Introduction to Neuroscience – Behavioral Neuroscience

Sexual dimorphism in brain and behavior: Hormonal and genetic regulation

Sexual Dimorphism

Sexual dimorphism is the difference in form between male and female members of the same species

Sexual dimorphism in body characteristics

Sexual Dimorphism in Social Behavior

Social behavior in mammalian species

- Most striking categories of sexually dimorphic behaviors
- Innate (genetically-predetermined) behaviors
- Controlled by simple sensory signals (e.g. pheromones)

Courtship behavior

Sexual behavior

Aggressive behavior (territoriality)

Parental behavior

The role of hormones in regulation of sexual dimorphism in behavior

Behavioral Neuroendocrinology

Arnold A. Berthold (1803-1861)
German physiologist and zoologist

In 1849, Berthold conducted one of the first experiments in behavioral endocrinology

Research question tested: Are the effects of prepubertal castration in males, dependent on neural connections to the testes?

Hypothesis: Intact testes are necessary for the development of male-typical characteristics

Animal model:

Castration

Castration +
Transplantation
in the same body

Castration +
Transplantation
in another body

Berthold's experiment- summary

Findings:

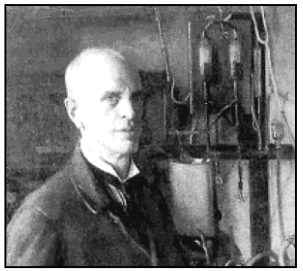
-Males that were castrated as juveniles later showed deficits as adults, in male-typical body characteristics and in behaviors such as aggression, mating and crowing.

-All of these effects could be reversed if the subject's testes, or the testes of another male, were implanted into the body cavity.

Conclusion:

Testes influence the development of male-typical morphology, and male-typical behavior, NOT through nerves, but by secreting a substance into the bloodstream (i.e. hormones).

Ernest Henry Starling (1866-1922), English physiologist



The first to use the term hormone.
"Hormones" from Greek " to excite"

"These chemical messengers, however, or <hormones> (from ορμάω=I excite or arouse), as we might call them, have to be carried from the organ where they are produced to the organ which they affect by means of the blood stream and the continually recurring physiological needs of the organism must determine their repeated production and circulation through the body"[6].

Starling (1905); Lancet

Hormone: "A substance, usually a peptide or steroid, produced by one tissue and conveyed by the bloodstream to another to effect physiological activity"

ORGANIZING ACTION OF PRENATALLY ADMINISTERED TESTOSTERONE PROPIONATE ON THE TISSUES MEDIATING MATING BEHAVIOR IN THE FEMALE GUINEA PIG[1]

CHARLES H. PHOENIX, ROBERT W. GOY, ARNOLD A. GERALL AND WILLIAM C. YOUNG

Department of Anatomy, University of Kansas, Lawrence, Kansas

Endocrinology, 1959, 65:369-382

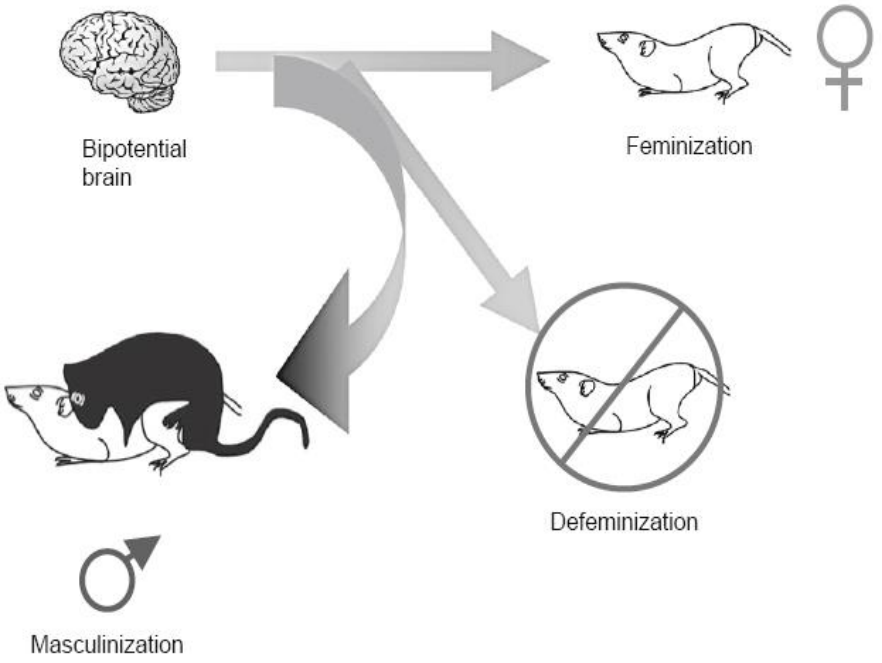
William C. Young (1899-1965)

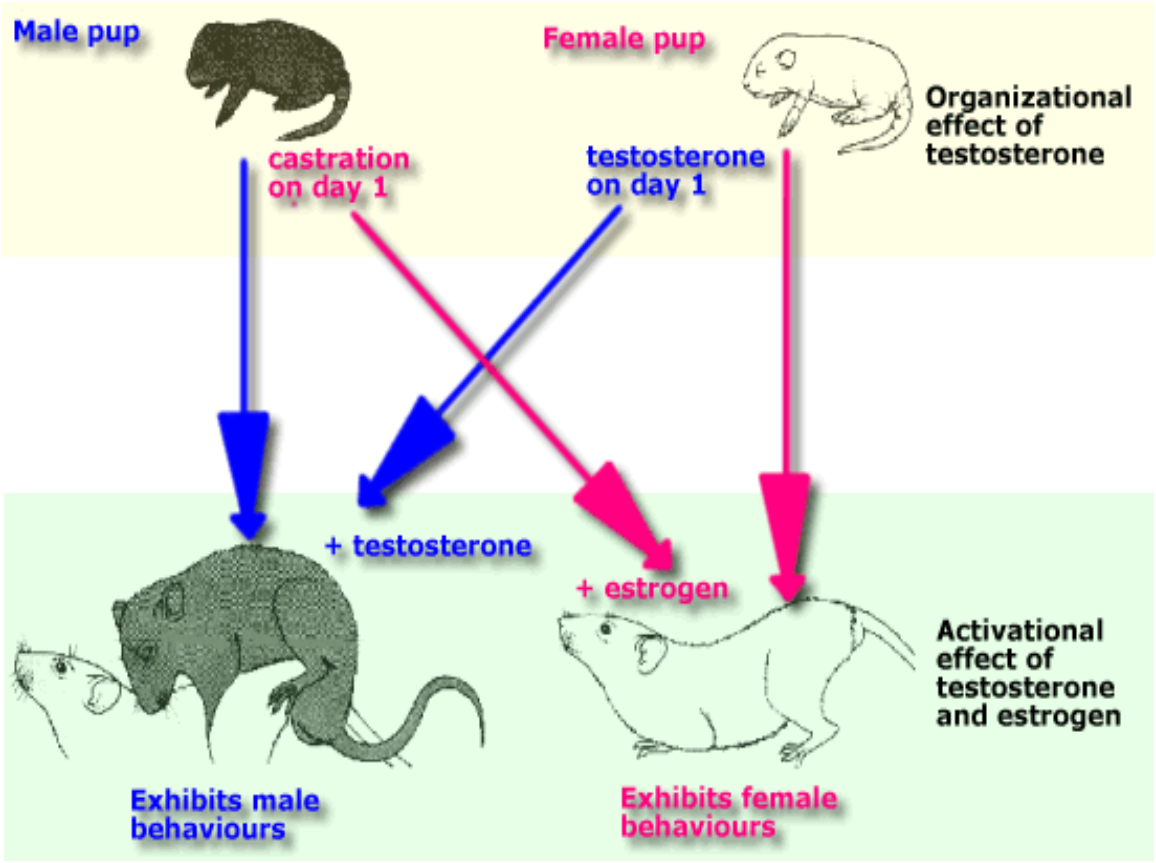
Findings: female guinea pigs prenatally exposed to testosterone did not show any female-typical behavior when given estradiol and progesterone during adulthood

The organization/activation hypothesize

•Sex hormones act during the prenatal stage to irreversibly organize the nervous system in a sex-specific manner

•During adult life, the same hormones possess activation effects, causing it to function in a sex-typical manner

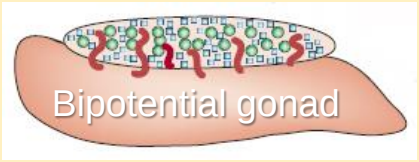



Male pup
Female pup
Organizational effect of testosterone
castration on day 1
testosterone on day 1
+ testosterone
+ estrogen
Activational effect of testosterone and estrogen
Exhibits male behaviours
Exhibits female behaviours

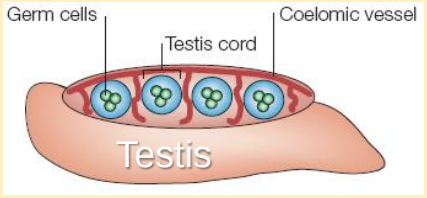
The classic model of brain sexual differentiation

Embryonic

XY ♂



♀ XX



SRY gene

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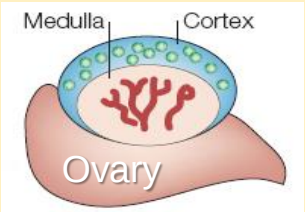
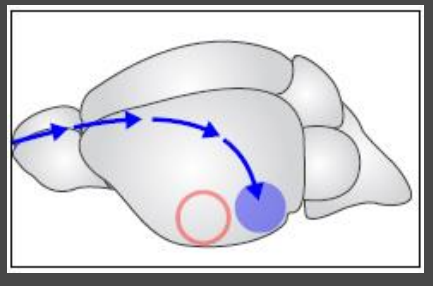
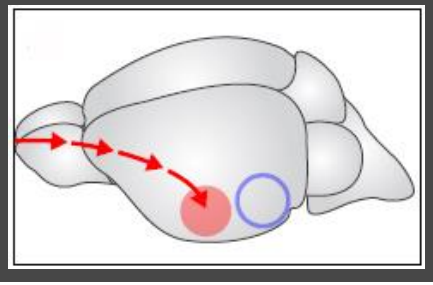


Perinatal

Testosterone/
Estradiol

Organization
(permanent changes)



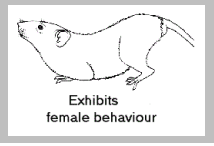


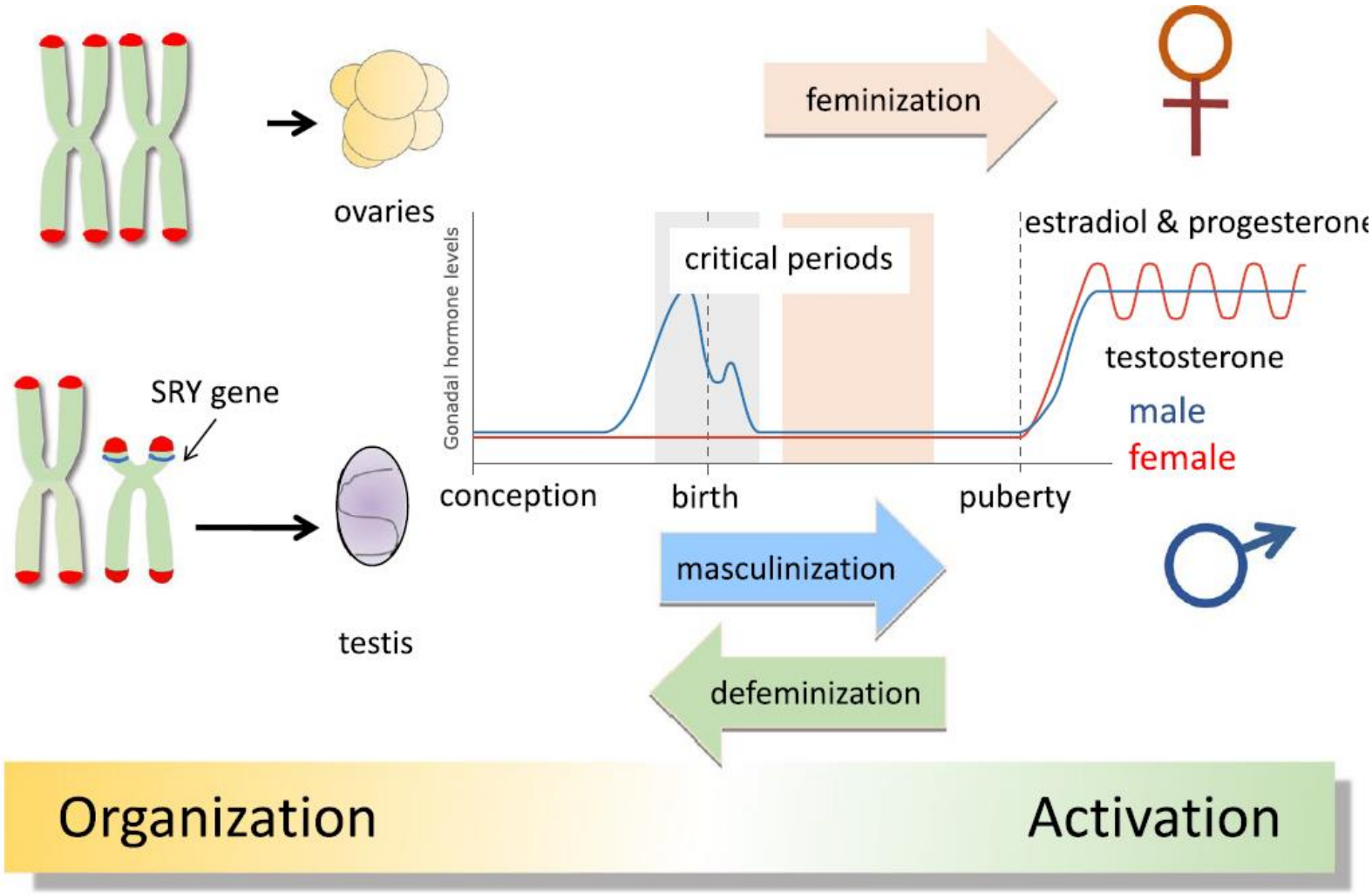
Adult

Testosterone

Activation

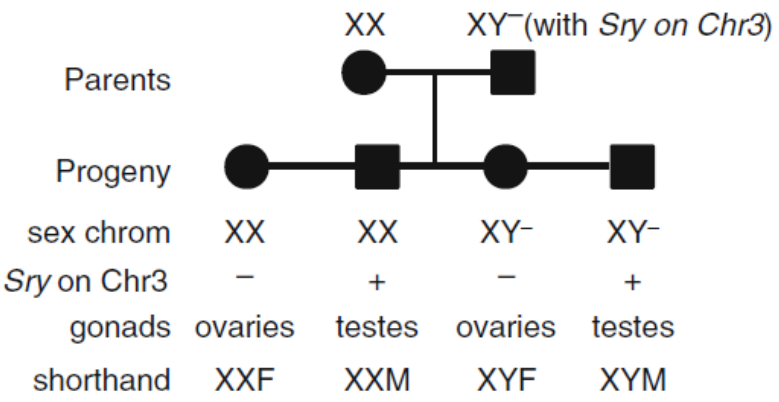
Estradiol &
Progesterone

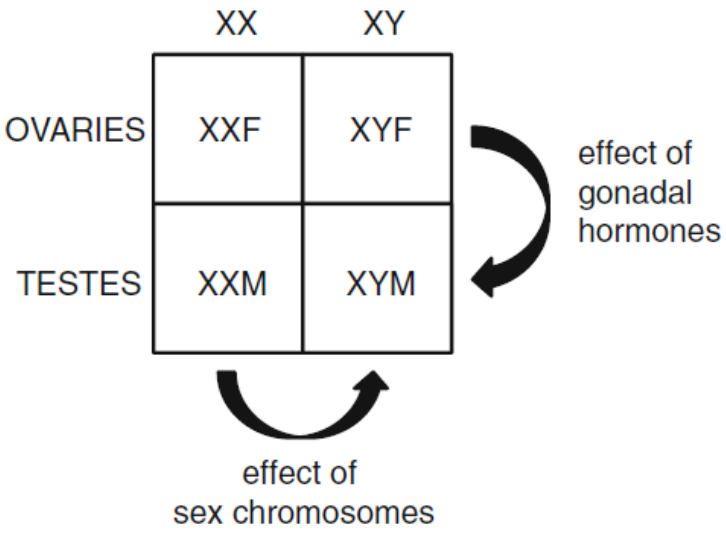


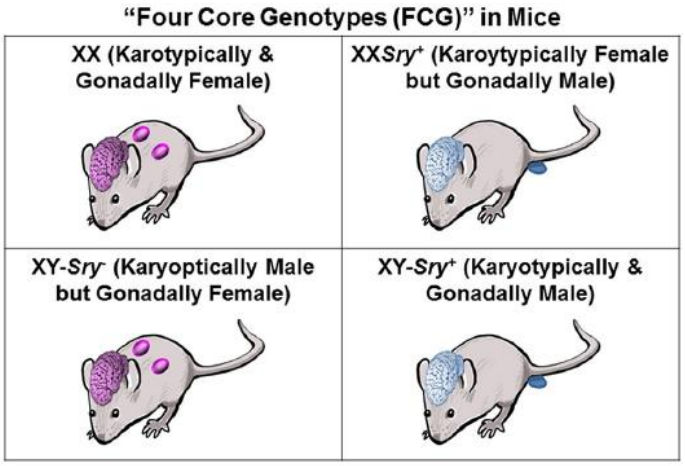


McCarthy 2020 J comp Physiol

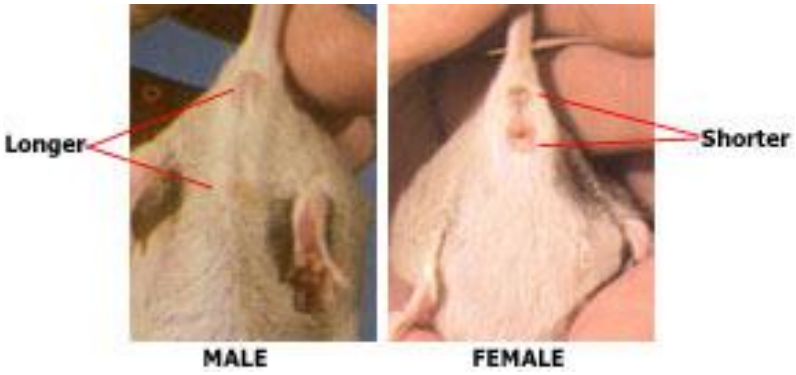
Genetic manipulation of SRY in mice



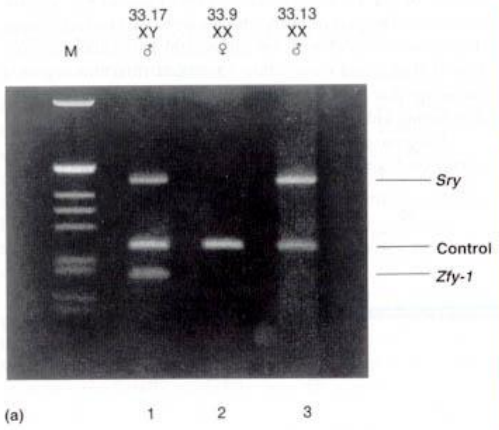


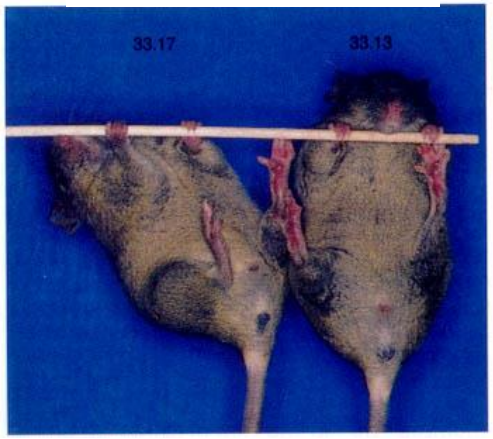


Genetic females expressing SRY gene are gonadally males

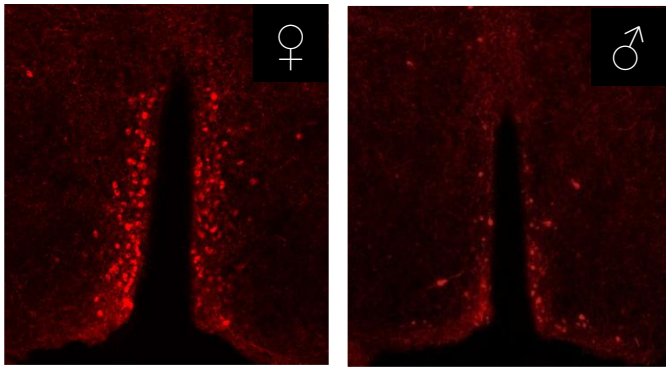


XX Sry (XXM)

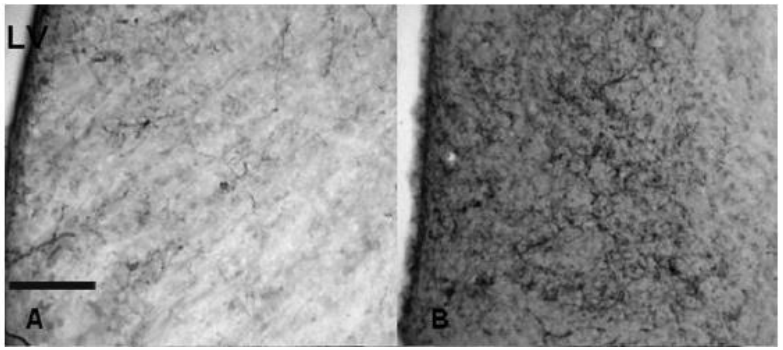


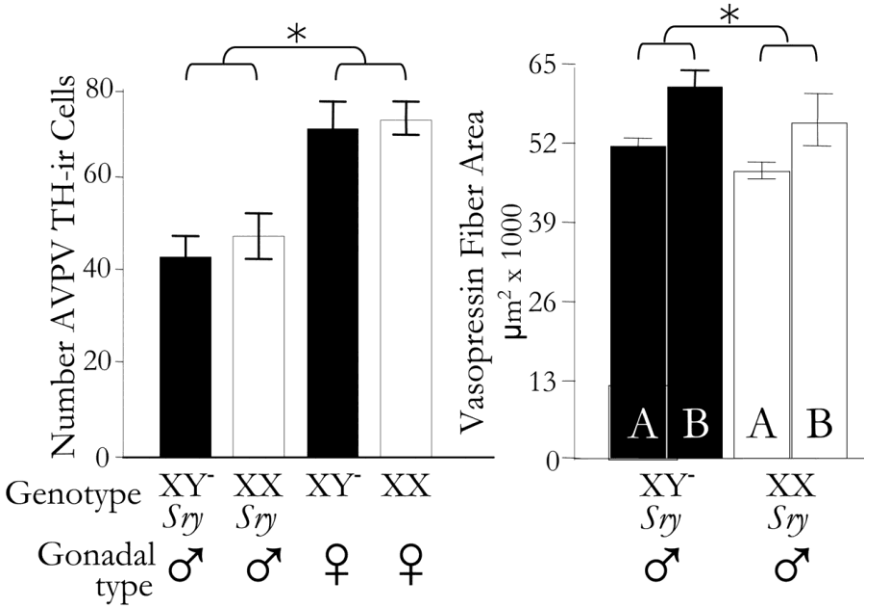


TH neurons in the AVPV in adult mice/rats



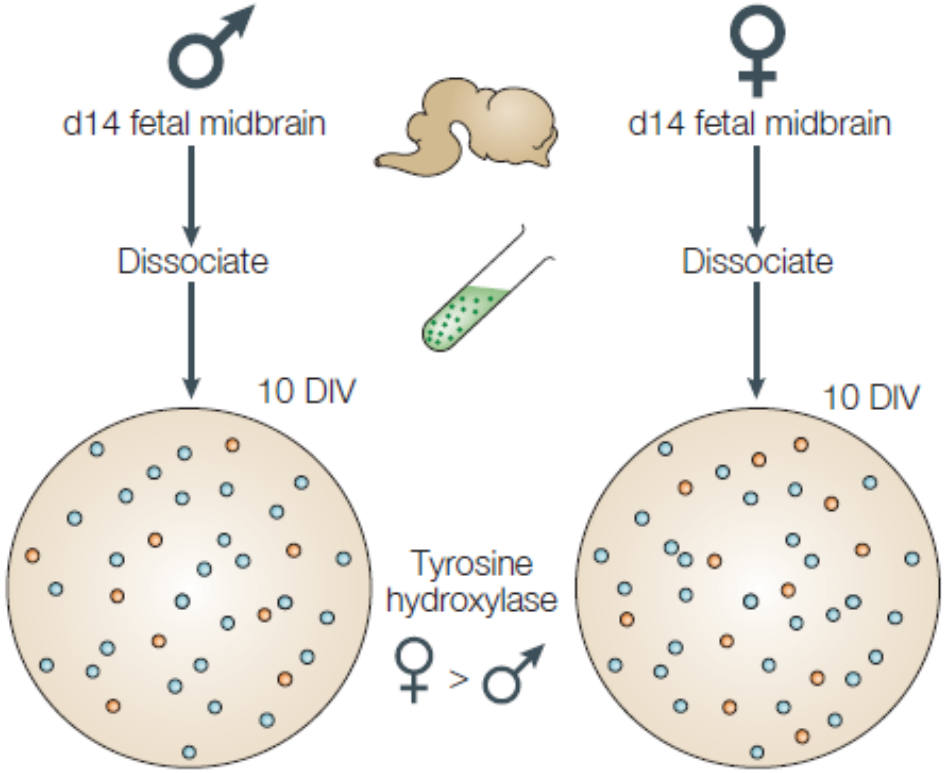
Dimorphic vasopressin fibers in the LS





Arnold et al 2004, Endocrinology

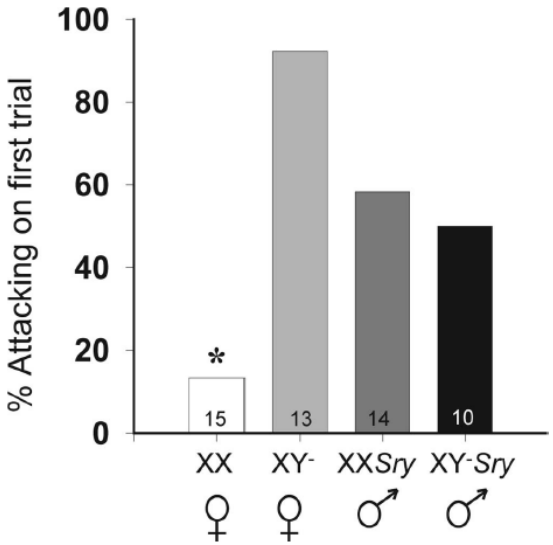
Evidence for the affect of Y-linked genes on brain sexual dimorphism



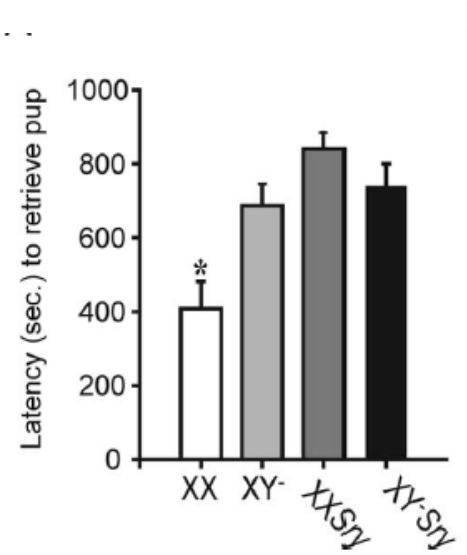
Arnold 2004 Nat Rev

The *Sry* gene and other genes on the sex chromosomes regulate sexual dimorphism in social behaviors

Aggressive behavior

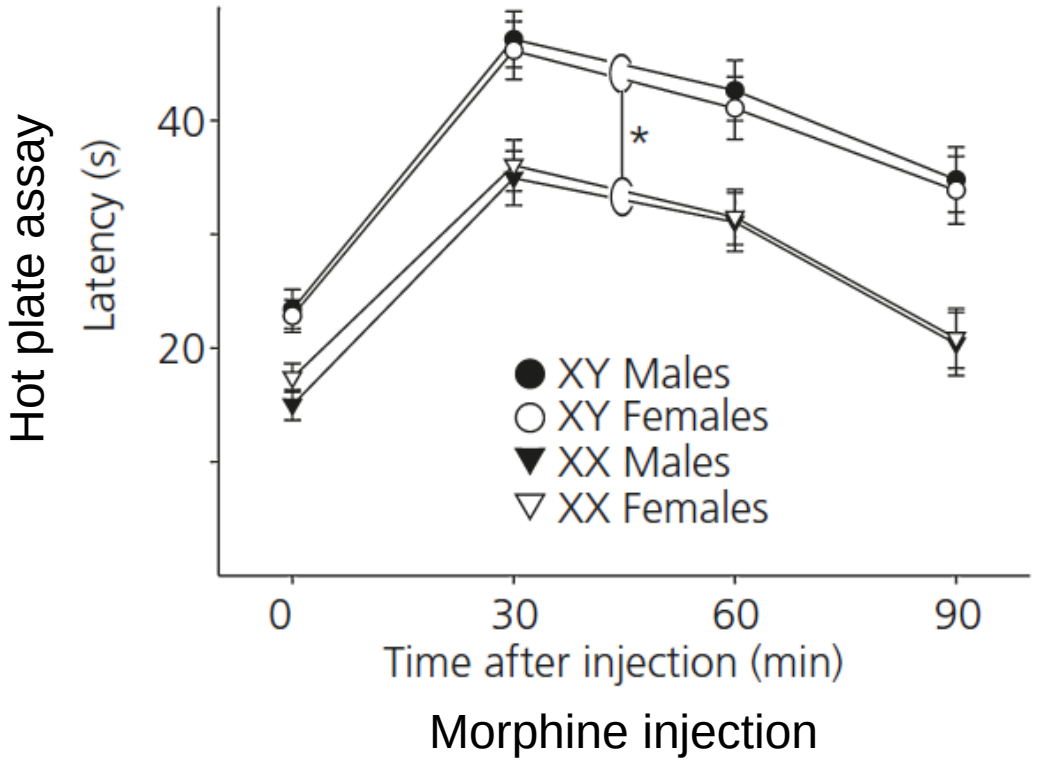


Maternal behavior



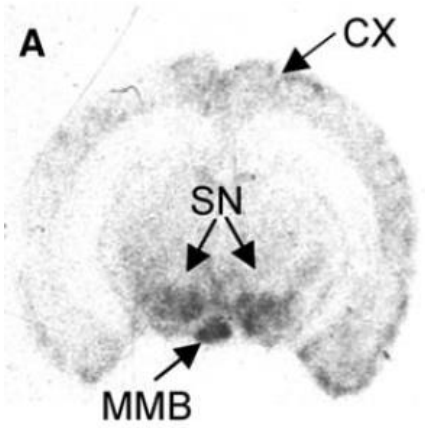
Gatewood et al 2006, J Neuros

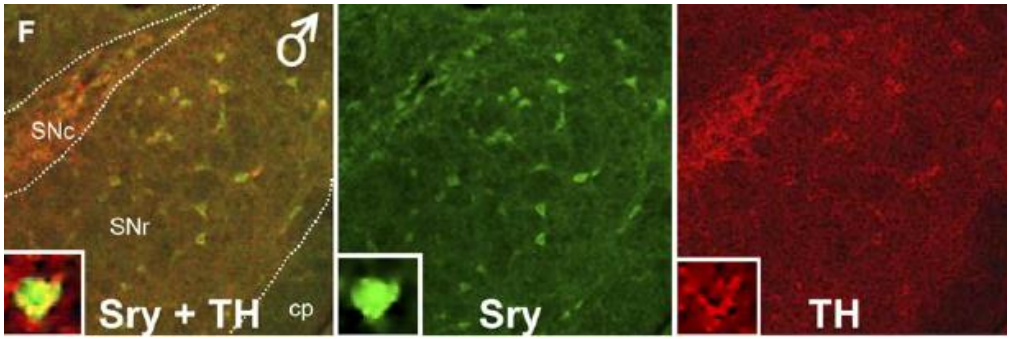
Effect of sex chromosomes on nociception



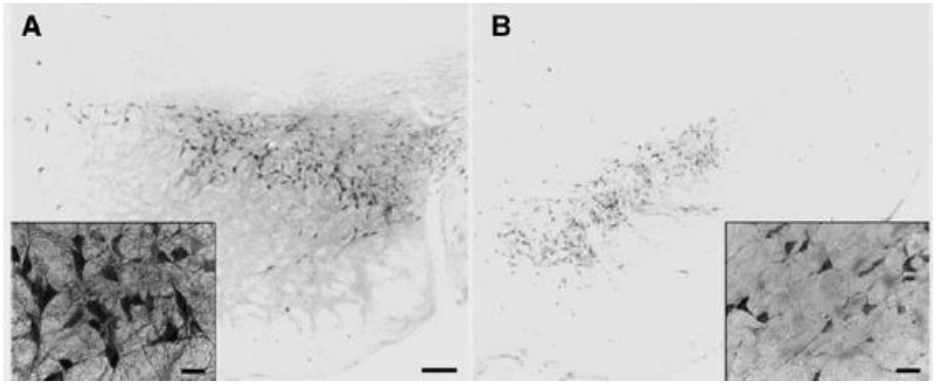
Gioiosa et al 2008, Horm Behav

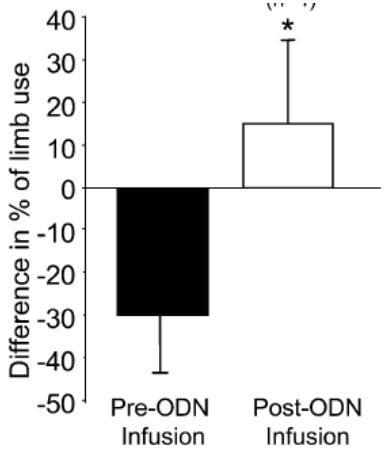
Direct regulation of the adult brain by SRY





Downregulation of SRY in the SN leads to decreased TH expression and deficient sensorimotor behavior





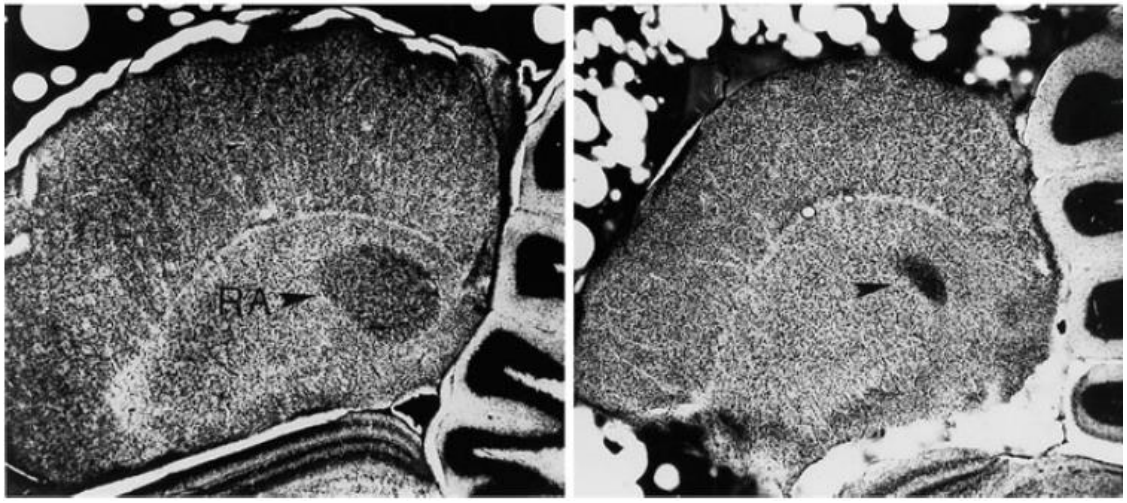
Dewing et al 2006 Curr Biol

The Klinefelter syndrome, also known as the **XXY genetic disorder**

symptoms include:

1. Reduced fertility or full infertility
2. Female-typical body characteristics

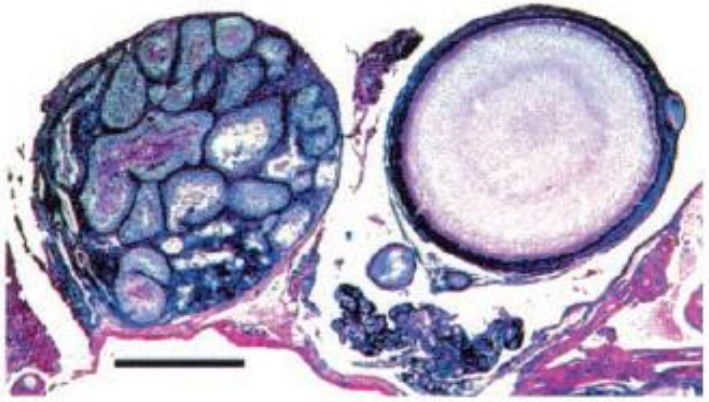
Sex difference in brain and behavior in Zebra finches



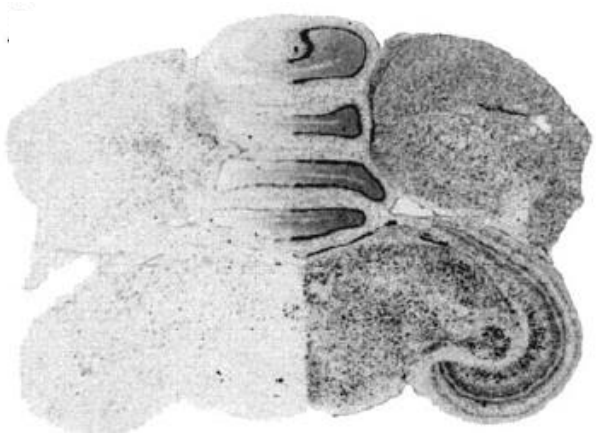
Gynadromorphic Finch

Agate et al 2003 *PNAS*

Testis Right Left Ovary

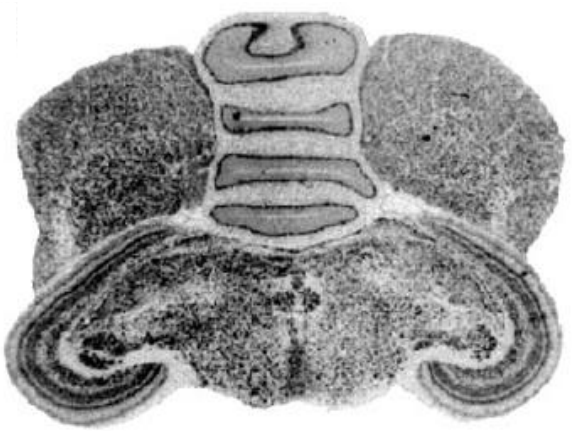


ZZ (male) ZW (female)



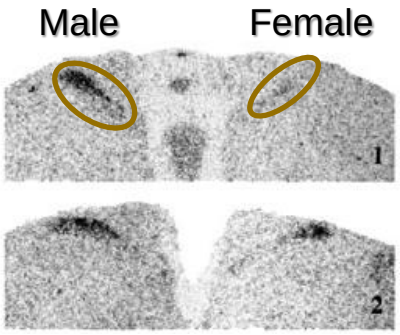
A gene expressed on the W chromosome

ZZ (male) ZW (female)

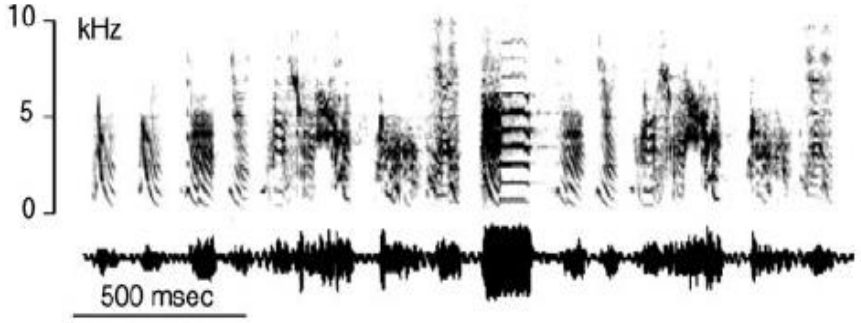


A gene expressed on the Z chromosome

AR expression in the song nucleus HVC (larger in males)



Typical song of a male

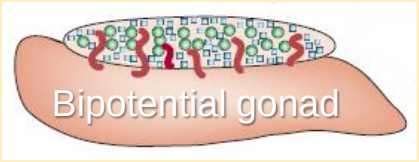


Agate et al 2003 PNAS

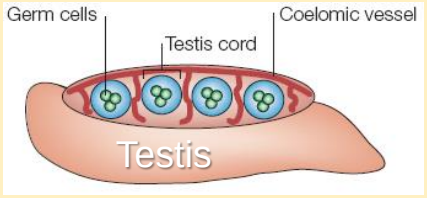
The classic model of brain sexual differentiation

Embryonic

XY ♂



♀ XX



SRY gene

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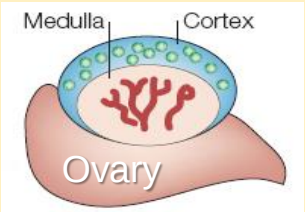
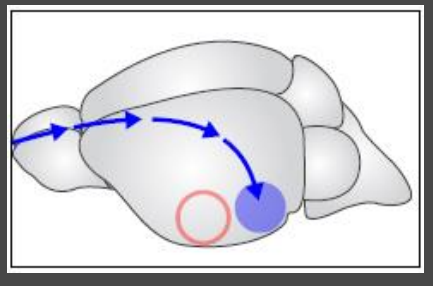
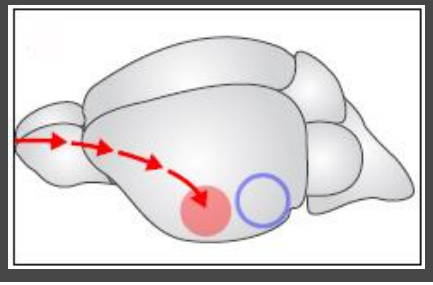


Perinatal

Testosterone/
Estradiol

Organization
(permanent changes)



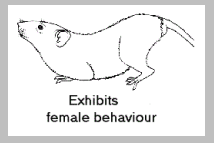


Adult

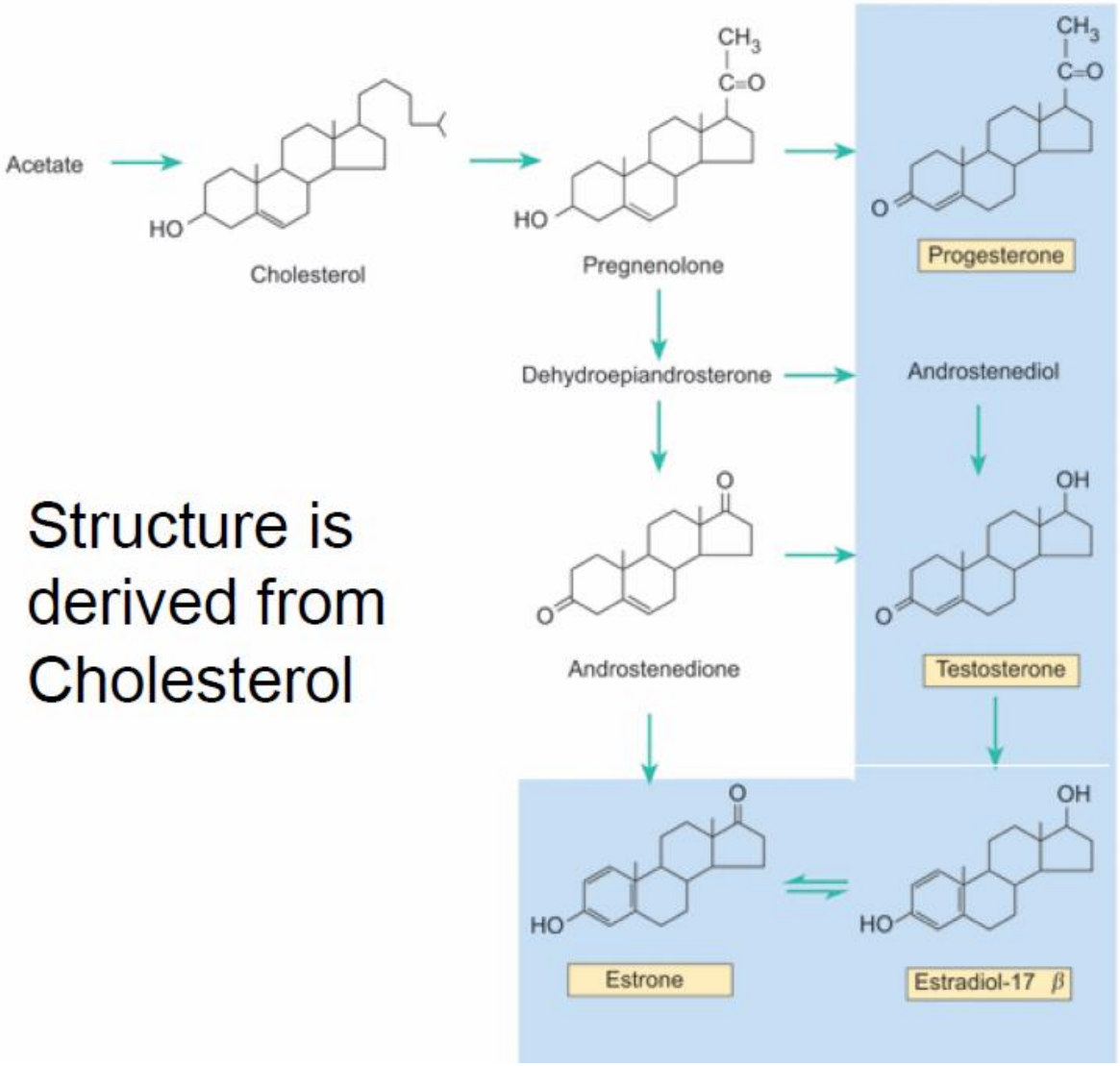
Testosterone

Activation

Estradiol &
Progesterone



The Sex Hormones



Structure is derived from Cholesterol

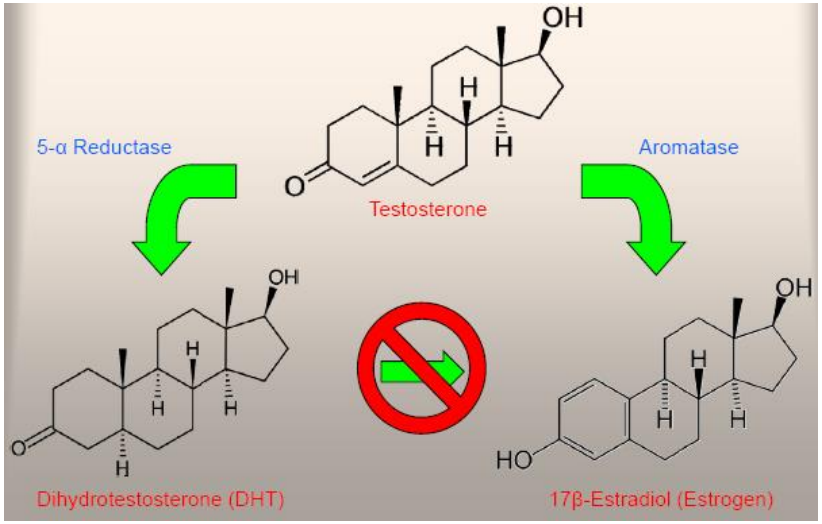
"Male" (androgenic) sex hormone

-Also secreted by the adrenal gland

"Female" (estrogenic) sex hormone

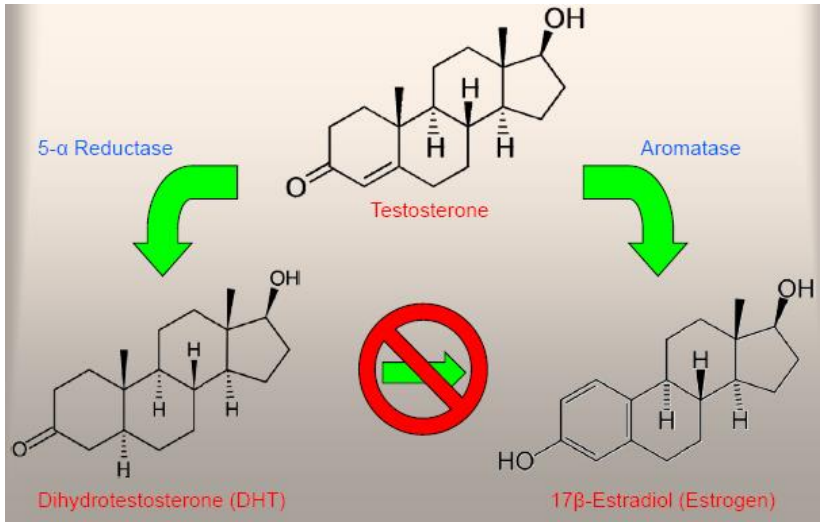
* Both are steroid hormones and secreted in both sexes

Testosterone, Estradiol or DHT masculinizes the brain ?



- Testosterone treatment in neonatal rats is blocked by prior administration of specific estrogen receptor antagonist
- DHT does not mimic the effect of testosterone
- Radio-labeled testosterone is recovered from the brain as radio-labeled estradiol
- Aromatase inhibitors counteract the effect of testosterone administration

Estradiol masculinizes the brain



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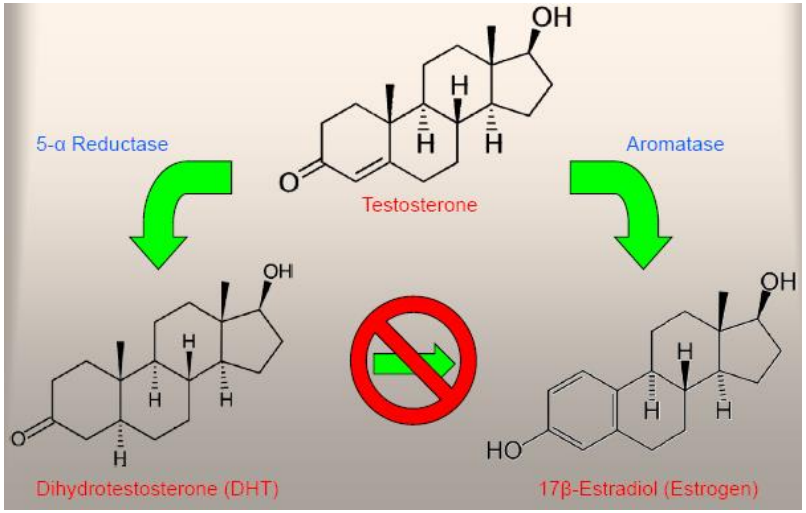
Why isn't the female brain masculinized by estrogen?

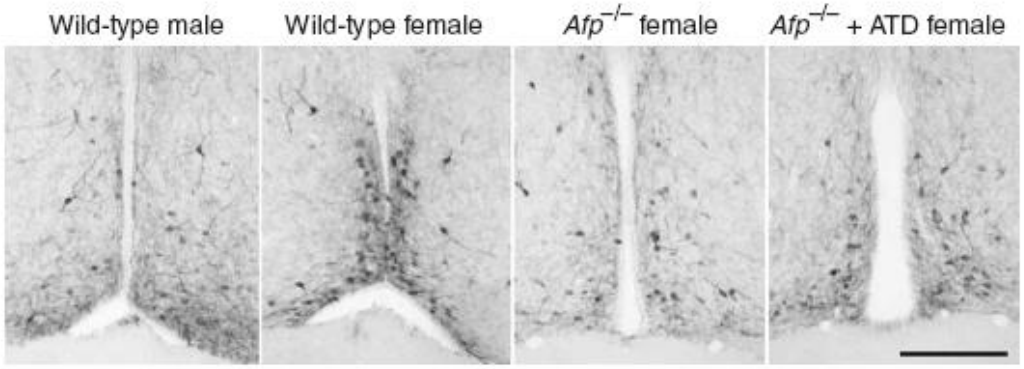
- Estradiol production by the fetal ovaries is minimal
- High levels of circulating α-fetoprotein (AFP) in embryos

AFP = Fetal plasma protein that binds estrogens with high affinity and prevents it's passage through the placenta.

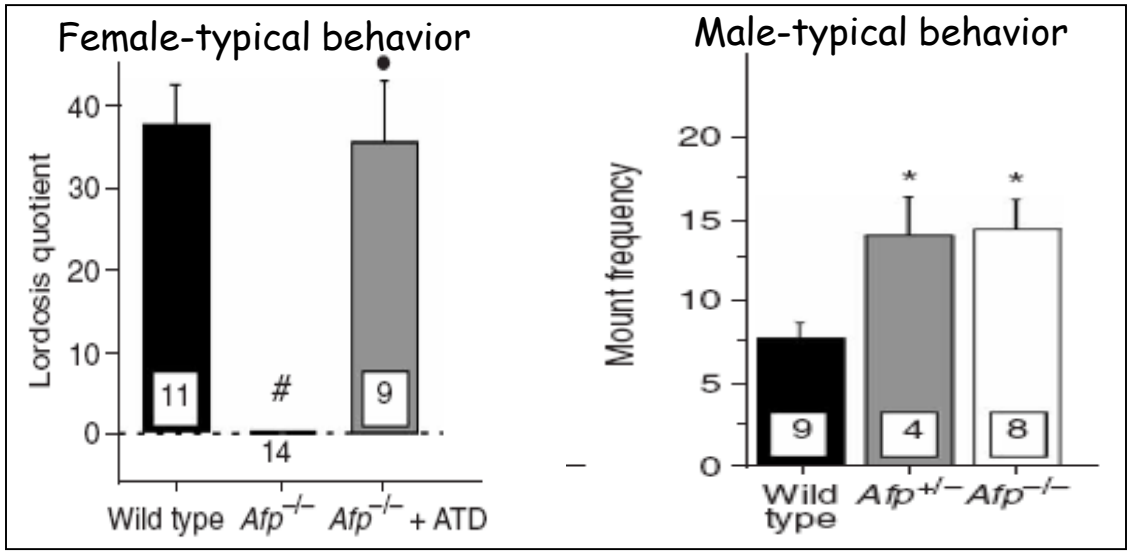


Role of Alpha-fetoprotein (AFP) in female brain development

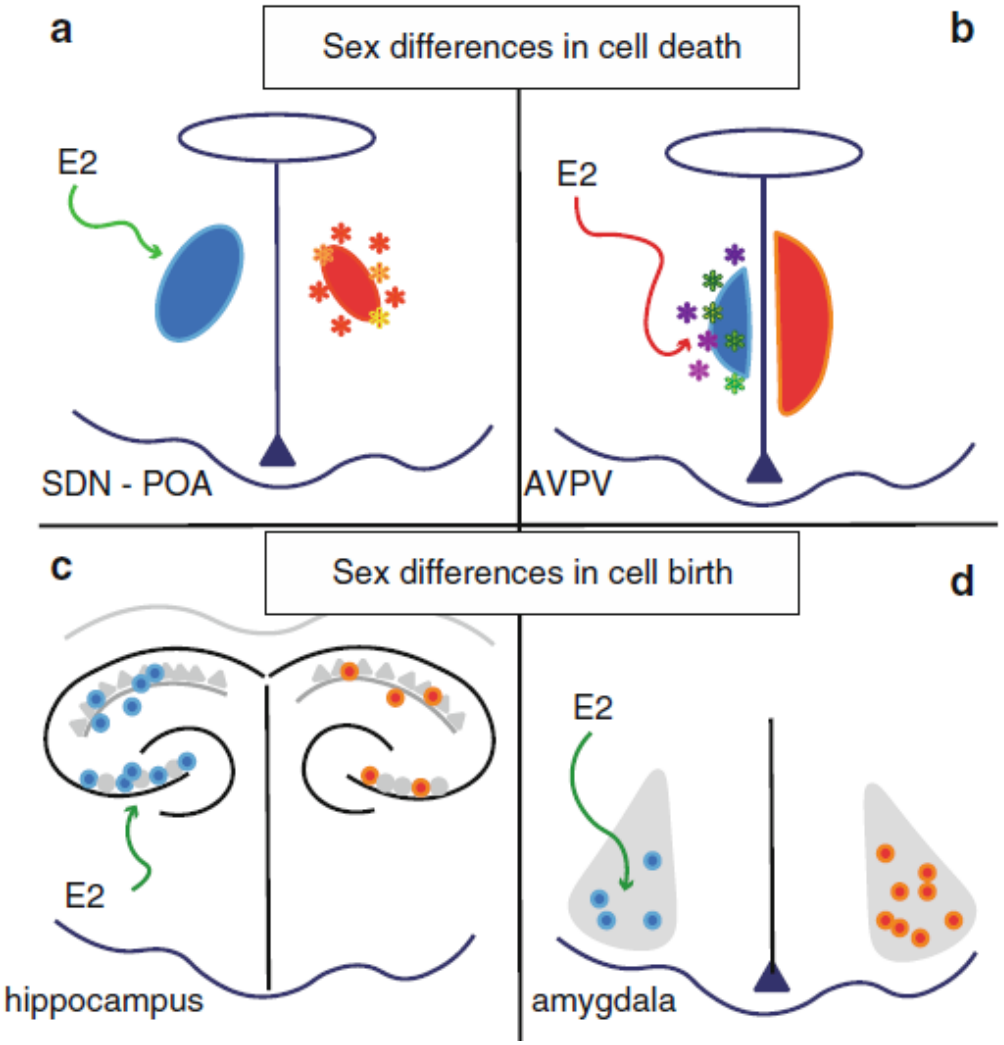
Expression of the Tyrosine Hydroxylase (TH) gene in the hypothalamus (AVPV)



ATD=
Aromatase inhibitor



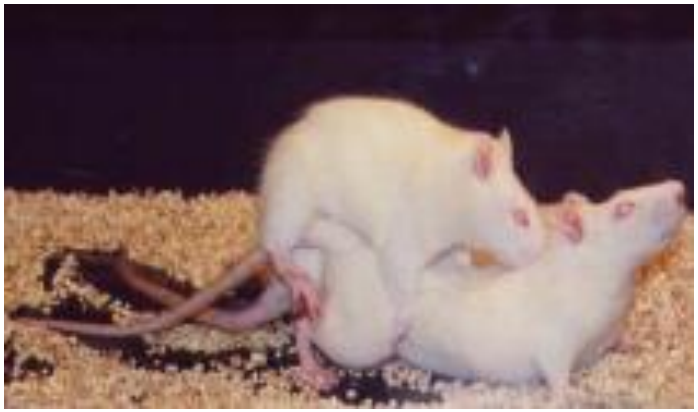
Baker et al 2005; Nature neuroscience



Arnold and McCarthy, 2016

Hormonal regulation of social behavior during adulthood

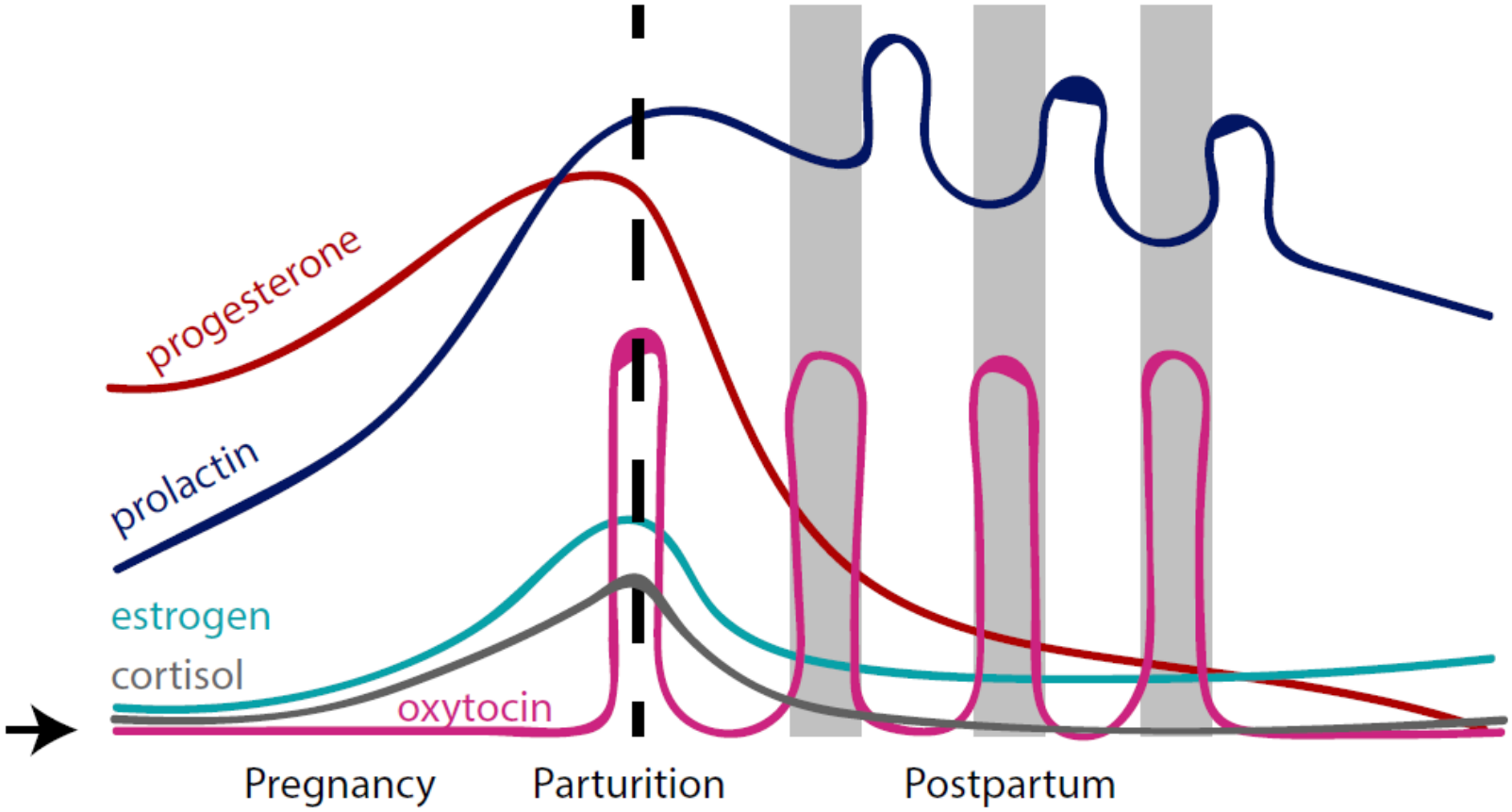
Aggressive behavior



Sexual behavior

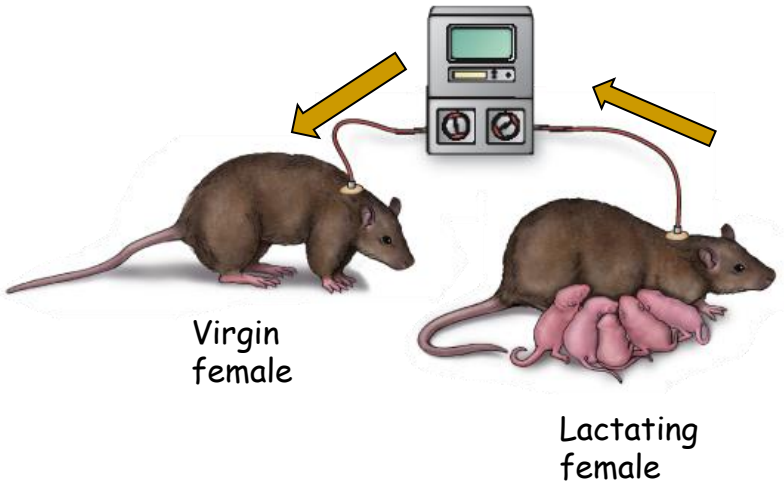
Maternal behavior

Maternal behavior in postpartum female rats


progesterone
prolactin
estrogen
cortisol
oxytocin
Pregnancy
Parturition
Postpartum

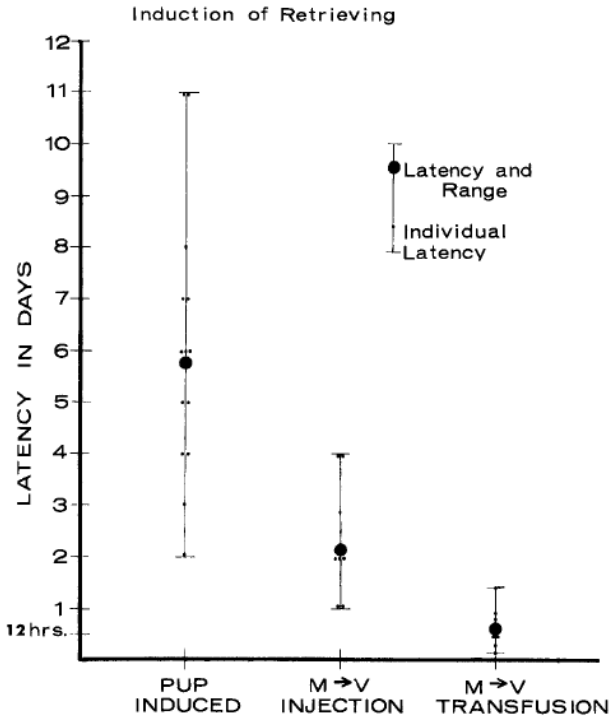
Terkel and Rosenblatt (1968)

Joseph Terkel



Blood was transfused from a parturient female (one that had given birth within 30 min prior to the onset of the transfusion) into a virgin female.

Hormonal factors underlying maternal behavior

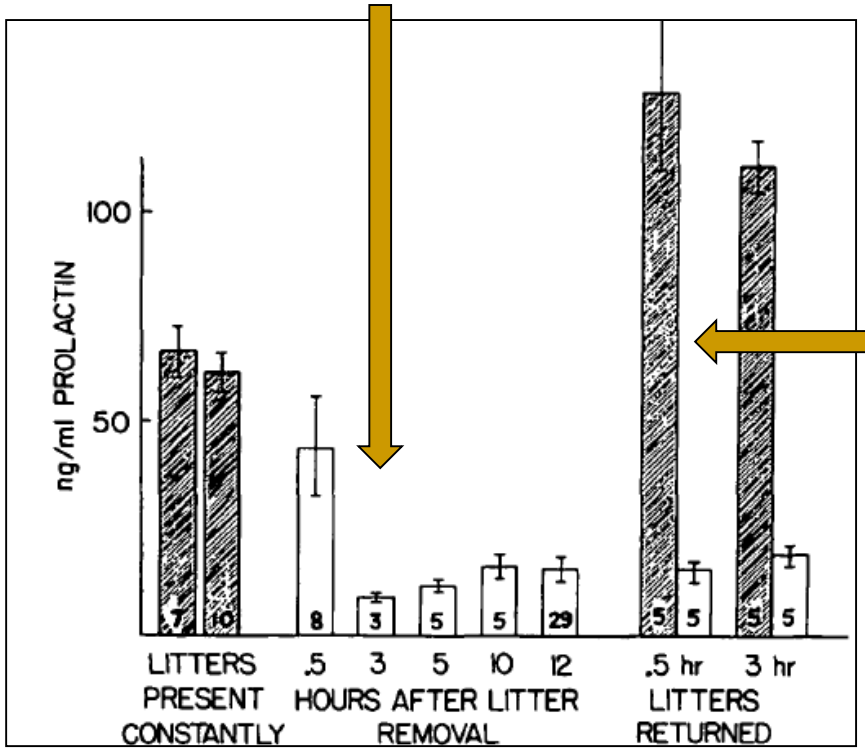


Maternal behavior of virgin females toward newborn (unfamiliar) pups is facilitated following blood transfusion from maternal females (lactating)

Terkel and Rosenblatt, 1972, J Comp Pysiol Psychol

Prolactin in serum and maternal care in rats

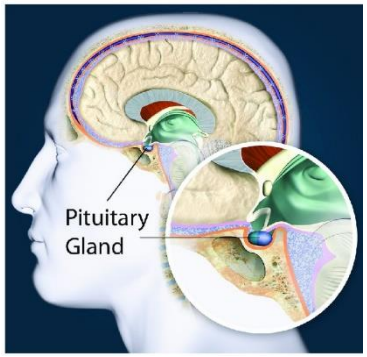
• Removal of litters from mother rats resulted in a rapid decline of serum prolactin levels, reaching pregnancy levels 3 hr later

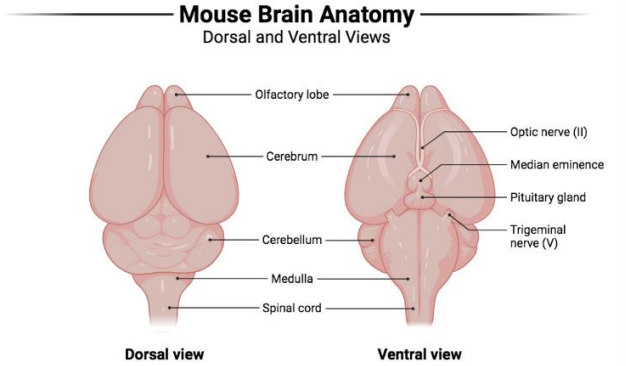


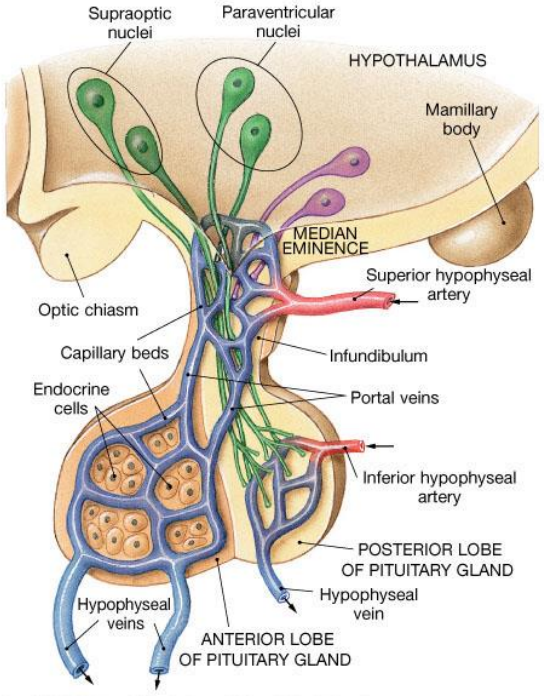
• When litters were returned to their mothers for 0.5-3 hr serum prolactin increased sharply

Amenomori et al 1970; Endocrinology

Prolactin is released from the pituitary gland



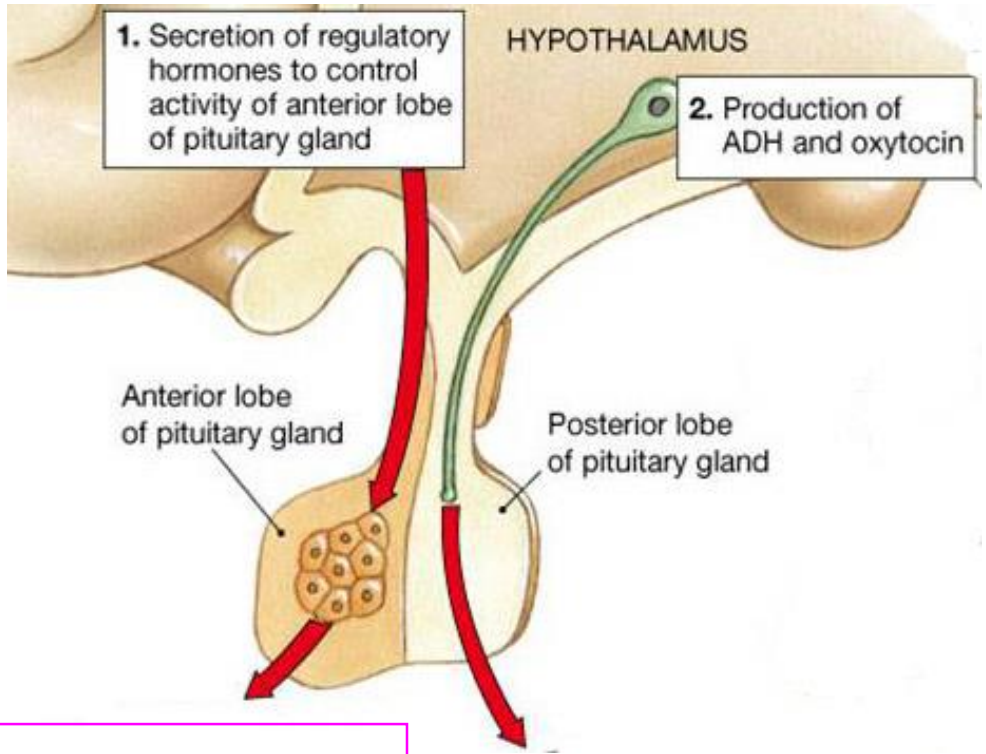




- It was shown that hypophysectomy (removing the pituitary gland) delayed the onset of maternal behavior in estrogen-treated females
- Prolactin injection with a pituitary gland implanted in the kidney capsule induced maternal care

Bridges et al. 1990, PNAS

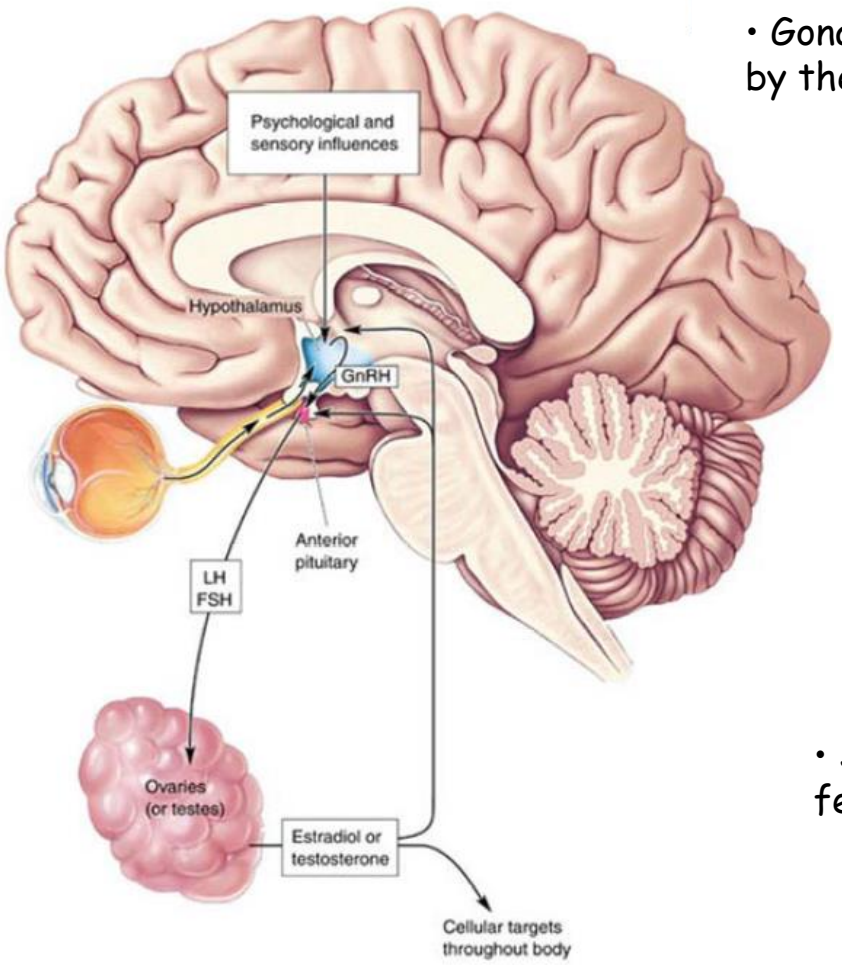
The Hypothalamus-Pituitary-Gonadal Axis



Prolactin (PRL)
Growth Hormone (GH)
Adrenocorticotropic hormone (ACTH)
Thyroid-stimulating hormone (TSH)
Follicle-stimulating hormone (FSH)
Luteinizing hormone (LH)

Vasopression
Oxytocin

The Hypothalamus-Pituitary-Gonadal Axis



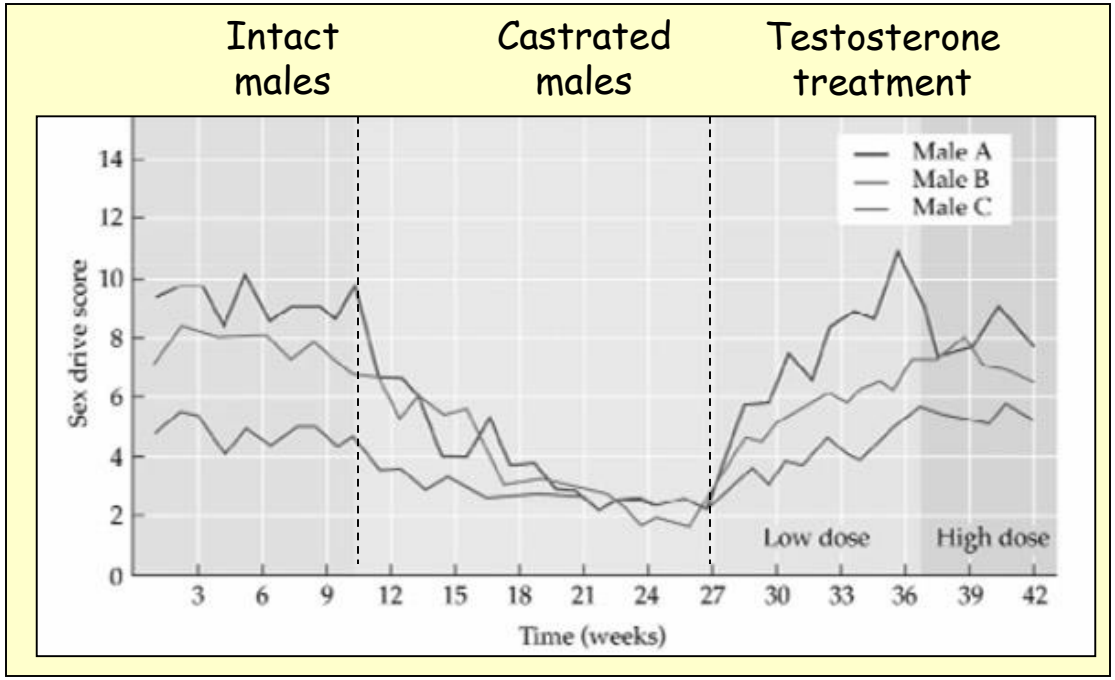
- Gonadotropin Releasing Hormone (GNRH) is released by the hypothalamus to stimulate anterior pituitary

- Gonadotroph cells in anterior pituitary release Luteinizing Hormone (LH) & Follicle-Stimulating Hormone (FSH).

- LH and FSH stimulates the gonads (Testes and Ovaries).

- Sex hormones released from the gonads feedback to influence brain functions

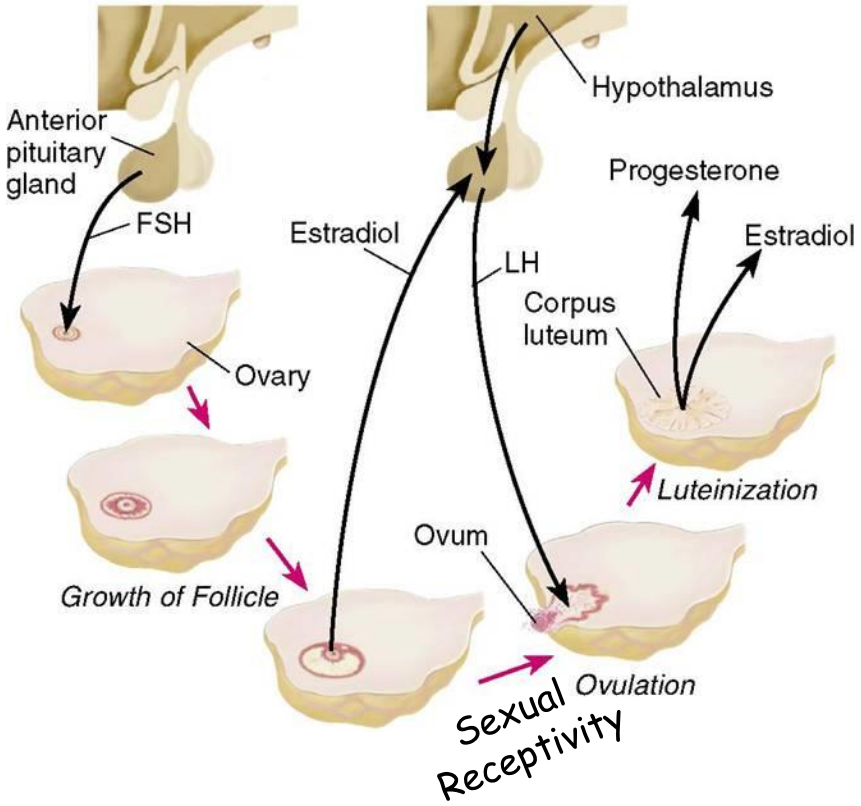
Effects of castration & testosterone treatment on males

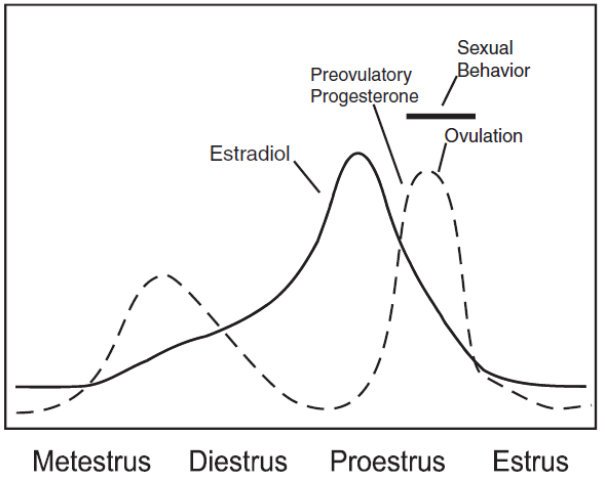


•In all rodents, gonadectomy decreases (abolishes) male courtship and sexual behavior

•Testosterone replacement reinstates sexual behavior in males

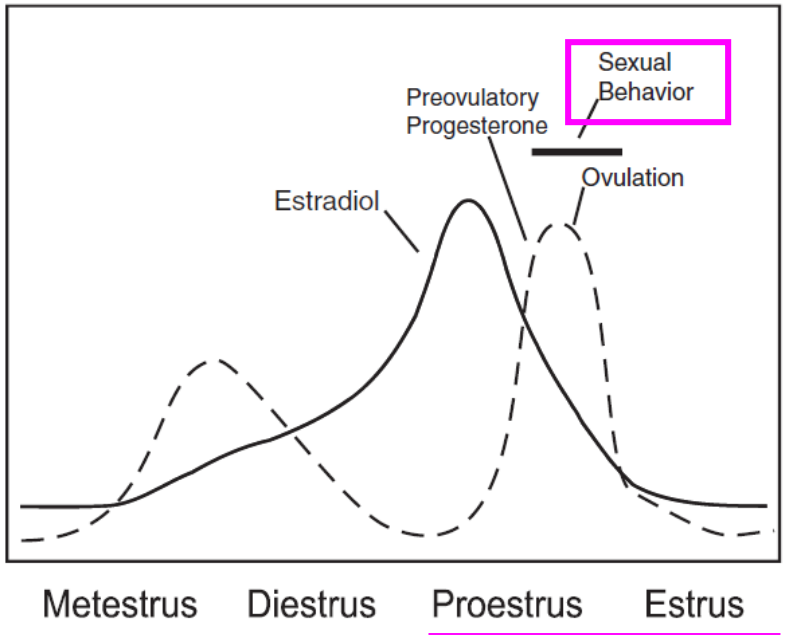
The Hypothalamus-Pituitary-Gonadal Axis and estrous cycle of female rats





Estrous cycle begins with secretion of gonadotropins from the hypothalamus, which stimulate the growth of ovarian follicles, and ovulation; the ruptured ovarian follicle becomes a corpus luteum and produces estradiol and progesterone

Hormonal activation of female-typical sexual behavior



0 hours	42 hours	Lordosis?[1]
Oil	Oil	No
Estradiol (low dose)	Oil	Usually low
Oil	Progesterone	No
Estradiol	Progesterone	High

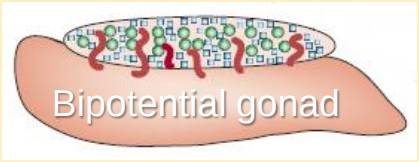
- In all rodents, gonadectomy decreases (abolishes) female sexual receptivity

- Estrogen and progesterone replacement reinstates sexual behavior of females

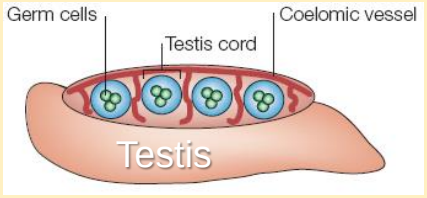
The classic model of brain sexual differentiation

Embryonic

XY ♂

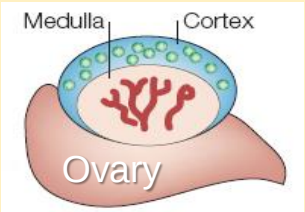


♀ XX



SRY gene

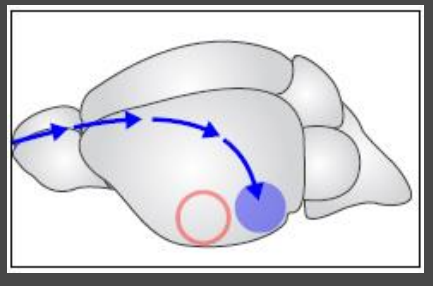
\+ -

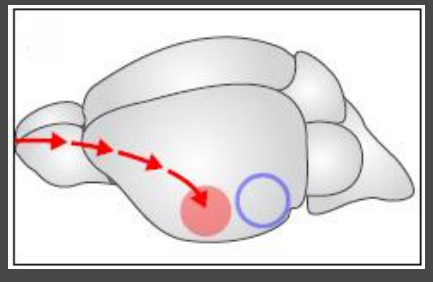


Perinatal

Testosterone/
Estradiol

Organization
(permanent changes)





Adult

Testosterone

Activation

Estradiol &
Progesterone

How can the female and male brains explain why females and males are so different?

Are the male and female brains wired differently?

Dimorphic brain functions/structures → Dimorphic social behaviors ?

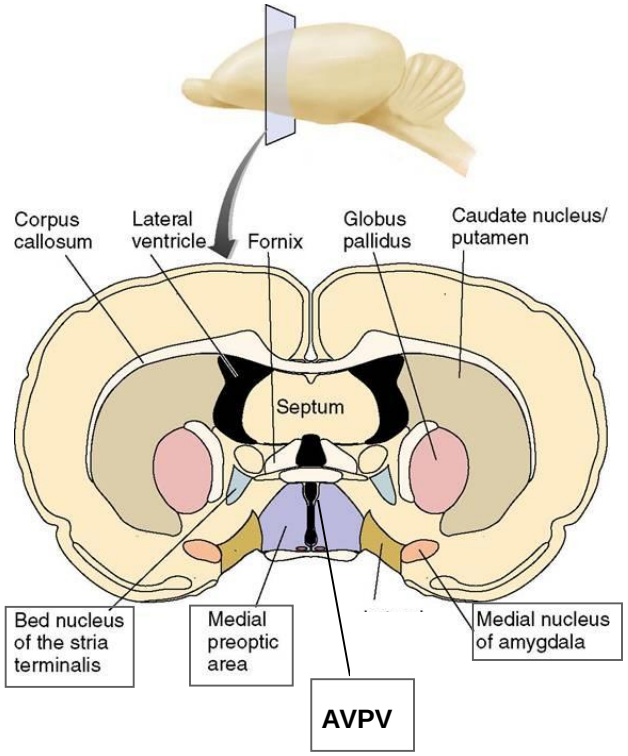
Sexually dimorphic brain nuclei in rodents

Bed Nucleus of the Stria Terminalis (BNST)
Sexually Dimorphic-Nucleus of Preoptic Area (SDN-POA)
Posterodorsal Medial Amygdala (MePD)

} Larger in male

Anteroventral Periventricular Nucleus (AVPV)

} Larger in Female

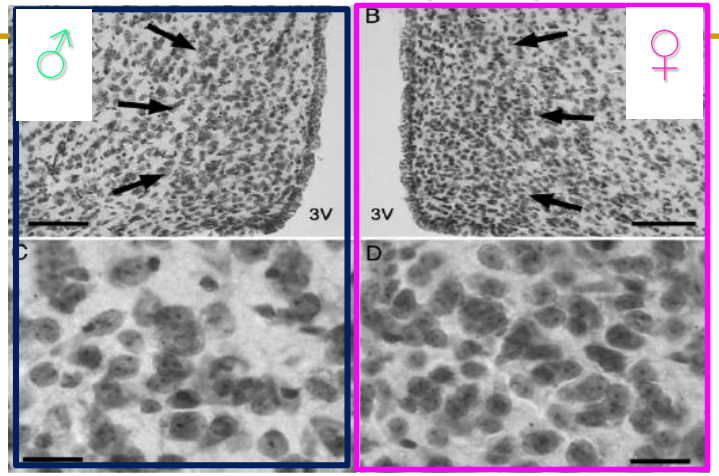


Sexual dimorphism: Morphology

Region	Volume larger in
AOB	Male
MeA	Male
PMv	Male
Posterior BNST	Male
Anterior BNST	Female
Central nucleus	Male
SDN-POA	Male
AVPV	Female
SON	Male
SCN	Male
VMN	Male
Locus Ceroleus	Female
SNB	Male
POA	Male
MePD	Male

Adapted from, Wilson & Davis, *Reproduction* 2007; Forger et al. 2015

AVPV (F>M)



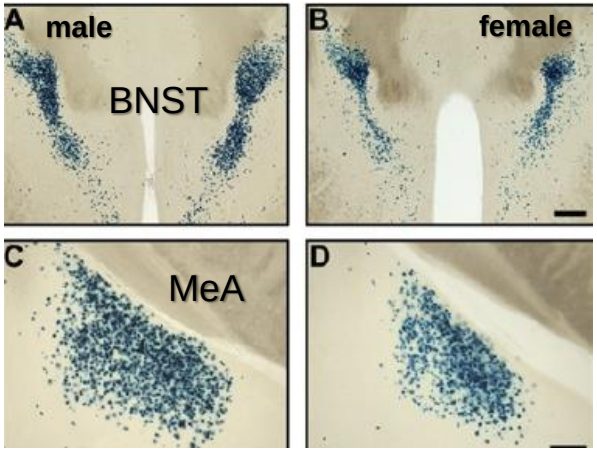
Forger et al 2004, *PNAS*

SDN-POA (M>F)

Gorski et al 1978, *Brain Res.*

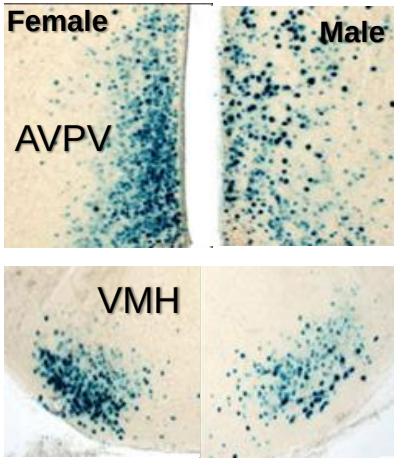
Sexual dimorphism: Gene expression

Androgen receptor



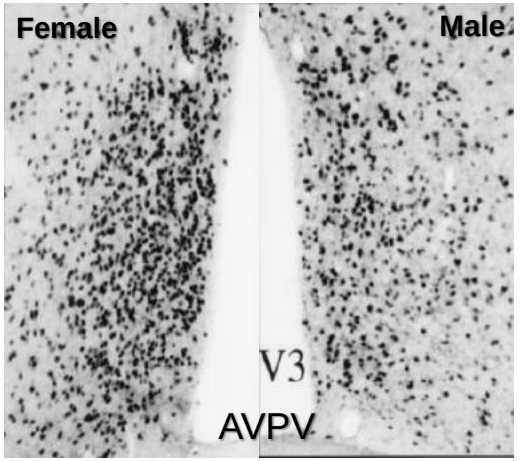
Juntti et al 2010, *Neuron*

Progesterone receptor



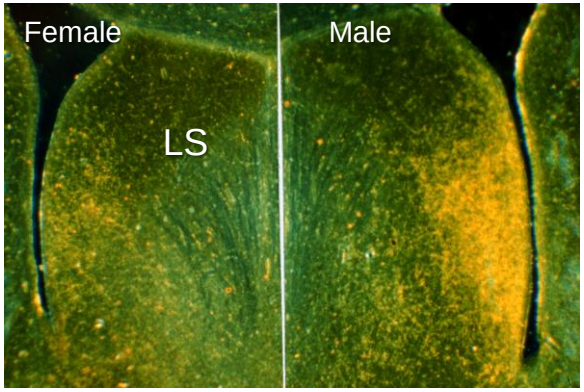
Yang et al 2013, *Cell*

Estrogen receptor α



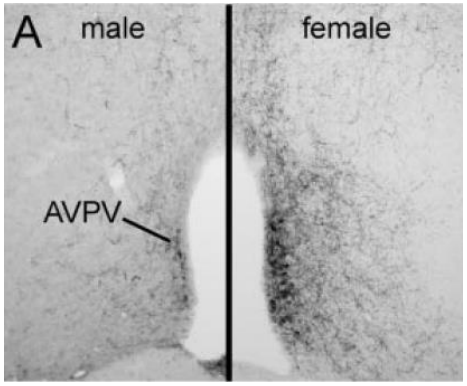
Simerly et al 1997, *PNAS*

Vasopressin fibers



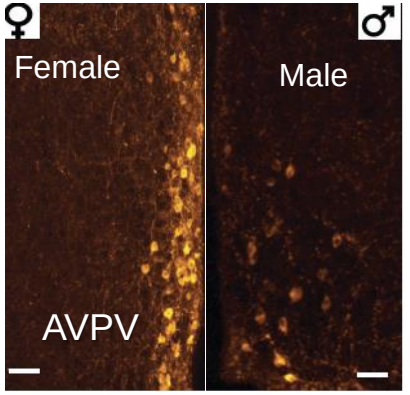
(Curtesy Geert de Vries)

Kisspeptin



Clarkson & Herbison 2006, *Endocrinology*

Tyrosine Hydroxylase

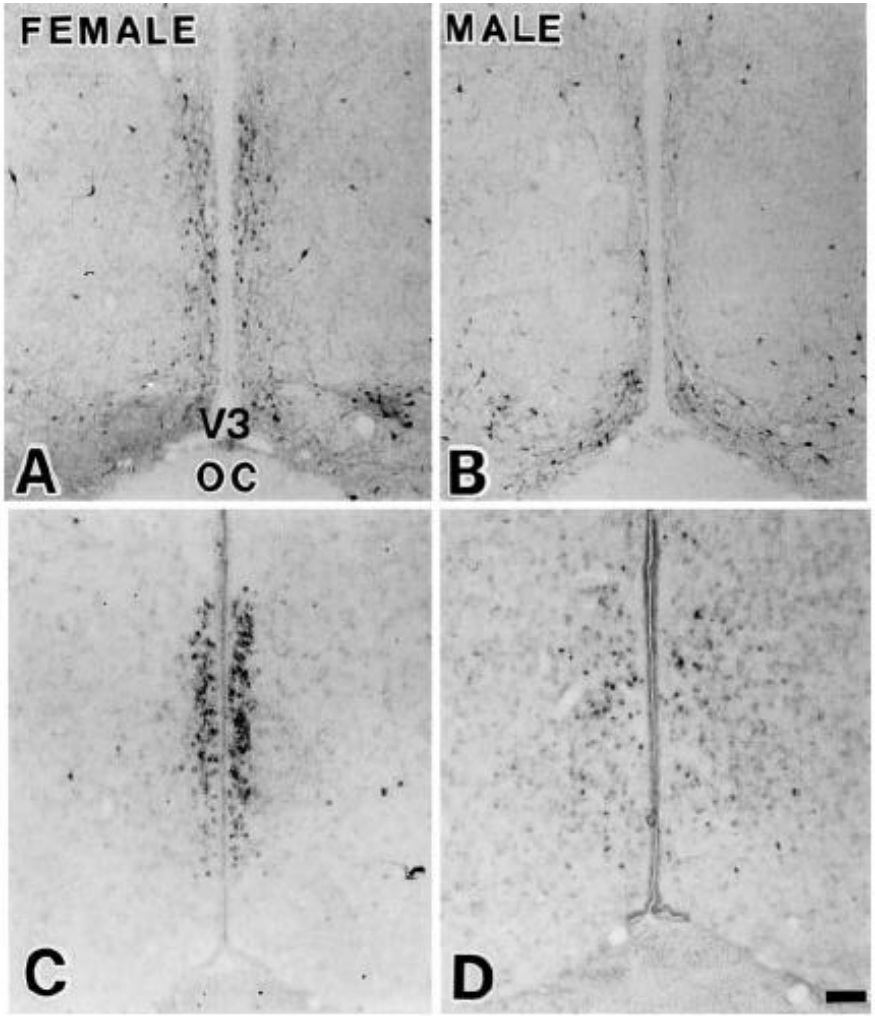


Scott et al 2015, *Nature*

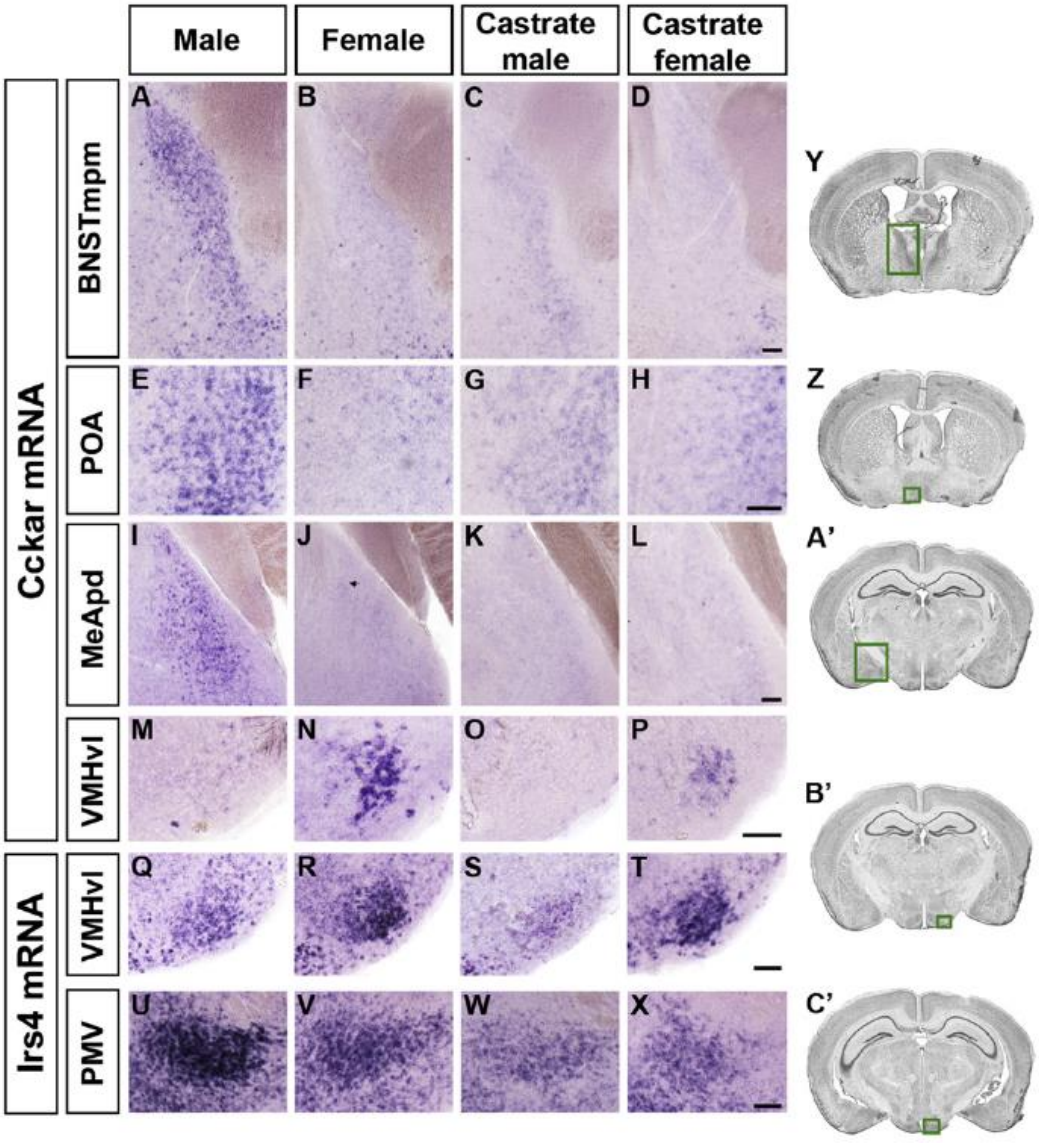
Sex differences in esrtogen-receptor-beta in the AVPV of rats can be altered by hormonal manipulation

Adult-intact

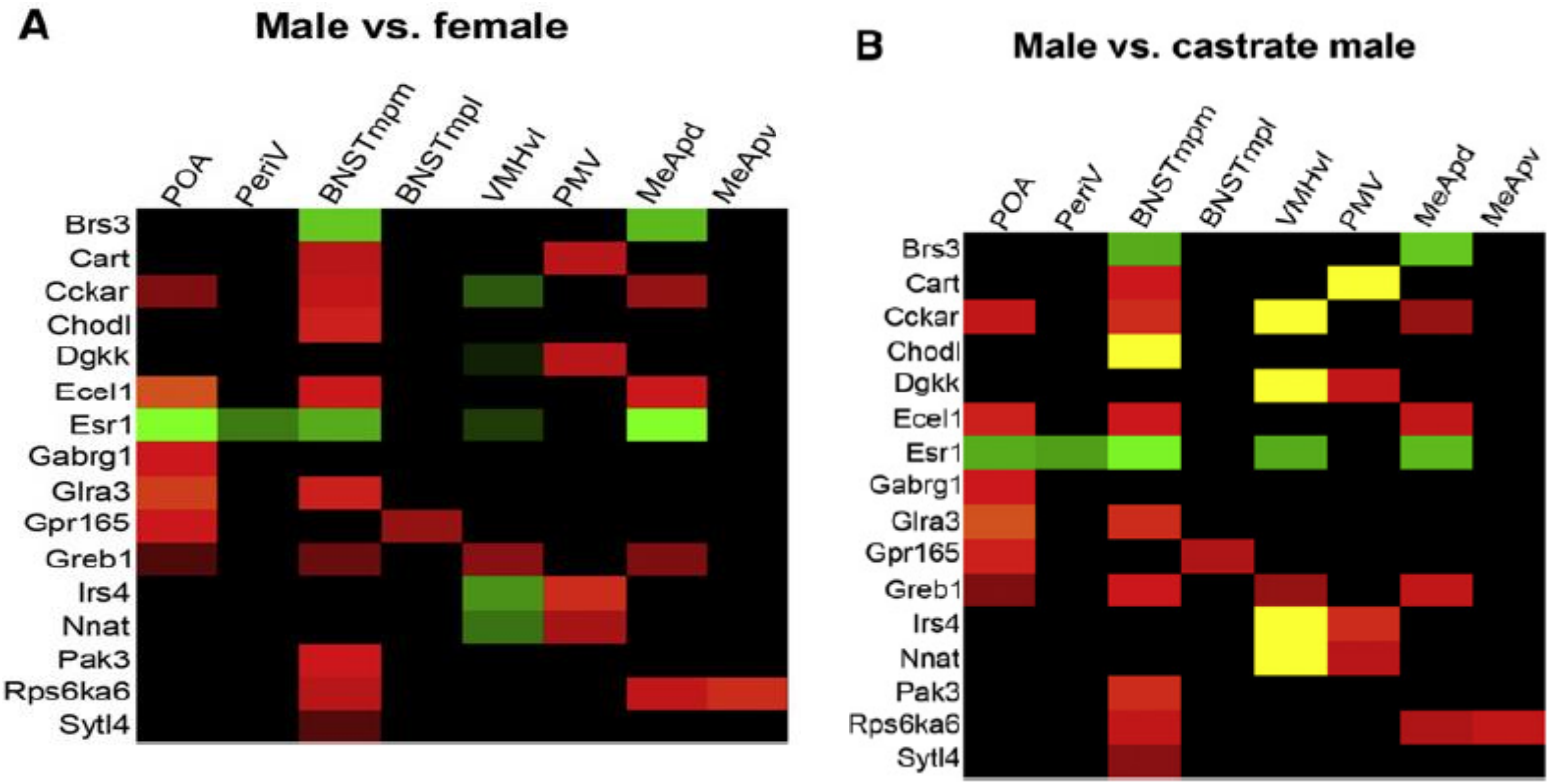
Prenatally hormone-manipulated



Orikasa et al 2001, PNAS

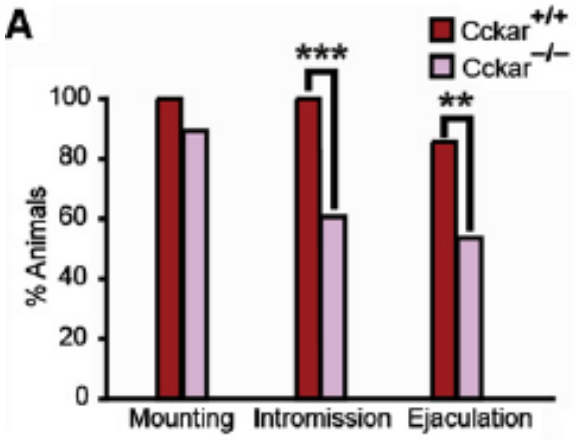


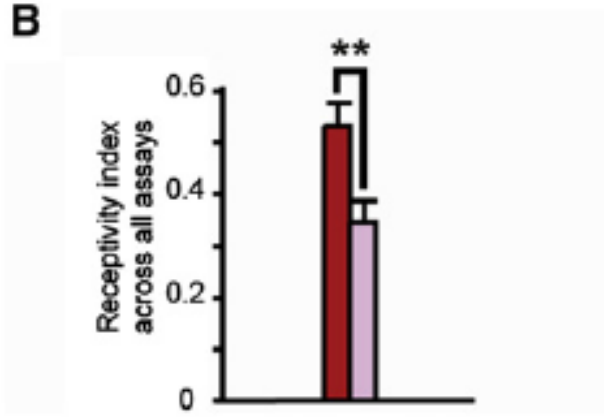
Xu et al 2012, Cell



Xu et al 2012, Cell

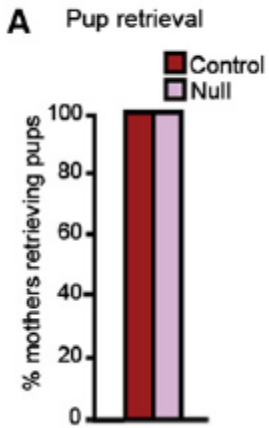
Control of female sexual behavior by *Cckar*

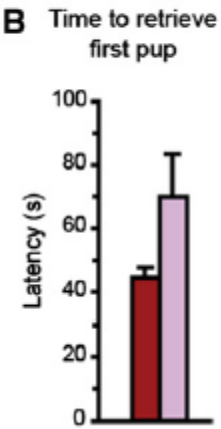


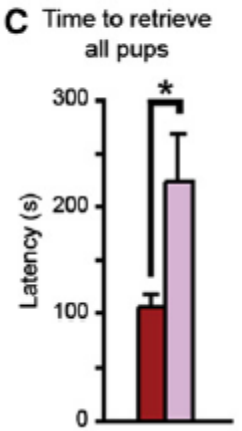


Control of maternal behaviors by *Irs4*

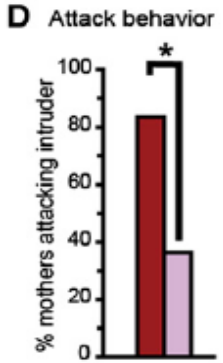
Maternal care

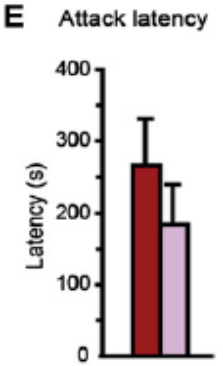


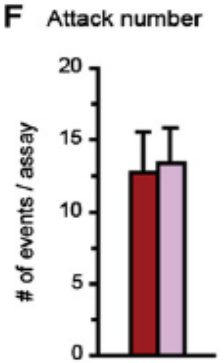


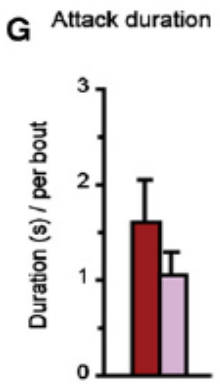


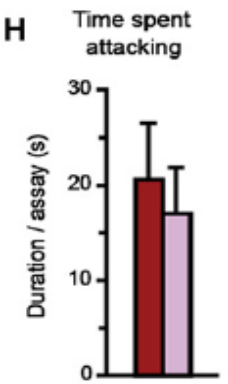
Maternal aggression

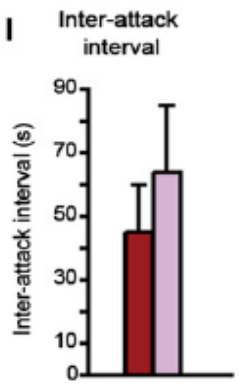




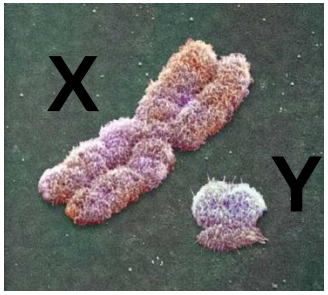


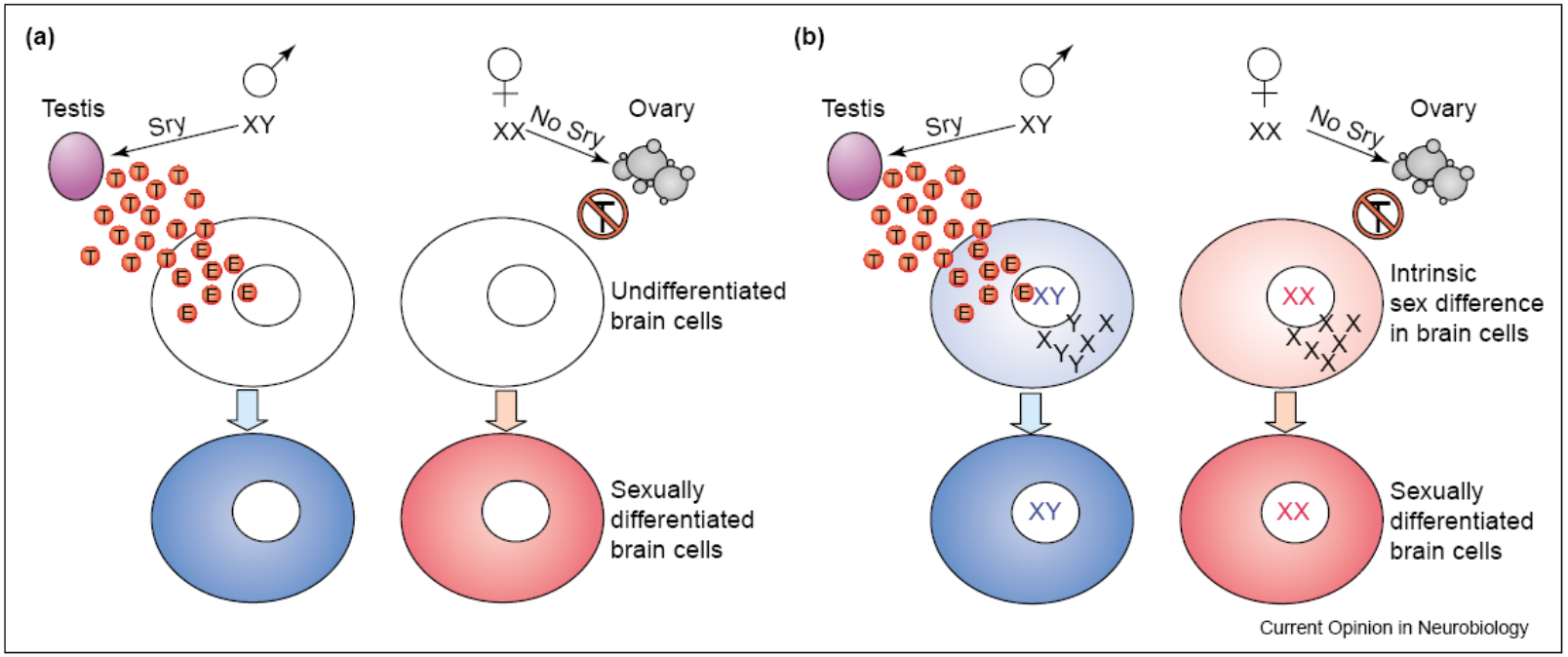






Sexual dimorphism can NOT be explained just by organization affects of sex hormones

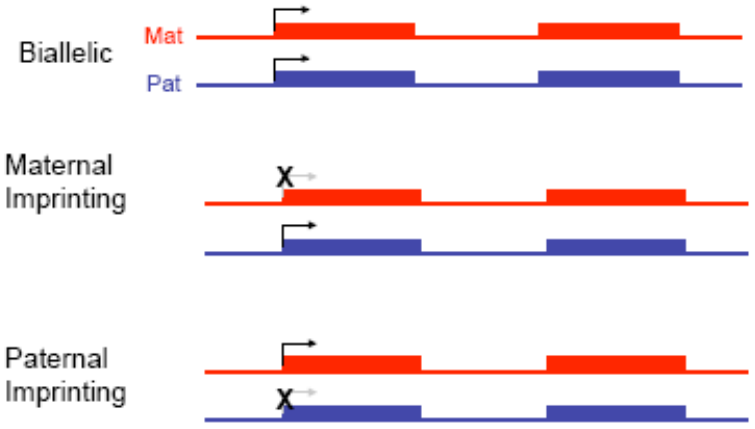


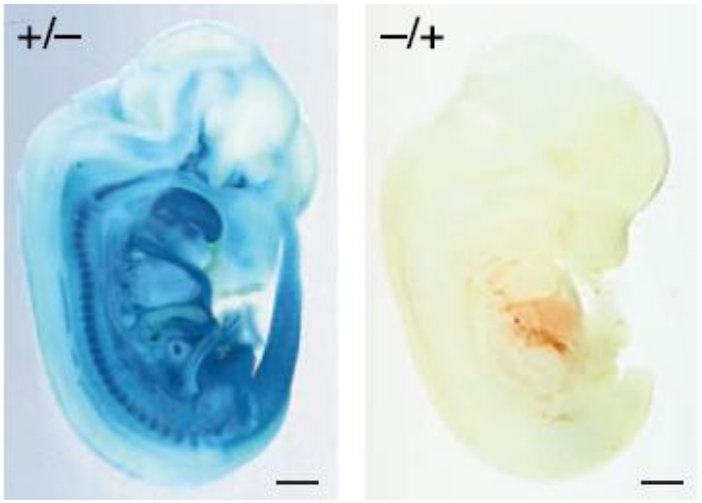


Imprinting genes

Definition:

A gene or chromosome region that is expressed when inherited from one (maternal or paternal) parent. But not when inherited from the other parent (i.e. parent-specific inactivation of a gene).



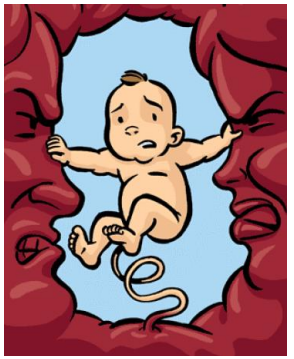


Imprinting genes

Mechanism:

Imprinting is determined by allele-specific DNA methylation at critical sites (e.g. promoter region) which represses the expression of the gene.

Imprinting genes



Biological function:
"The battle of the sexes theory" or "parental conflict theory"

- The father is more "interested" in the growth of the offspring, at the expense of the mother.
- The mother's interests are to conserve resources for her survival and provide sufficient nutrition to her offspring.

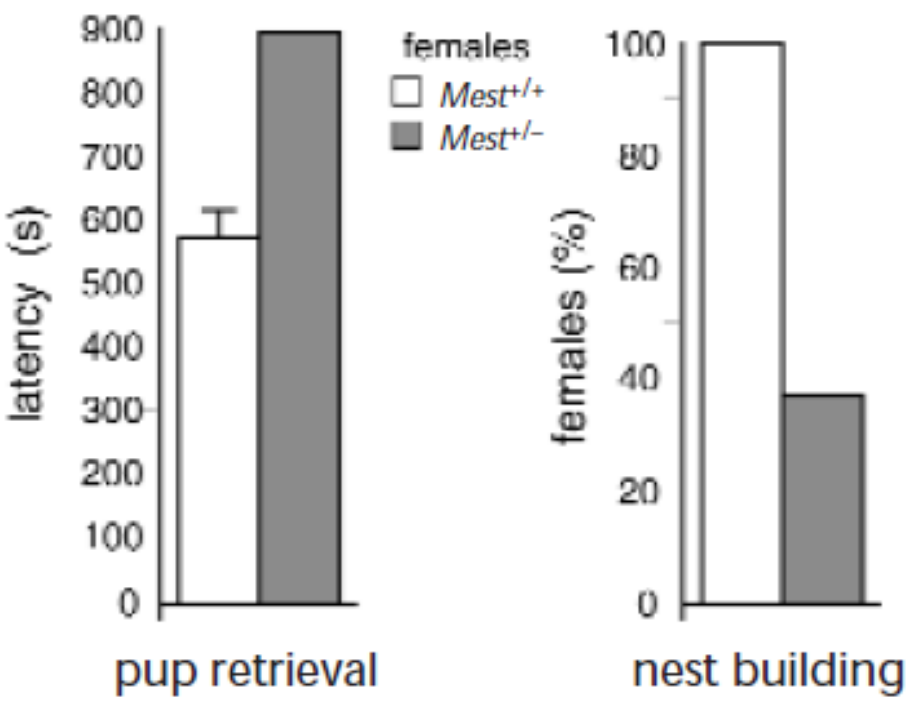
- Paternal imprinting genes are selected to extract resources from the mother for the fetus, while maternal imprinting genes are selected to inhibit this transfer of resources

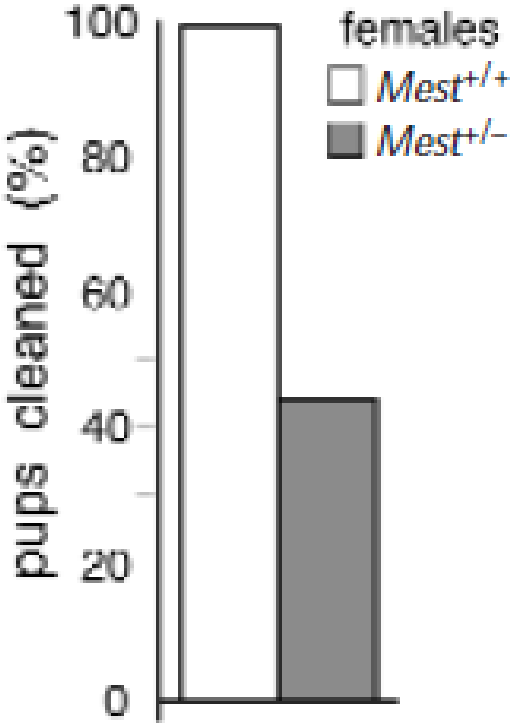
Maternal imprinting genes will repress growth of pups and paternal imprinting genes will enhance growth.

Paternally-imprinted genes

Intact Peg1 enhance maternal care

Peg1 mutant females exhibit deficiency in maternal behaviors

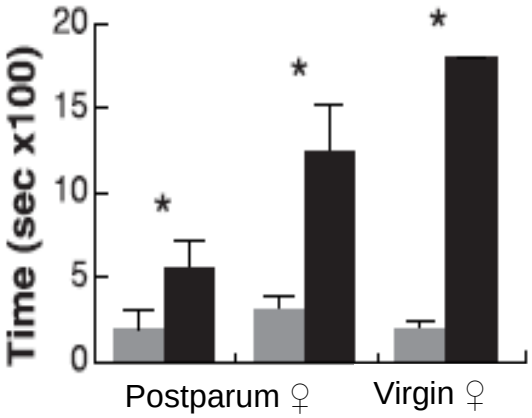




Curley et al 2004 *Proc R Soc B*

Paternally-imprinted genes (Peg3)

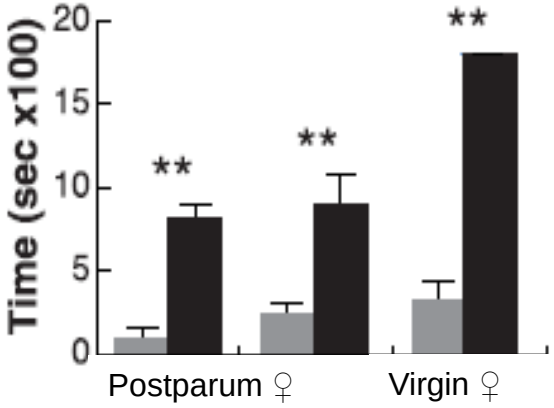
Time to retrieve pups

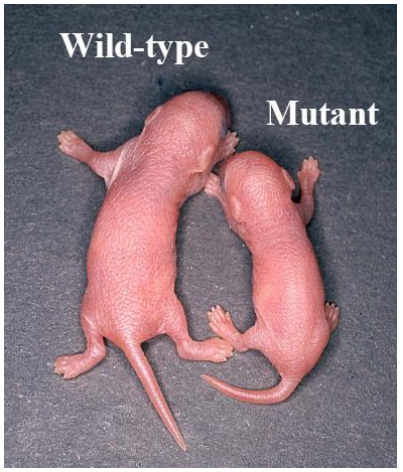


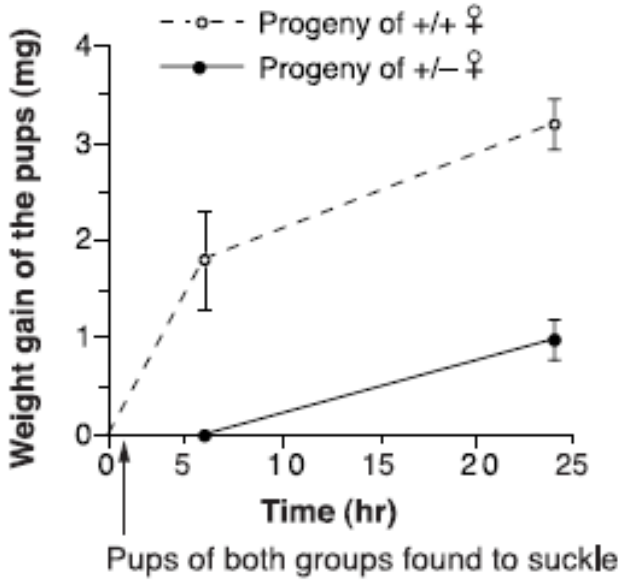
Mutant

Wild type

Latency of nest building

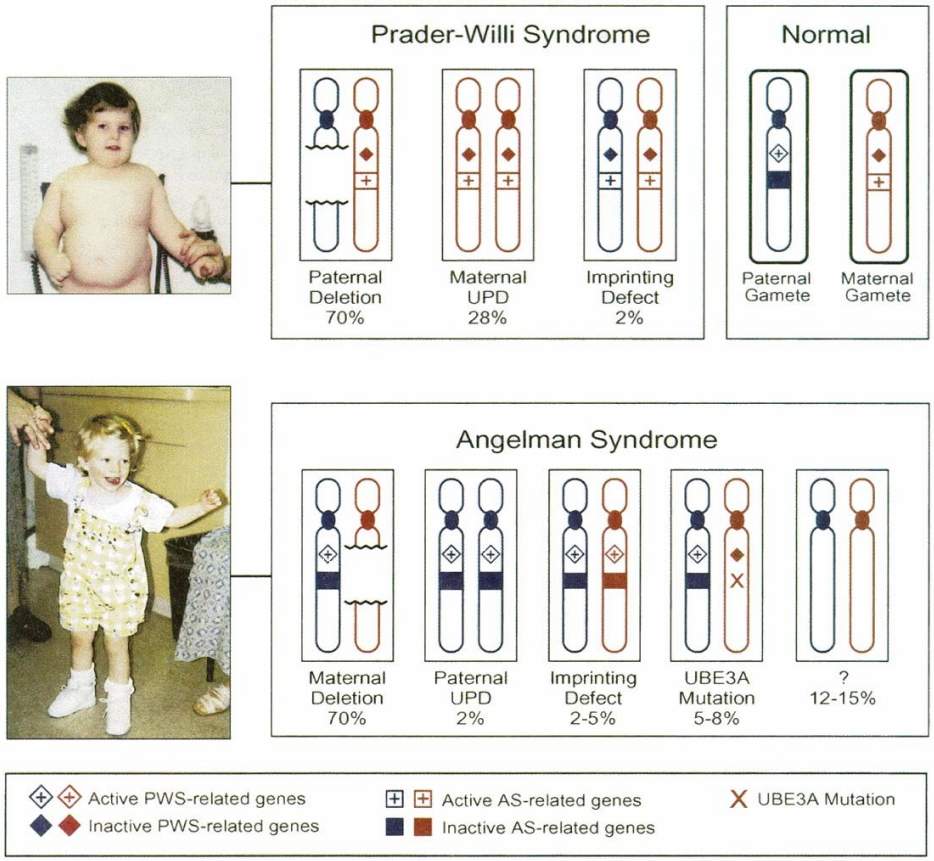






Lefebvre et al 1998; Nature Genetics
Keverne et al 1999; Science

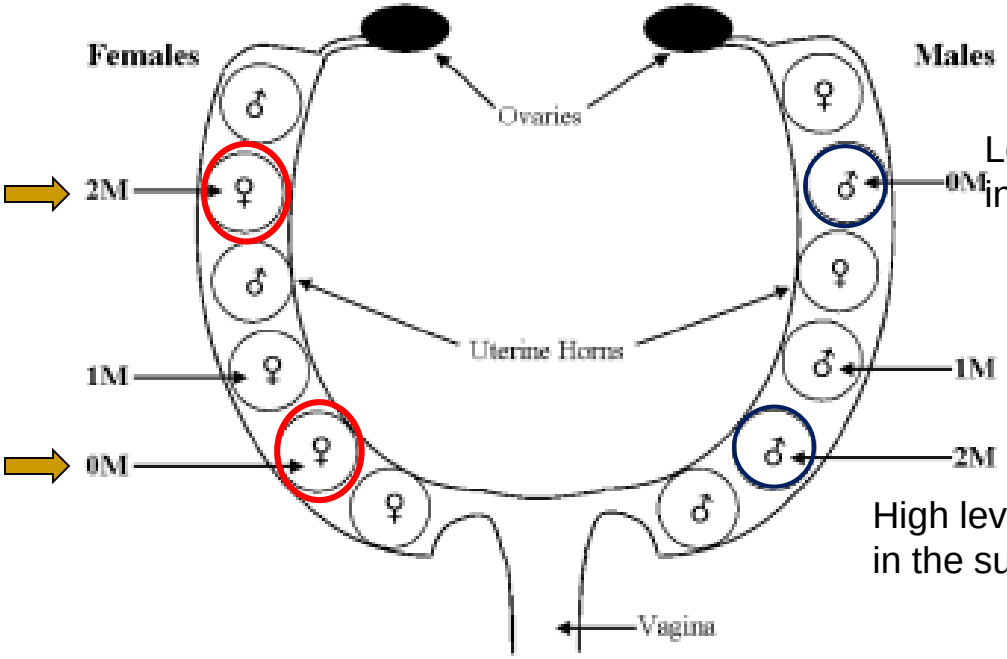
Imprinting genes and human disease



Effects of exposure to different levels of testosterone in uterus on female/male behavior

High level of testosterone in the surrounding

Low level of testosterone in the surrounding



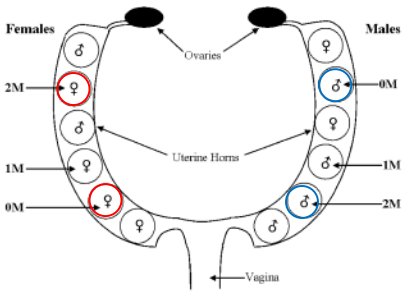
Low level of testosterone in the surrounding

High level of testosterone in the surrounding

Rayan and Vandernbergh 2002; Neuroscience and Biobehavioral Reviews

Effects of exposure to testosterone in uterus on female behavior

Sex	0M	2M
Physiology		
♀	Lower fetal testosterone levels	Higher fetal testosterone levels
♀	Earlier vaginal opening	Later vaginal opening
♀	Less male offspring	More male offspring
♀	Mate and impregnated earlier	Mate and impregnated later
♀	More sensitive to bisphenol-A	Less sensitive to bisphenol-A
♂ & ♀	Less sensitive to testosterone	More sensitive to testosterone
Morphology		
♀	Shorter AGD	Longer AGD
♂	Lower 5α-reductase levels	Higher 5α-reductase levels
Behavior		
♀	Less likely to mount other females	More likely to mount other females
♂	Less parental behavior	More parental behavior
♂ & ♀	Smaller home range	Larger home range
♂ & ♀	Less aggressive	More aggressive



Rayan and Vandernbergh 2002; Neuroscience and Biobehavioral Reviews

Effect of prenatal stress on sexual dimorphism in brain and behavior

Effect of prenatal stress on sexual dimorphism in the rat brain

	Control	*Environmental*	*Nutritional*
Litter size	11.3 ± 1.4	10.3 ± 1.3	9.2 ± 1.8
Neonatal weight (g)			
Males	6.93 ± 0.13	*5.03 ± 0.13	*5.36 ± 0.27
Females	6.52 ± 0.08	**5.76 ± 0.07	*5.35 ± 0.07

SDN measurements

Treatment	*Days postnatally*		
	Birth	*20 Days*	*60 Days*
Males			
Control	0.259 ± 0.015	**0.858 ± 0.083	**0.643 ± 0.035
ES	*0.471 ± 0.034	*0.419 ± 0.049	*0.345 ± 0.034
NS	*0.447 ± 0.027	*0.553 = 0.086	*0.278 ± 0.039
Females			
Control	0.261 ± 0.021	0.369 ± 0.027	0.378 ± 0.025
ES	0.324 ± 0.034	0.440 ± 0.076	0.258 ± 0.023
NS	0.363 ± 0.033	0.502 ± 0.066	0.339 ± 0.036

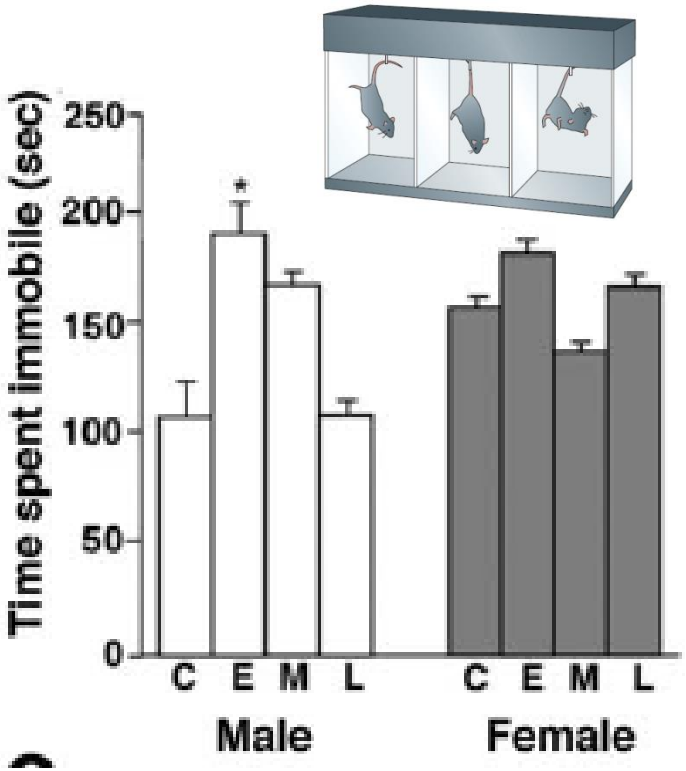
ES: Environment stress (change in lighting/ temperature)
NS: nutritional stress (50% of total food of control males)

Anderson et al 1985, Brain Research

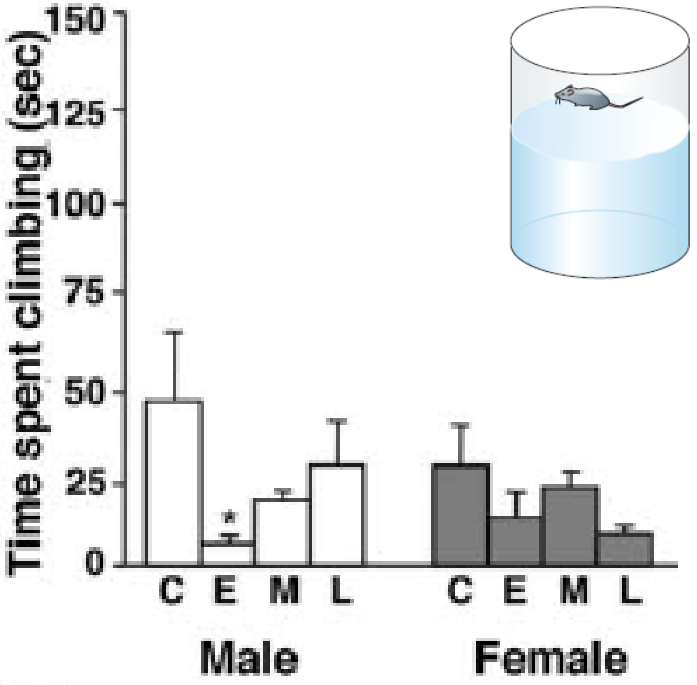
Sex-Specific Programming of Offspring Emotionality after Stress Early in Pregnancy

Bridget R. Mueller and Tracy L. Bale

Tail suspension assay



Forced swim test



C: control;
Prenatal stress during (E) early, (M) mid or (L) late gestation

Mueller and Bale 2008, JNS

The control of pheromone signals on sexually dimorphic reproductive behaviors

What are pheromones?

Chemical (odor) signals that are emitted by animals to communicate information to their own species

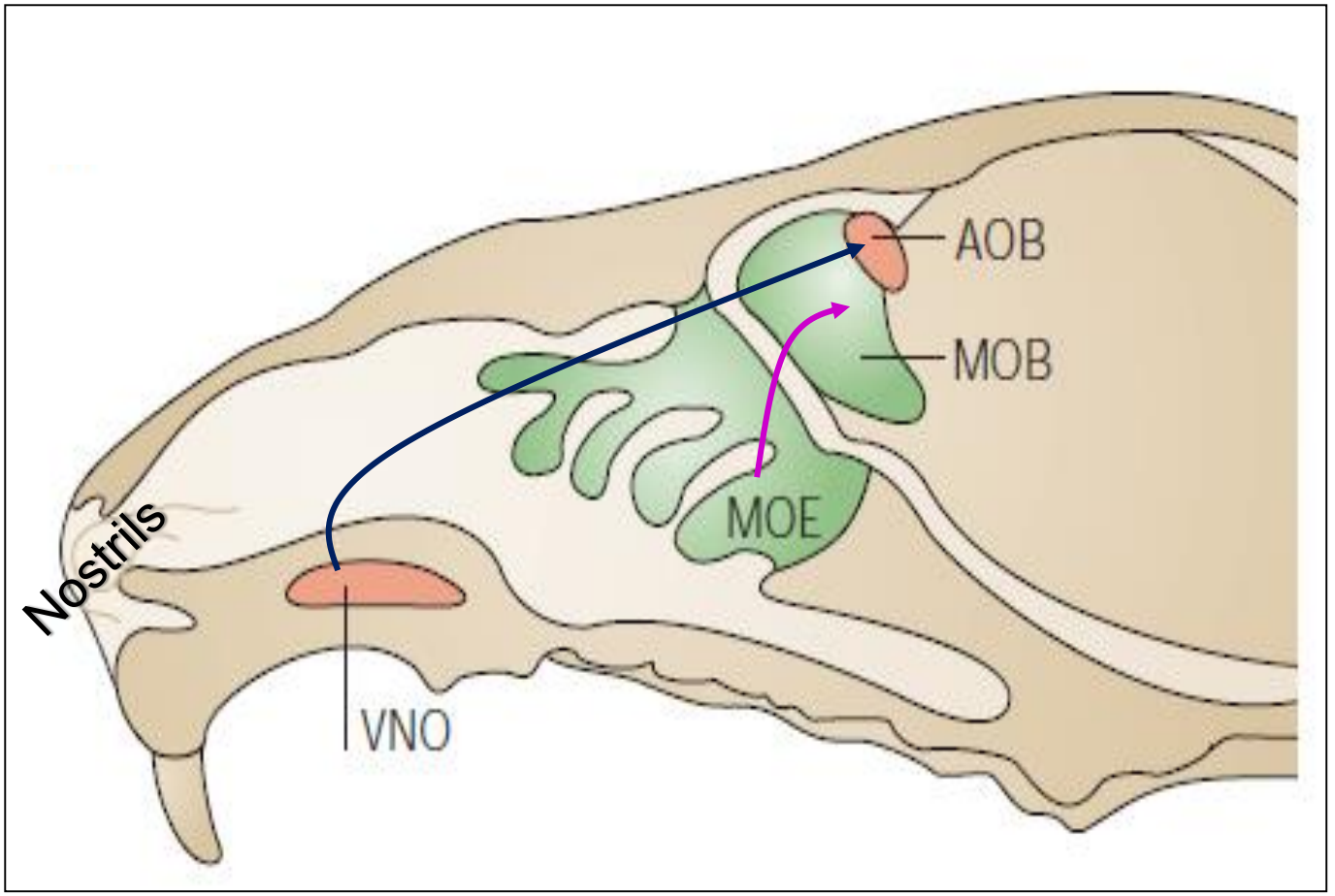
Pheromone signals are largely involved in the regulation of social and reproductive behaviors in most animals (including in human)

Attracting mate partner

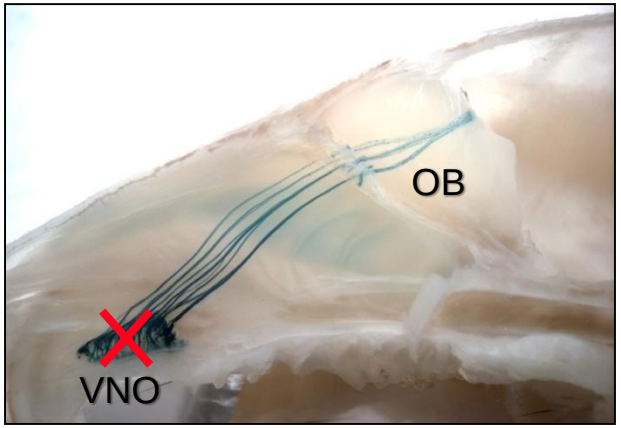
Pup recognition

Male territoriality

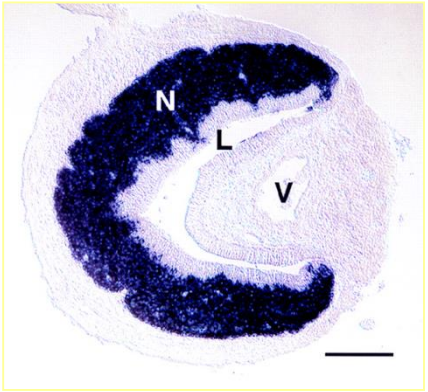
The olfactory systems

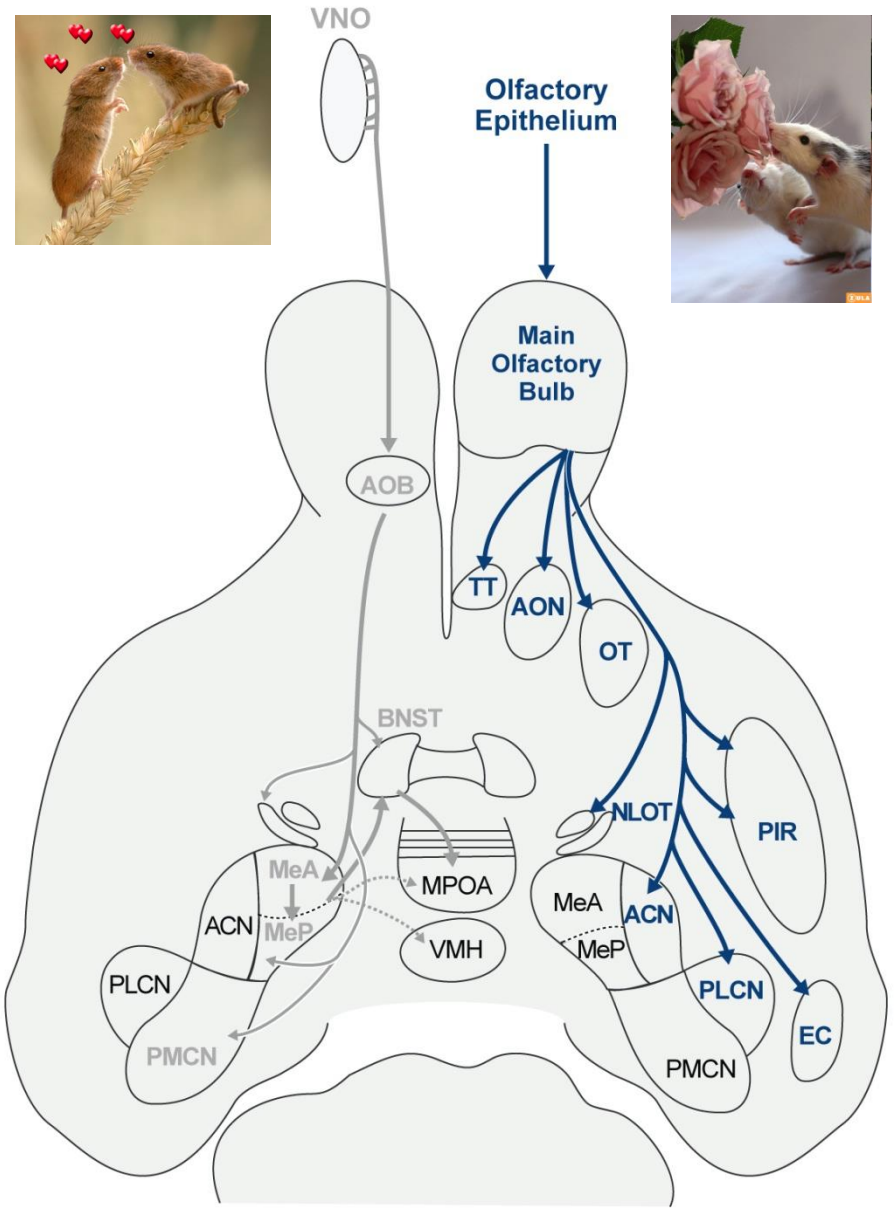


Detection of chemosensory signals in mice

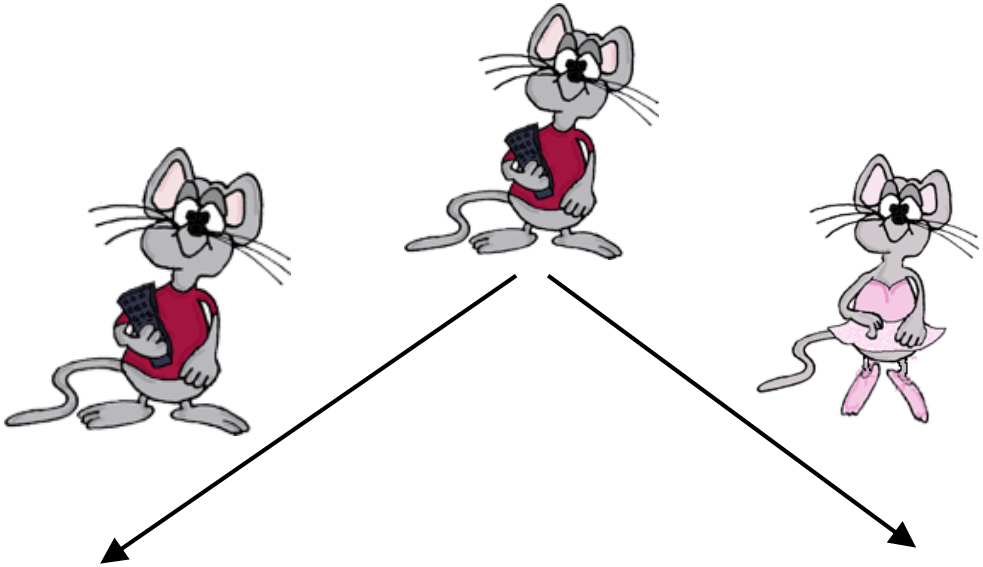


TRPC2 expression in the VNO





Typical male-female reproductive behaviors



Aggressive behavior

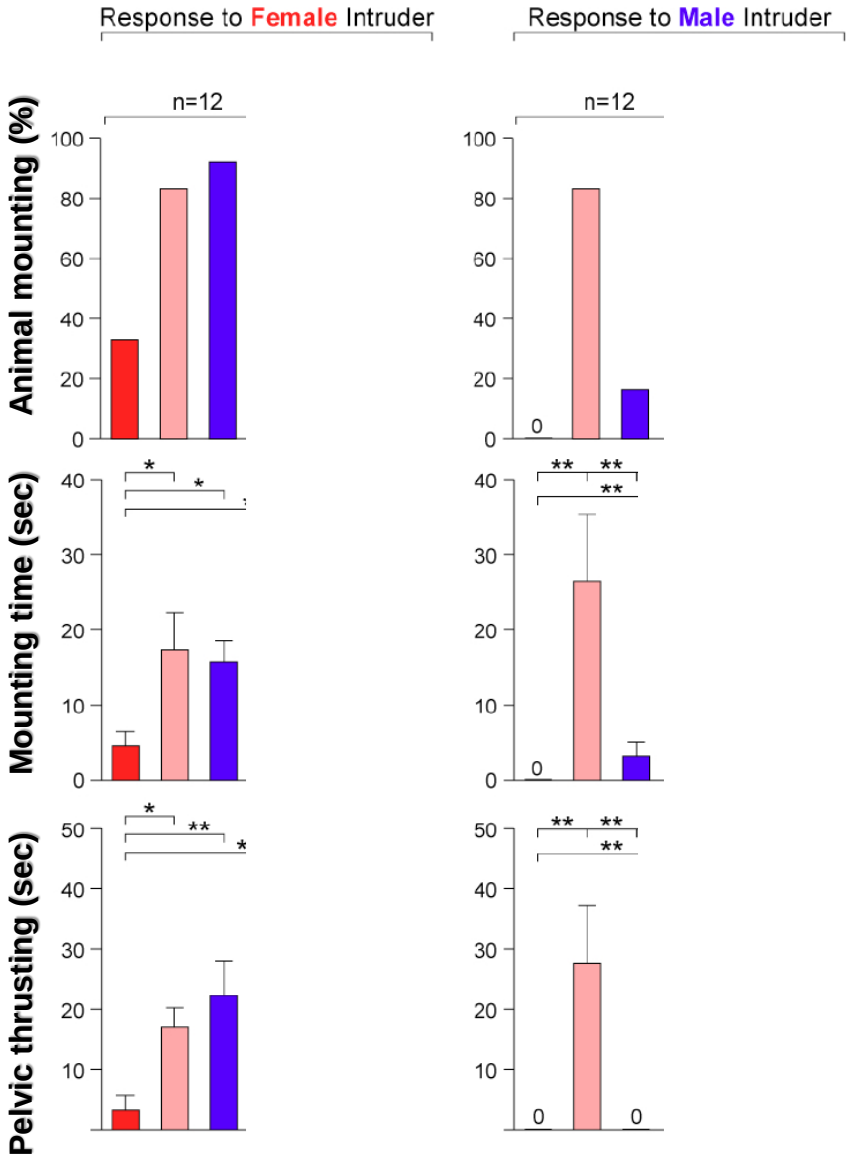
Sexual behavior

Sexual behavior of TRPC2-KO lab females

TRPC2 mutant female (brown) with normal male (black)

Kimchi et al. 2007; *Nature*

Male-typical sexual behavior in TRPC2-KO females



♀ WT

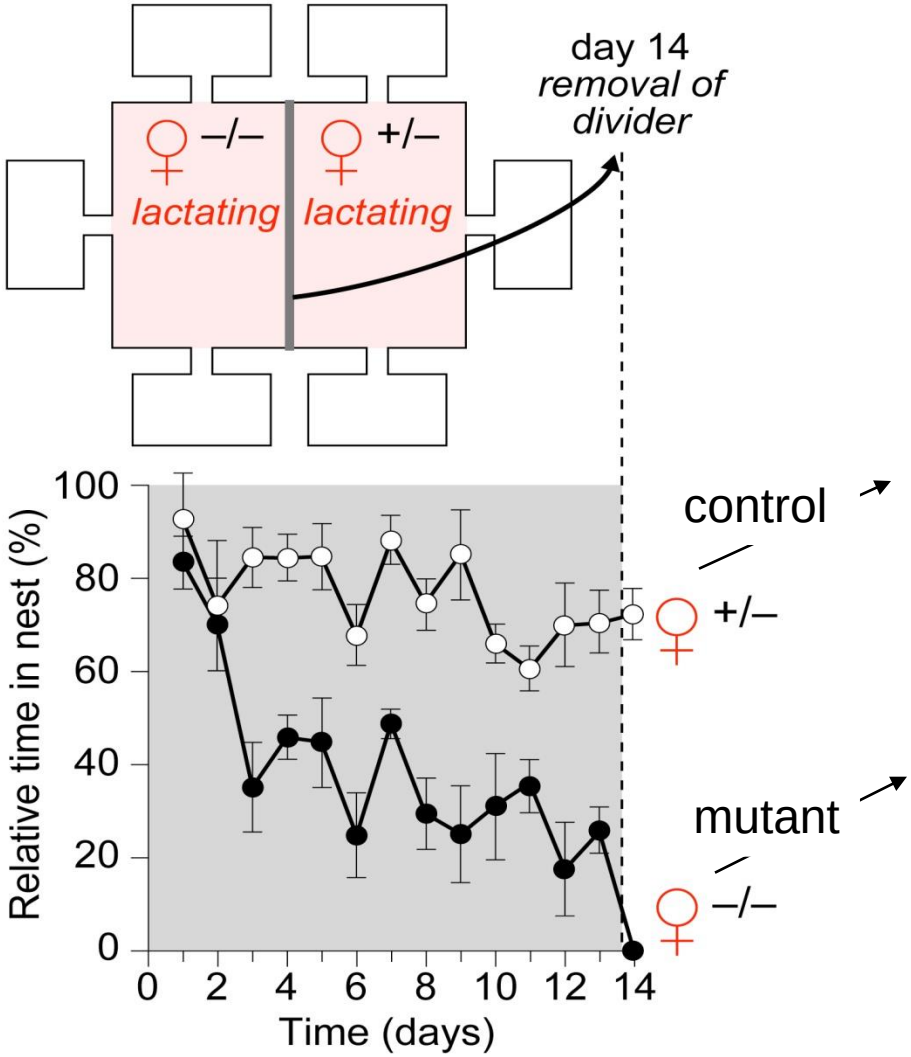
♀ TRPC2-KO

♂ WT

Kimchi et al. 2007; *Nature*

♀ **TRPC2$^{-/-}$ mutant (light) +**
♂ **Sexually experienced intruder (dark)**

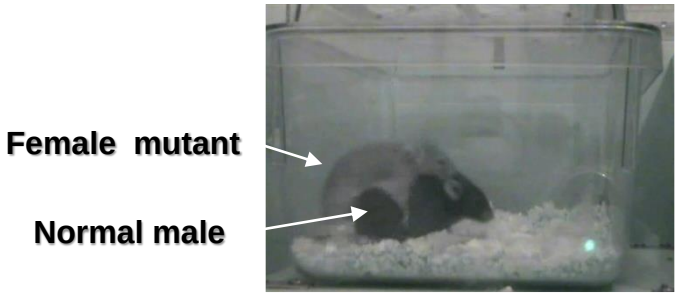
Maternal behavior



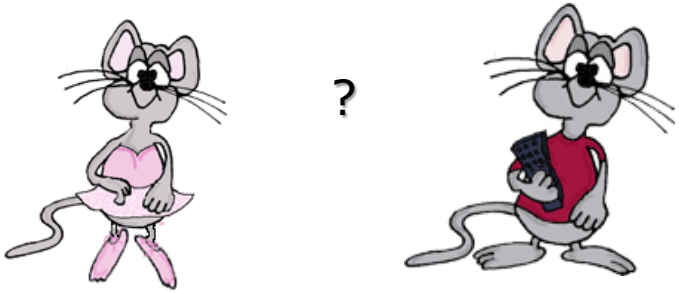
	TRPC2$^{+/-}$	TRPC2$^{-/-}$	P value
Weight of animals (grams)			
Males (n=15)	25.67 ± 0.66	25.96 ± 0.68	NS
Females (n=26)	21.41 ± 0.69	22.43 ± 0.56	NS
Duration of estrous cycle (days)			
Females (n=10)	5.20 ± 0.25	5.40 ± 0.26	NS
Steroid hormone level in blood			
Total testosterone (ng/ml)			
Males (n=5)	3.10 ± 0.30	4.50 ± 0.60	NS
Females (n=6)	<0.1	<0.1	
Free testosterone (pg/ml)			
Males (n=5)	14.10 ± 1.30	15.30 ± 1.50	NS
Females (n=6)	0.19 ± 0.07	0.41 ± 0.03	<0.05
17-β estradiol (pg/ml)			
Males (n=5)	21.31 ± 3.20	20.58 ±2.80	NS
Females (n=6)	14.29 ± 2.10	14.91 ± 1.50	NS

Behavioral phenotype of TRPC2-KO females

↑ Male-typical sexual behavior
(courtship and mounting behaviors)

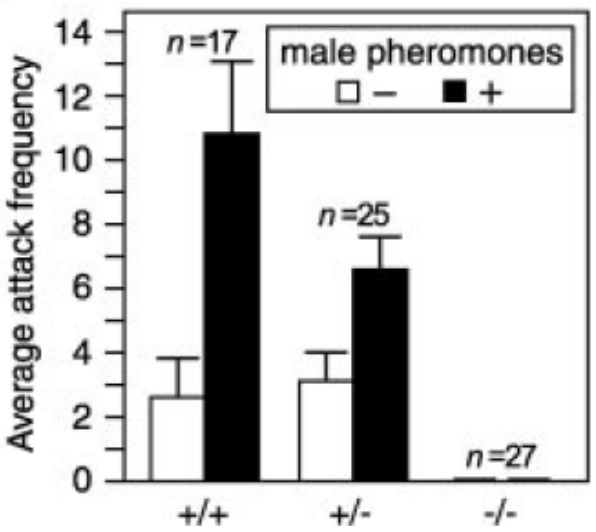


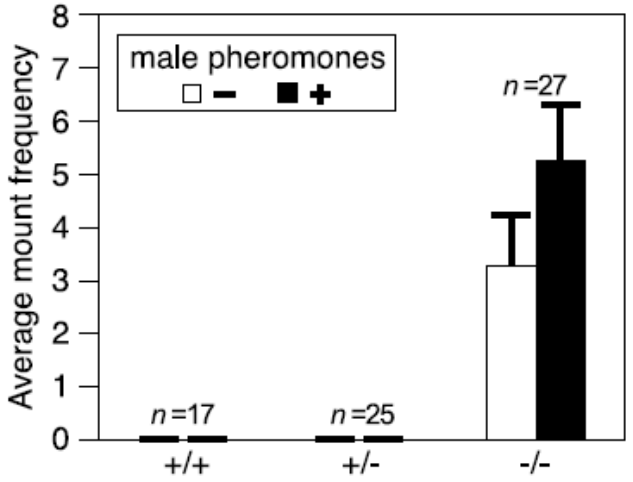
Failure to discriminate between
male and female

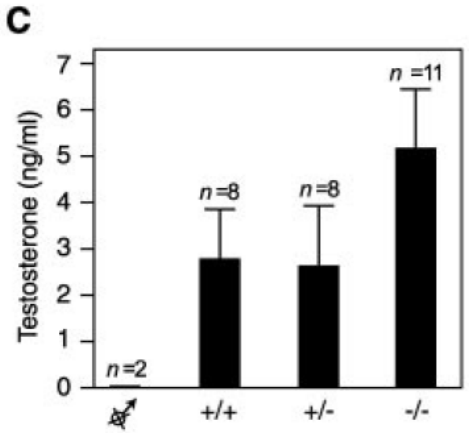


↓ Female-typical behavior
(maternal behavior)

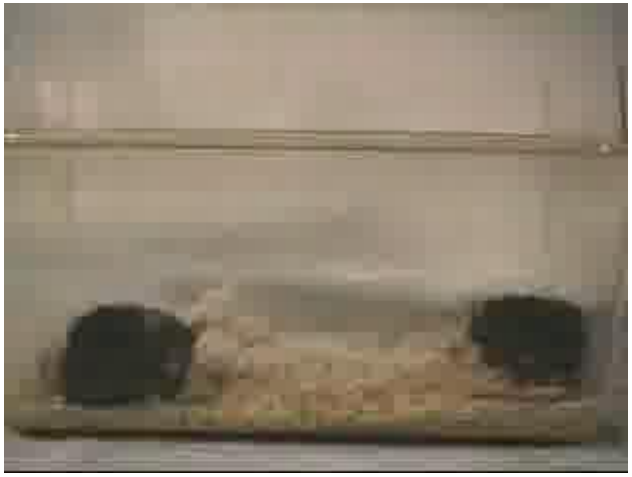
Behavioral phenotype of TrpC2$^{-/-}$ males







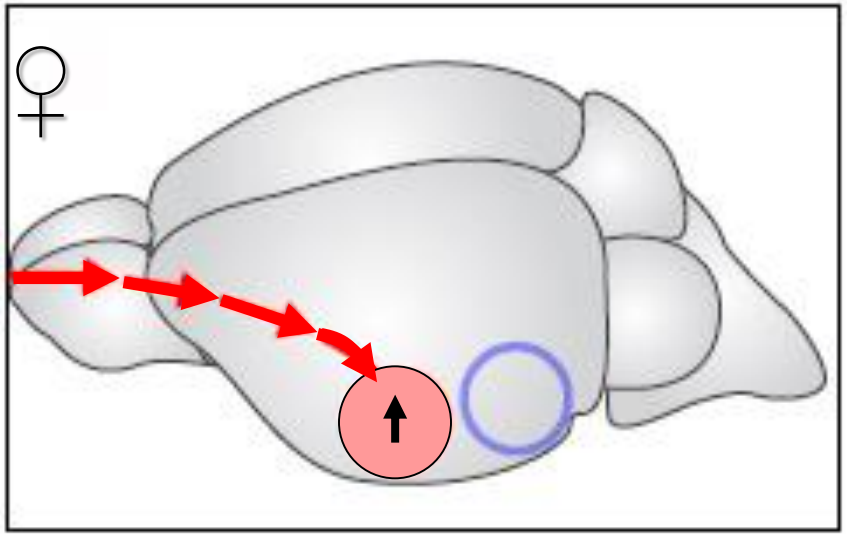
Stowers et al 2002; Science



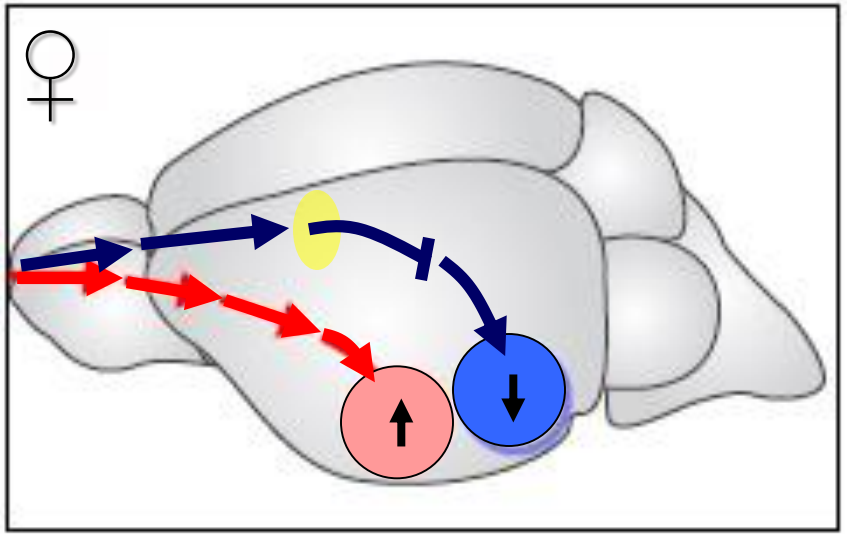
2 control (WT) males

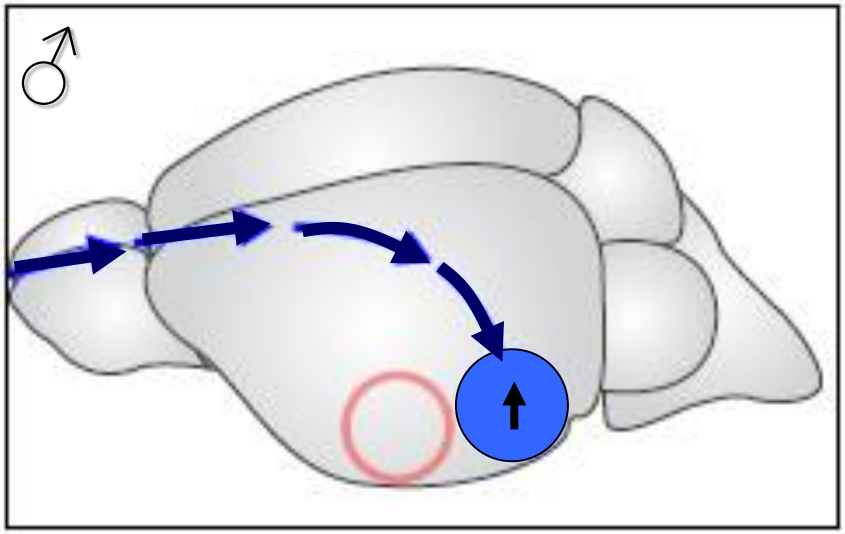
4 mutant males

Old model



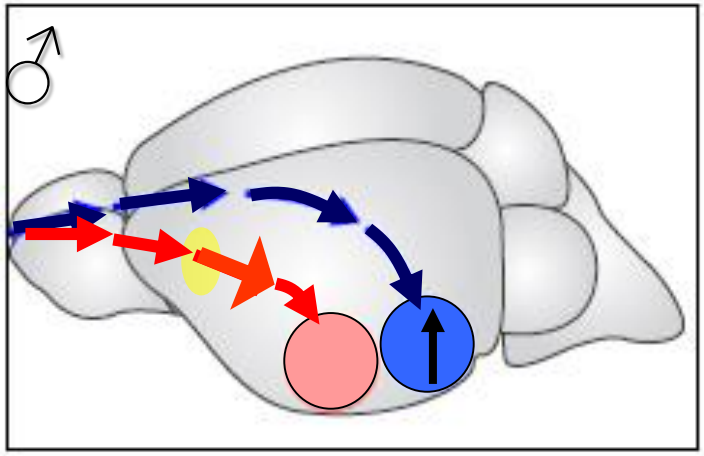
New model

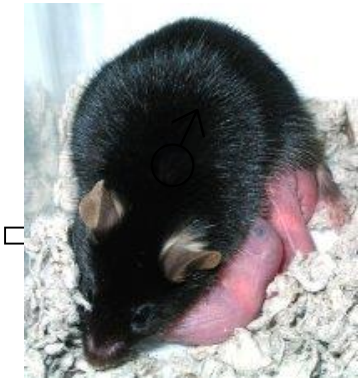




Model: Pheromonal inputs repress neuronal circuits for female-typical behavior in males

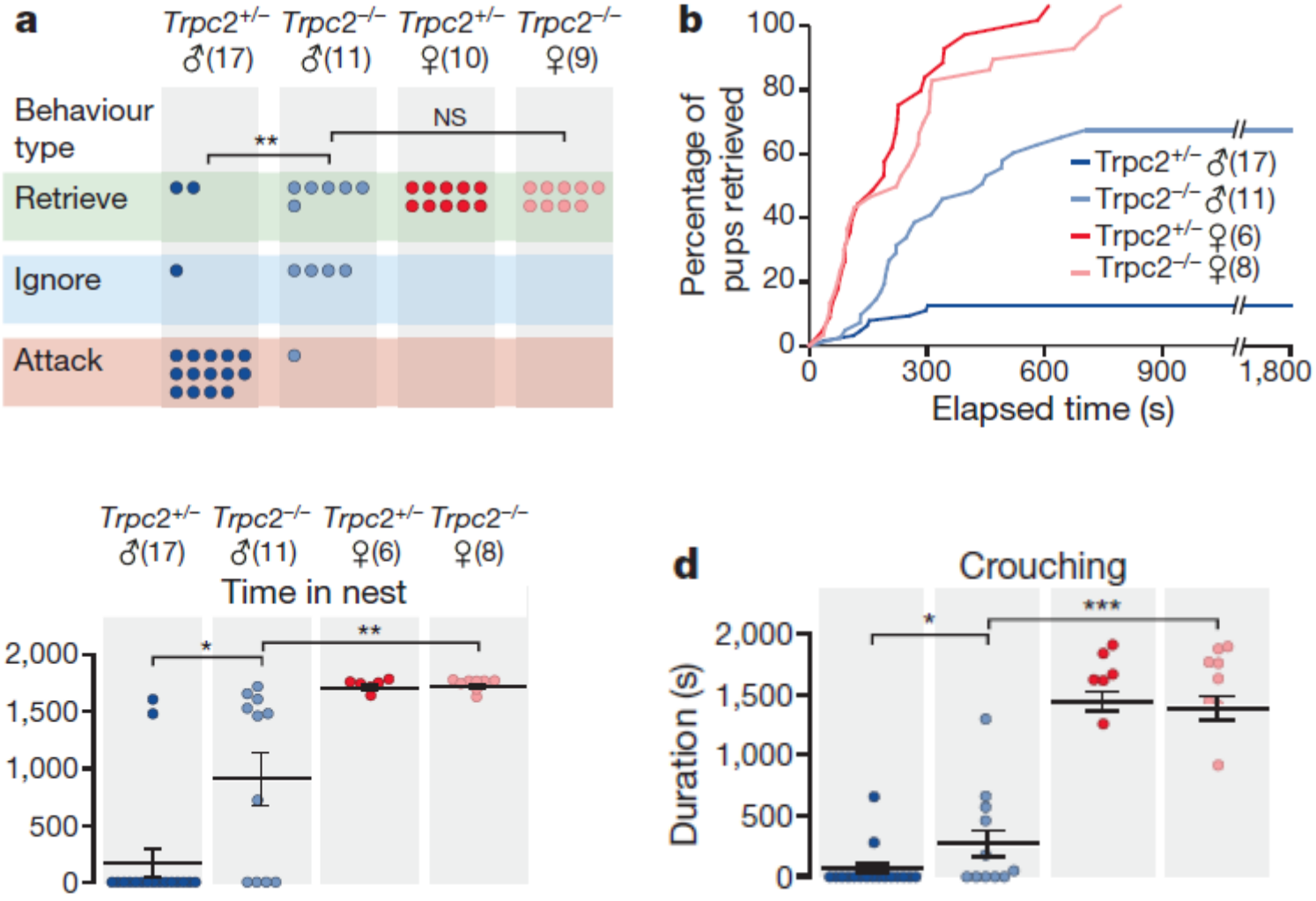
Sex-specific pheromone signals





Dulac and Kimchi, 2007, CONB

Behavioral phenotype of TrpC2$^{-/-}$ males



Wu et al 2015, *Nature*

Social and sexual behaviors of male mutant mice

↓ Aggressive behavior

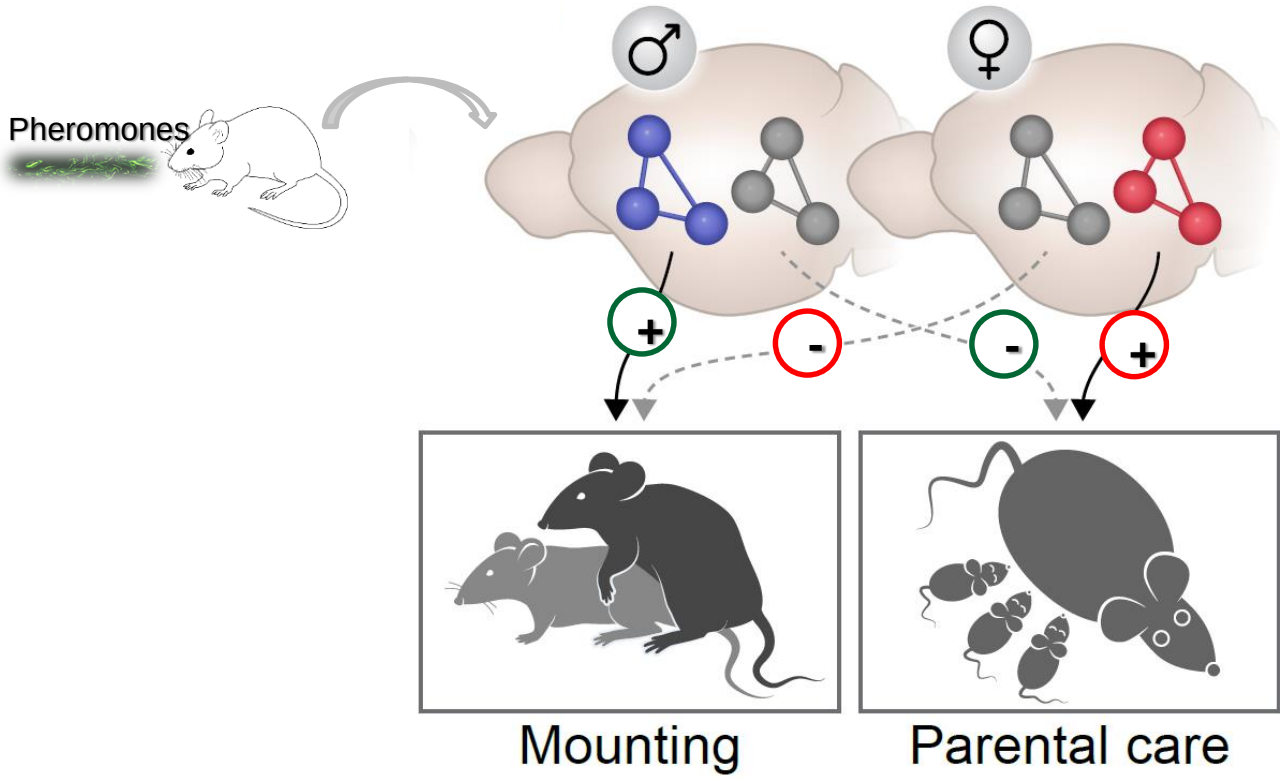
Failure to discriminate between male and female

?

↑ Female-typical behavior
(pup caring / nursing behavior)

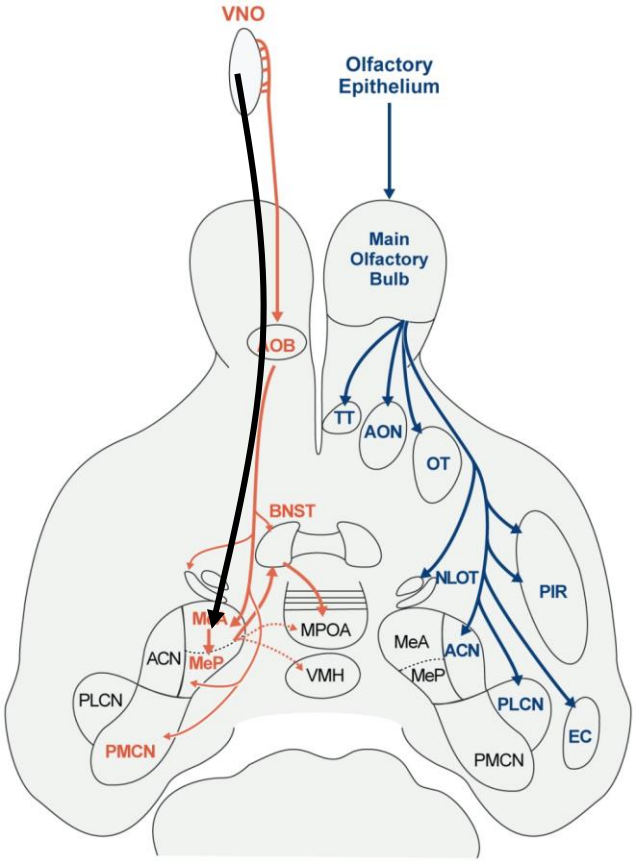
Normal testosterone basal level

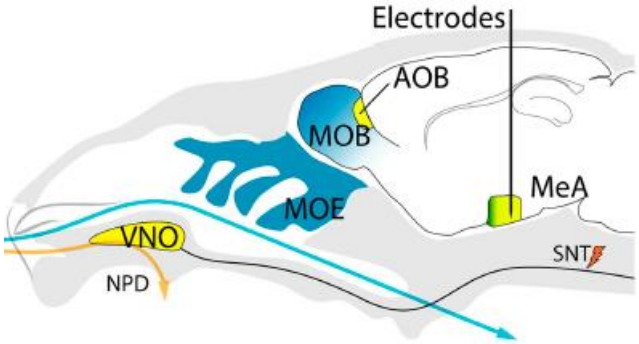
Sex-typical networks exist in both sexes



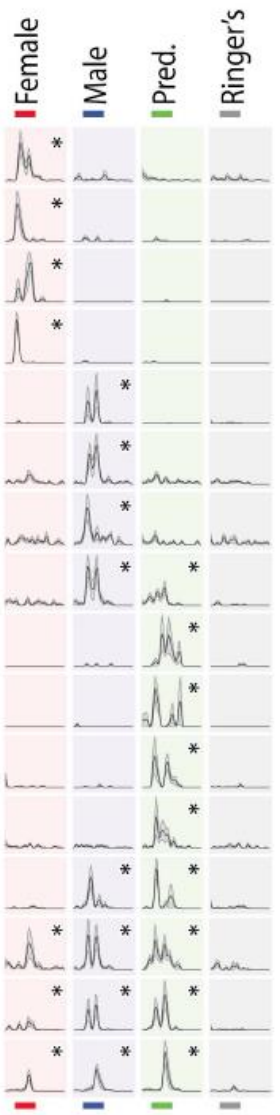
Kimchi et al. 2007, *Nature*
Zilkha et al. 2021, *Curr Opin Neuro*

MeA sensory responses to VNO stimuli



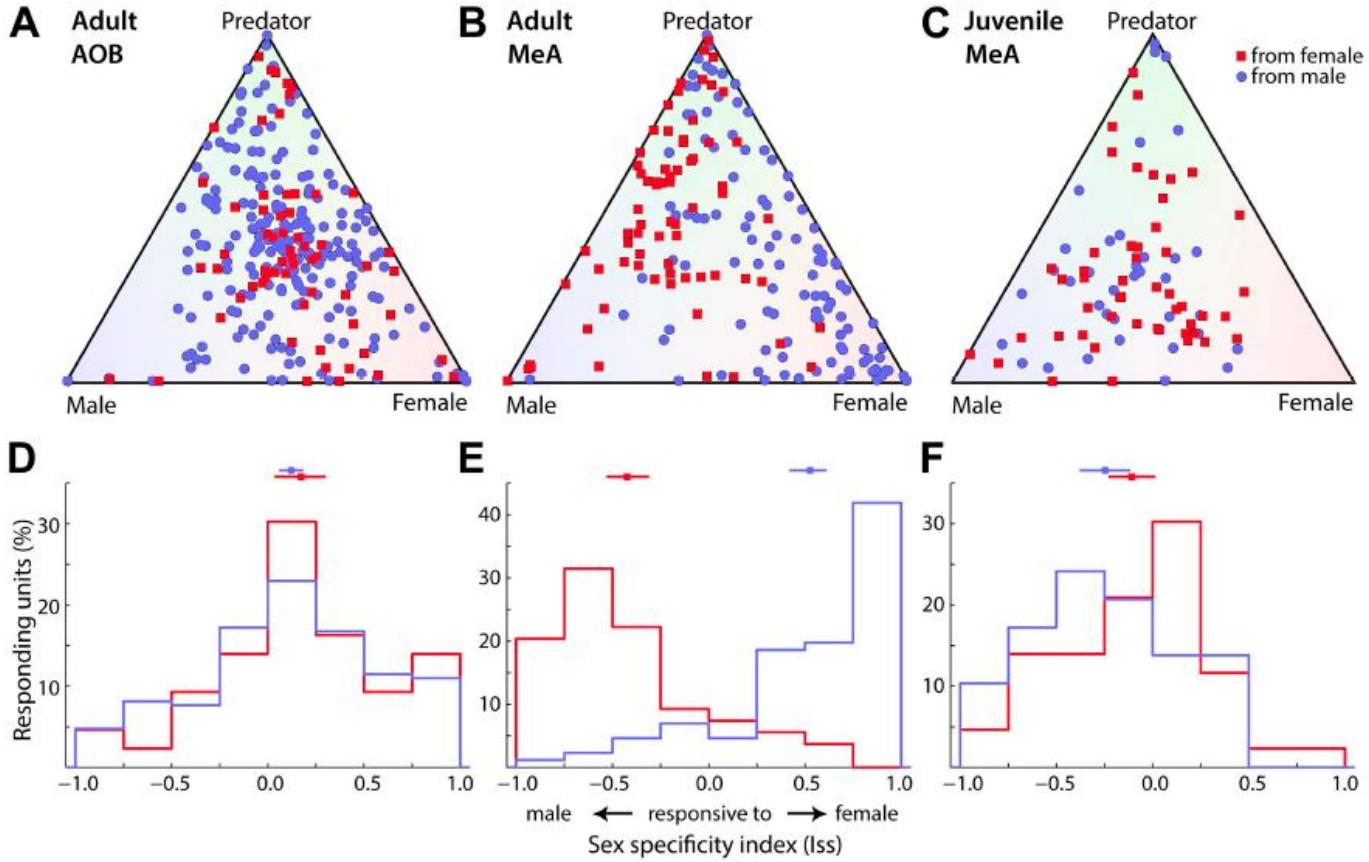


Electrical stimulus to artificially activate the VNO pump



Bergan et al 2014, eLife

Sexual dimorphism in neural responses of the adult medial amygdala (MeA) to chemosignals



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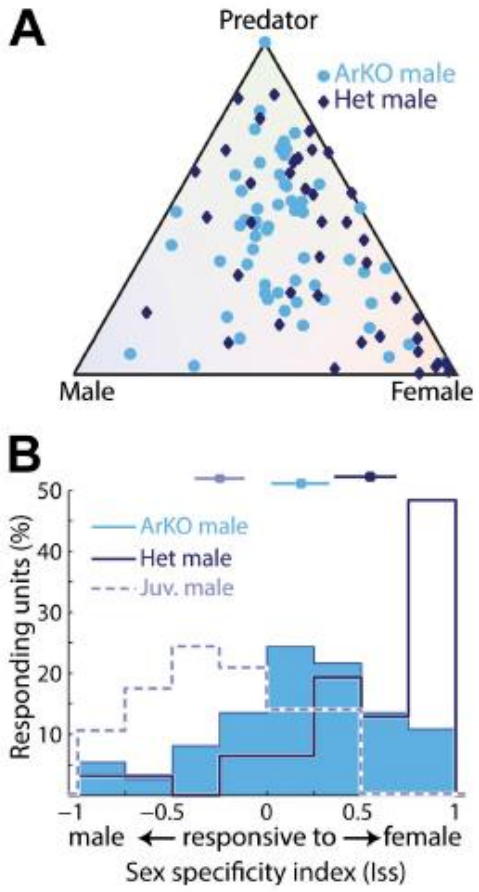
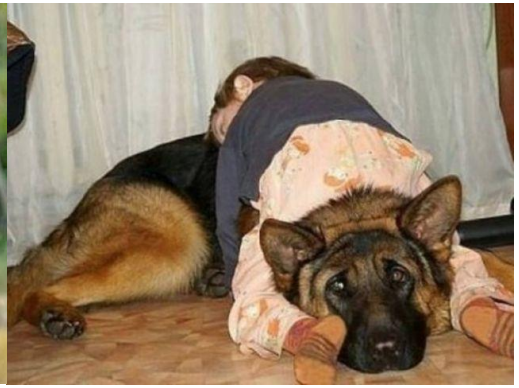


ArKO=aromatase knockout mice

Bergan et al 2014, eLife

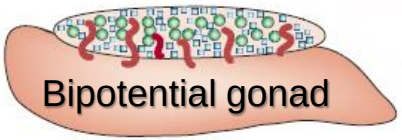
Parental care- evolutionary conserved behavior



Dimorphism of the brain: differentiation and activation

XY ♂

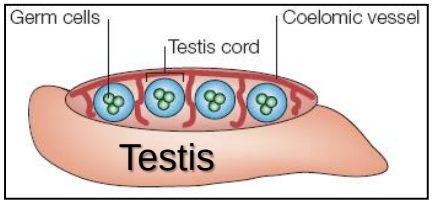
♀ XX

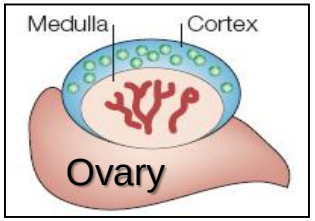


SRY gene

\+

-

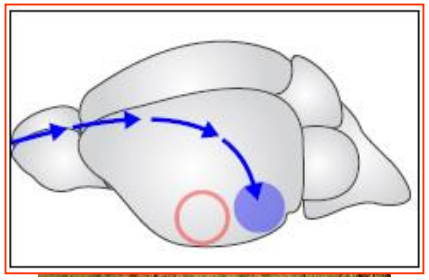


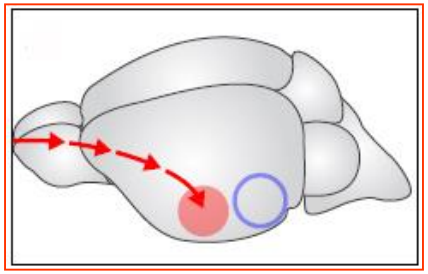


Testosterone & Estradiol

Organization (permanent changes)

Estradiol & Progesterone





Testosterone & Estradiol

Activation

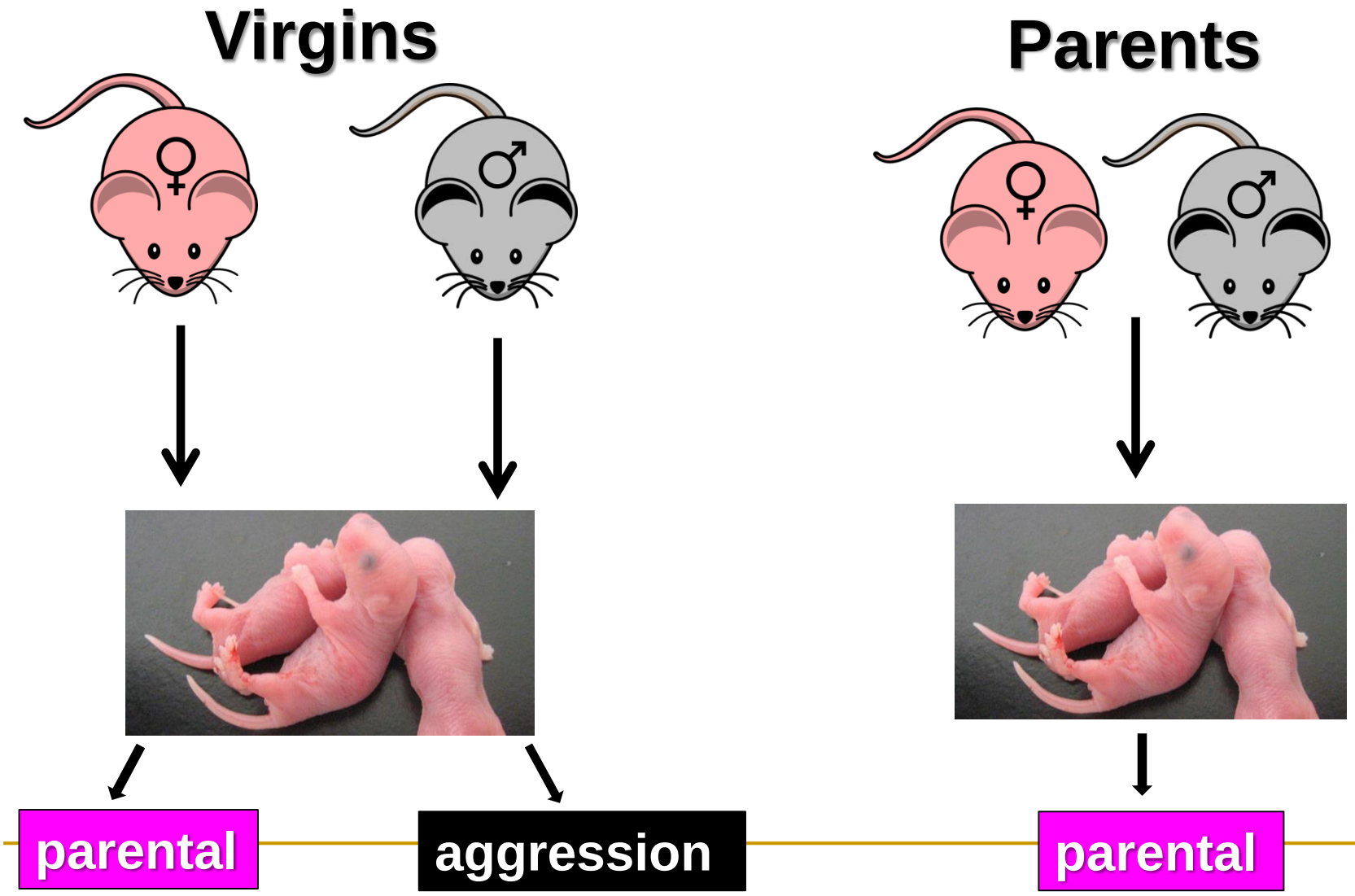
Estradiol & Progesterone

Sex-specific behaviors

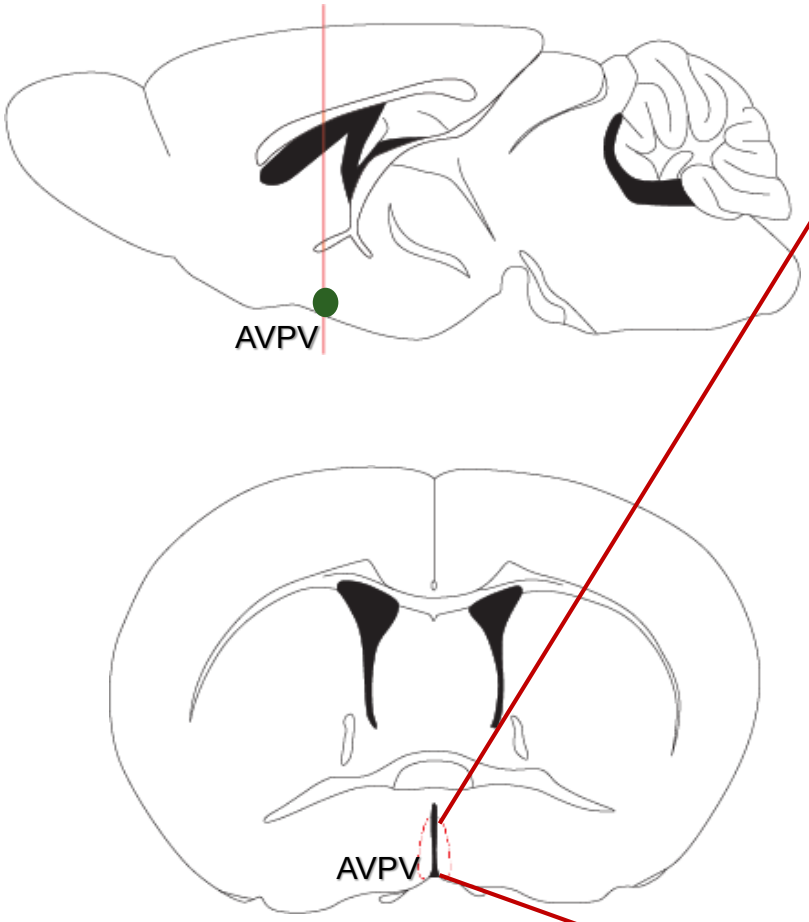
How are sexually dimorphic reproductive behaviors encoded by the male and female brain?

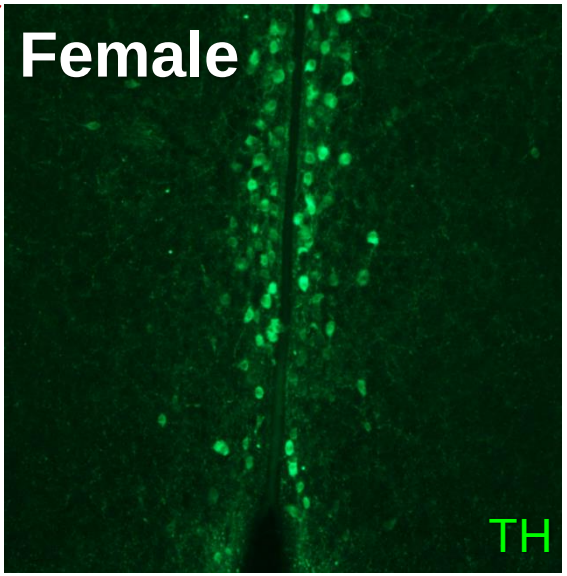
Dimorphic brain functions/structures ⇨ **Dimorphic social behaviors ?**

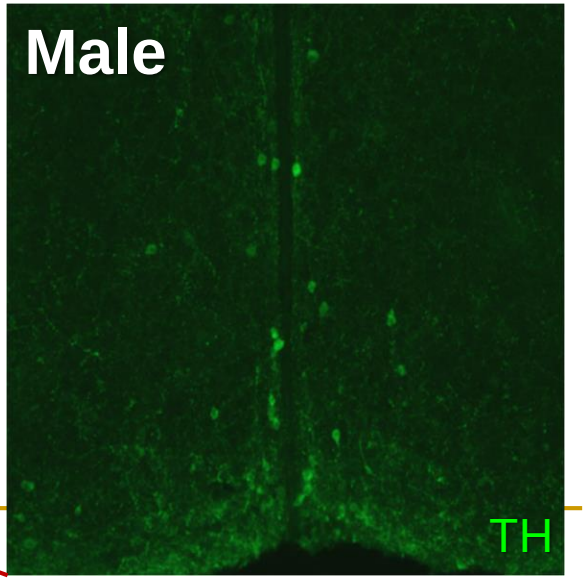
Sexual dimorphism in pup-directed behaviors



Sexual dimorphism in tyrosine hydroxylase-positive neurons in the Anteroventral Periventricular Nucleus (AVPV)

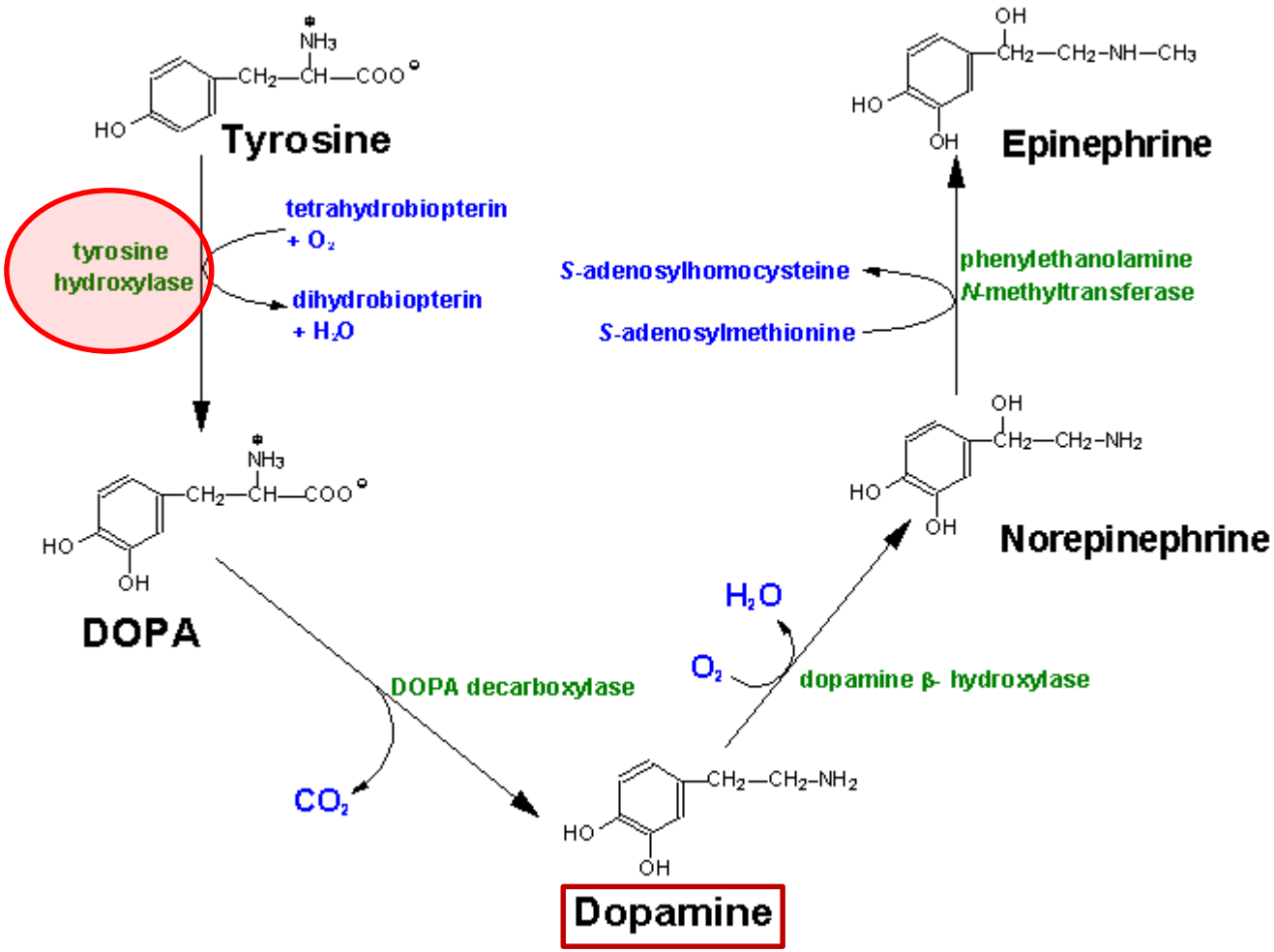




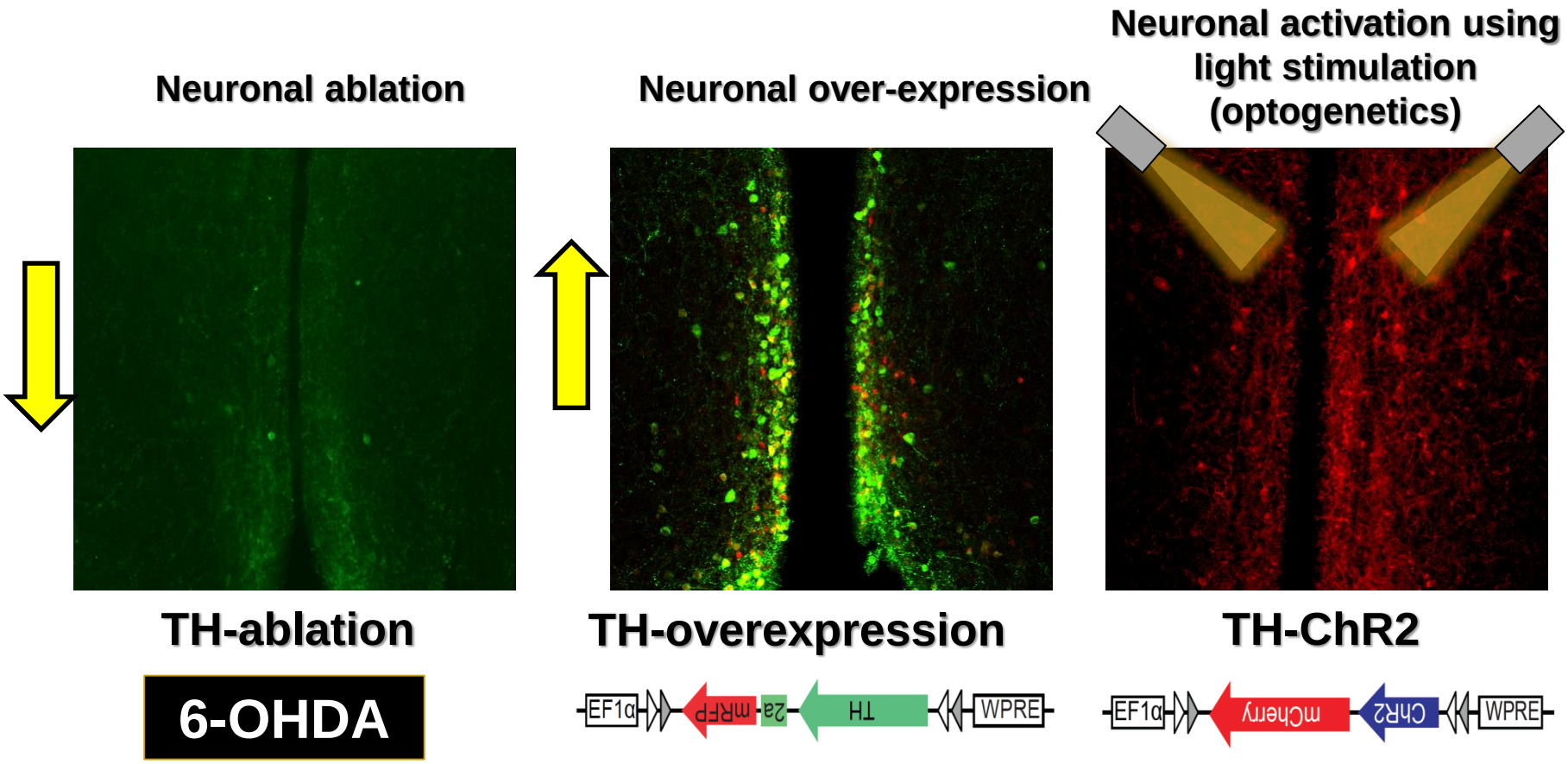


TH= Tyrosine hydroxylase

TH-expressing neurons in the AVPV can produce dopamine



Selective manipulations of TH^{+} AVPV neurons in adult males and females

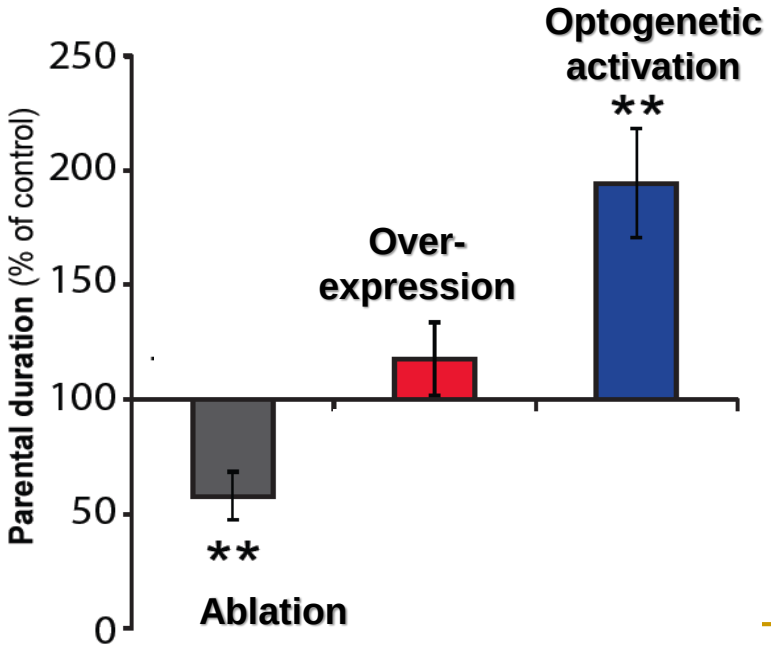


Scott et al. 2015, Nature

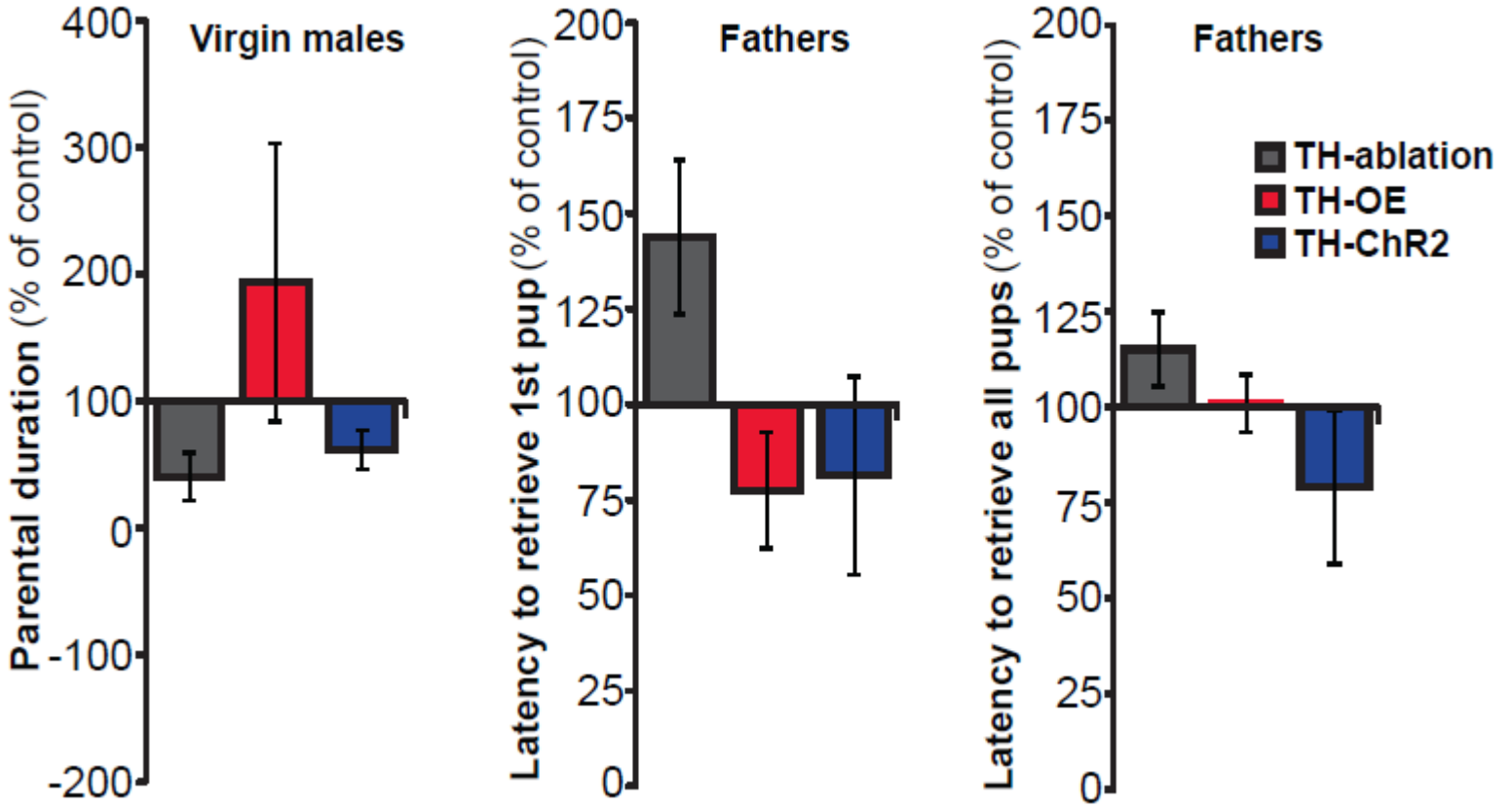
In females, hypothalamic dopaminergic (TH^+ AVPV) neurons promote maternal care

Crouching over the pups

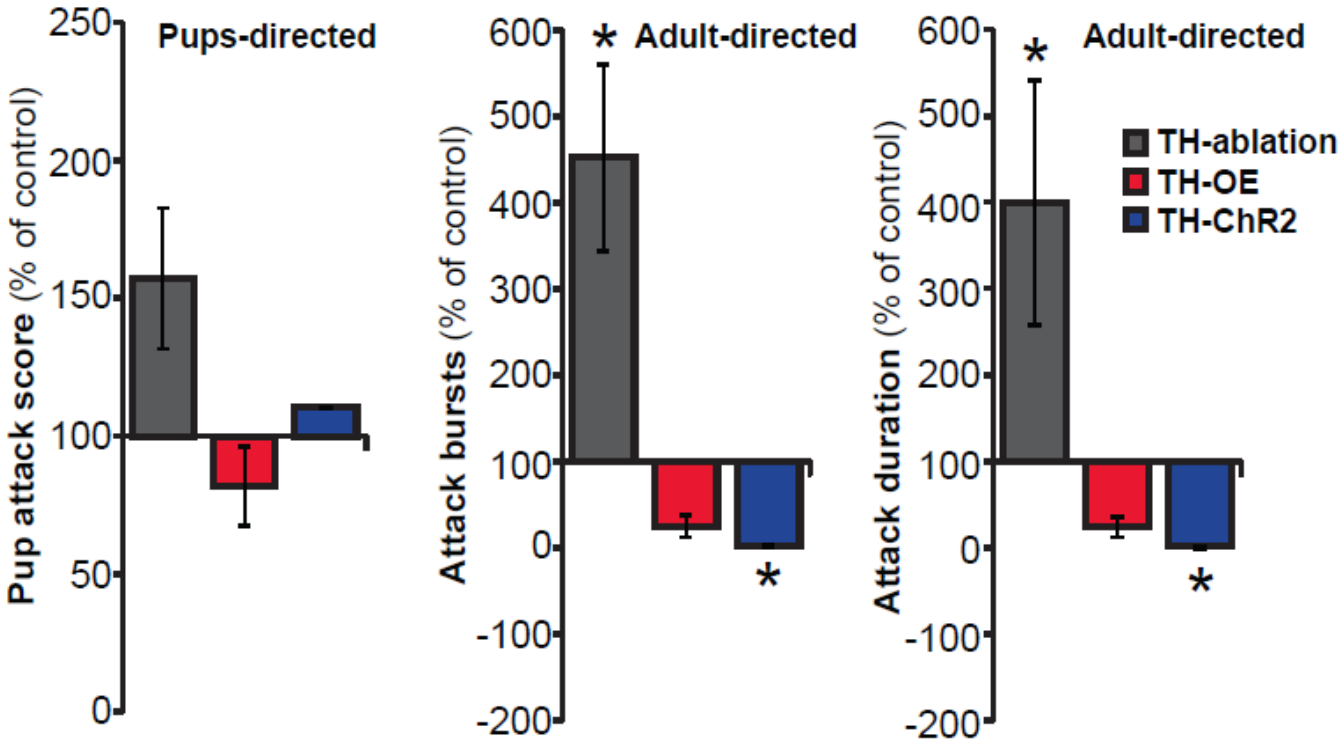
Pup retrieval back to the nest



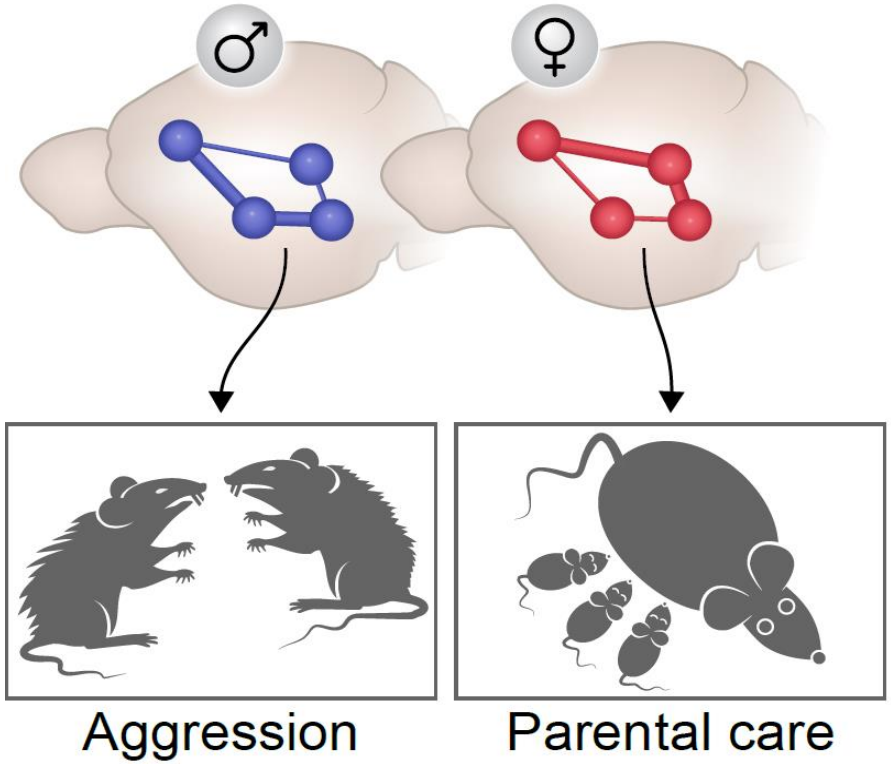
TH^{+} AVPV neurons are not involved in the regulation of parental behavior in males



TH^+ AVPV neurons are involved in suppression of conspecific aggressive behaviors

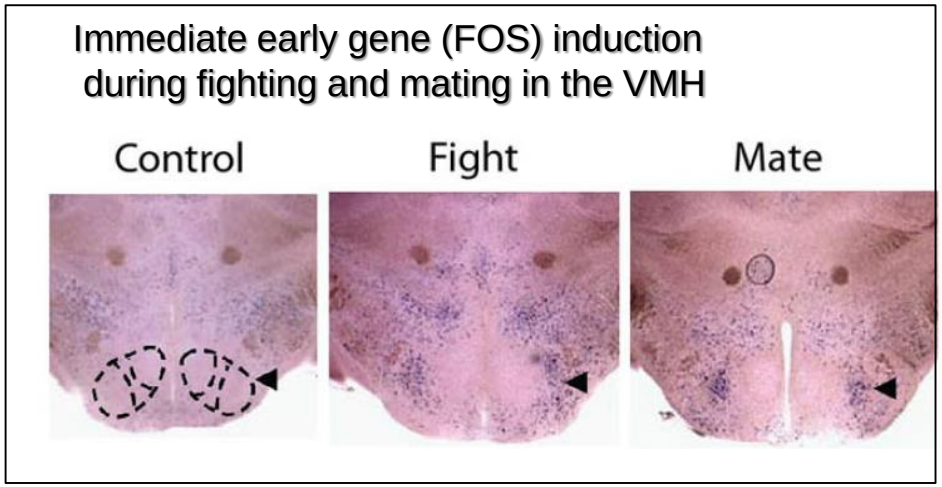


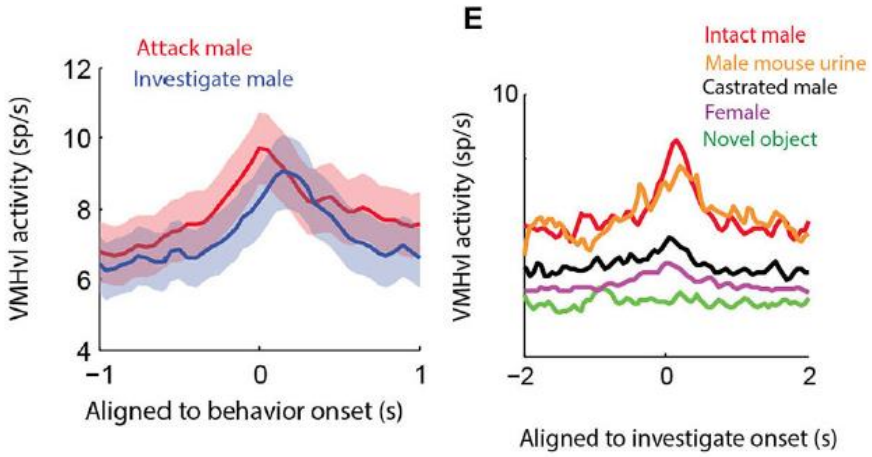
Dimorphic TH$^+$ AVPV neurons control sex-typical behavior in both sexes



Zilkha et al. 2021, *Curr Opin Neuro*

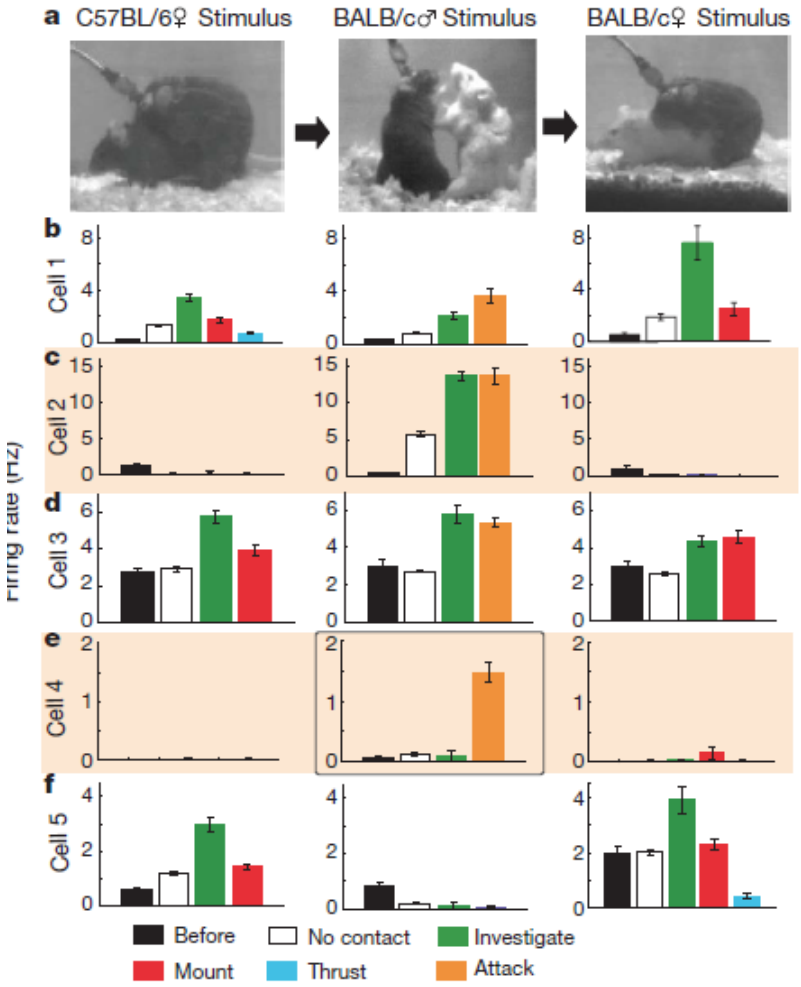
Functional identification of an aggression locus in the mouse hypothalamus (VMH)





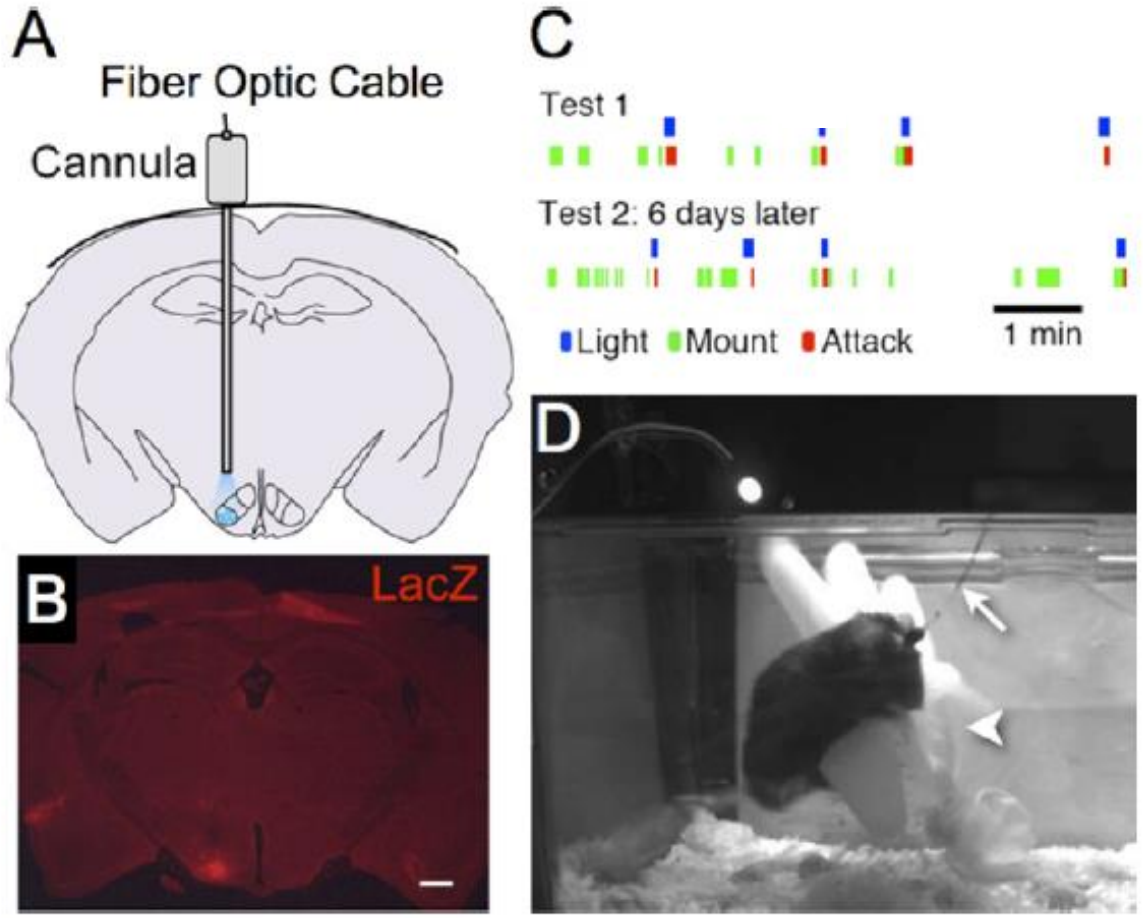
Lin et al 2011, Nature
Falkner and Lin 2014, Front Sys Neuros

Functional identification of an aggression locus in the mouse hypothalamus (VMH)



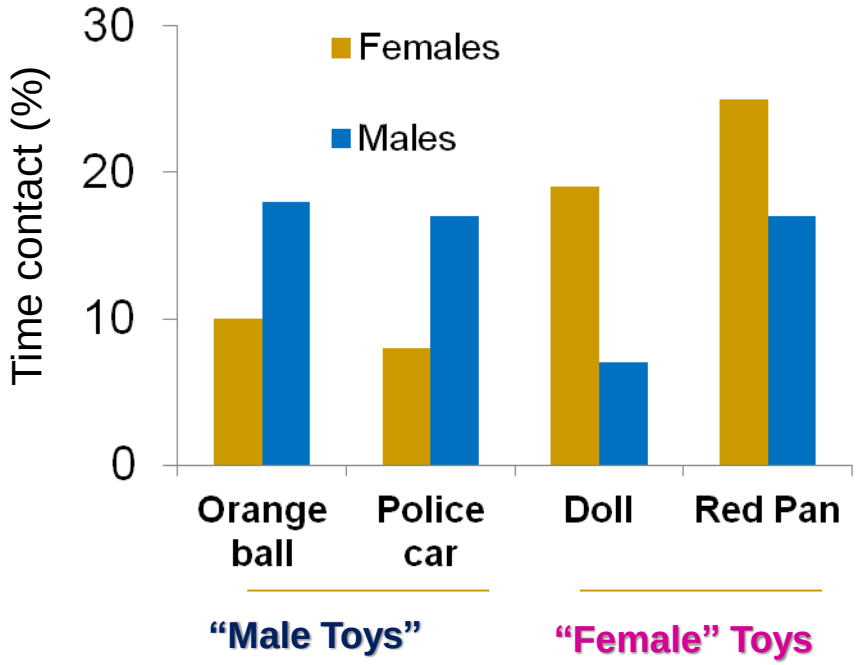
Lin et al 2011, Nature
Falkner and Lin 2014, Front Sys Neuros

Activation of aggressive behavior using optogenetics in the VMH



Lin et al 2011, Nature

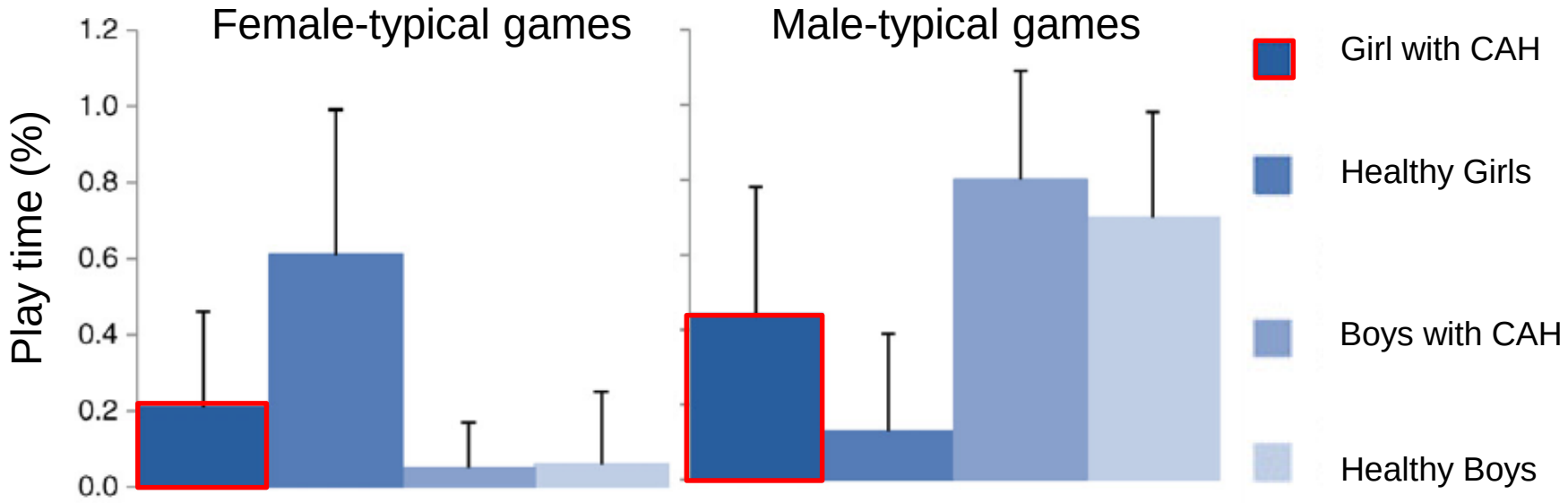
Sexual dimorphism in human behavior: Nature versus Nurture



Alexander and Hines, 2002, Evol Hum Behav

Congenital Adrenal Hyperplasia (CAH)- Genetic disease

Elevated exposure to testosterone during development



Pasterski et al 2005, Child Develop

The boy who was raised as a girl

Twins Bruce and Brian Reimer were born in Canada as two perfectly normal boys

Bruce's penis was damaged
During an unsuccessful surgery for urinary problems

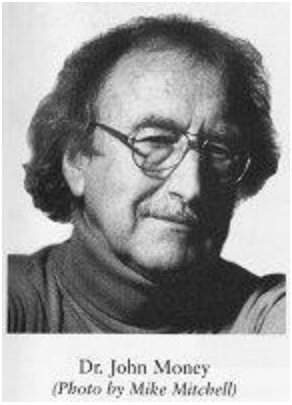
Suggested the “ideal” sex change experiment

Dr John Money was a psychologist specializing in sex changes

The boy who was raised as a girl

Dr Money genuinely believed that Bruce had a better chance of living a happy life as a woman than as a man without a penis

Suggested the “ideal” sex change treatment



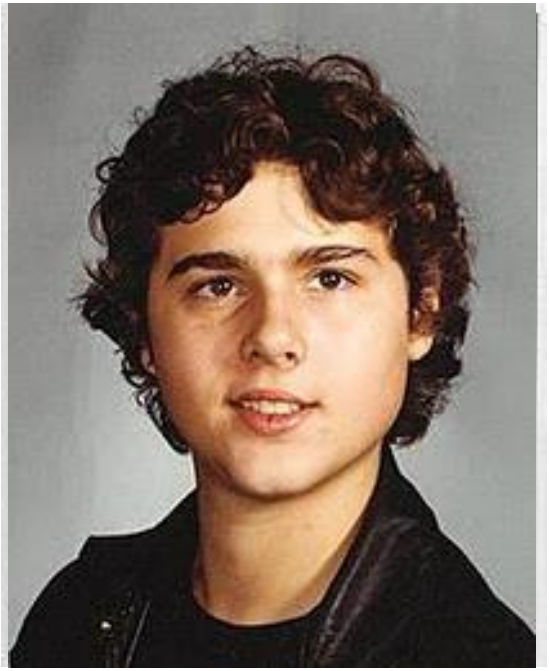
Bruce raised as Brenda

At the age of ~2 years old Bruce is castrated and treated with female sex hormones

The boy who was raised as a girl

At the age of 38 David committed suicide (2 years after his brother died from a drug overdose)

David got married but later became depressed



At the age of 15 Brenda switched again
To a male named David

http://youtube/MUTcwqR4Q4Y

http://www.bbc.co.uk/news/health-11814300