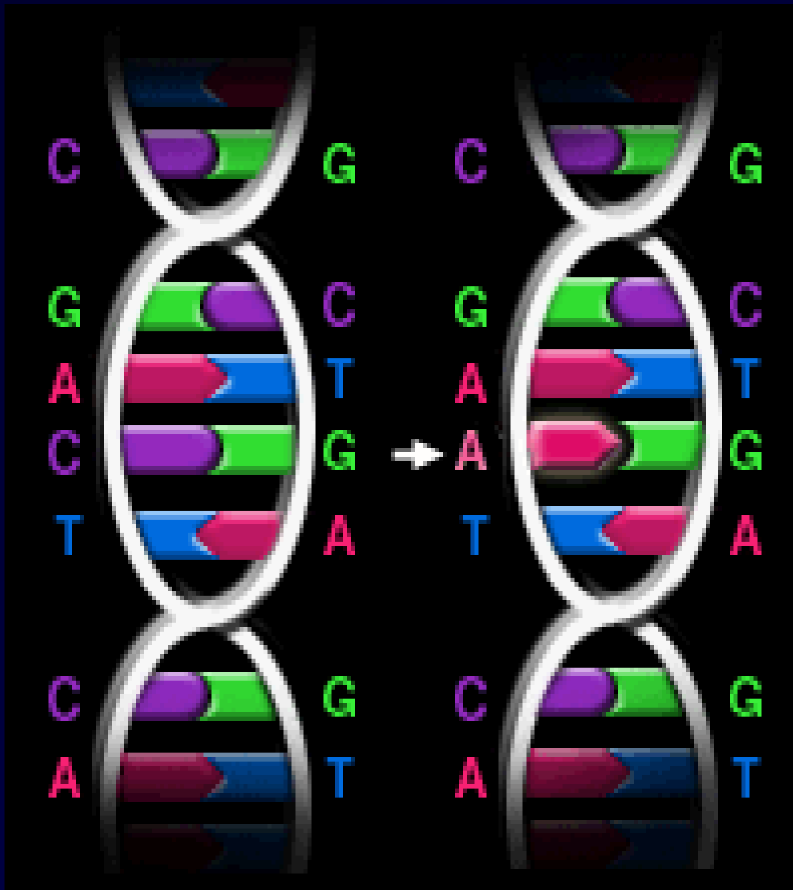
Φύλο και εγκέφαλος

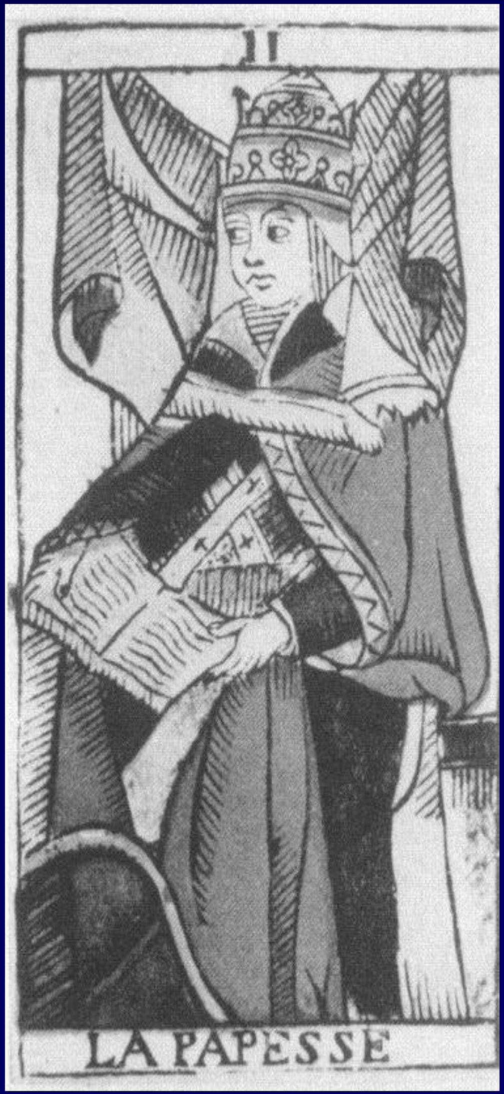
Νεοκλής Α. Γεωργόπουλος
Ενδοκρινολόγος



Genes & Jeans

Για την ανάπτυξη άρρενος τύπου ταυτότητας φύλου απαραίτητη η άμεση δράση των ανδρογόνων στον εγκέφαλο μέσω του ανδρογονικού υποδοχέα

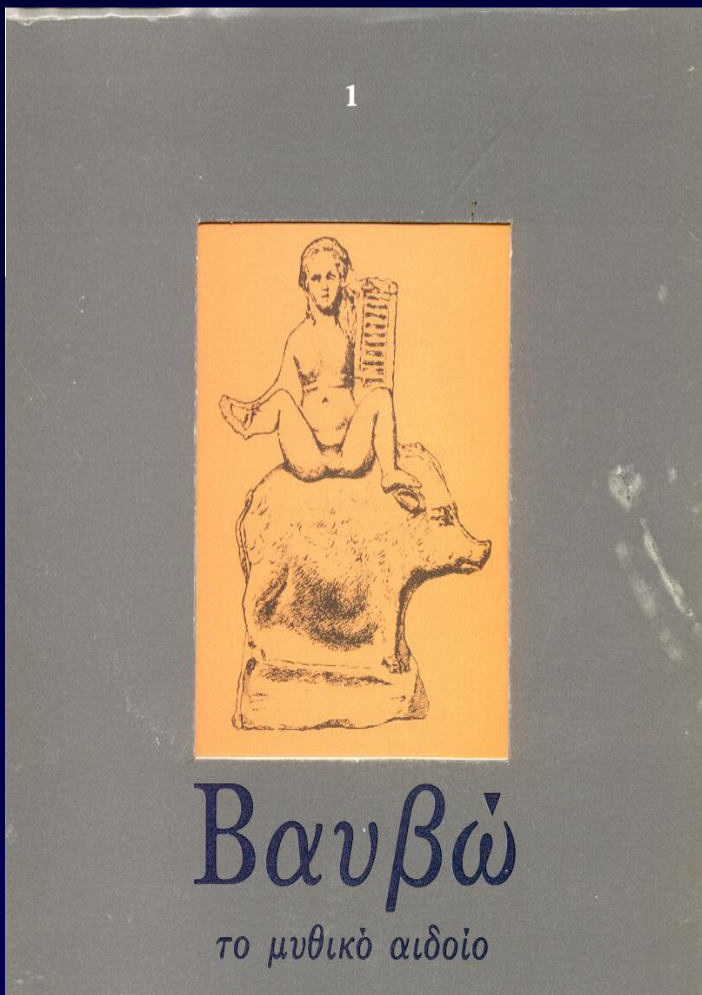
Pope Joan: A Recognizable Syndrome*
Maria I. New and ElizabethS. Kitzinger, JCEM 1993



Baubo:a Case of Ambiguous Genitalia in the Eleusinian Mysteries

Neoklis A. Georgopoulos, George A. Vagenakis, Apostolos L. Pierris

Hormones 2003



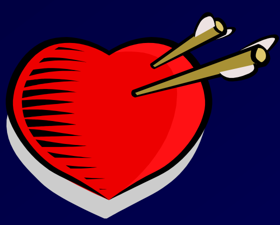
Ως ειπούσα πέπλους ανεσύρετο, δείξε δε πάντα σώματος ουδέ πρέποντα τύπον.

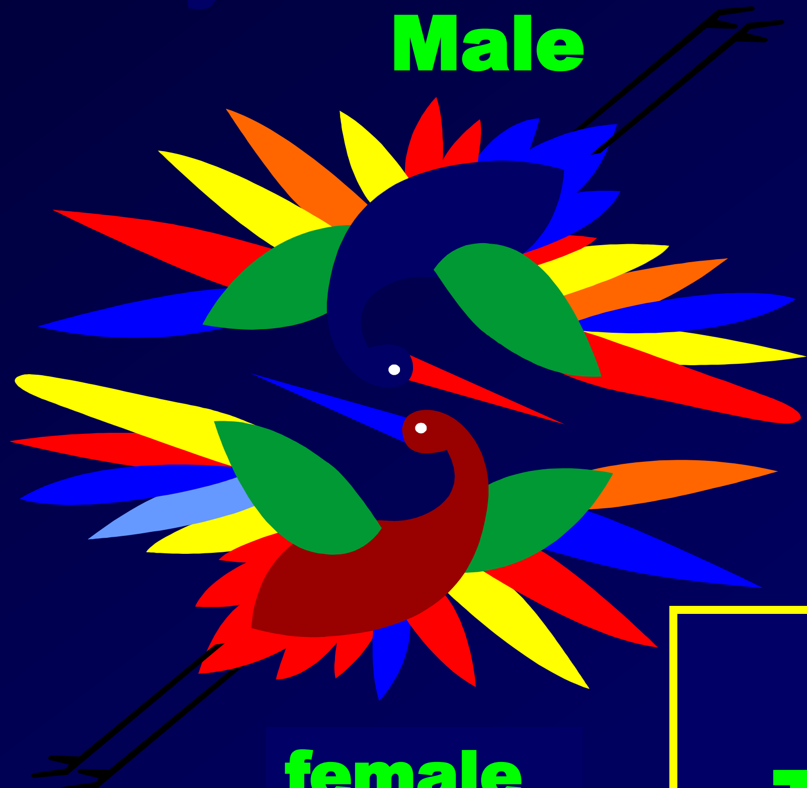
Παίς δ’ήεν Ίακχος Βαυβούς υπο κόλπους

Masculinization of the brain

The sing of the canary

Male

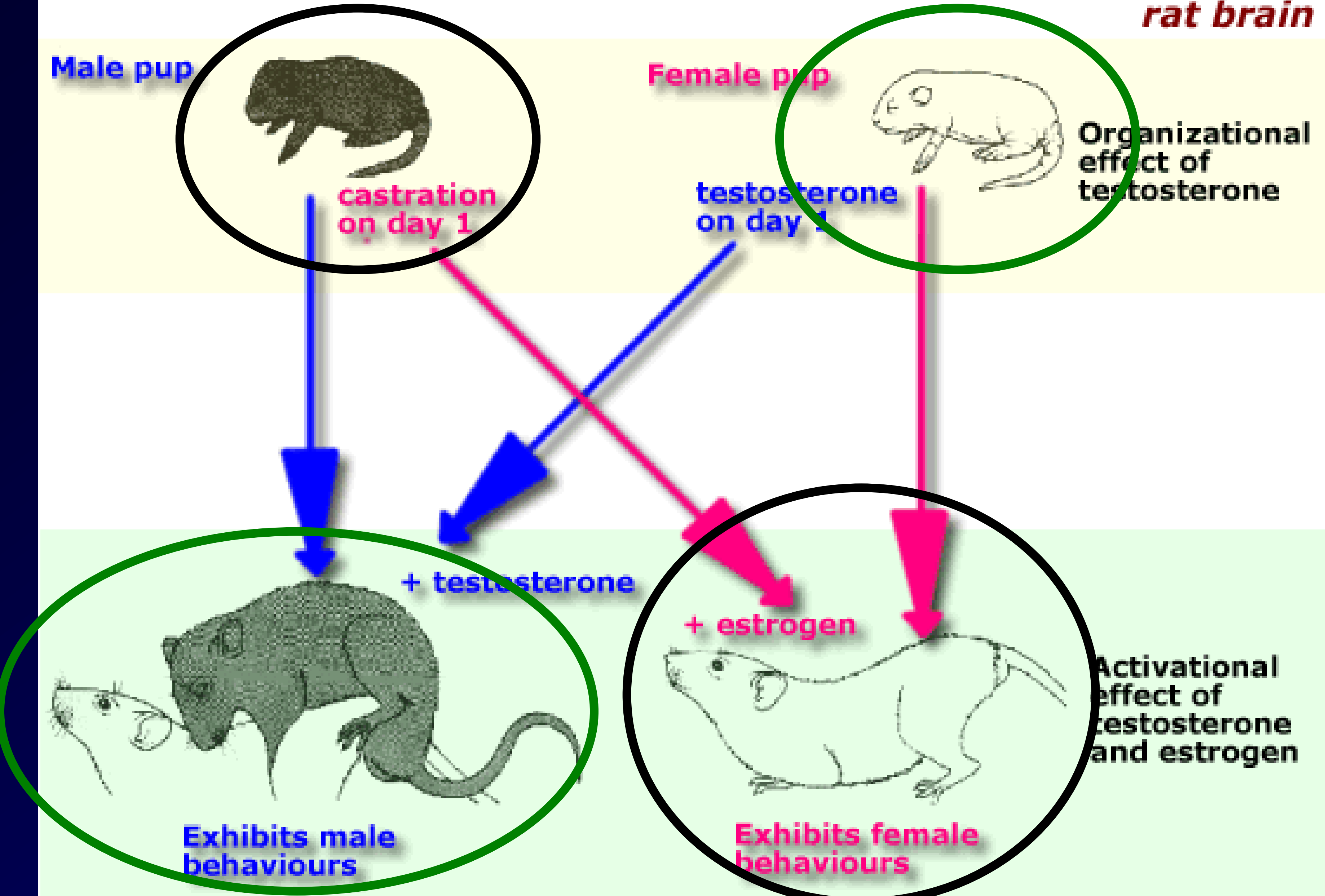




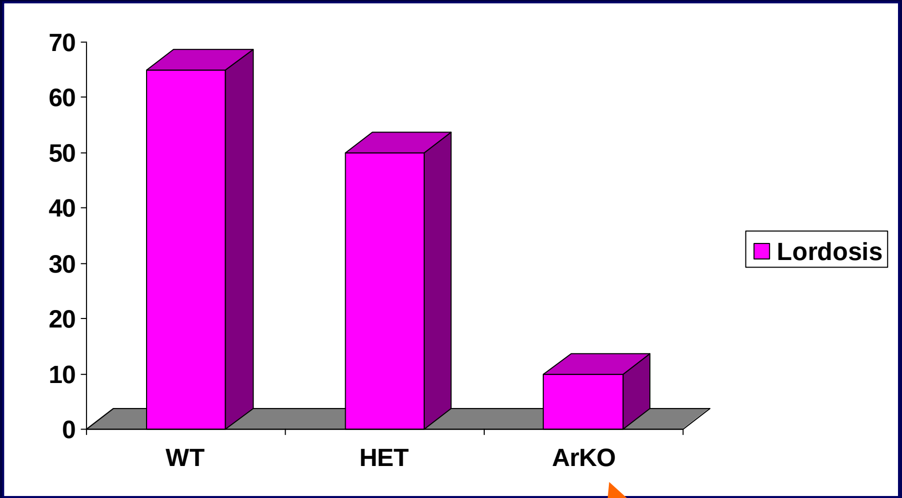
female

Female + Testosterone

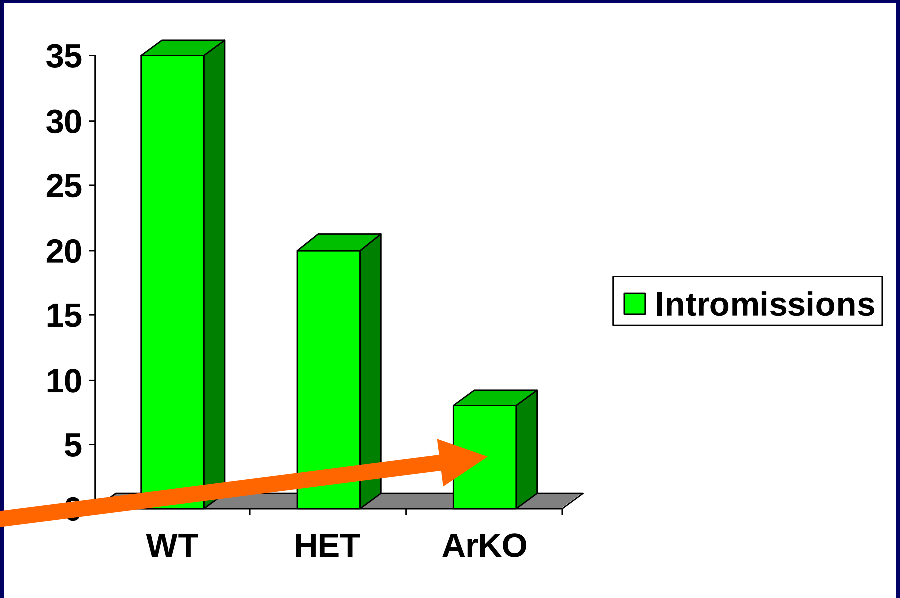
Testosterone masculinizes and defeminizes rat brain



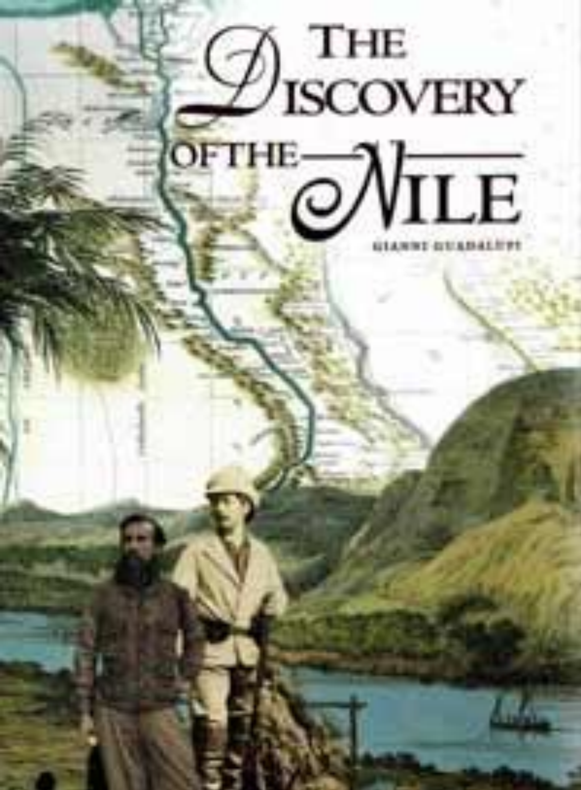
Estrogens are required for female typical brain and behavioral sexual differentiation

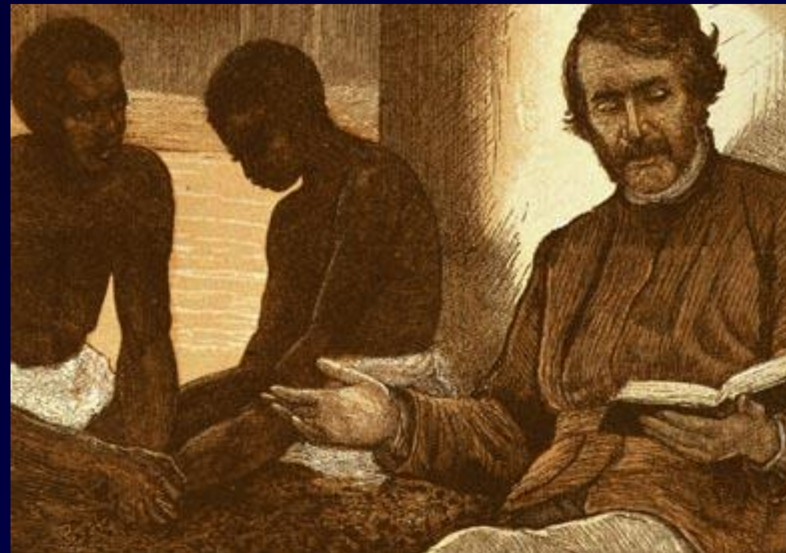


Aromatase Knock out mice

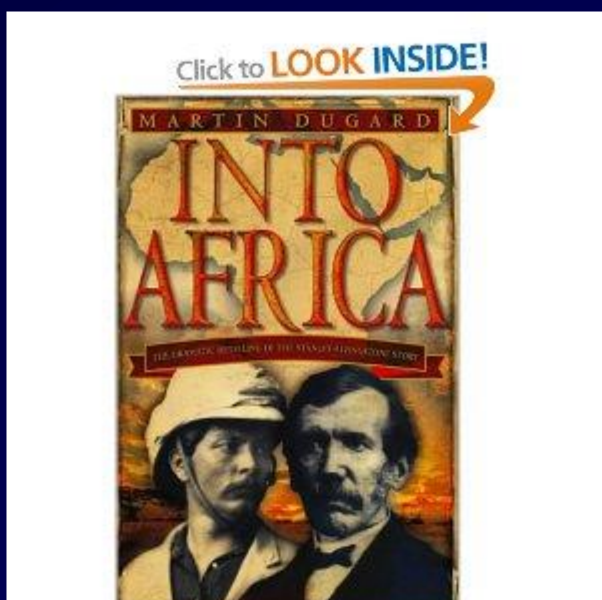


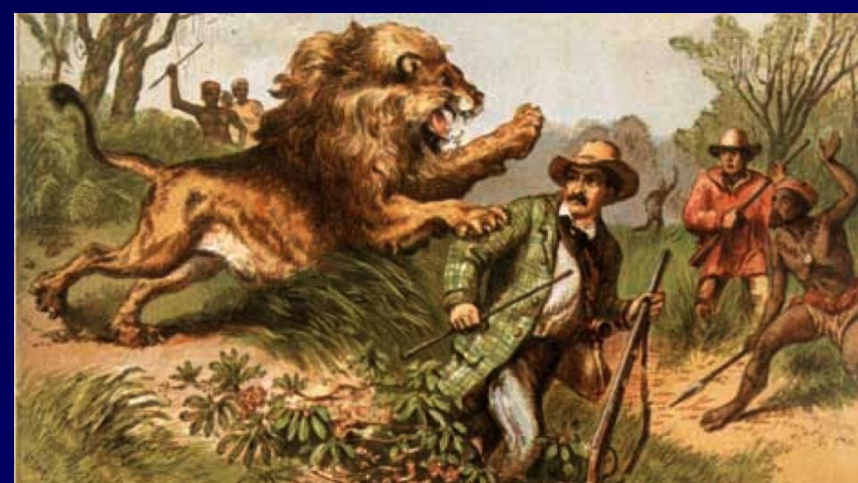
Bakker J. Neuroendocrinology 2007


THE DISCOVERY OF THE NILE
GIANNI GUADALUPI




ARABIA FELIX
DISCOVERY OF
THE NILE


Click to LOOK INSIDE!
MARTIN DUGARD
INTO AFRICA



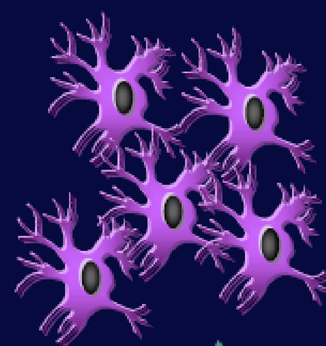
Φυλετικός διμορφισμός ΚΝΣ

Brain Sexual Differentiation
Multisignaling process

Brain development | Adult brain | Behavior

XX

XY



Female

Male

ORGANIZATIONAL ACTIONS

ACTIVATIONAL ACTIONS

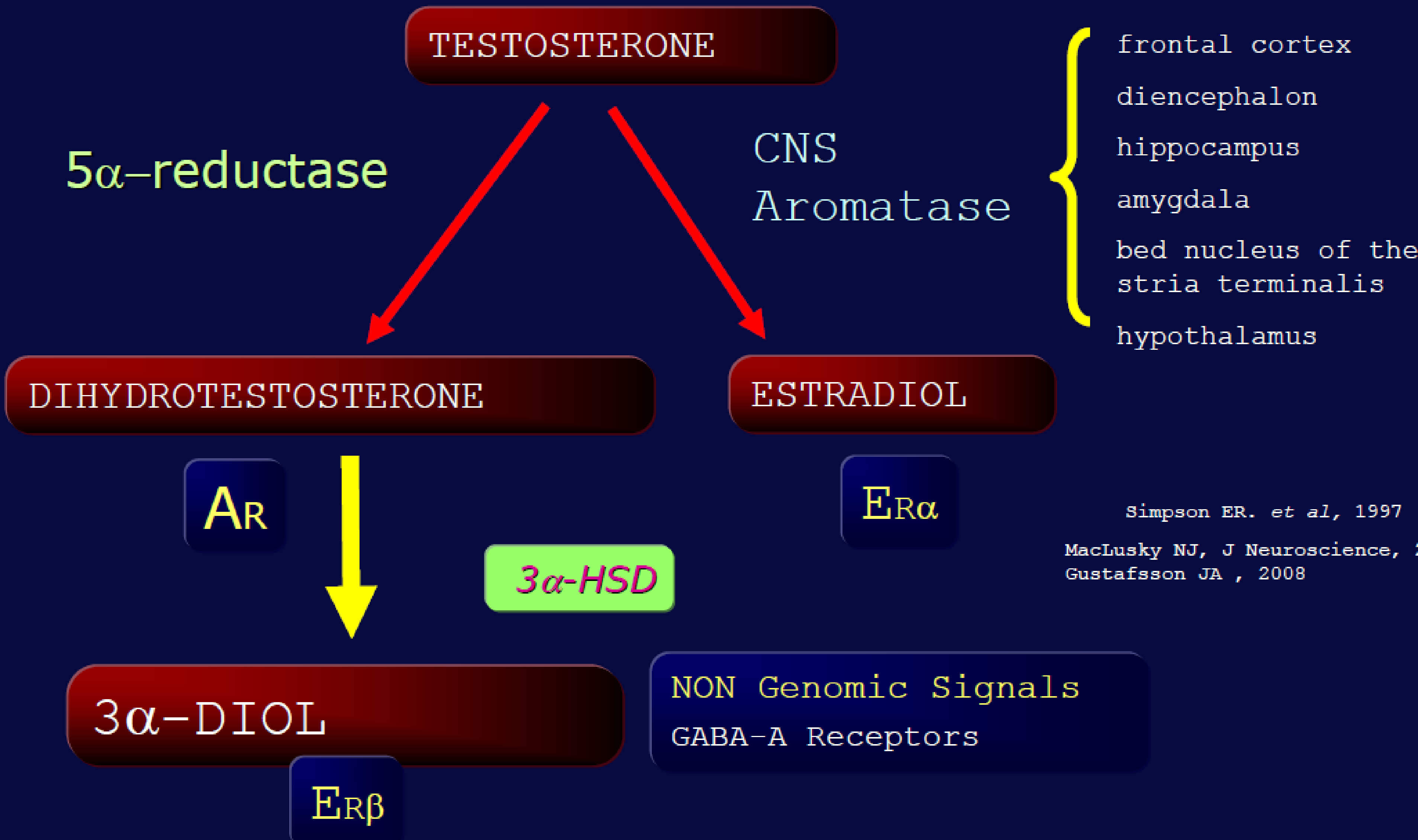
NEUROACTIVE STEROIDS
Neurotrophic Factors
Neurotransmitters Second
Messenger Pathways Cross-Talks

NEURAL and ENDOCRINE CONDITIONS

Endocrine Disruptors

Dick F. Swaab 2004

Central Metabolism of Sex Steroids

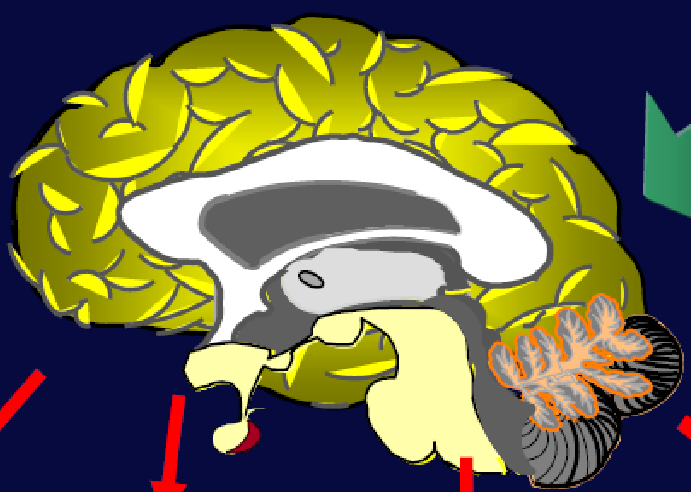


The Brain as a Target Tissue for Sex Steroids

CNS Sexual Dimorphism

FUNCTIONAL SEX DIFFERENCES

- Ers, PRs, ARs different expression in brain areas
- ER polymorphisms
- Enzyme induction



STRUCTURAL SEX DIFFERENCES

- Different neuronal subpopulations in brain areas

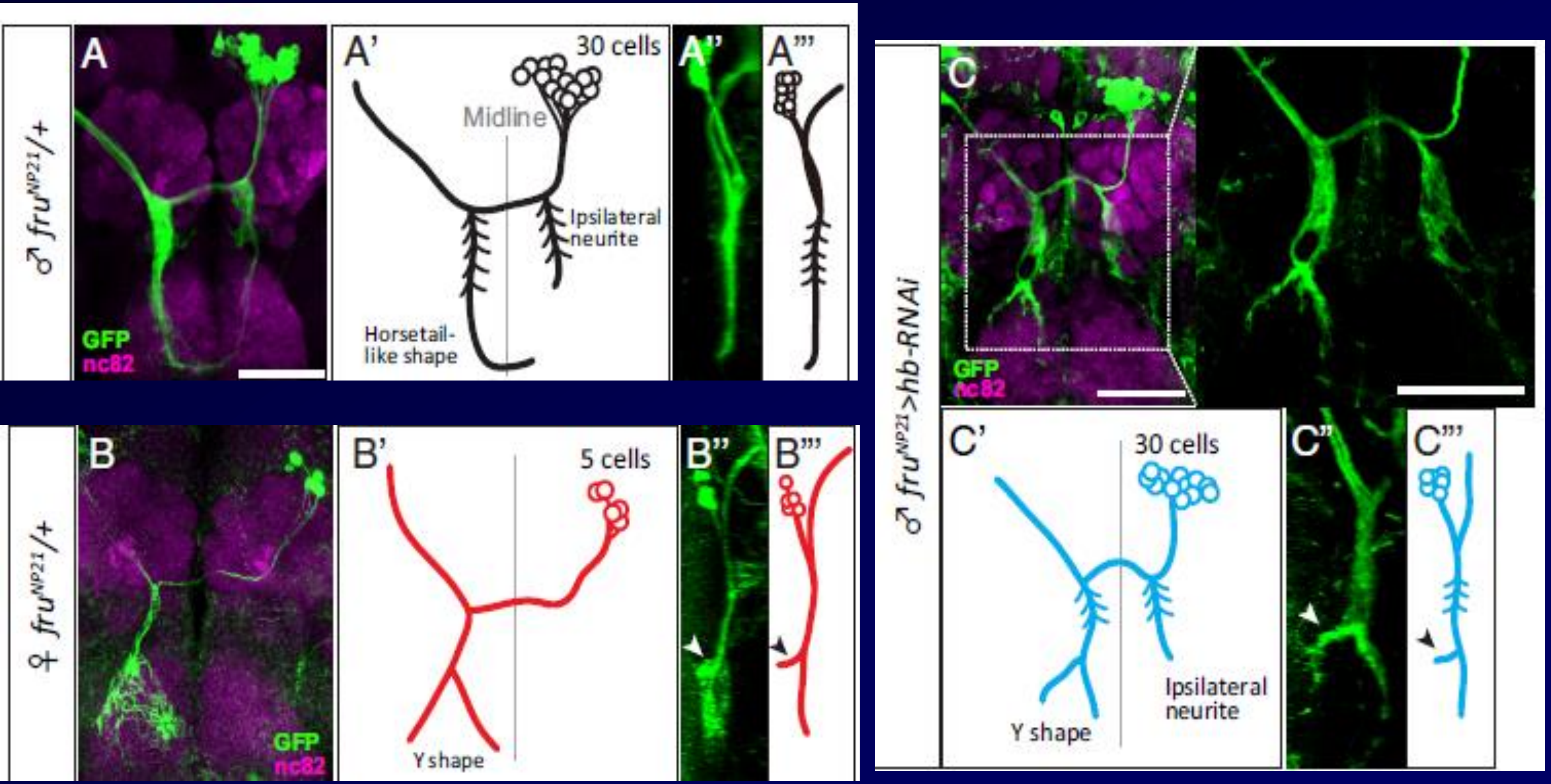
SEXUAL ORIENTATION

GENDER IDENTITY

COGNITIVE DIMORPHISM

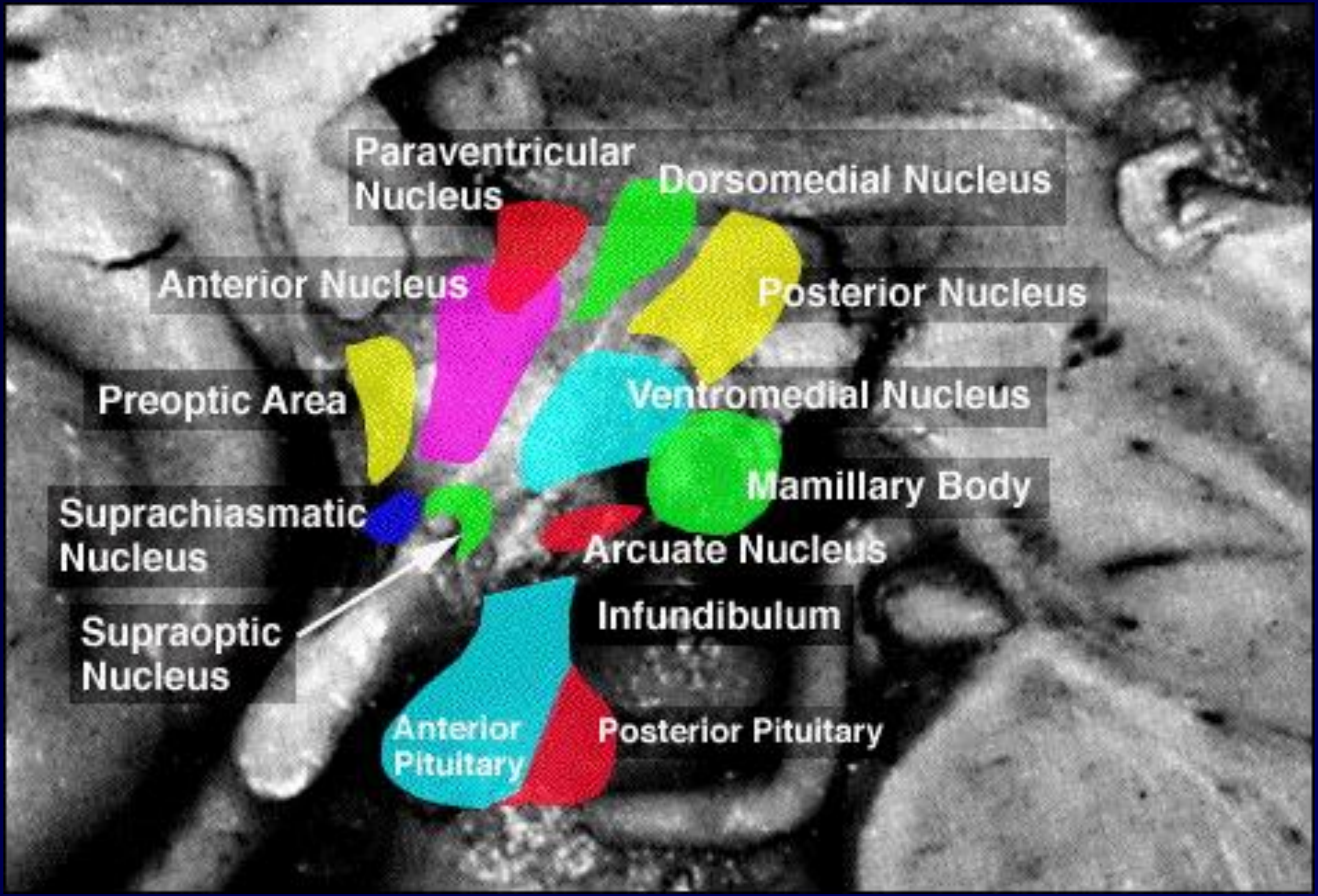
PREVALENCE OF NEUROLOGICAL AND PSYCHIATRIC DISEASES

Male-typical shape of neurites: substantial evidence



Goto et al, 2011

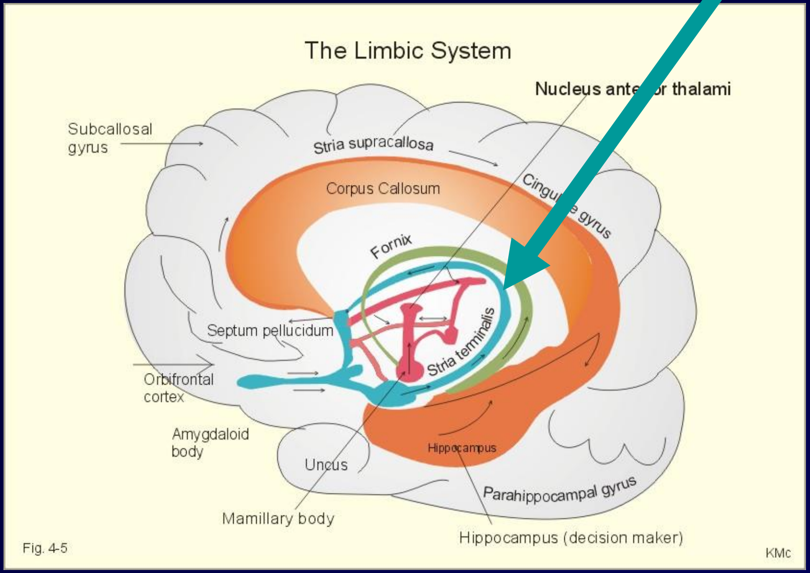
Sexually dimorphic nuclei - Hypothalamus



Πυρήνες - SDN of MPOA, SCN, BST, INAH 2
Μέγεθος, σχήμα, αριθμός νευρώνων
Οι περιοχές του εγκεφάλου διαφοροποιούνται μέχρι και την ενήλικο ζωή

BST Bed nucleus of the Stria Terminalis

- Males : increased size and number of neurons

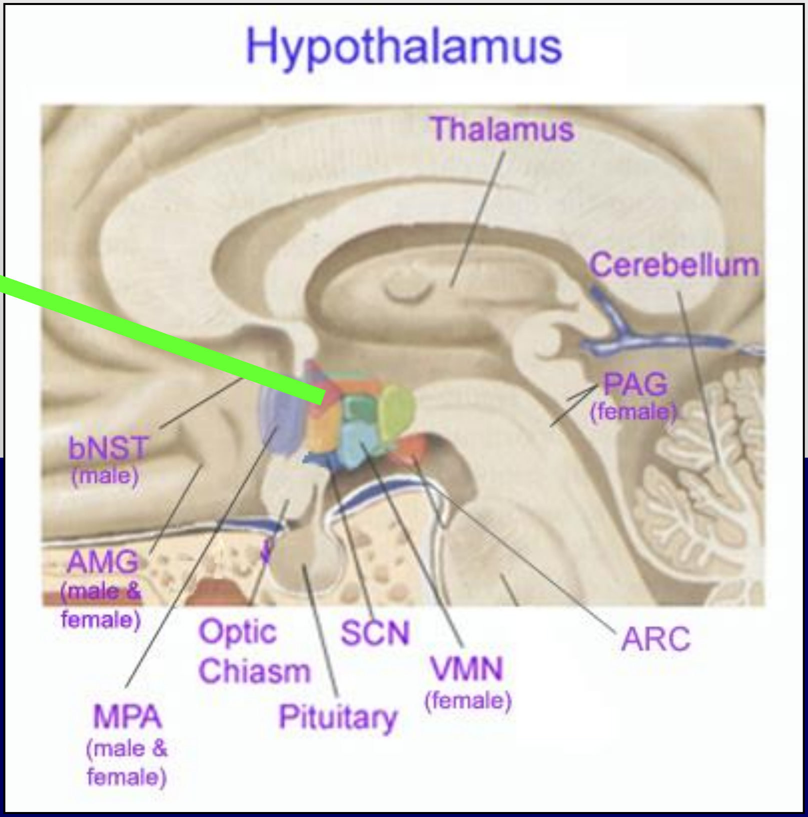


Males : Spherical vs

Elongated in Females

SCN

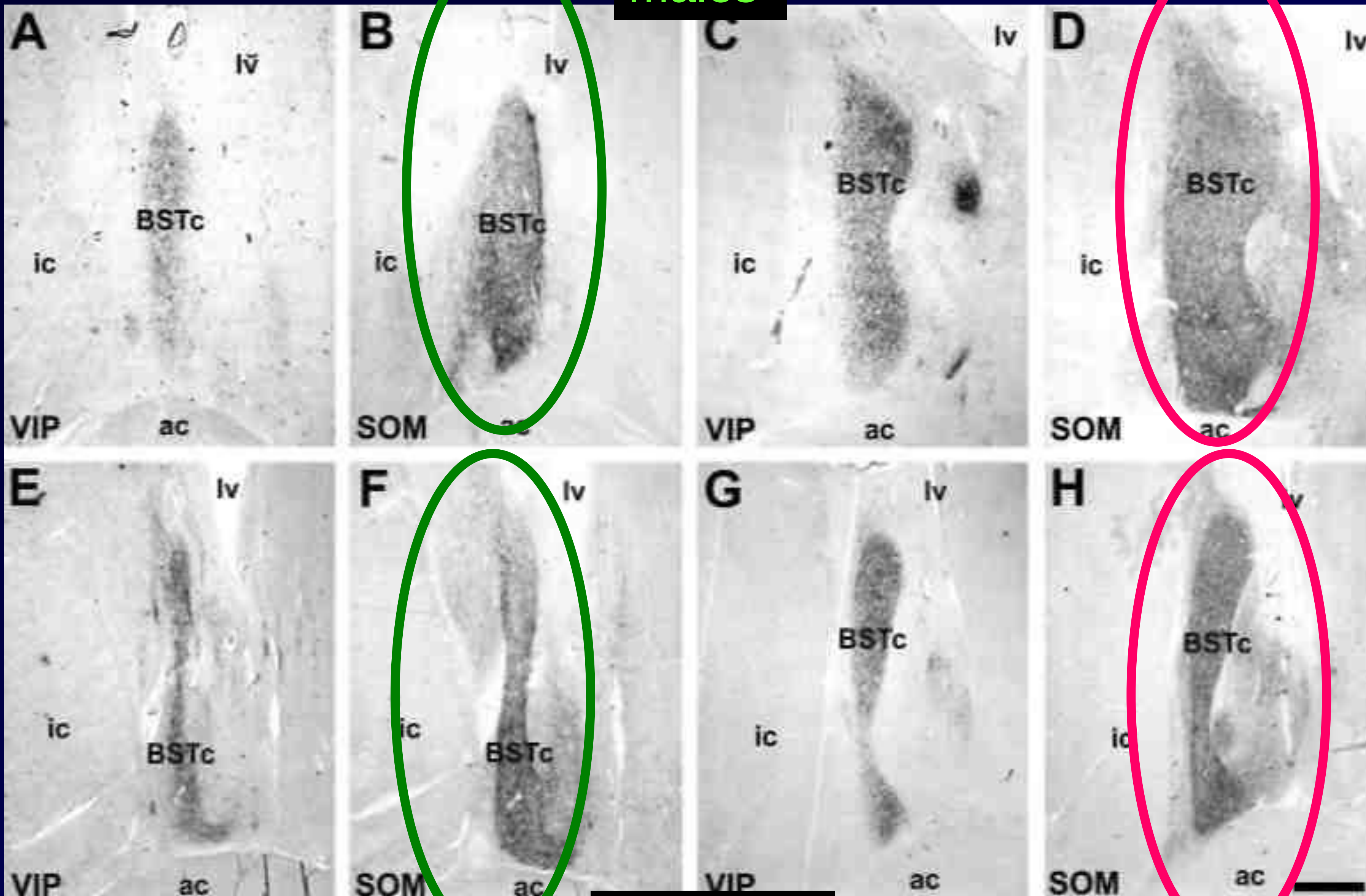
Suprachiasmatic Nucleus



14 y

males

39 y

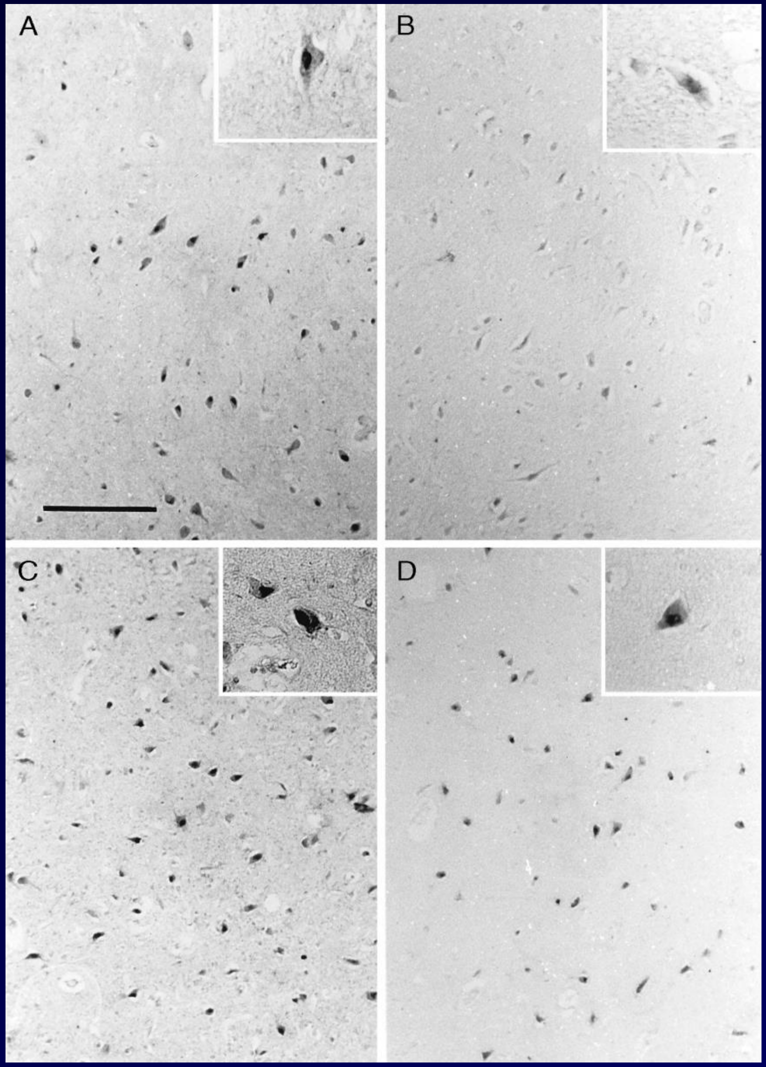


16 y

females

32 y

Sex differences in androgen receptors (AR) of the human mamillary bodies: differences in circulating levels of androgens



A: Heterosexual man

B: Heterosexual woman

C: Homosexual man

D: Woman with high levels of androgens

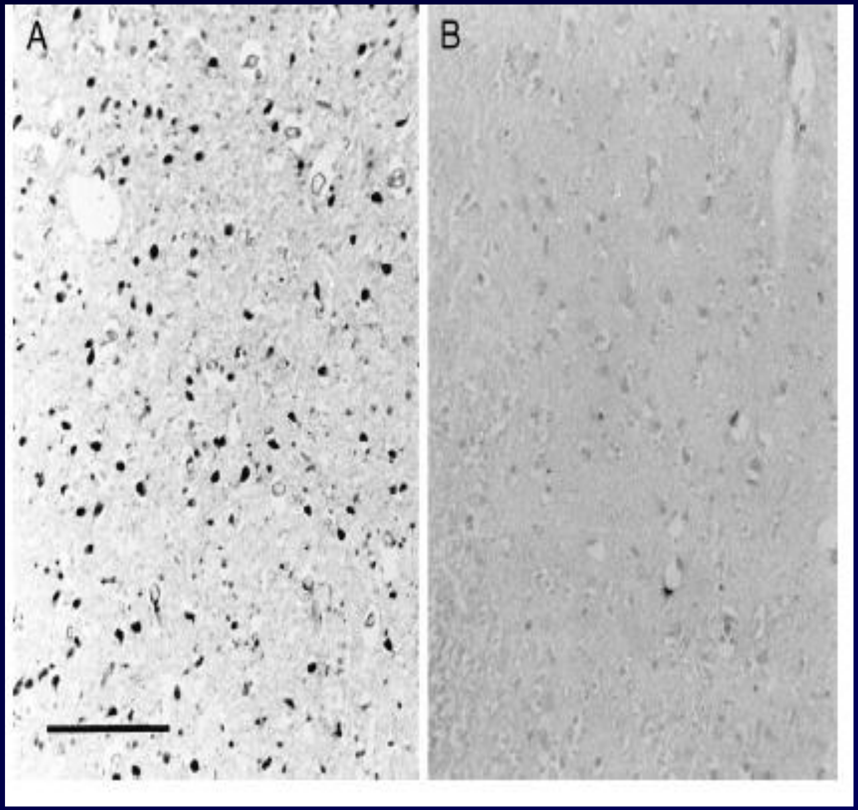
LEGEND

Conclusions:

1. Sex difference in the nuclear AR immunoreactivity between A and B.
2. No difference in the intensity of AR staining between A, C and D.

Kruijver et al, 2001

Sex differences in androgen receptors (AR) of the human mamillary bodies: differences in circulating levels of androgens



A: Non-castrated male-to-female transsexual

B: Castrated male-to-female transsexual

LEGEND

Conclusions:

Sex difference in the nuclear AR immunoreactivity between A and B.

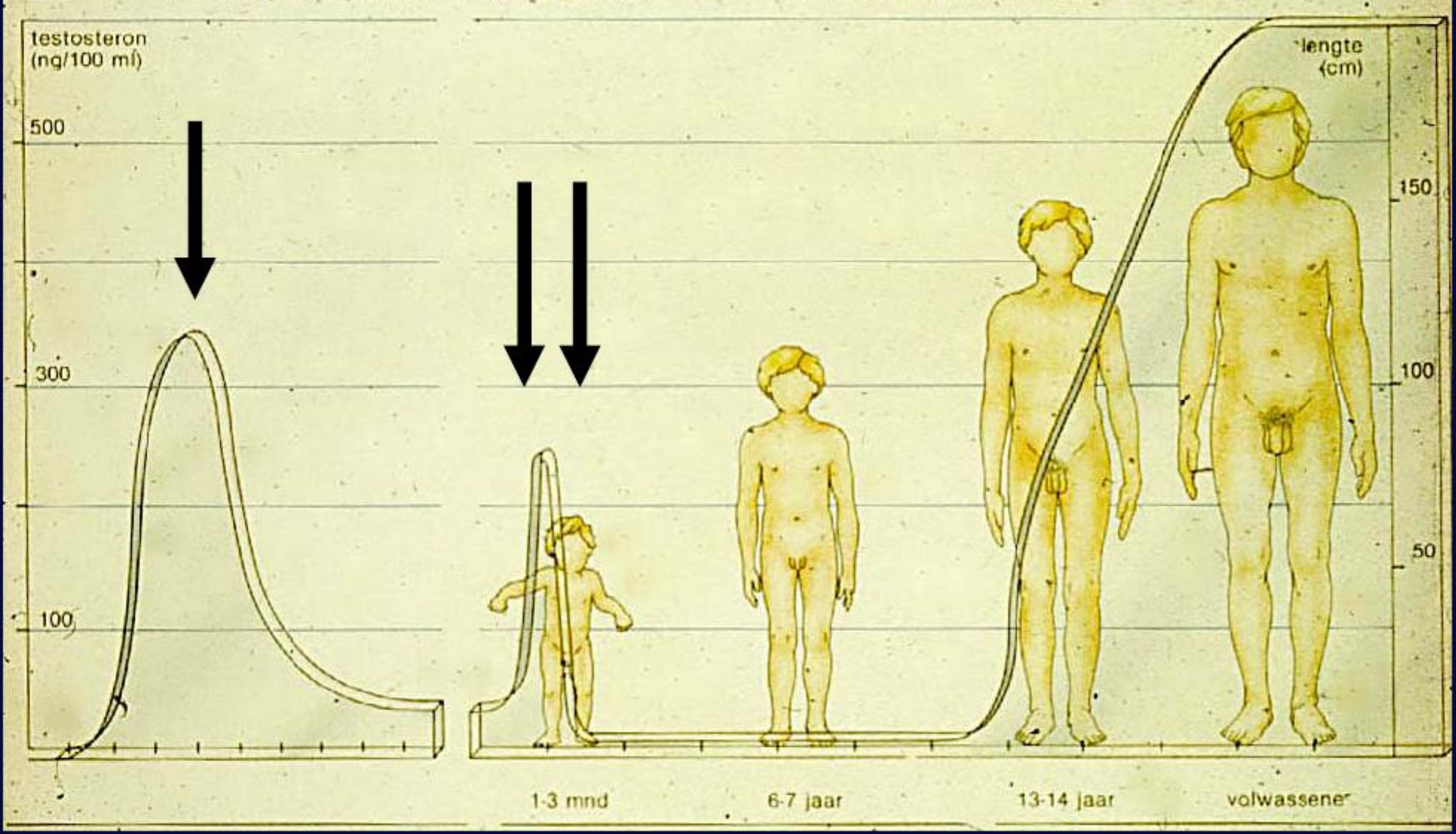
Kruijver et al, 2001

Φυλετικός διμορφισμός ΚΝΣ

Πως και πότε δημιουργείται;

Testosterone Plasma Levels in Men

Testosteronconcentraties in het plasma op verschillende leeftijden (naar Butt en London, Clinics in Endocrinology and Metabolism 1975; 4, 3: 585)



Phoenix et al, 1959: Organizational-activational hypothesis of hormone-driven sex differences in brain and behavior

A. Prenatal/early postnatal transient rise in testosterone: Masculinizes and defeminizes neural circuits in males
B. Absence of the transient rise in testosterone: Feminine neural phenotype
C. Puberty: Testicular and ovarian hormones act on previously sexually differentiated circuits to facilitate expression of sex-typical behaviors in particular social contexts.

Revised Organizational hypothesis: **One** protracted sensitive period for the organizing actions of testosterone

Schulz et al, 2009

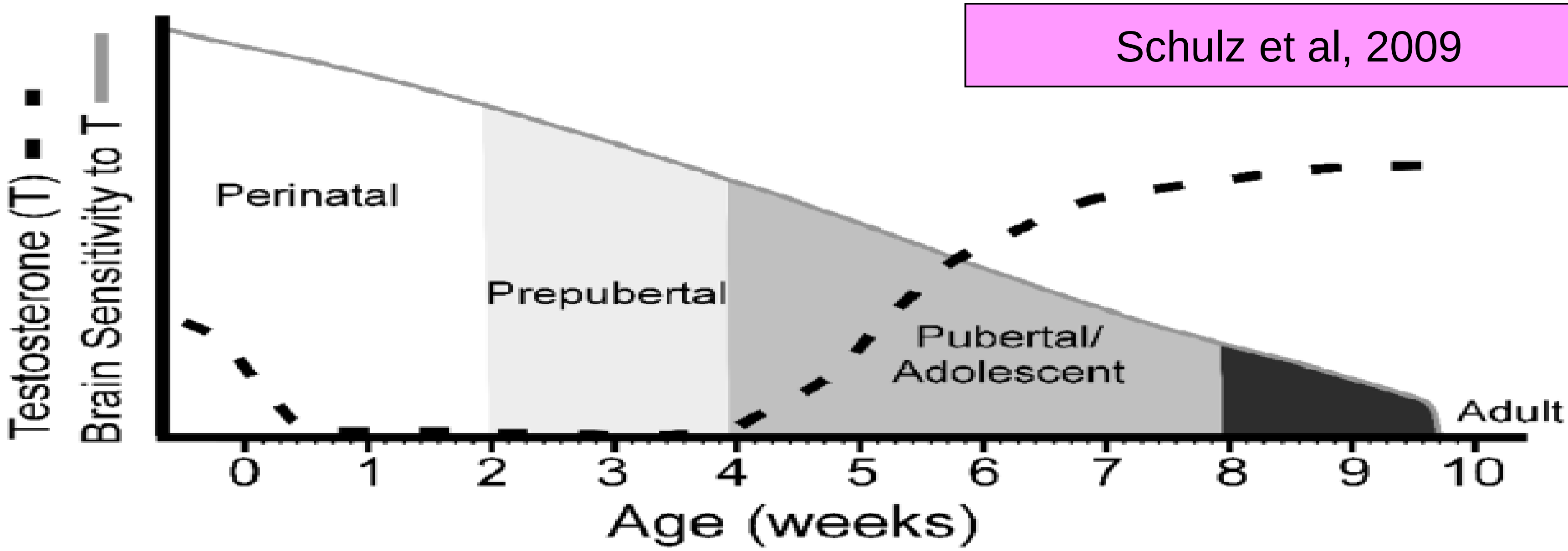
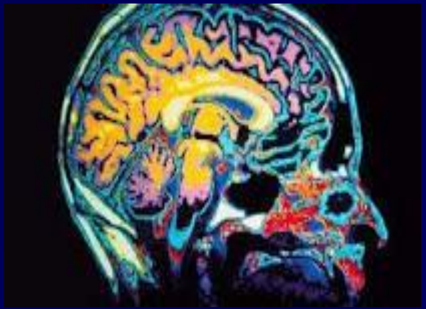


Fig 3.
Illustration depicting the overall findings of our study investigating the effects of early, on-time, and late adolescent testosterone treatments on adult mating behavior. Given that early adolescent testosterone treatment was initiated immediately following the period of sexual differentiation (postnatal day 10), our data suggest that adolescence is part of a protracted sensitive period for the organizing actions of testosterone (area under the solid gray curve). In addition, because early adolescent treatments most effectively organized adult mating behavior, we propose that sensitivity to the organizing actions of testosterone decreases across postnatal development. The dashed line approximates testosterone secretions across development, whereas the solid line depicts decreasing sensitivity to the organizing actions of testosterone across development. Shading approximates the timing of perinatal, prepubertal, adolescent periods in the Syrian hamster.

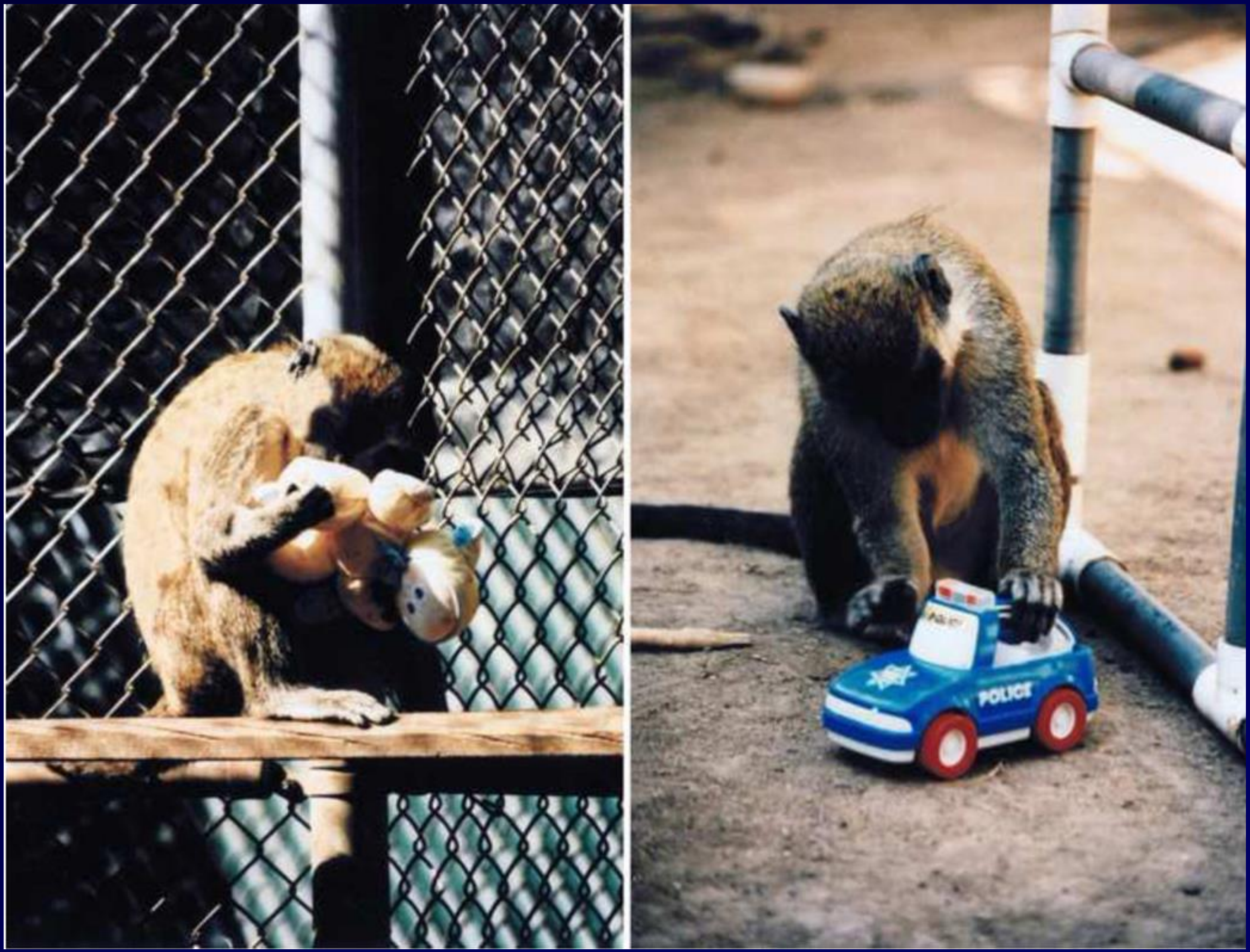
Masculinization of behavioral traits

Organizational effect of prenatal androgen exposure



Sex dimorphism of the central nervous system

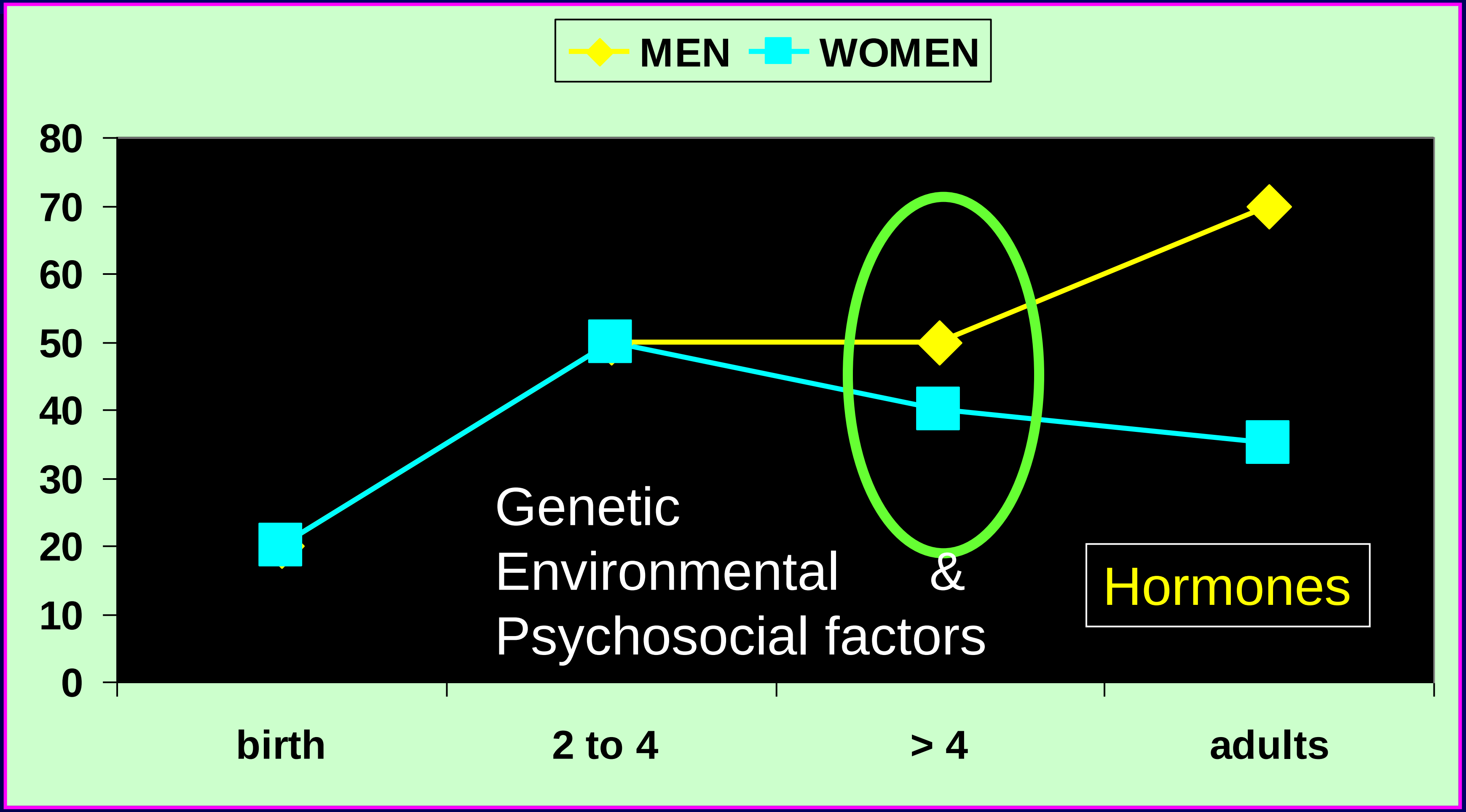
We can not evaluate the organizational effect of prenatal androgen exposure in humans based on animal studies



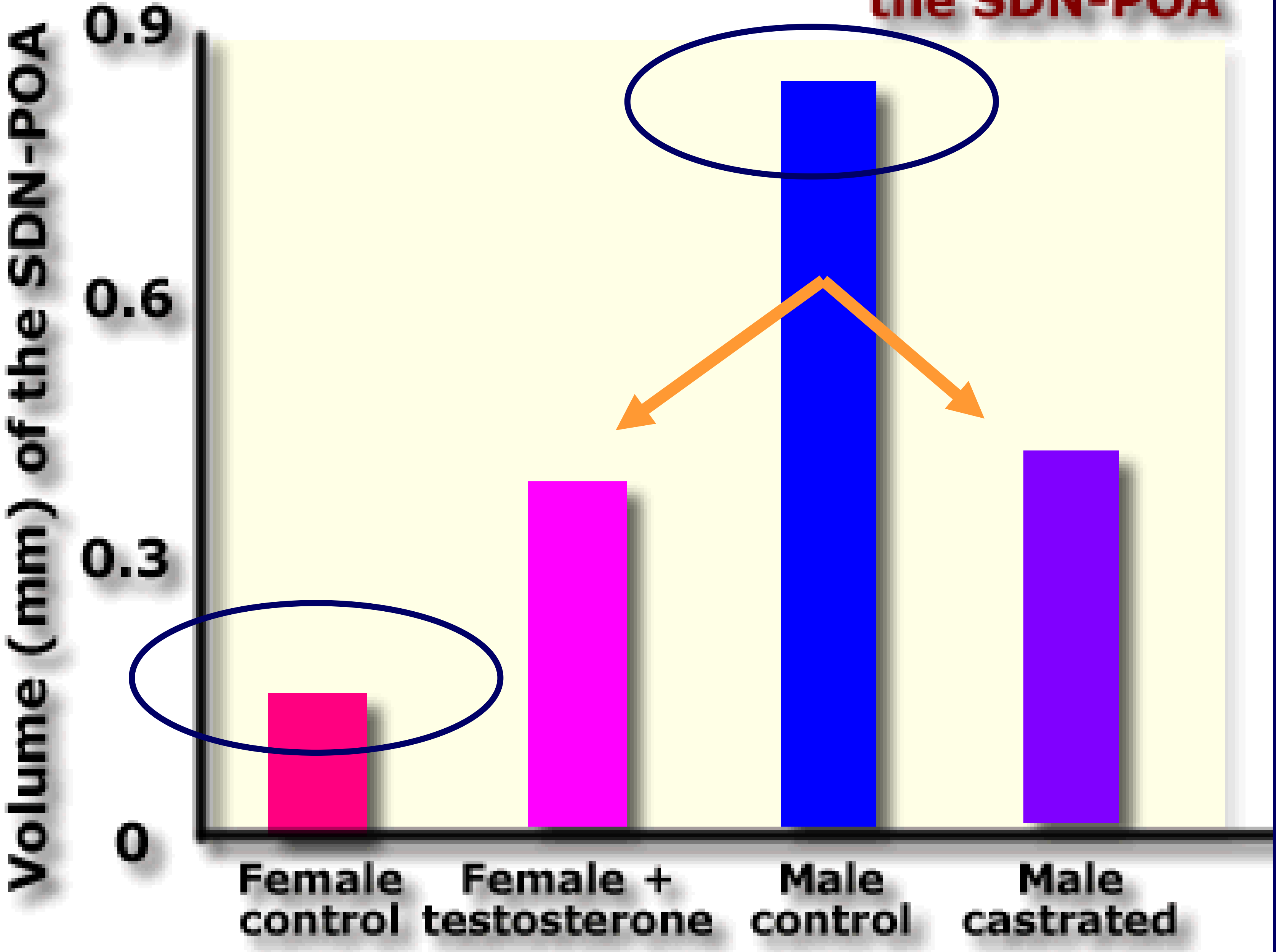
Postnatal period of hypothalamic differentiation

Sexual differentiation of **SDN**

Sexually **D**imorphic **N**ucleus



Neonatal testosterone influences size of the SDN-POA



Intrauterine androgen exposure of the female fetus and behavior

(i) individuals who have genetic disorders that cause abnormalities in the amount or activity of testosterone, beginning prenatally;
(ii) individuals whose mothers were prescribed hormones during pregnancy for medical reasons; and
(iii) individuals with no history of hormone abnormality, but for whom information on prenatal hormone levels is available and can be related to postnatal behaviour.

Causes of hyperandrogenic states in pregnancy

A. Fetal causes

- Congenital adrenal hyperplasia (CAH)

B. Maternal causes

1. Ovarian tumors
2. Non- tumor ovarian conditions (pregnancy luteoma, hyperreactio luteinalis, PCOS)
3. Adrenal tumors (rare)
4. Non-tumor adrenal causes (Cushing’s syndrome, irregular secretion of CRH in the placenta, non-functional adenomas in the cortex of the adrenal glands containing receptors with aberrant activity for CRH)
5. Iatrogenic (preparations containing androgens or progestins)

Congenital Adrenal Hyperplasia as a model of prenatal exposure to androgens

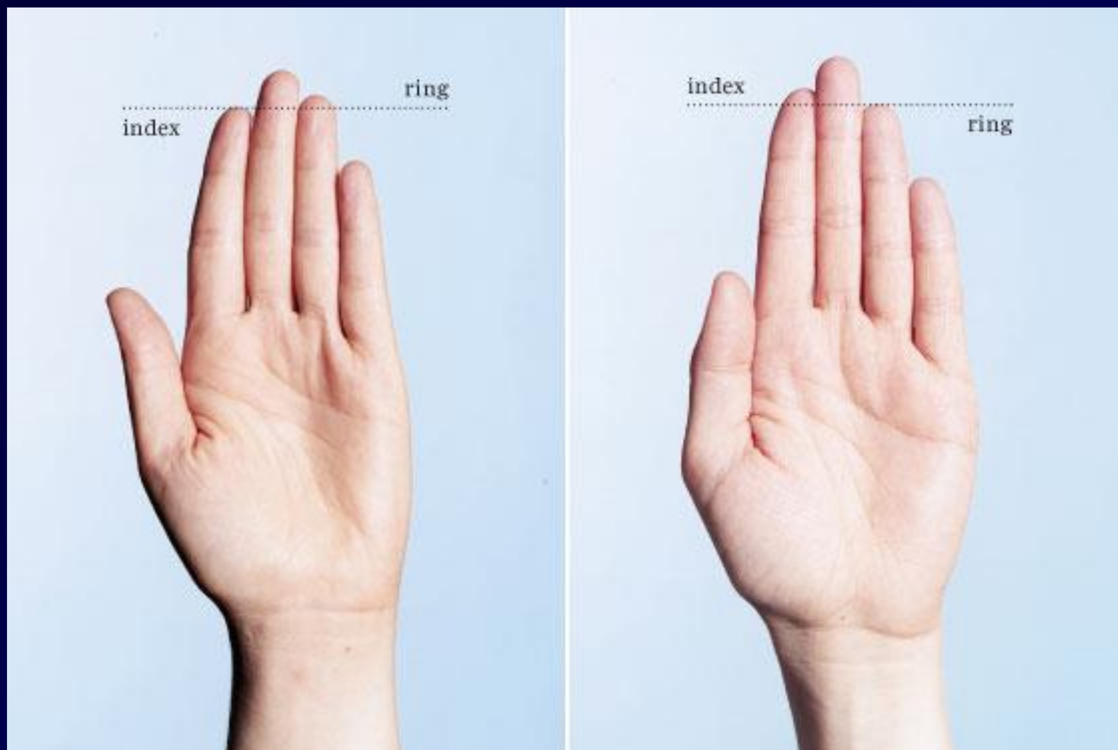
Sizes of sex differences in human behavior/psychological characteristics

Behavior/Psychological characteristic	approximate size in standard deviation units (d)
Core gender identity[23,74]	11.0 to 13.2
Sexual orientation[24,75]	6.0 to 7.0
Childhood Play	
Play with girls' toys[8]	1.8
Play with boys' toys[8]	2.1
Feminine preschool games[76]	1.1
Masculine preschool games[76]	0.7 to 1.8
Playmate preferences[76]	2.3 to 5.6
Composite of sex-typed play (PSAI)[77,78]	2.7 to 3.2
Cognitive and Motor Abilities (adolescents/adults)	
Targeting[37,38,79-81]	1.1 to 2.0
Fine Motor Skill[38,82,83]	0.5 to 0.6
Mental rotations[84,85]	0.3 to 0.9
Spatial perception[84,85]	0.3 to 0.6
Spatial visualization[84,85]	0.0 to 0.6
SAT Mathematics[86]	0.4
Computational skills[86]	0.0
Math concepts[86]	0.0
Verbal fluency[87,88]	0.5
Perceptual speed[89]	0.3 to 0.7
Vocabulary[90]	0.0
SAT Verbal[90]	0.0
Personality (assessed with questionnaires)	
Tendencies to physical aggression[35,91]	0.4 to 1.3
Empathy[34,92]	0.3 to 1.3
Dominance/Assertiveness[92]	0.2 to 0.8

Hines, 2010

Ratio of the length of the second digit divided by the length of the fourth digit (2D:4D):

♂



♀

Prenatal androgens?

Perinatal androgens?

AMH?

Sex chromosomes?

Behavioral?

Ratio of the length of the second digit divided by the length of the fourth digit (2D:4D):

CAH

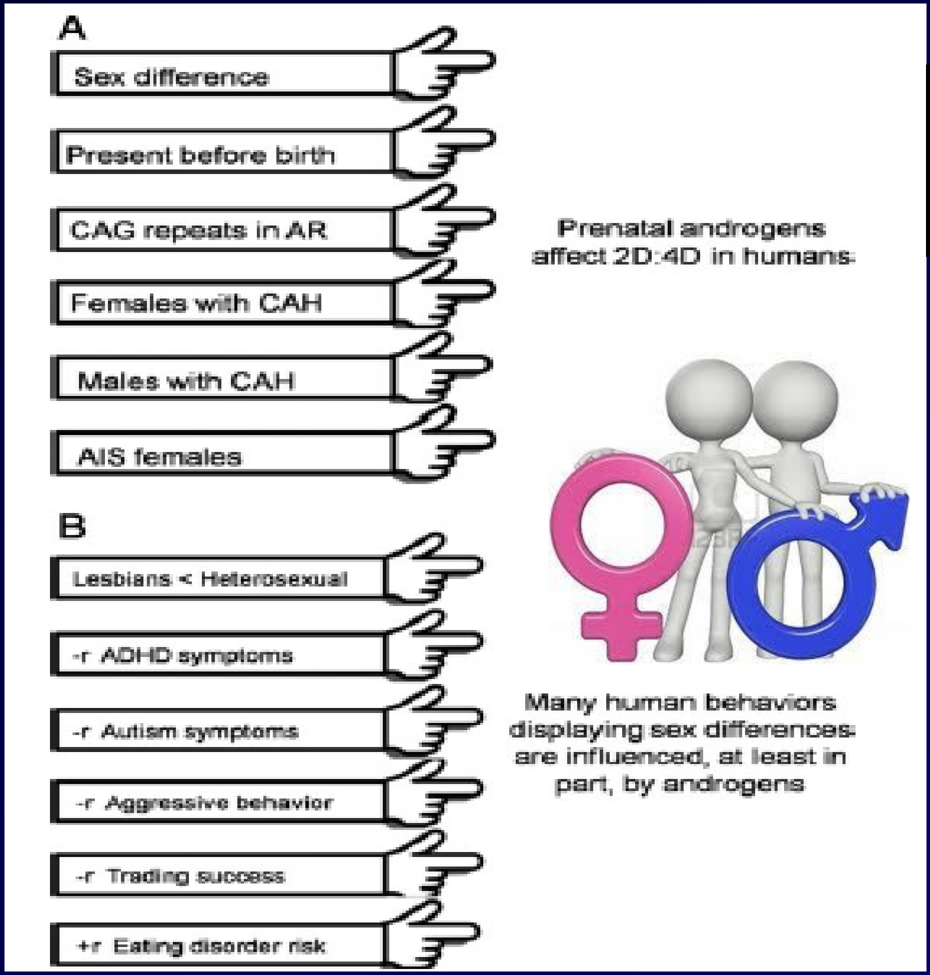
Females with CAH had a significantly smaller 2D:4D on the right hand than did females without CAH.
Males with CAH had a significantly smaller 2D:4D than did males without CAH.
A subset of six males with CAH had a significantly smaller 2D:4D on both hands compared with their male relatives without CAH.
These results are consistent with the idea that prenatal androgen exposure reduces the 2D:4D and plays a role in the establishment of the sex difference in human finger length patterns.

Brown WM, Hines M, Horm Behav 2002

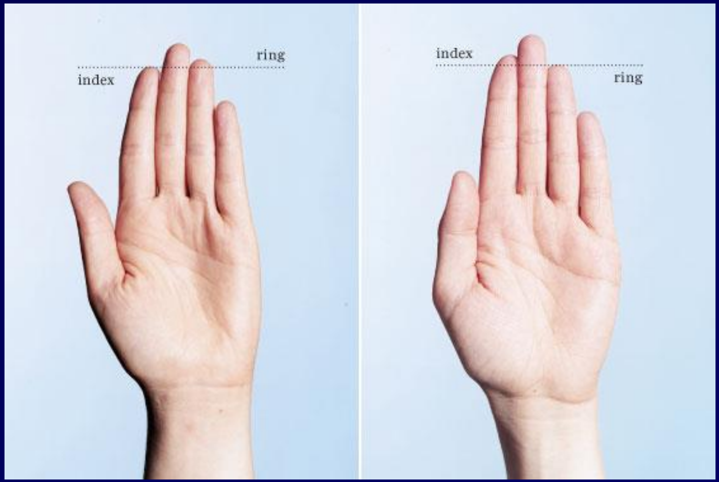
We found lower 2D/4D ratio in female patients with 21-hydroxylase deficiency compared to healthy girls (p=0.000) and equal 2D/4D ratio for female patients when compared to male controls. Male patients with 21-hydroxylase deficiency had significantly lower 2D/4D ratio than female and male controls in the right hand. Healthy boys had lower 2D/4D ratio than healthy girls.

Okten A, Kalyoncu M, Early Hum Dev 2002

Ratio of the length of the second digit divided by the length of the fourth digit (2D:4D): a test of the organizational hypothesis that androgens act early in life to masculinize various human behaviors



Fingerpost reflect total androgenic stimulation rather than just prenatal androgen exposure



Breedlove, 2010

Congenital Adrenal Hyperplasia as a model of prenatal exposure to androgens

- **Low rates of child-bearing in CAH?**
- **Low rates of heterosexual drive in CAH?**

FORMS

	SIMPLE VIRILIZING (SV)	**SALT WASTING (SW)**
PREGNANCY	**60%**	**7%**

Among SV + SW with adequate and heterosexual activity

Low "maternalism" in CAH

↓Interest in getting married -
performing childcare/housewife role

"… Jim and I can't stand children. They' re cute and everything, but I had never had any maternal feeling like that, like I wanted to have a baby… Most people look at babies and think they' re cute and they coo over them. I never felt anything. It' s just a baby. I have cats. Those are my babies…"

Sexual interest in women with CAH

- Low levels of sexual interest and activity associated with low fertility have been reported in women with CAH.

Meyer-Bahlburg, 1999

Possible cause

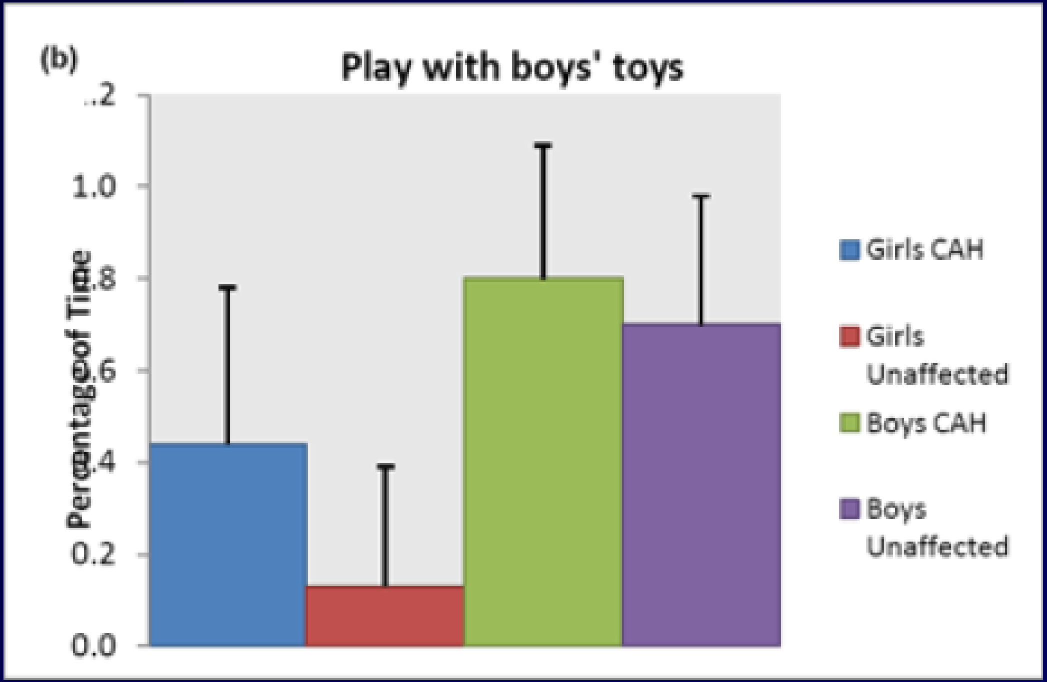
Desensitization hypothesis (Bancroft, 2003)

1. Exposure to high levels of testosterone during fetal and early postnatal life desensitize CNS to testosterone effects in males.
2. If males were as sensitive to CNS effect of testosterone as females, then the behavioral masculinizing effects could be maladaptive.
3. Physiologically, no such desensitization process occurs in females.

Congenital Adrenal Hyperplasia

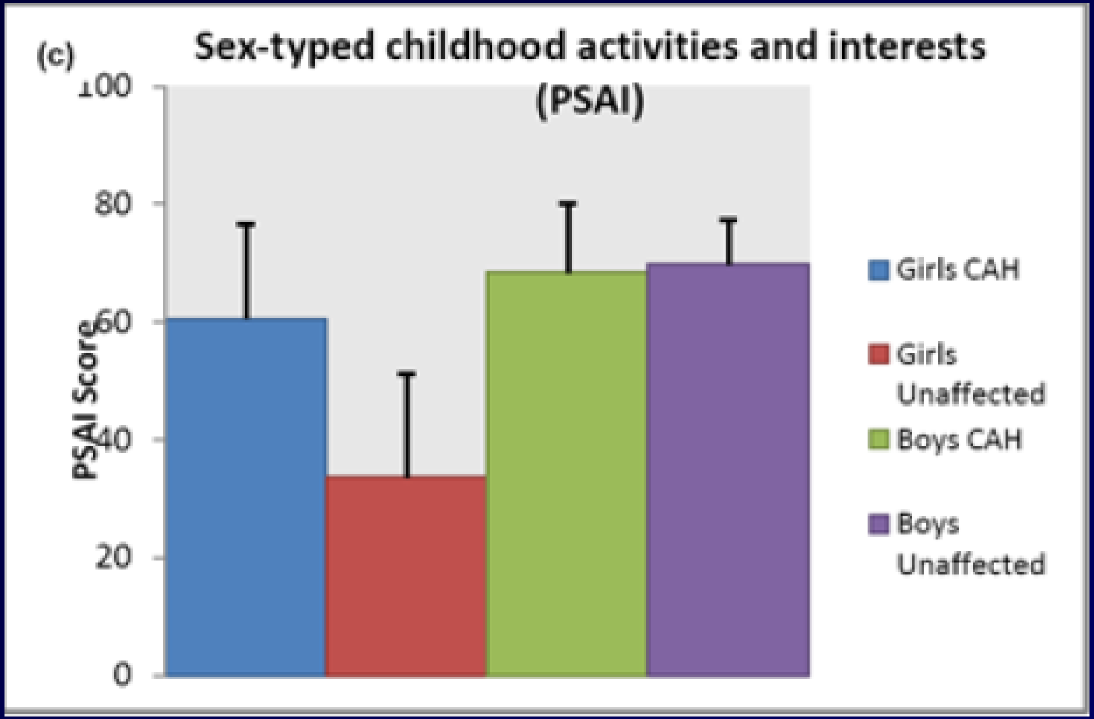
Hines M, Trends Cogn Sc 2010

Congenital Adrenal Hyperplasia



Hines M, Trends Cogn Sc 2010

Congenital Adrenal Hyperplasia



Hines M, Trends Cogn Sc 2010

Sexual orientation in women with CAH

TABLE 2. Relationships and sexuality in the 62 women with CAH and the different *CYP21A2* genotype groups compared to controls

	CAH	Null	I2splice	I172N	Miscellaneous	V281L	Controls
n	62	14	15	25	3	5	62
Relationships							
Partner	38 (61%)	4 (29%)	8 (53%)	21 (84%)		2 (40%)	50 (81%)
P value (patients *vs.* controls)	0.01	0.0004	0.04	NS (0.7)		NS (0.3)	
Not debuted sexually	8 (13%)	2 (14%)	5 (33%)	1 (4%)		0 (0%)	1 (2%)
P value (patients *vs.* controls)	0.02	NS (0.09)	0.0008	NS (0.5)		NS	
Sexual orientation							
Heterosexual	43	5	10	21	2	5	56
Bisexual	7	3	2	1	1	0	0
Homosexual	3	2	1	0	0	0	1
Total	53	10	13	22	3	5	57
No answer	9	4	2	3	0	0	5
Bi/homosexual	19%	50%	30%	5%	33%	0	2%
P value (patients *vs.* controls)	0.005	0.0001	0.02	NS (0.5)	NS (0.1)	NS	

	CAH	controls
Active sexually	52%	71%
Sexual interest	73%	90%

Mutations
1. Null,I2splice: salt-wasting (SW)
2. I172N: simple virilizing (SV)
3. V281L: non-classical (NC)

Frisen et al, 2009

Sexual orientation in women with CAH in correlation with genotype

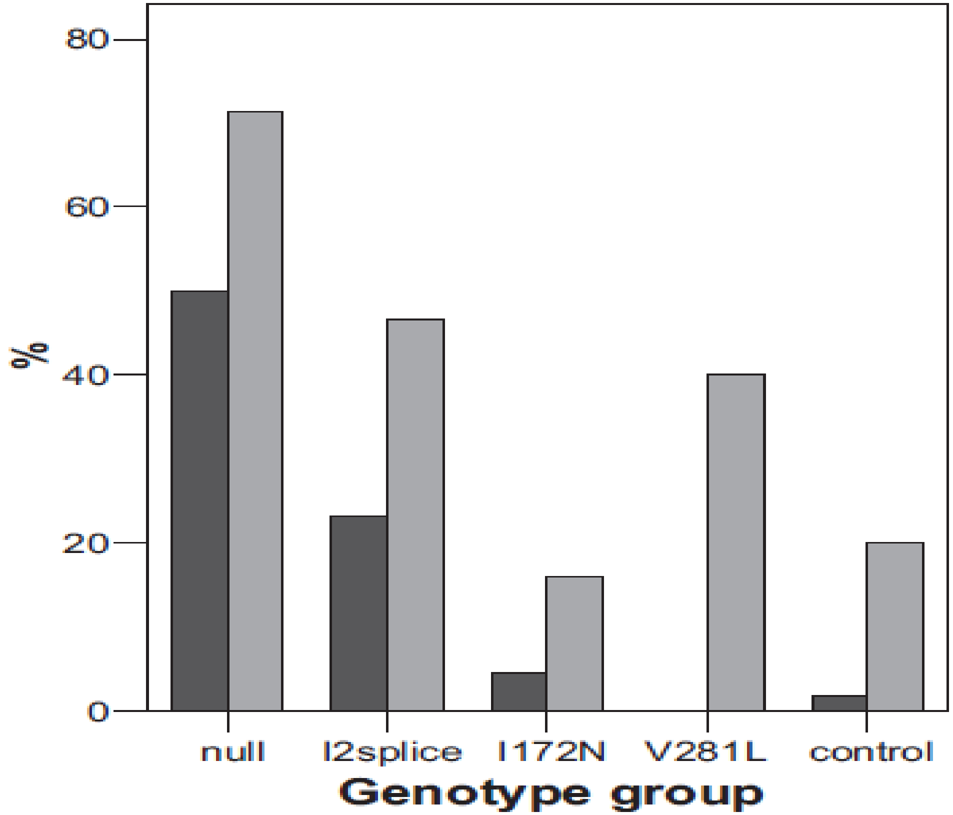


FIG. 2. Women with bi- or homosexual orientation and women with no partner given as percentage for the *CYP21A2* genotype groups and the controls.

Frisen et al, 2009

Testosterone effect of CAH on gender identity is smaller than the effect on sex-typed childhood play behavior and similar to the effect on sexual orientation

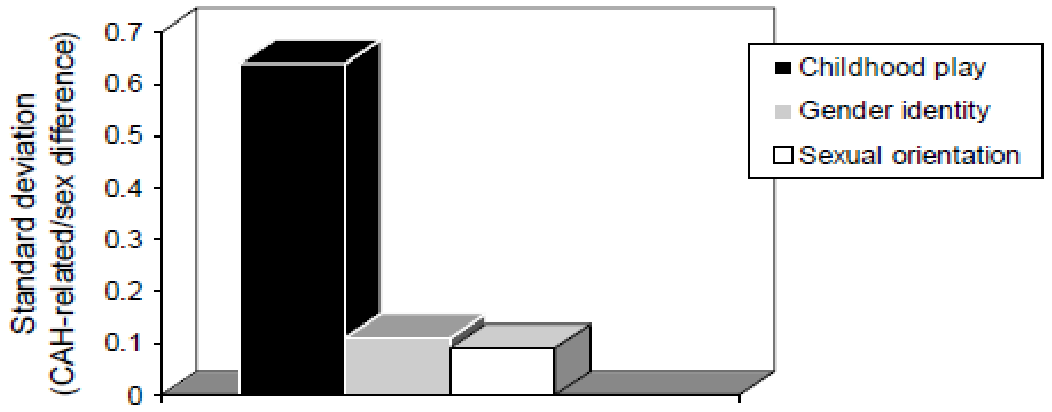


Figure 1 The size of the difference between females with congenital adrenal hyperplasia (CAH) and those without CAH relative to the size of the sex difference in three characteristics: childhood play behaviour (sex-typed toy, activity, temperamental and playmate preferences); sexual orientation (preferences for erotic partners of ... same or the other sex); and core gender identity (sense of self ... male or female). Group differences (CAH versus control; male ... sus female) are expressed in standard deviation units.

Childhood play behaviour: females with CAH moved about 60% of the distance toward mean male-typical behaviour.

Sexual orientation: 10%

Hines, 2006

Occupation and interests in women with CAH in correlation with genotype

TABLE 1. Choice of occupation and leisure activities in the 62 women with CAH and the different *CYP21A2* genotype groups compared to controls

	CAH	Null	I2splice	I172N	V281L	Controls
n	62	14	15	25	5	62
Occupation						
Male dominant	13/43	6/11	3/12	2/17	2/3	6/47
P value (patients *vs.* controls)	0.04	0.006[a]	NS (0.3)	NS (0.7)	NS	
Extreme male dominant	6/43	5/11	1/12	0/17	0/3	1/47
P value (patients *vs.* controls)	0.04	0.0005[b]	NS (0.4)	NS	NS	
Females in occupation (%)	50	35	48	61	41	63
P value (patients *vs.* controls)	0.009	0.01	NS (0.1)	NS (0.6)	NS	
Interests						
Sports	47/57	12/13	10/14	20/25	5/5	41/60
P value (patients *vs.* controls)	NS (0.06)	NS (0.07)[c]	NS (0.5)	NS (0.2)	NS	
Rough sports	42/57	12/13	10/14	17/25	3/5	30/60
P value (patients *vs.* controls)	0.007	0.004[d]	NS (0.1)	NS (0.1)	NS	
Motor vehicles	8/57	4/13	3/14	1/25	0/5	0/60
P value (patients *vs.* controls)	0.002	0.000	0.006	NS (0.3)	NS	

Mutations
1. Null,I2splice: salt-wasting (SW)
2. I172N: simple virilizing (SV)
3. V281L: non-classical (NC)

Frisen et al, 2009

Occupation and interests in women with CAH in correlation with genotype

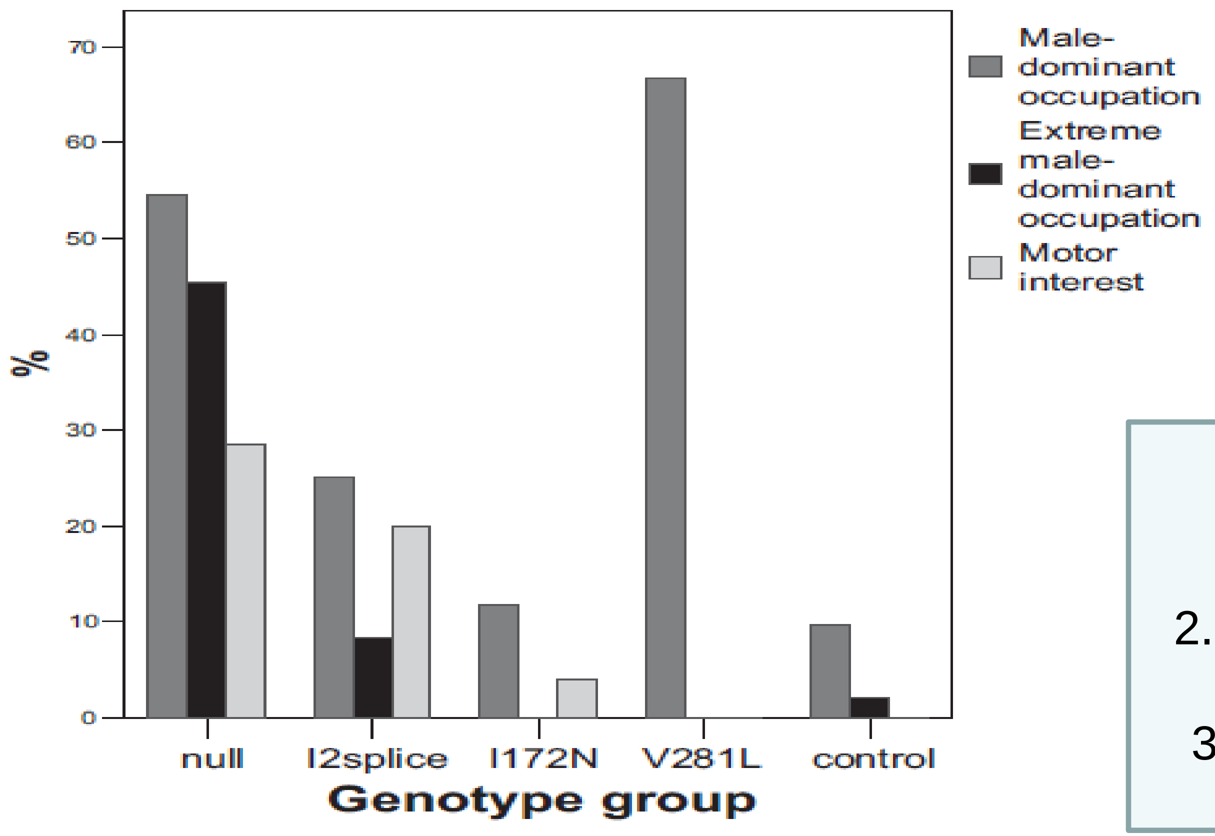


FIG. 1. Male-dominant occupations (≤25% females in occupation), extreme male-dominant occupations (≤11% females in occupation) and motor vehicles as main interest, given as the percentage for the different *CYP21A2* genotype groups and the controls.

Mutations

1. Null,I2splice: salt-wasting (SW)
2. I172N: simple virilizing (SV)
3. V281L: non-classical (NC)

Frisen et al, 2009

Core gender identity, sexual orientation and recalled childhood gender role behavior in women with CAH

Table 1. Control Variables and Psychosexual Outcomes in Women and Men With and Without CAH (Means + *SD*)

	Women		Men	
	CAH (n = 16)	Control (n = 15)	CAH (n = 9)	Control (n = 10)
		Control variables		
Age (years)	23.6+6.7	22.7+3.4	28.1+8.4	24.3+7.8
Vocabulary	8.19+1.51	9.07+1.62	9.00+2.45	8.90+2.01
		Psychosexual outcomes		
Recalled childhood gender role behavior [a]	60.5+16.1***	33.6+17.6	68.3+11.8	69.8+7.4***
Core gender identity [b] (past 12 months)	5.44+3.01*	3.93+1.28	3.22+0.67	3.80+1.13
Core gender identity [b] (lifetime)	6.75+4.84*	4.27+1.22	3.44+0.88	4.20+1.14
Sexual orientation[c] (past 12 months)	3.75+2.62*	2.27+0.59	2.44+1.33	2.10+0.32
Sexual orientation[c] (lifetime)	3.69+2.60*	2.33+0.72	2.22+0.67	2.20+0.42

[a] Numbers of participants for recalled childhood gender role behavior = 14 women with CAH, 11 control women, 8 men with CAH, and 8 control men. [b] Scores can range from 3 to 21. Lower scores indicate stronger identification with the assigned gender. [c] Scores can range from 2 to 10. Lower scores indicate stronger heterosexual orientation.

* Differs from mean for control women, $p < .05$. *** $p < .001$.

Hines et al, 2004

Those girls who are most behaviorally masculinized as children are also the most likely to evolve a bisexual or homosexual orientation as adults

Gender identity in women with CAH

TABLE 1. Frequency of male-typical responses to items on the gender identity interview

	CAH girls (n = 43)	Tomboys (n = 7)	Control girls (n = 29)	Significant group differences
1. Prefers short hair	10 (23%)	3 (43%)	6 (21%)	
2. Does not like dresses	25 (58%)	3 (43%)	10 (35%)	cah/ctl[a]
3. Better to be boy	2 (5%)	2 (29%)	0 (0%)	cah/tb[a], tb/ctl[b]
4. Not happy as girl	4 (9%)	3 (43%)	0 (0%)	cah/tb[a], tb/ctl[c]
5. Wishes to be boy	12 (28%)	3 (43%)	5 (17%)	
6. Try boy for a while	23 (54%)	5 (71%)	11 (38%)	
7. Boy forever	1 (2%)	3 (43%)	0 (0%)	cah/tb[c], tb/ctl[c]
8. Rather be father	2 (5%)	3 (43%)	0 (0%)	cah/tb[c], tb/ctl[c]
9. Pretends male	9 (21%)	5 (71%)	2 (7%)	cah/tb[b], cah/ctl[b], tb/ctl[c]

cah, Girls with CAH; tb, tomboys; ctl, control girls.
Group differences on items scored 0, 1, or 2 tested by χ^2, [a] $P < 0.10$; [b] $P < 0.05$; [c] $P < 0.01$.

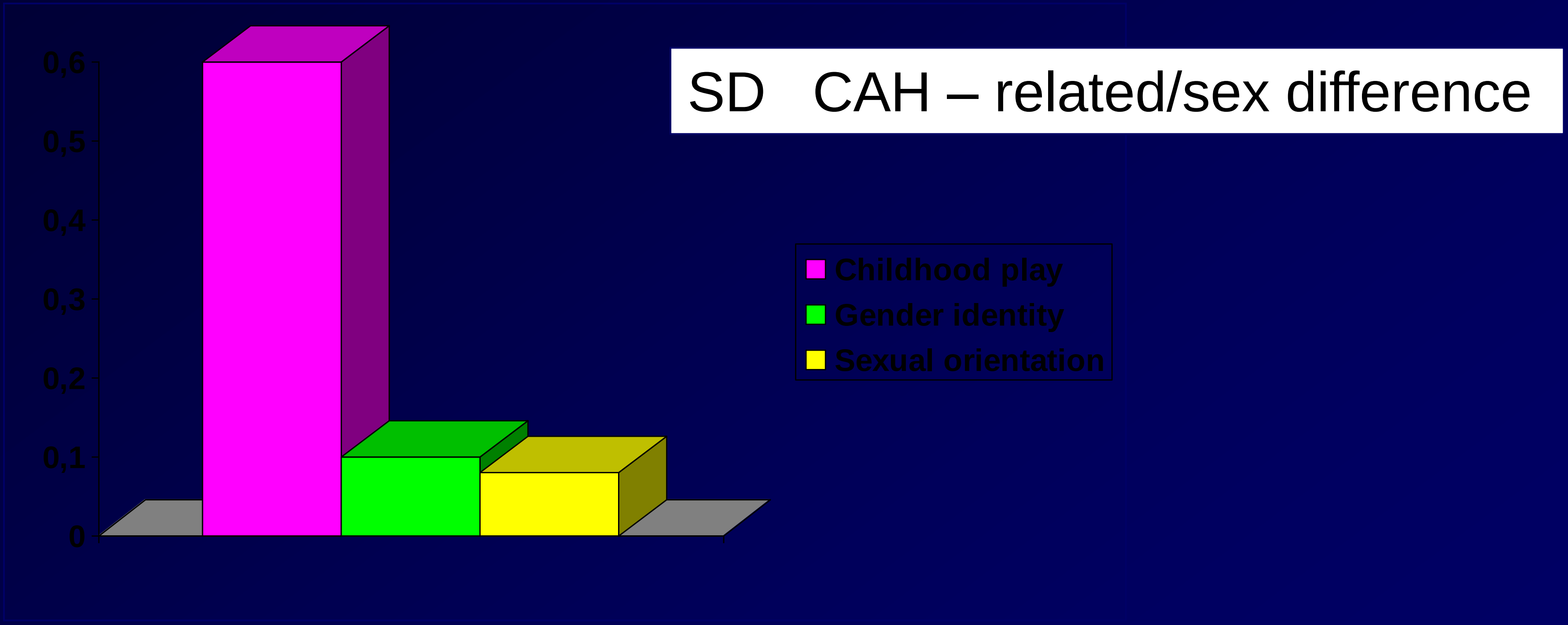
Berenbaum et al, 2003

Gender dysphoria and gender change in chromosomal females with CAH

- Patients raised as females: 94.8% later developed a gender identity as girls and did not feel gender dysphoric.
- 5.2% of those girls, expressed gender identity dysphoria.

- Among patients raised as males, 12.1% of those expressed gender identity problems.

Difference between females with CAH and those without CAH relative to the size of the sex difference in 3 characteristics



Gender identity and gender role

5α Reductase deficiency as a model of prenatal exposure to androgens

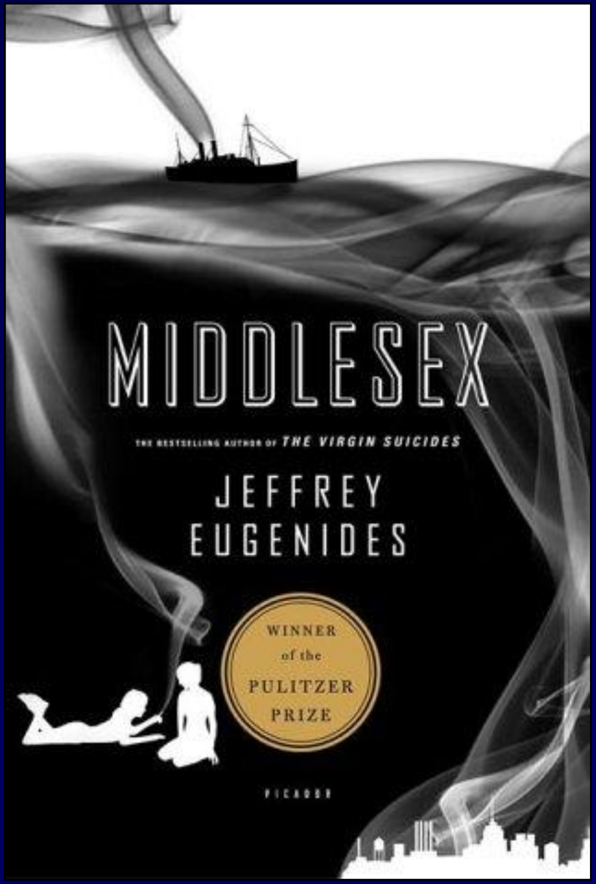
Prenatal Hormones and Sexual Orientation

5-α Reductase deficiency

Clinical presentation

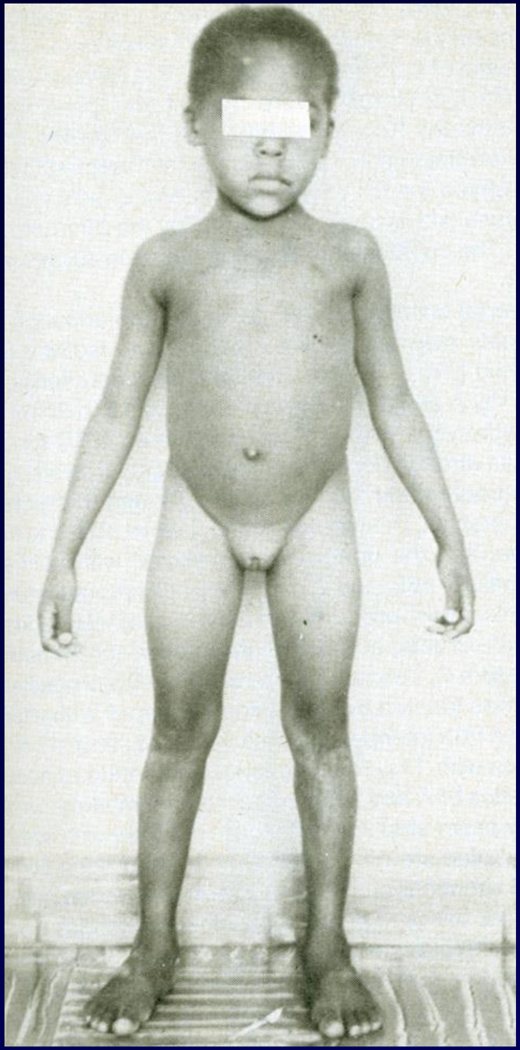
46 XY neonate with

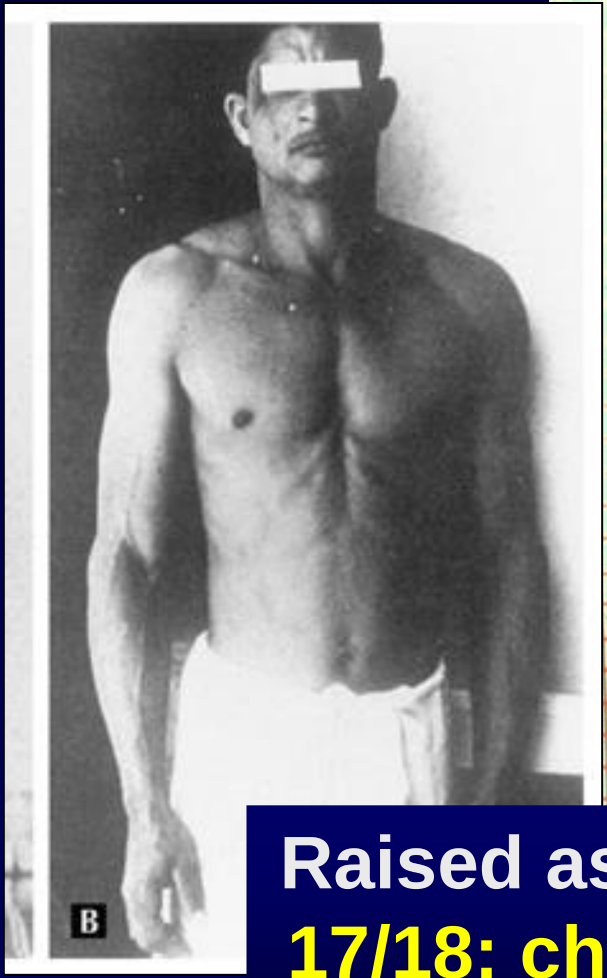
- Female phenotype
- Ambiguous genitalia
- Blind vagina

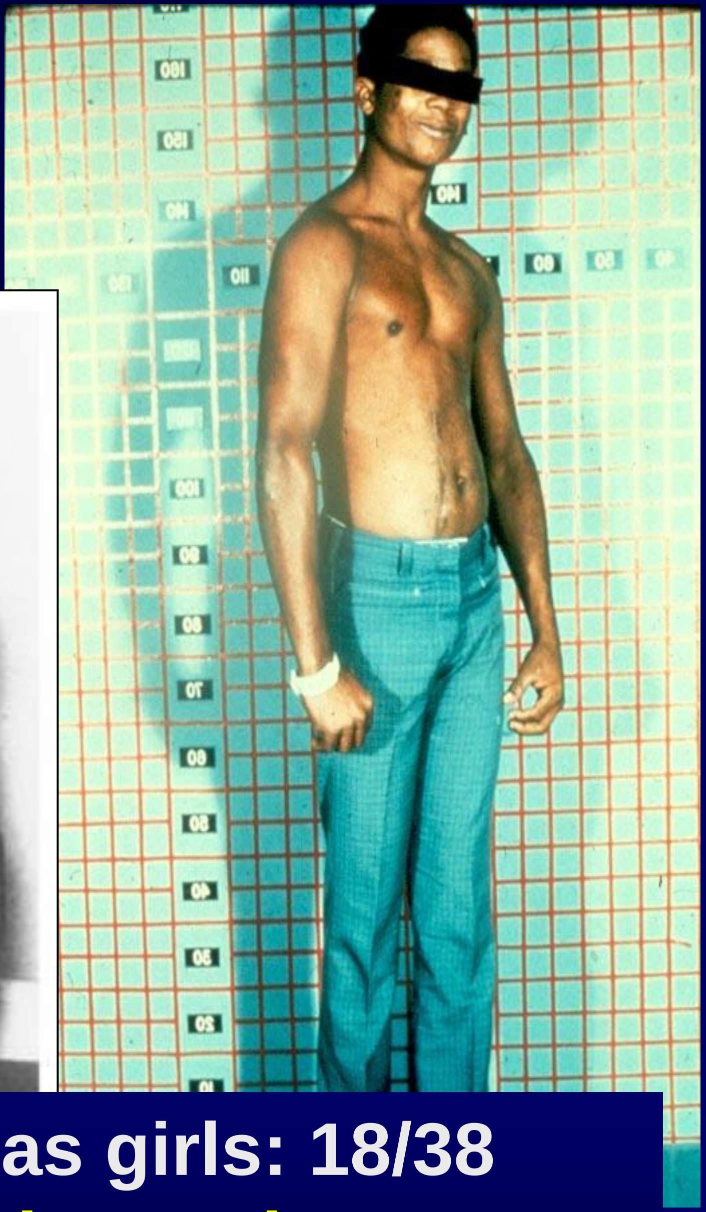


Bifid scrotum, Urogenital sinus, Small phallus.

Virilization at puberty
Gender change







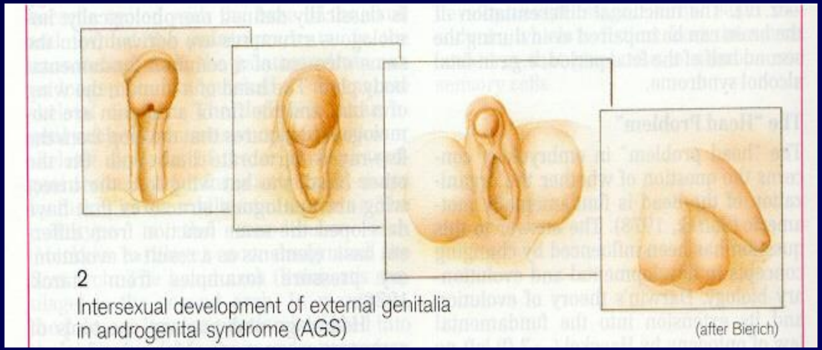
Raised as girls: 18/38
17/18: changed to a male-gender role

Androgen Insensitivity Syndrome (AIS) as a model of prenatal exposure to androgens

Androgen role in male gender identity

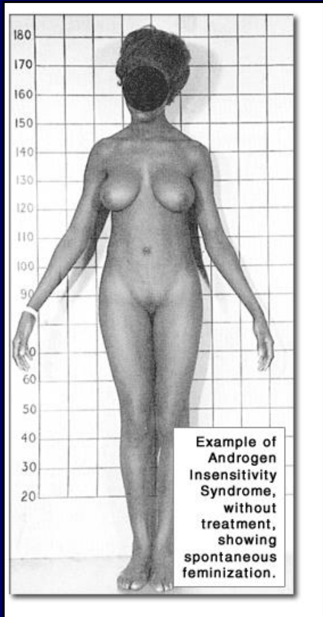
- Gender: Gender identity (self estimation)
  Gender role (objective estimation)
  Sexual orientation (hetero- or homosexual)
- Female gender identity: presence of ovaries or lack of gonads (gonadal dysgenesis)
- Male gender identity: testicular issue irrespective of female or hermaphrodite (intersex) phenotype.
- Complete androgen insensitivity syndrome: Female gender identity
- Partial androgen insensitivity syndrome:

  Female or male gender identity.



2
Intersexual development of external genitalia in androgenital syndrome (AGS)
(after Bierich)

Kula et al, 2000



Ταυτότητα φύλου και ΚΝΣ

Het MAN

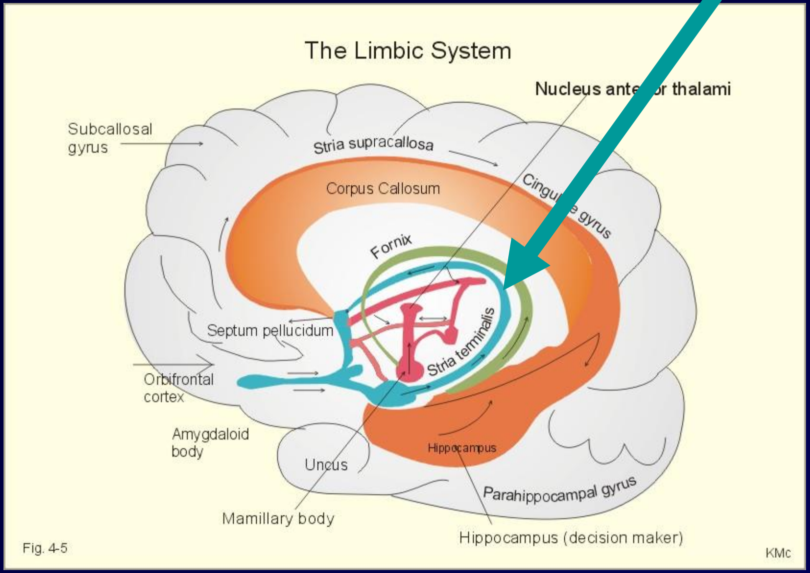
Het FEMALE

Male to female transsexuals have female SOM neuron numbers in BSTc

Hom MAN

M to F TRANS

Kruijver JCEM 2000



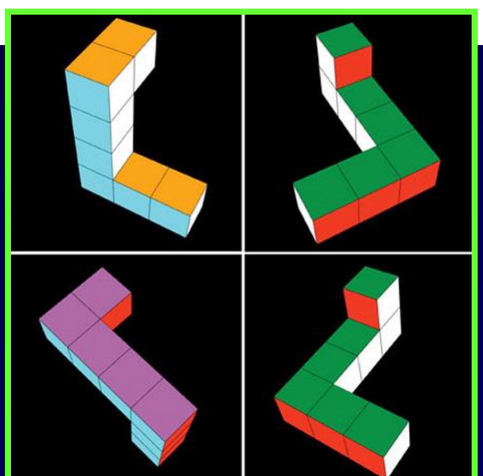
BST Bed nucleus of the Stria Terminalis

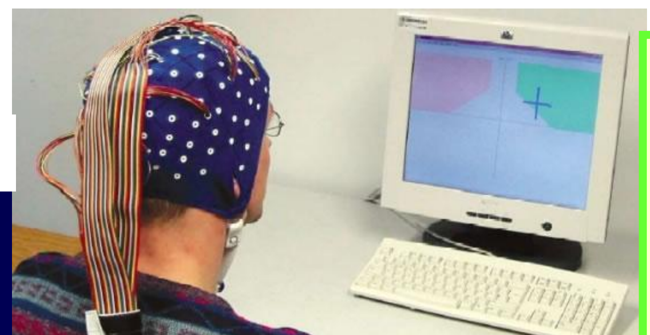
- Males : increased size and number of neurons
- Male to Female transsexuals have 1. female size and 2. number of neurons

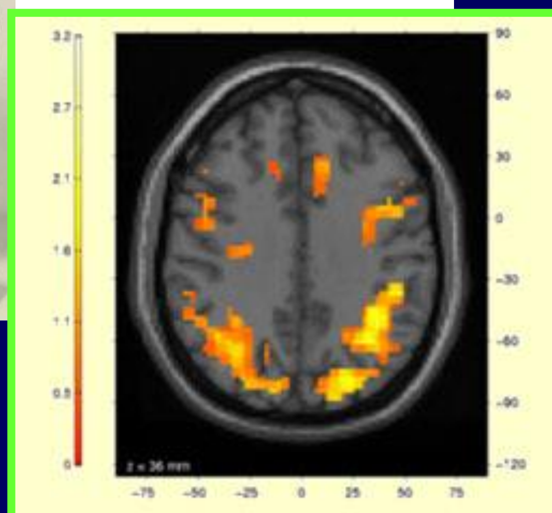
Sex atypical cerebral asymmetry and functional connections in Transsexuals ? Linked to neurobiological entities

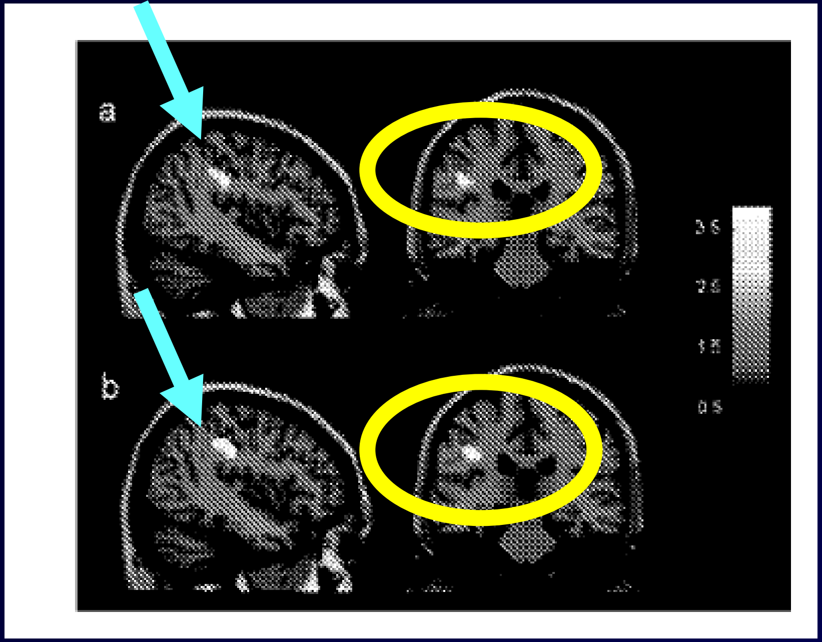
Neuroimaging Differences in Spatial Cognition between Men and Male-to-Female Transsexuals Before and During Hormone Therapy

Schoning S. J Sex Med 2009









Before Hormonal treatment

After Hormonal treatment

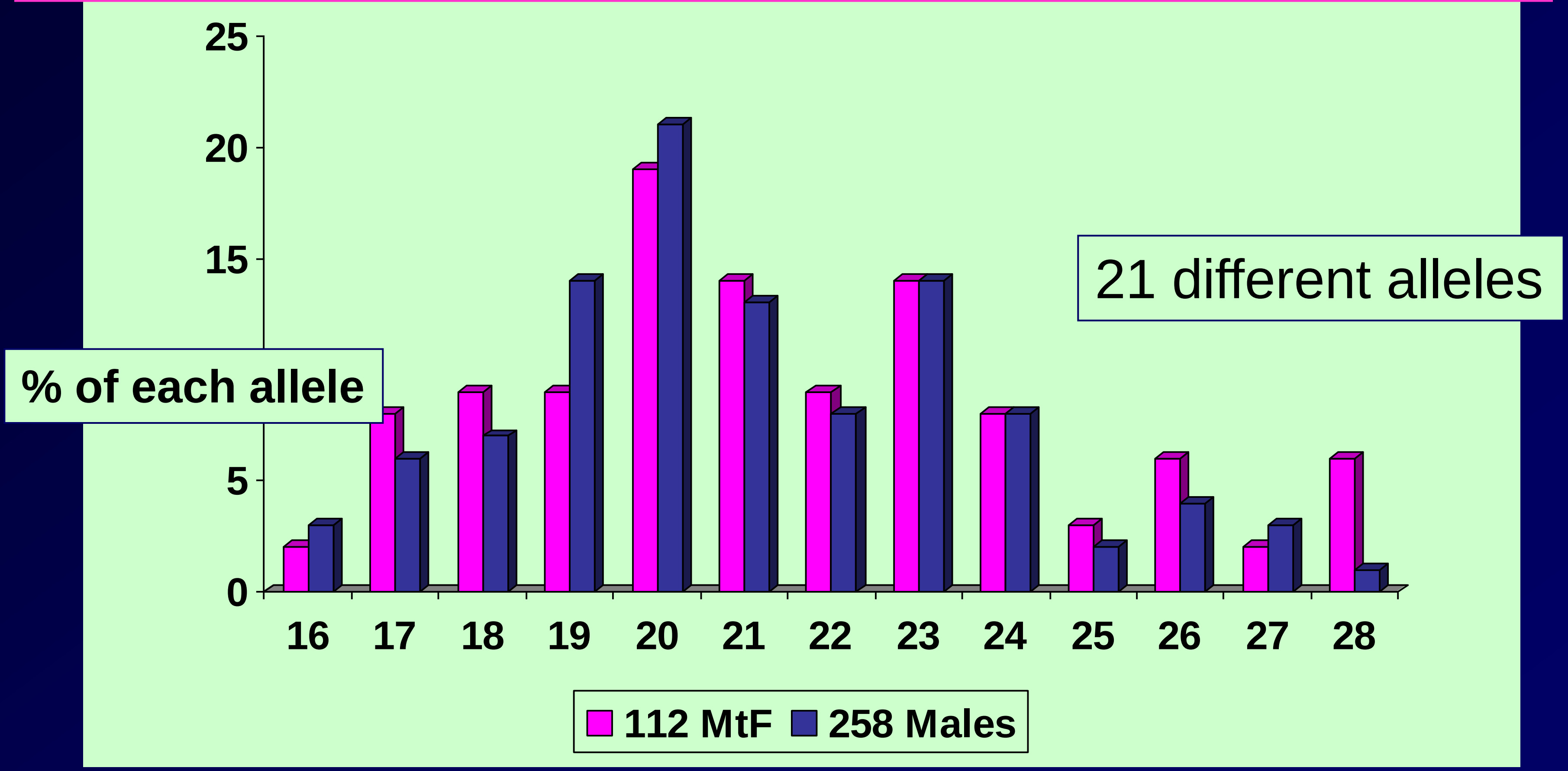
Trans show cortical activation patterns for a mental rotation distinct from their biological sex

a priori Neuroimaging differences
in spatial cognition between MEN and M to F trans
caused by different Neurobiological processes,
which remain stable over hormonal therapy

Androgen Receptor repeat length polymorphism associated with Male to Female Transsexualism

Hare L. Biol Psychiatry 2009

MTF trans have significantly longer mean repeat lengths



Number of CAG repeats in the Androgen Receptor gene

Σεξουαλικότητα και ΚΝΣ

Michael Crichton (2003): "…the work of science has nothing whatever to do with consensus.

Consensus is the business of politics.

Science, on the contrary, requires only one investigator who happens to be right, which means that he or she has results that are verifiable by reference to the real world. In science consensus is irrelevant. **What is relevant are reproducible results. The greatest scientists in history are great precisely because they broke with the consensus** . . . There is no such thing as consensus science. If it's consensus, it isn't science. If it's science, it isn't consensus…

Consensus is invoked only in situations where the science is not solid enough"

Προγεννητικοί παράγοντες που πιθανώς επηρεάζουν τον σεξουαλικό προσανατολισμό

Swaab, Best Practice&Research Clinical endocrinology&Metabolism,2007

Γενετικοί

Ορμόνες

Χημικοί

Ανατομικοί

Κοινωνικοί

Ανοσολογικοί

Παιδιά από οικογένειες transsexual ή ομοφυλοφίλων δεν εμφανίζουν διαταραχή σεξουαλικού προσανατολισμού

Males : Spherical vs

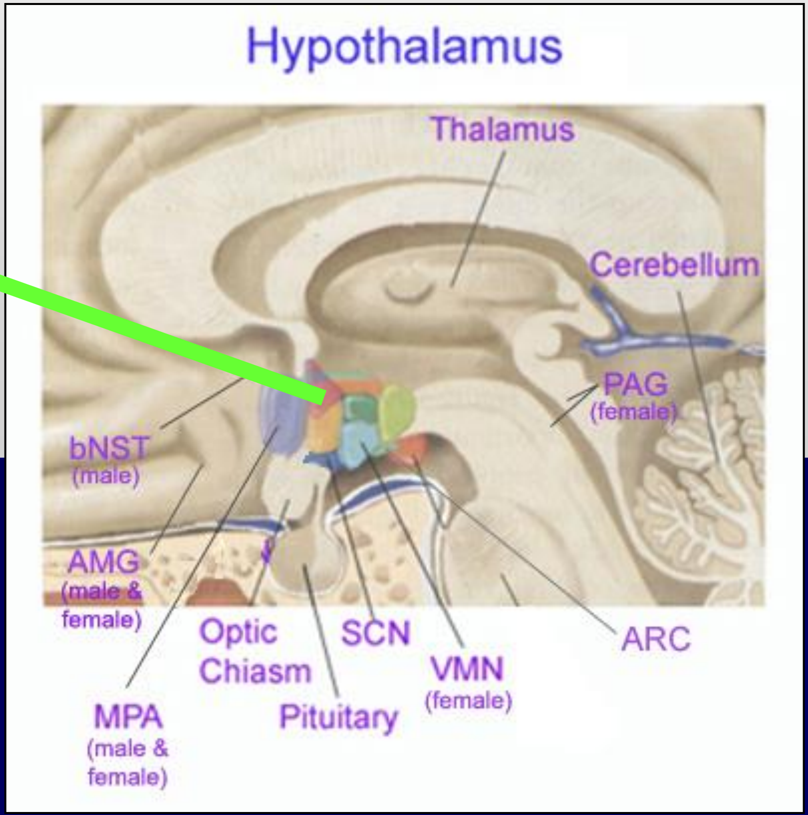
Elongated in Females

Homo- twice as many cells vs

Hetero- sexual men

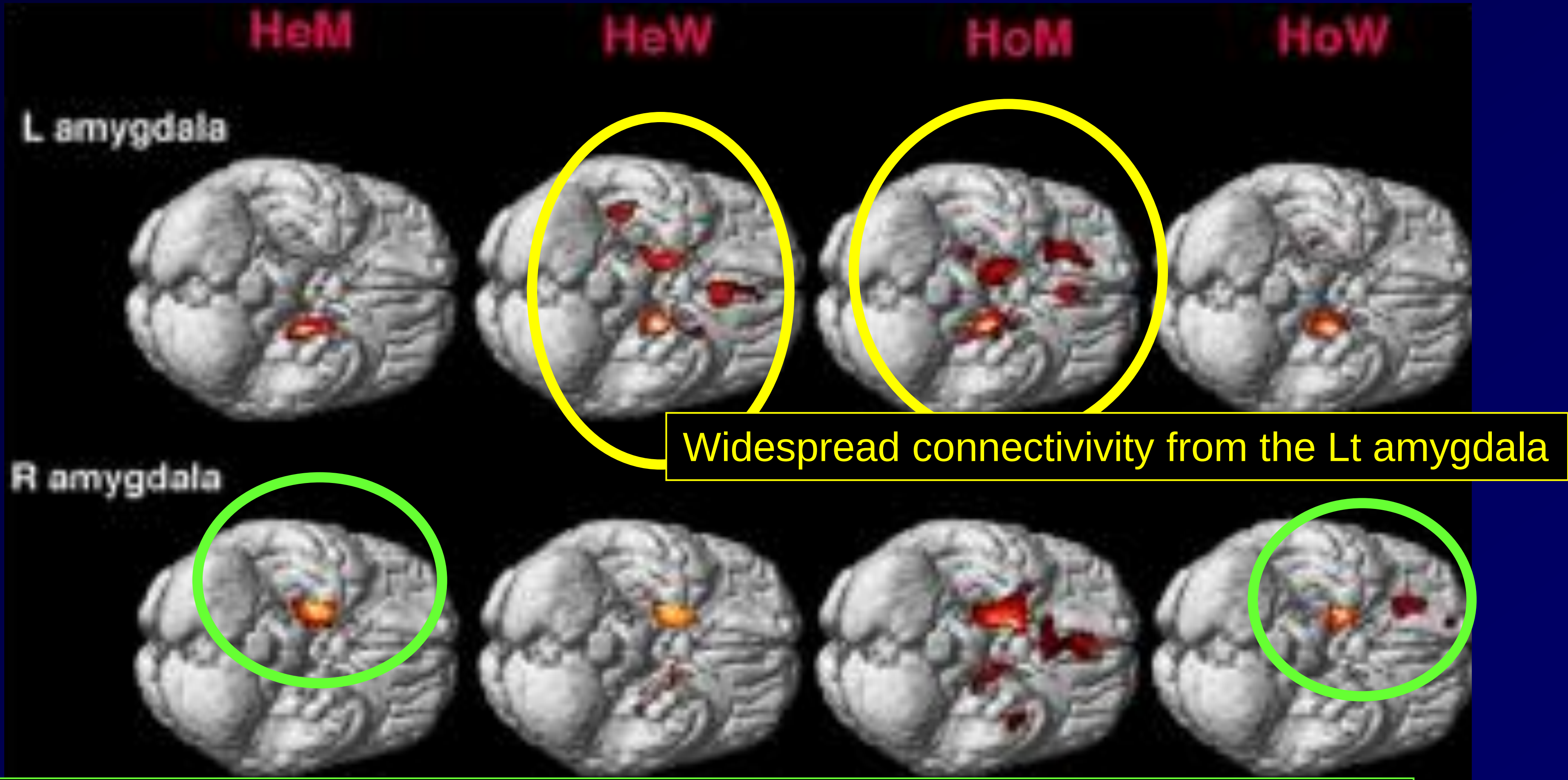
SCN

Suprachiasmatic Nucleus



PET and MRI show differences in cerebral asymmetry and functional connectivity between homo and heterosexual subjects

Savic I. PNAS, 2008

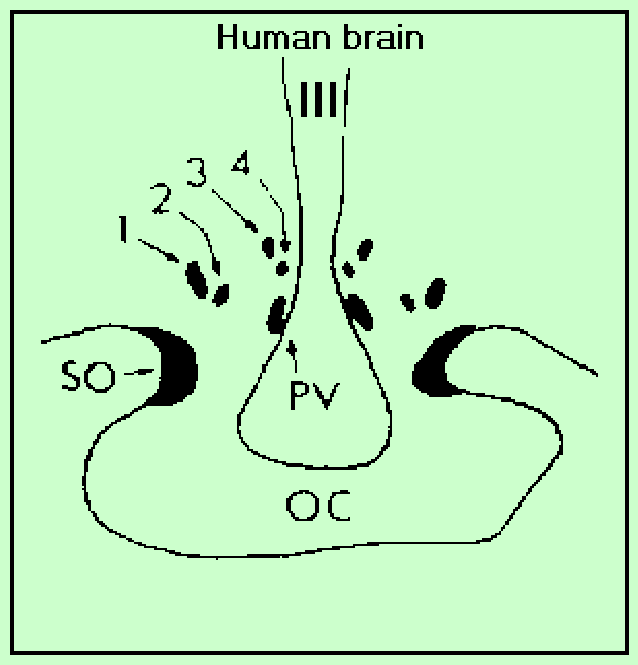


Rightward cerebral asymmetry widespread connectivity from the Rt amygdala

INAH-3

Interstitial **N**uclei of

Anterior **H**ypothalamus



Le Vay, Science,1991

larger in Het men VS Women and Hom men

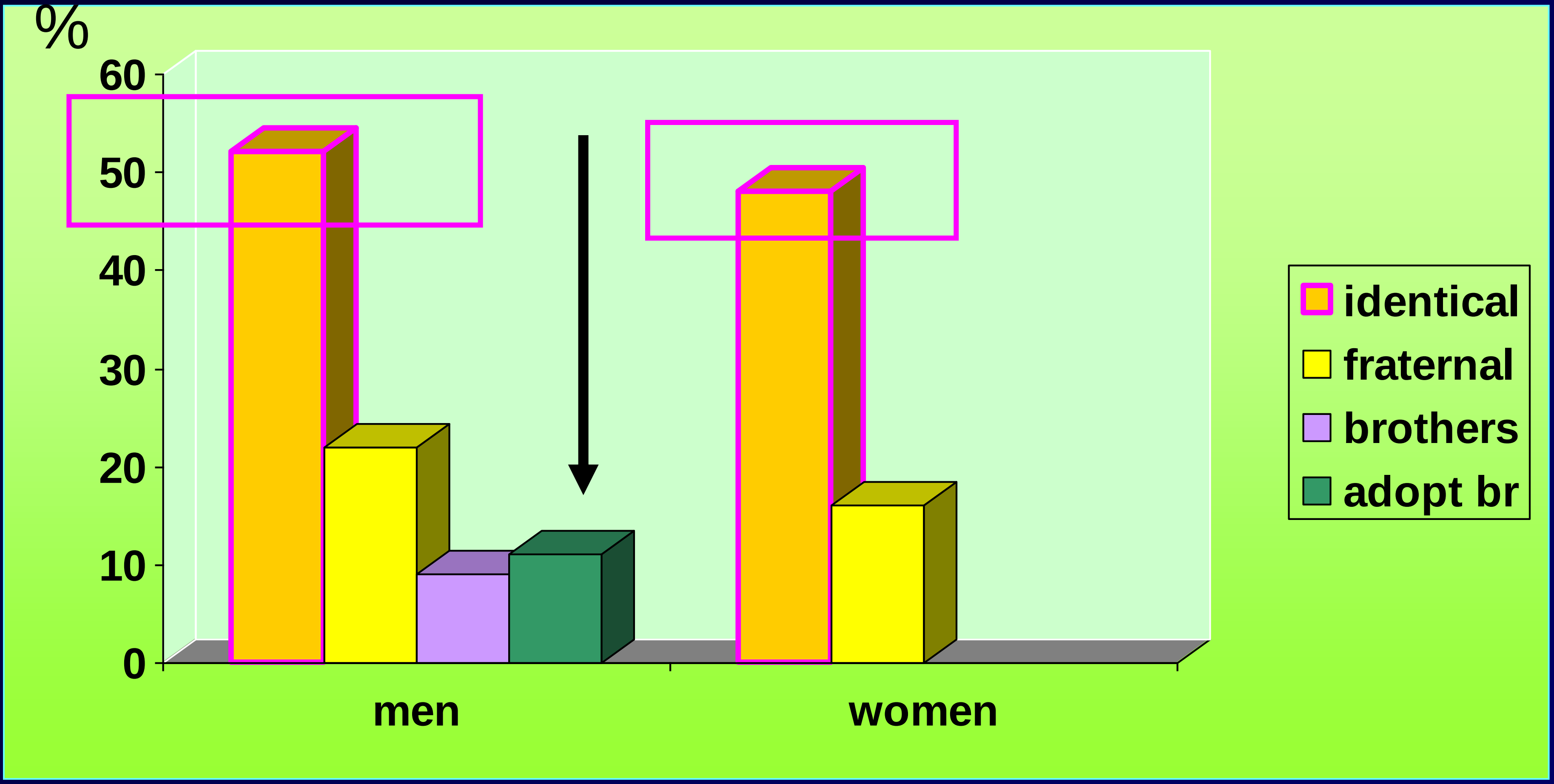
- ? a small INAH3 cause homosexuality
- ? homosexuality reduce the size of INAH3
- ? unknown 'third factor' responsible for homosexuality and reduced INAH3 volume

? Certain sexually dimorphic features in the brain may differ between individuals of the same sex but different sexual orientation

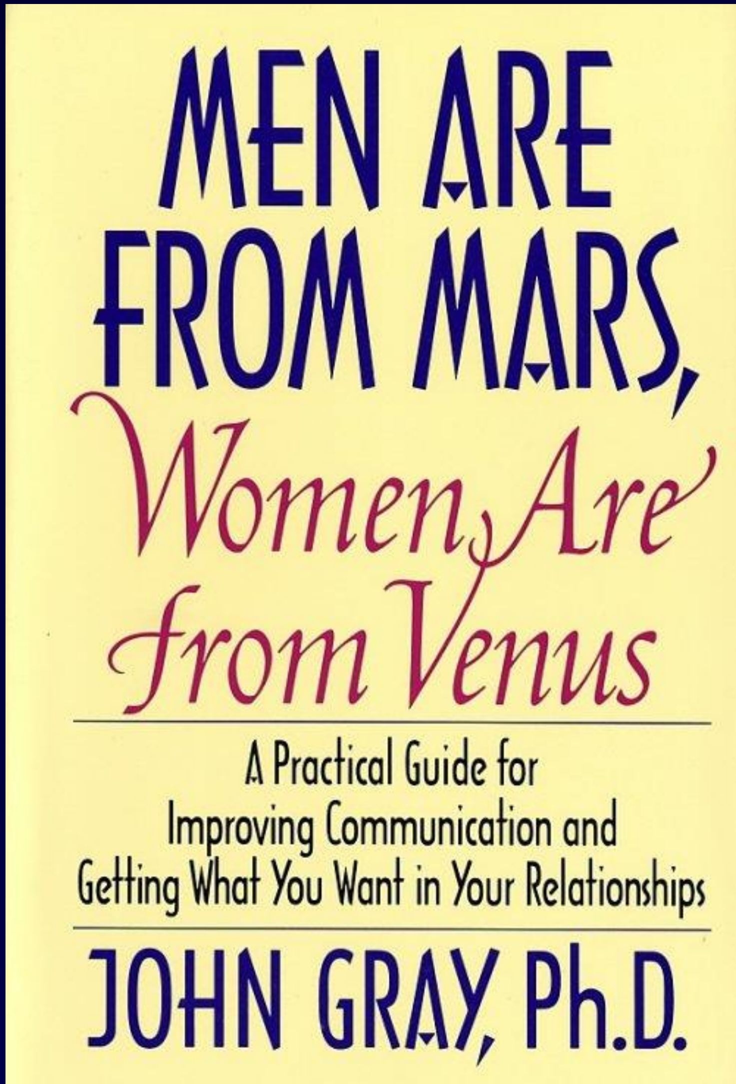
PET and MRI : Sexual dimorphism with respect to hemispheric asymmetry and the functional connections from the RT and LT amygdala

1. MRI volumetry of cerebral hemispheres
2. PET measurement of cerebral blood flow for analysis of functional connections from the RT to the LT amygdalae

Genetic basis of sexual orientation



Bailey J, Pillard R. Arch Gen Psychiatry , 1991
Carlson, Niel R. 2001


MEN ARE FROM MARS,
Women Are from Venus
A Practical Guide for Improving Communication and Getting What You Want in Your Relationships
JOHN GRAY, Ph.D.


shaaubmagazine.com


OXYTOCIN
TESTOSTERONE