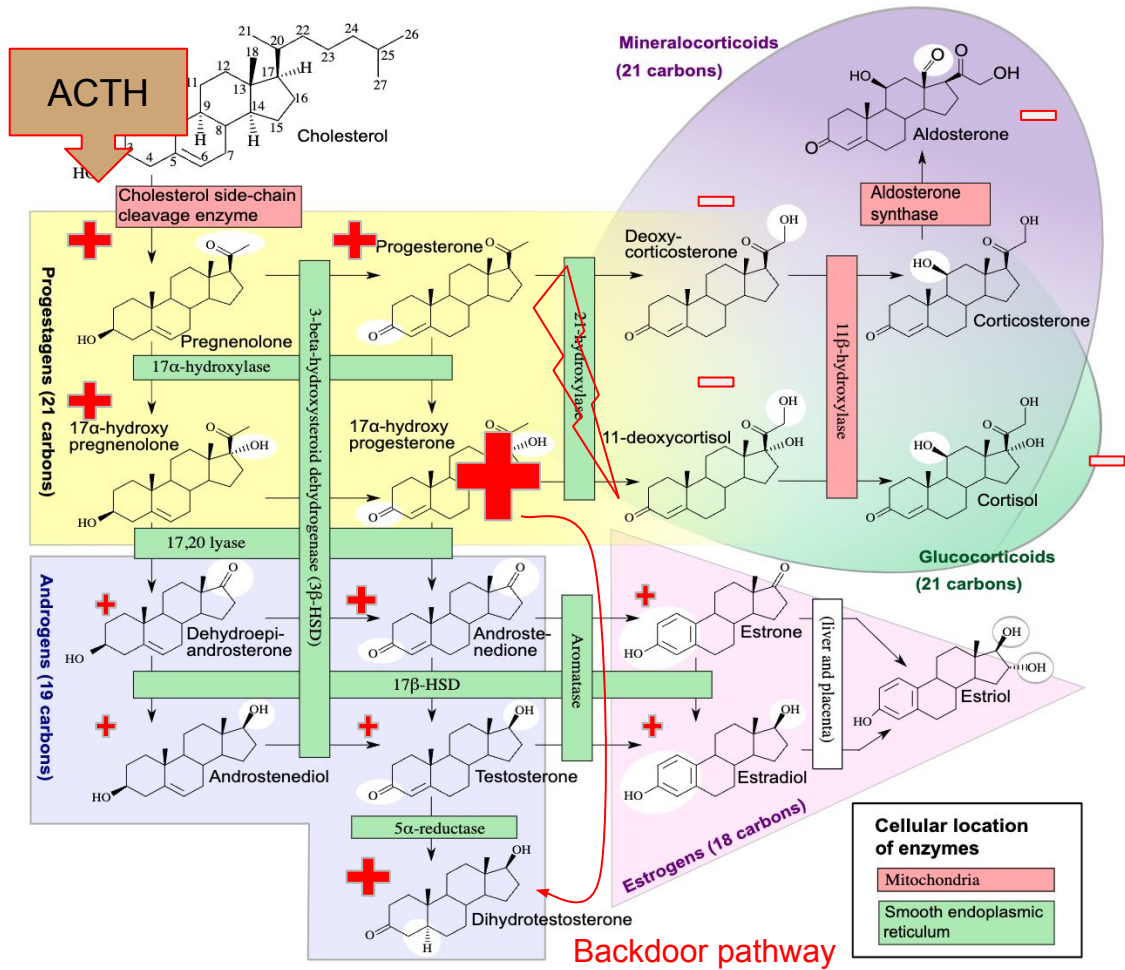
⊕

⊕ ⊕ ⊕

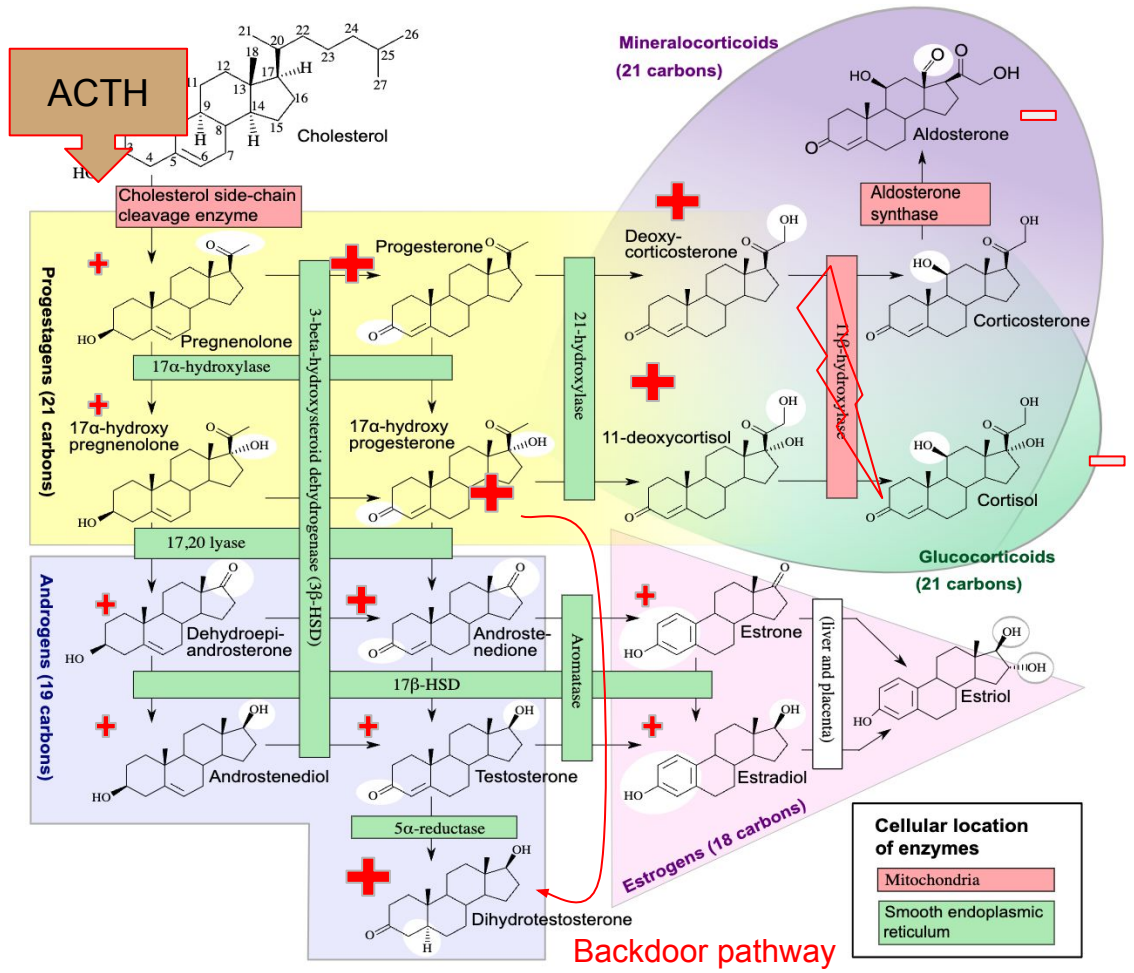
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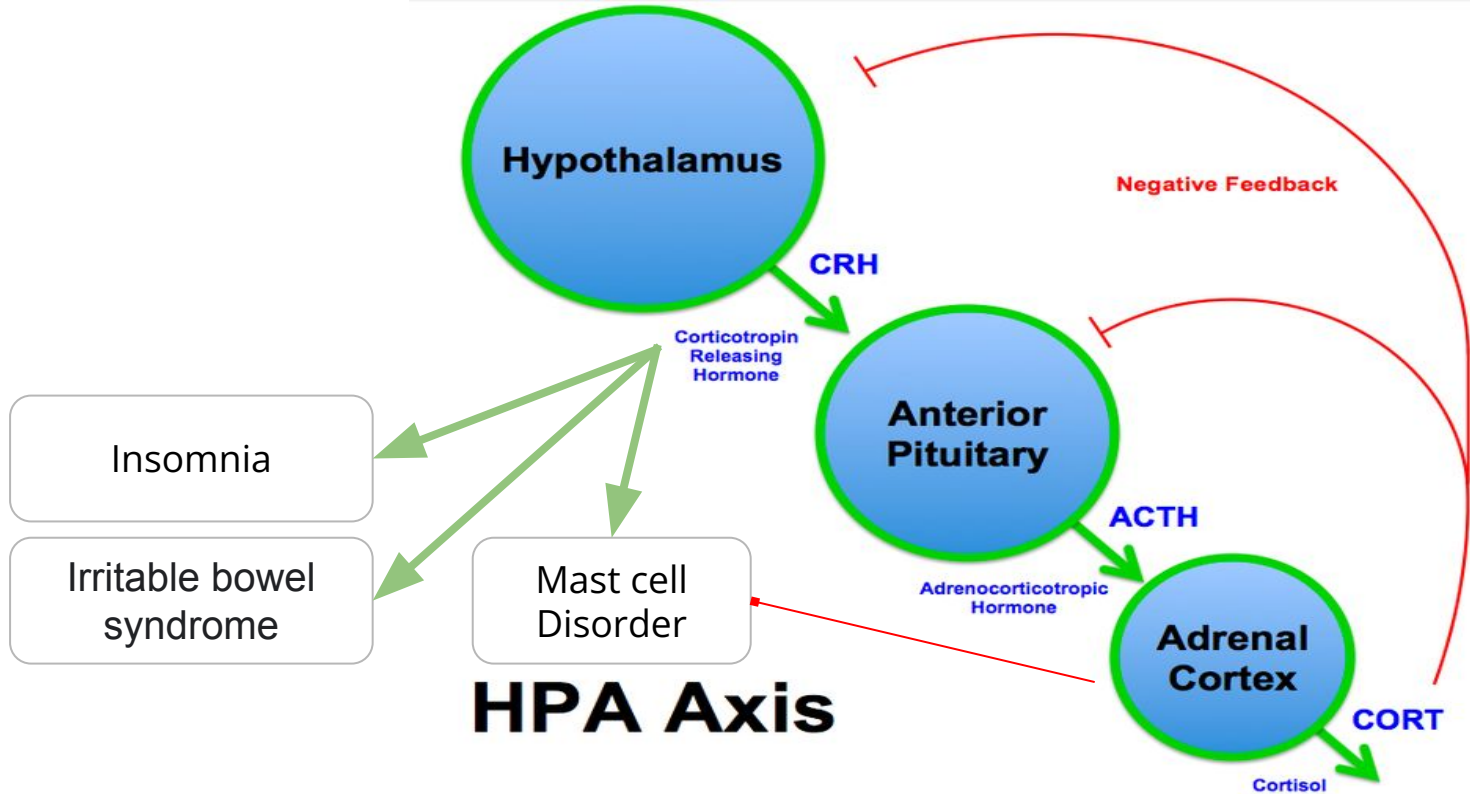
CAH (21-OHD)



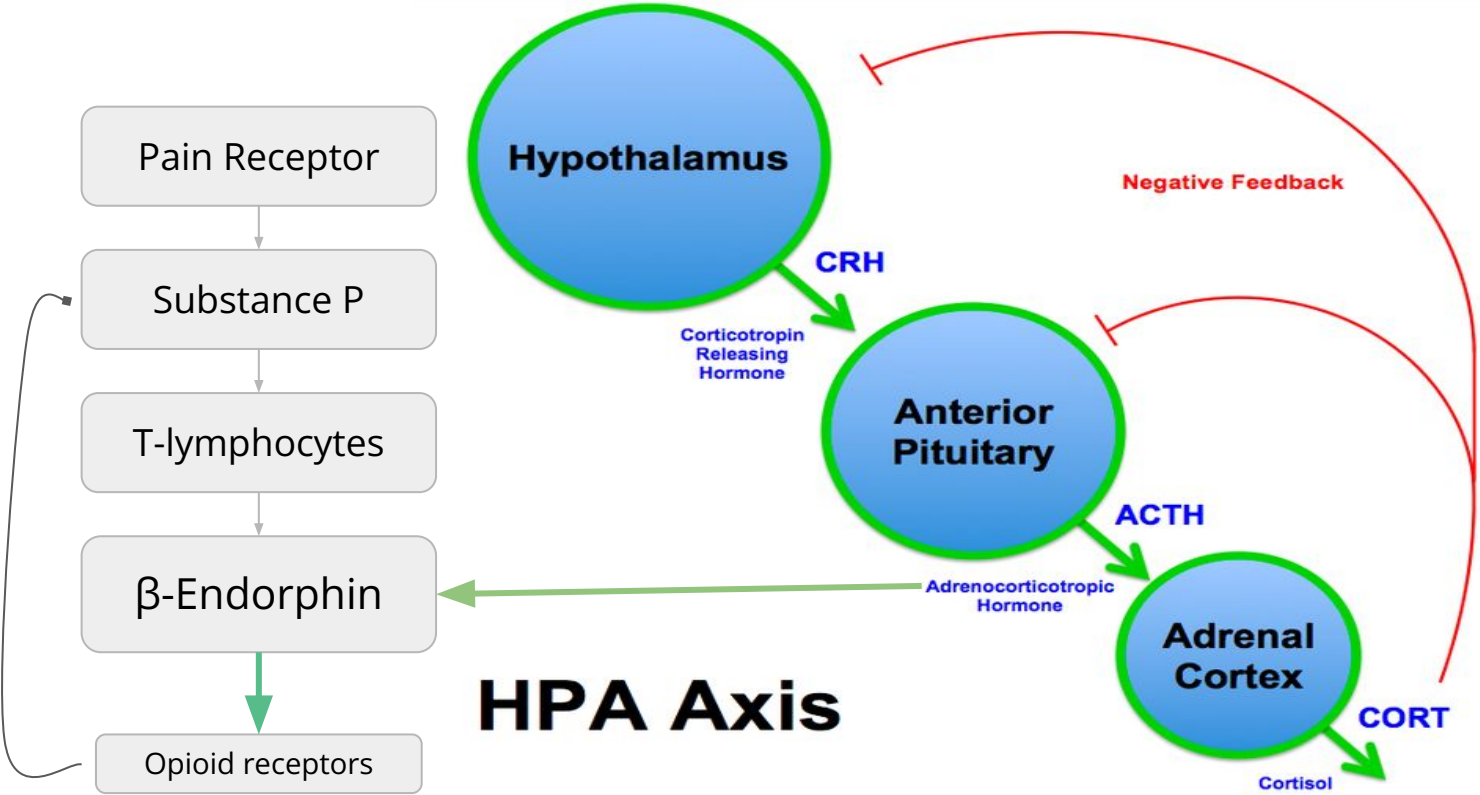
CAH (11BD)



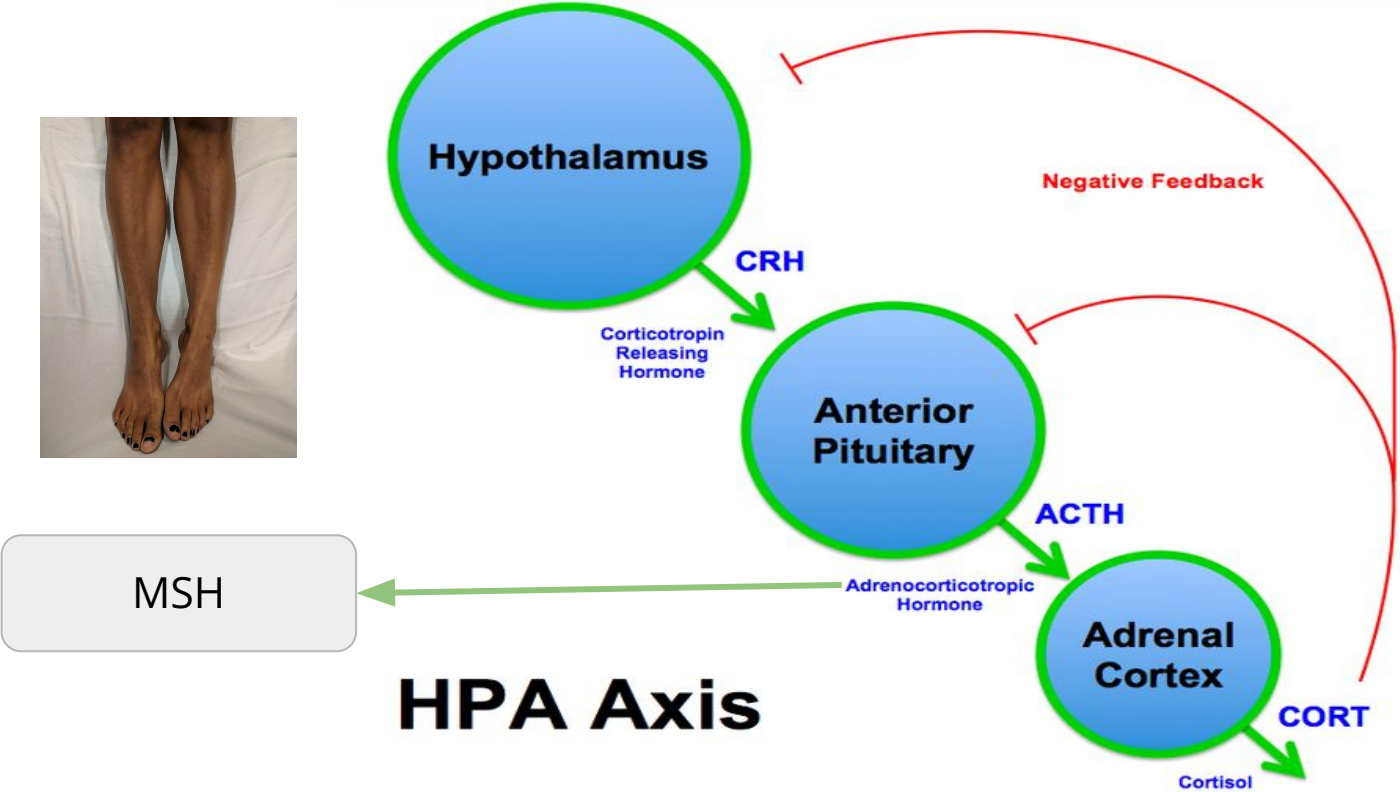
CAH & CRH



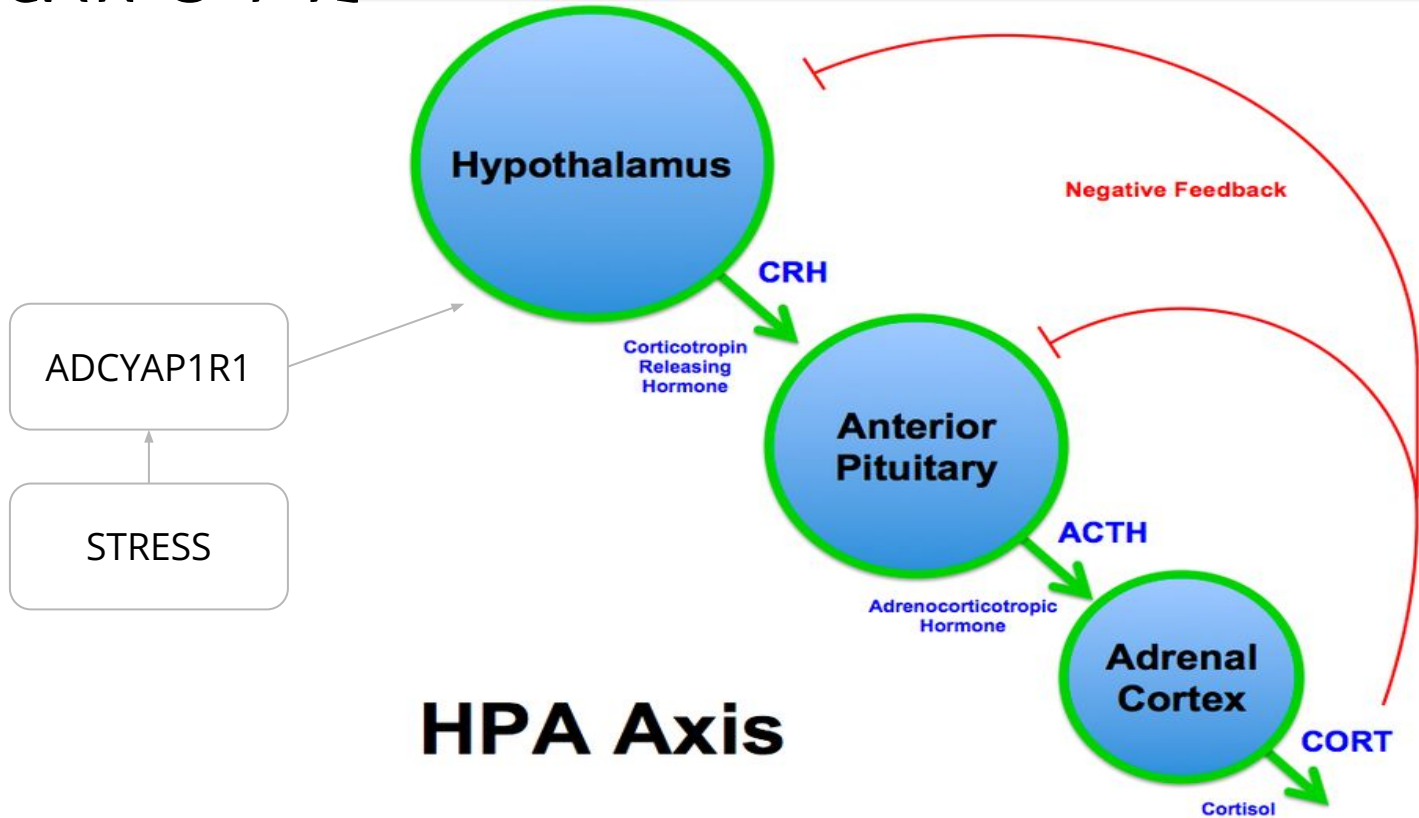
CAH & CRH & Pain tolerance && depression && Anxiety



CAH & MSH (Pale addison's disease)



CAH & PTSD



Primary adrenal insufficiency in the Trans community?

EDS is common in the transgender community

- [17% of adolescents with EDS reported gender dysphoria.](#)
- [2.6% of patients presenting for GAS had EDS diagnosis](#)

Partial 21-hydroxylase deficiencies were observed in most transgender patients

- [Genetic and epigenetic effects on sexual brain organization mediated by sex hormones](#)

17 α -hydroxylase excess is associated with trans men

- [A polymorphism of the CYP17 gene related to sex steroid metabolism is associated with female-to-male but not male-to-female transsexualism - Fertility and Sterility](#)

POTS is seen in a “preponderance of female to male patients”

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6868651/>

Eating Disorder / Anorexia nervosa which is associated with reduced cortisol production is common in the transgender community.

- [Prevalence of Eating Disorder Symptoms in Transgender and Gender Diverse Adolescents Presenting for Gender-Affirming Care](#)
- [Eating disorders among queer and trans individuals: Implications for conceptualization, assessment, and treatment](#)

LGBTQ people showed an increased risk of PTSD and transgender people showed the highest risk of PTSD

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10387489/>

Hypothyroidism is more common in the transgender community than in the general population.

- [Characterization of Thyroid Disease Prevalence Among Transgender and Gender-Diverse Patients | Journal of the Endocrine Society | Oxford Academic](#)

Transgender women had similar or worse pain tolerance to cisgender women, both worse than cisgender men.

- [Sex and Gender are Not the Same: Why Identity Is Important for People Living with HIV and Chronic Pain](#)

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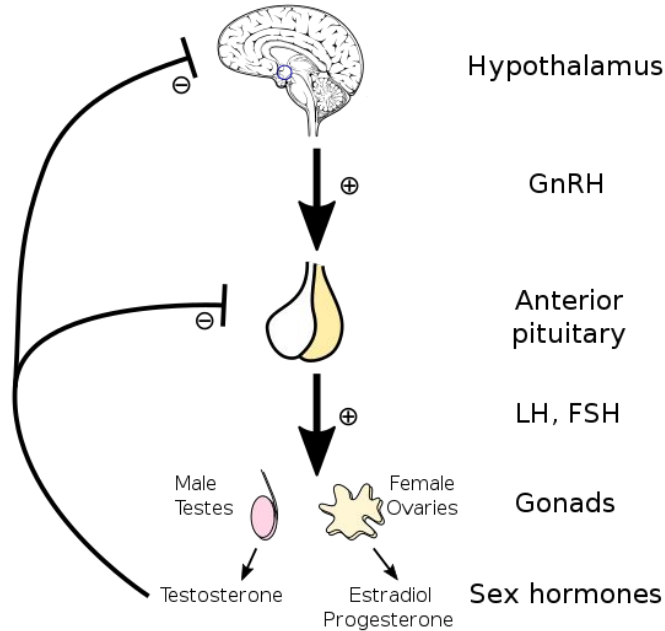
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Estrogen Signaling

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- Hypospadias
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- Alzheimer's
- ...

Hypothalamic–pituitary–gonadal axis



Androgen signaling

Androgen insensitivity syndrome (AIS)

- Complete androgen insensitivity syndrome (CAIS)
 - external genitalia are those of a typical female (a vulva)
- Partial androgen insensitivity syndrome (PAIS)
 - external genitalia are partially, but not fully, masculinized
- Mild androgen insensitivity syndrome (MAIS)
 - external genitalia are those of a typical male (a penis and a scrotum) but smaller than average
 - sufficient to impair spermatogenesis and / or the development of secondary sexual characteristics at puberty in males

Inverted sex hormone signaling / discordant phenotype

AMAB

- Hips development
- Breast development
- No voice drop

AFAB

- Voice drop
- Muscle development
- Male scent

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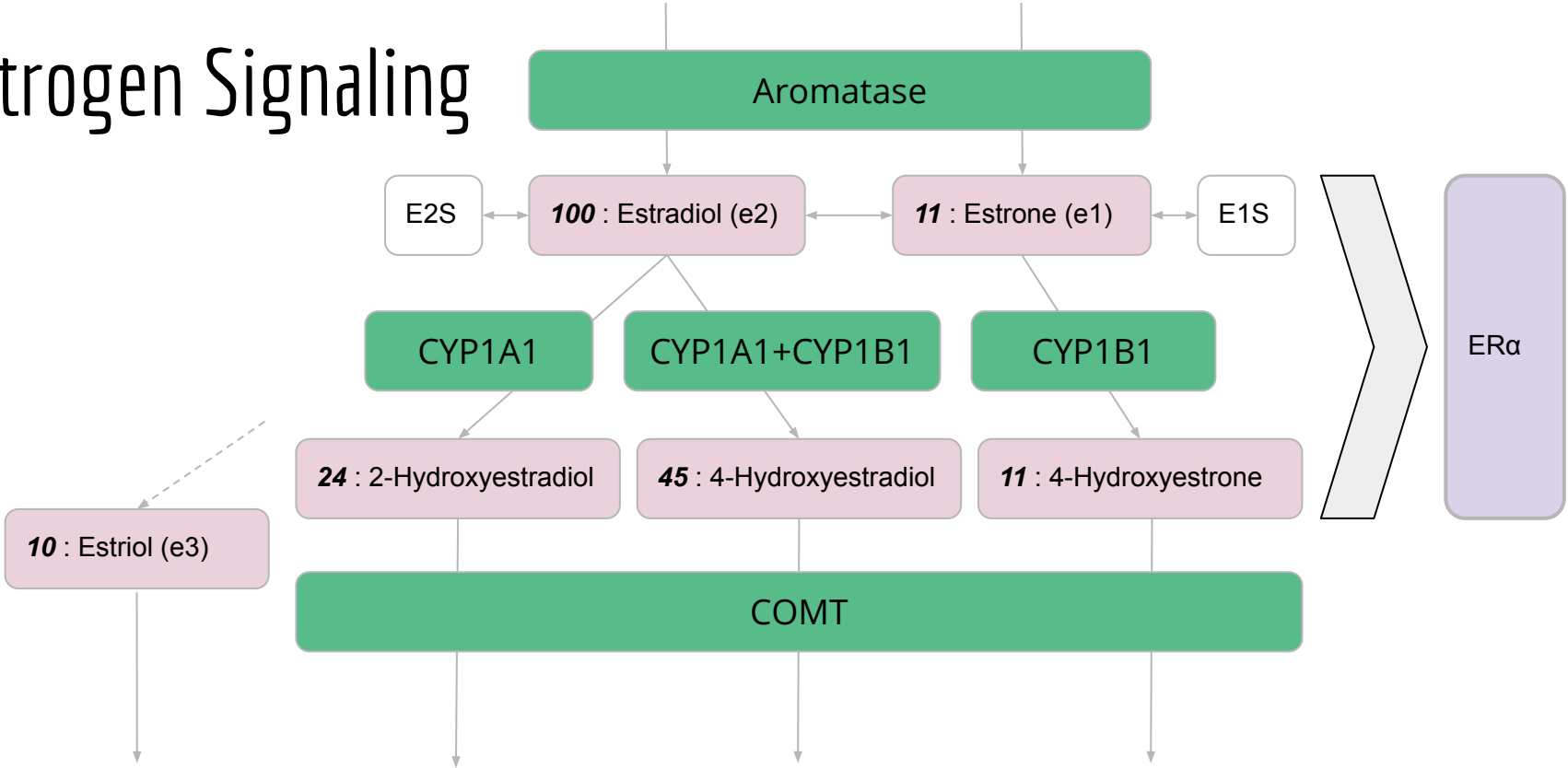
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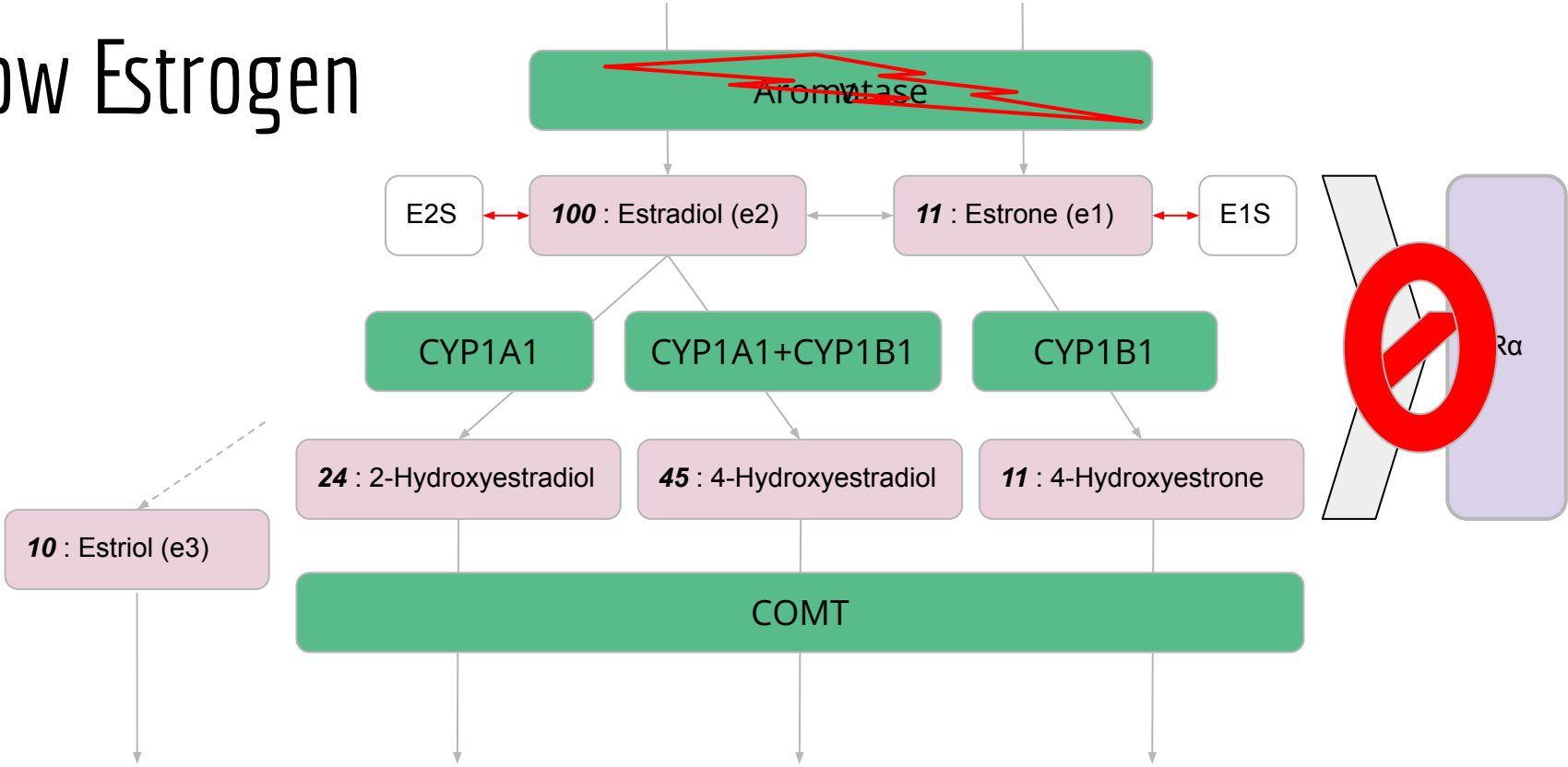
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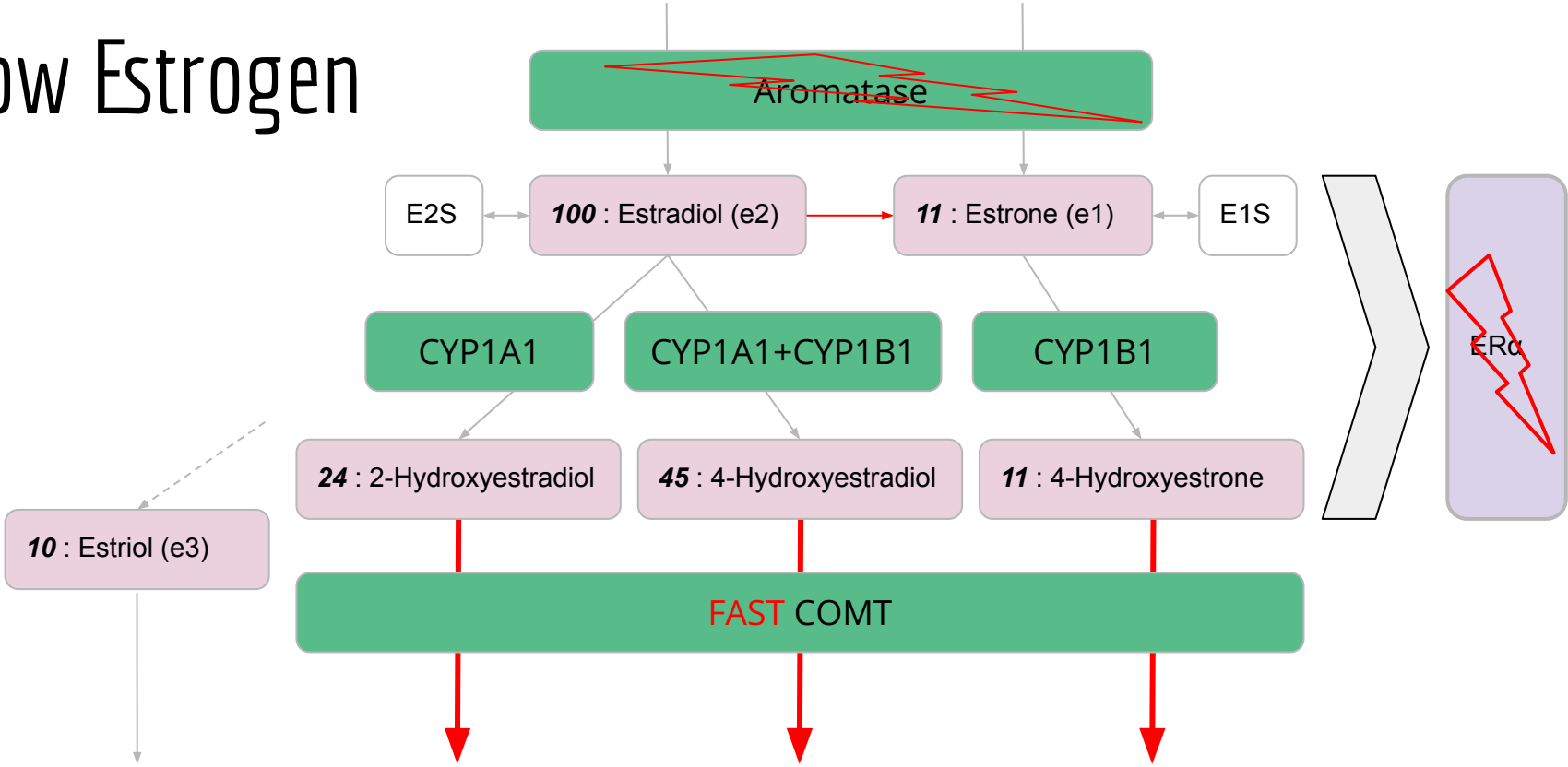
Estrogen Signaling



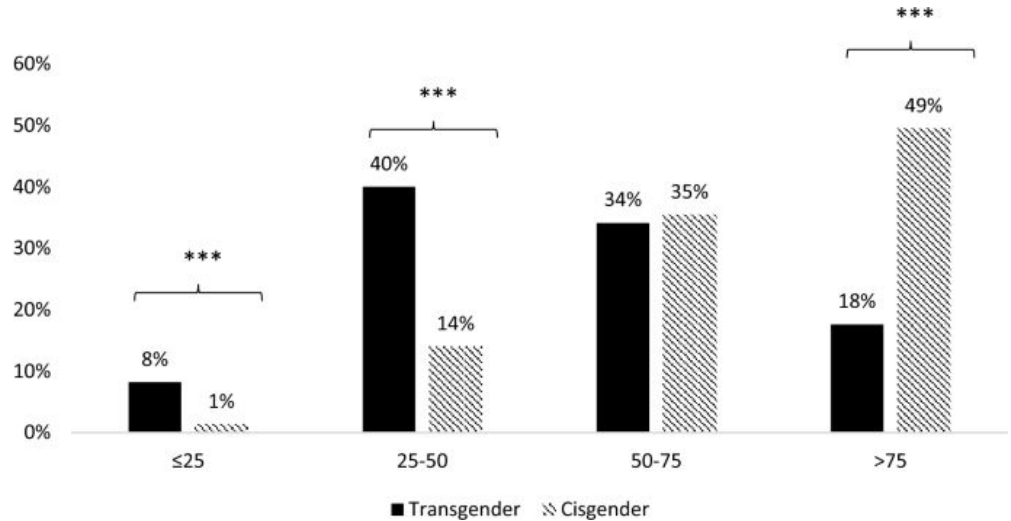
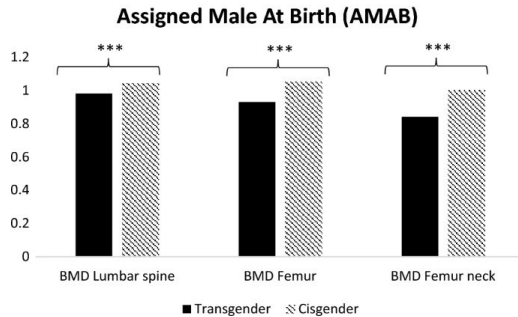
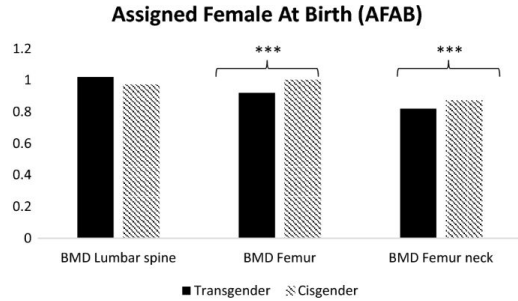
Low Estrogen



Low Estrogen



Low Estrogen: Bone density & Vitamin D



Low Estrogen: Hypospadias & Cryptorchidism



Subcoronal



Midshaft



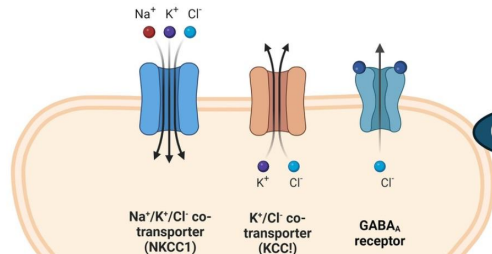
Penoscrotal

Autism : Low estrogen

Excitatory: depolarization

Shift delaying factors

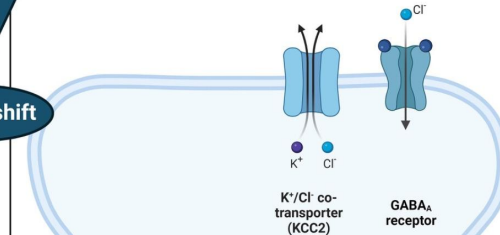
- **Estradiol (E2)**
- Prenatal stress
- Spontaneous neural activity before receiving external signals
- Postnatal aberration of thalamic input from *external stimuli*



Inhibitory: hyperpolarization

Shift acceleration factors

- Testosterone
- Dihydrotestosterone
- **Oxytocin**
- Postnatal stress
- *External sensory input*



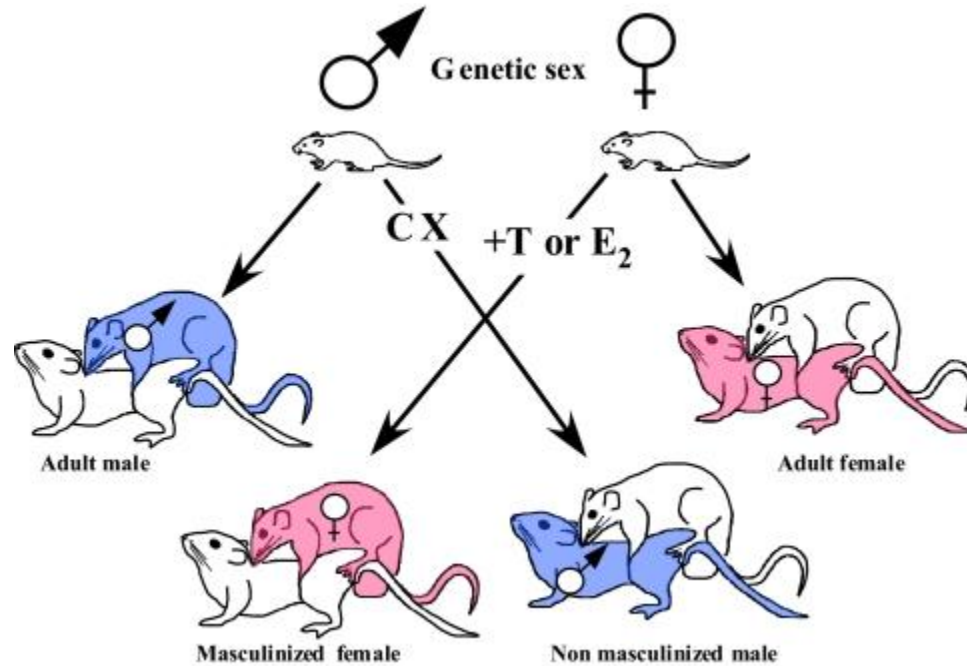
<https://doi.org/10.3389/fendo.2024.1343759>

Low Estrogen: Alzheimer's

Associated with Alzheimer's

- Higher risk: Primary Ovarian Insufficiency: aka Early Menopause
- Seen in more women than men
- etc

Low/High Estrogen: ER α & Copulatory role preference



A year of helping

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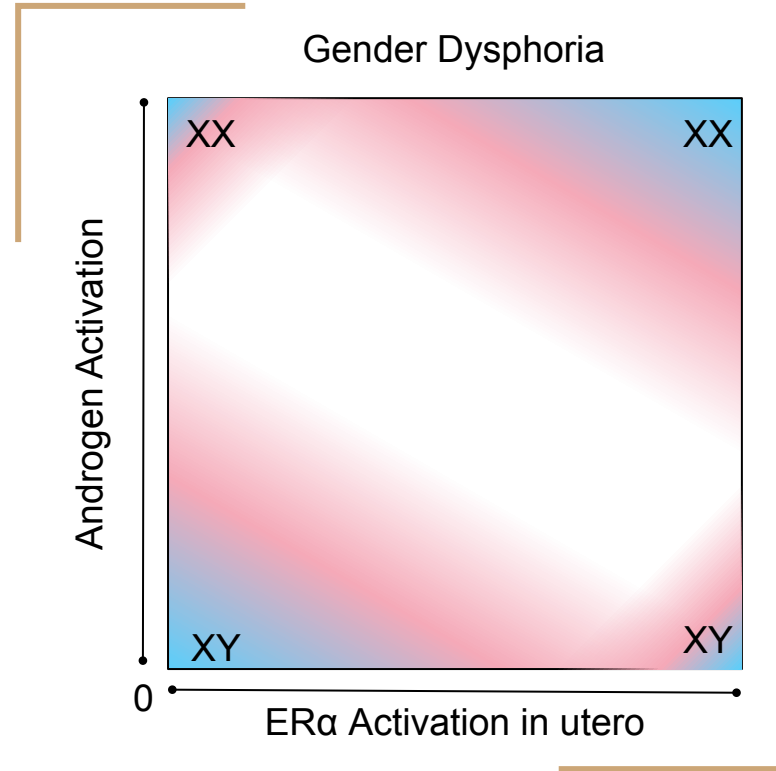
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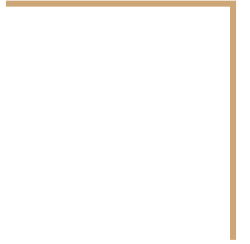
Gender Dysphoria

- Copulatory role preference
- Inverted sex hormone signaling / discordant phenotype

Kate's Hypothesis on the cause of gender dysphoria



What's next?





Questions?





Link for more
information



https://new.reddit.com/r/DrWillPowers/wiki/meyer-powers_syndrome_faq/