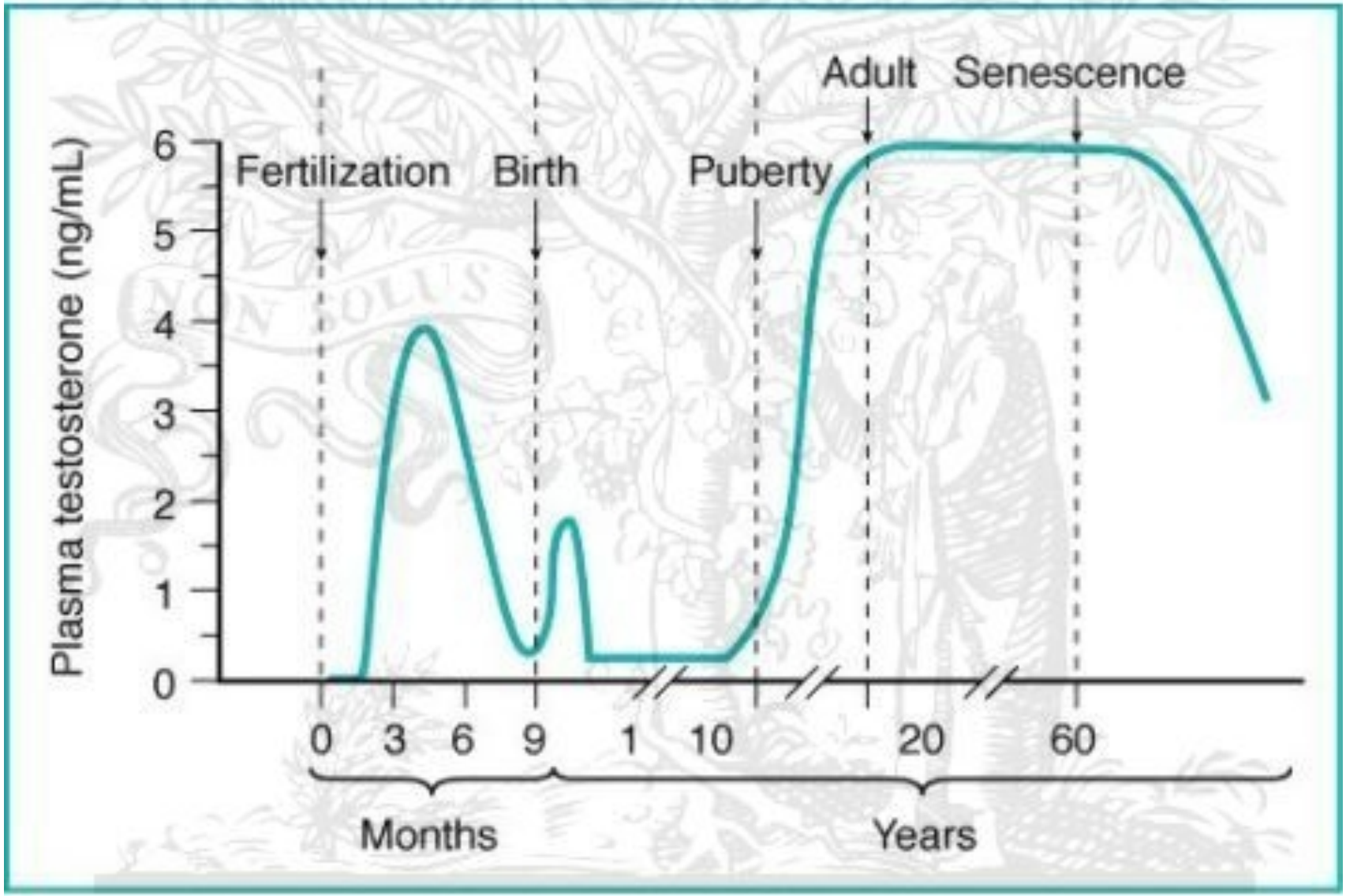
Plan

- Finish video/discussion
- Organizational/activational effects
  - Reading (text – not quizzable)
  - Kruijver (quizzable on Thursday)
- Slides on gender identity


Plasma testosterone (ng/mL)
6
5
4
3
2
1
0
Fertilization
Birth
Puberty
Adult
Senescence
0
3
6
9
1
10
20
60
Months
Years

Gender identity of children and young adults with 5 alpha-reductase deficiency.

Praveen EP, Desai AK, Khurana ML, Philip J, Eunice M, Khadgawat R, Kulshreshtha B, Kucheria K, Gupta DK, Seith A, Ammini AC.
Department of Endocrinology and Metabolism, All India Institute of Medical Sciences, New Delhi, India.

- Dysfunctional 5-alpha reductase enzyme fails to act on testosterone to make DHT
  - Can have male, female, or ambiguous genitalia
- Four of five patients were reared as females
- Of the four, three chose to switch to identifying as male at puberty
  - Male sexual characteristics began to appear
- Researchers believe their gender identity was male from childhood
- Possible social factors → more comfortable gender identity?

46, XY karyotype, primary amenorrhea, female internal tract
Gonadal streaks (min. dev. gonad tissue in place of differentiated teste or ovaries)
child looks, and in most cases identifies as, female
hormone replacement therapy (estrogen and androgens) needed during puberrty
SRY gene mutations 10-15% cases (reference 1), majority cases may be linked to deficient genes involved in sex differentiation pathways.

2 Cases: Both reared female, female external genitalia, karyotype

1st case) [1] at 16, a girl experiencing primary amenorrhea was given the diagnosis after a medical evaluation. FSH and LH were given, after which secondary sexual characteristics developed and menarche followed 1.5 years later.

2nd case) [2] at 21, sexually ambiguous person reared as a female was discovered to be phenotypically male. The person had already for some years begun to identify himself as male. Gonadotropins were elevated.

Swyer Syndrome (46,XY Gonadal Dysgenesis)

References:

Matthew Herrmann - Psyc 132

1] [PURE 46,XY GONADAL DYSGENESIS]
http://www.ncbi.nlm.nih.gov/pubmed/21084251

2] 46 XY gonadal dysgenesis in adulthood 'pitfalls of late diagnosis'
http://casereports.bmj.com/content/2012/bcr.12.2010.3626.full

Cloacal Exstrophy

By Kristopher Jhang

7/15/13

Psyc 132

Cloacal exstrophy

A child with cloacal exstrophy (a rare congenital malformation) is typically born with many intra-abdominal structures exposed and it can be diagnosed prenatally. Although it is a serious condition, and requires a series of operations, the long-term outcome is good for many children. The pattern of inheritance is still unknown due to the small number of patients. This is a rare disorder and is found in one in 400,000 births.

- In cloacal exstrophy, a portion of the large intestine lies outside of the body, and on either side of it—and connected to it—are the two halves of the bladder. In boys, the penis is usually flat and short with the exposed inner surface of the urethra on top. The penis is sometimes split into a right and left half. In girls, the clitoris is split and there may be one or two vaginal openings. The testes may not come down into the scrotum (sac). In the female child, the vagina may be absent and the clitoris is split into two halves.

References

- 1. John P. Gearhart, Robert D. Jeffs: Exstrophy of the Bladder, Epispadias and other Bladder Anomalies in Campbell's Urology, Sixth Edition. Eds. Walsh PC, Retik AB, Stamey TA, Darracott Vaughan E, Jr., WB Saunders Co. Vol. 2 1772-1821.
- 2. John P. Gearhart: The bladder exstrophy-epispadias complex. In pediatric Urology. Es Gearhart JP, Rink RR, and Mouriquand P. Saunders, Philadelphia. Chapter 32, p 511-546.
- 3. https://www.hopkinschildrens.org/cloacal-exstrophy.aspx
- 4. http://www.childrenshospital.org/az/Site2187/mainpageS2187P0.html

Table 1. Participant characteristics

Participant No.	Age at Assessment	Sex	
		Chromosomal	Rearing
Reassigned			
1	23	XY male	Female
2	34	XY male	Female
3	37	XY male	Female
Nonassigned			
4	11	XX female	Female
5	14	XY male	Male
6	17	XY male	Male
7	19	XX female	Female
8	19	XX female	Female
9	22	XY male	Male

Core GI in all patients was stable and matched assignment.

Psychopathology, Psychosocial, Gender and Cognitive Outcomes in Patients With Cloacal Exstrophy

Bipasha Mukherjee[a], Elizabeth McCauley[a, b], , , Russell B. Hanford[b], Matthew Aalsma[c], Amy M. Anderson[b]

[a] University of Washington, Seattle Children's Hospital, Seattle, Washington

[b] Regional Medical Center, Seattle, Washington

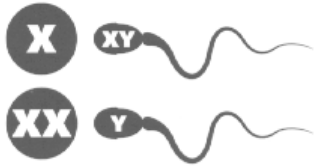
Congenital Adrenal Hyperplasia

- Reference: http://www.tandfonline.com/doi/abs/10.1080/00224490409552215#.UeTBIWTwKgE
- This was a study looking at psychosexual development, following Congenital Adrenal Hyperplasia (CAH) patients of both male and female background in an age bracket of 18-44.
- CAH is the most common genetic endocrine disorder, resulting from mutations in a gene responsible for cortisol and aldosterone synthesis
- It was found that women with CAH were significantly more likely to feel homosexual or bisexual than the control group of women, but men had no change in sexual orientation.
- Women with CAH described themselves as feeling decidedly less female, and men did not have any difference between the group with CAH and the control group.

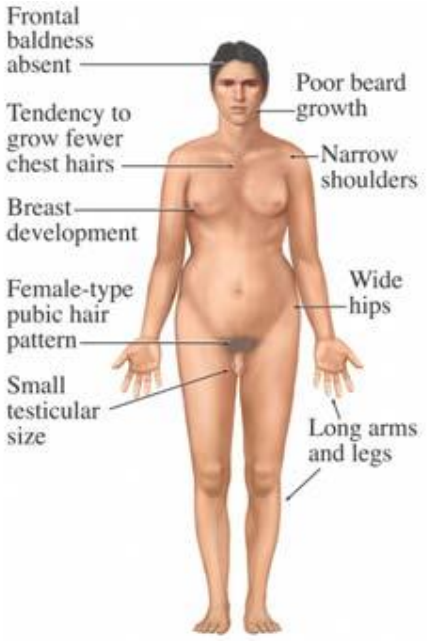
Aphallia

- 1 in 30 million births (75 total)
- Impaired mesenchymal proliferation at cloacal eminence → Absence of genital tubercle → absence of phallus (female OR male)
- Chibber paper:
  - Normal testis with normal testosterone production
  - Previously: males w/ aphallia were raised as female
    - Gonadectomy, if done, must be before postnatal testosterone surge
    - Estrogen therapy later performed
- Modern days: gender reassignment carefully evaluated
- Ex. 16 year old male, aphallic but otherwise normal
  - Raised as male
  - Phalloplasty; implantation of penile prosthesis planned
  - asymptomatic
- Chibber, Percy Jal, Hemendra N. Shah, Pritesh Jain, and Prabha Yadav. "Male Gender Assignment In Aphallia: A Case Report And Review Of The Literature." *International Urology and Nephrology* 37.2 (2005): 317-319. Print.

http://ghr.nlm.nih.gov/condition/klinefelter-syndrome http://www.isna.org/faq/conditions/klinefelter http://www.genetic.org/Support/PersonalStories.aspx



Klinefelter Syndrome 47XXY/ XXY Syndrome/XXY trisomy



- Inherits an extra X-chromosome from their mother or father
- Affects 1 in 500-1000 newborn males
- Affects physical and cognitive development
- Small testes → less testosterone →delayed or incomplete puberty
- Gender-related outcome: male
- Variants (for example: 48-XXYY, 48-XXXX, 49-XXXXY, Mosaic 46-XY/47-XXY)
  - ~1 in 50,000 newborns
  - health risks increases as the number of extra sex chromosomes increase

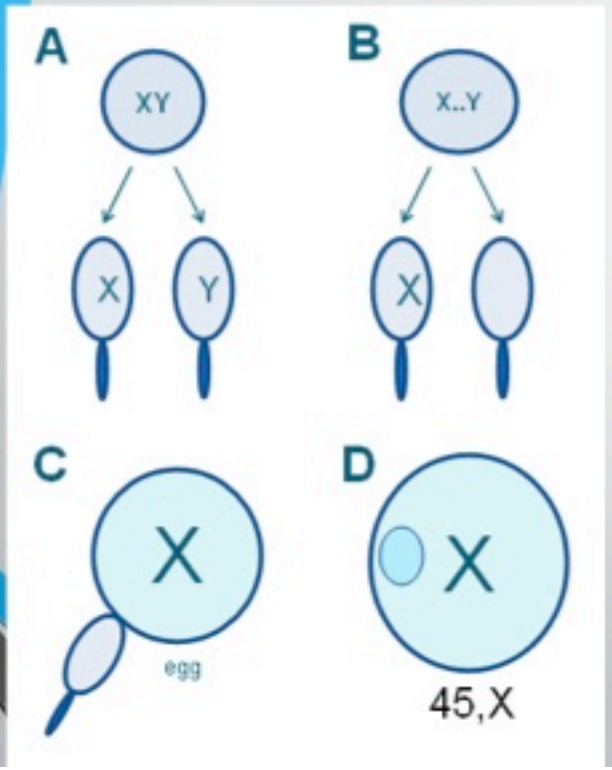
Turner Syndrome

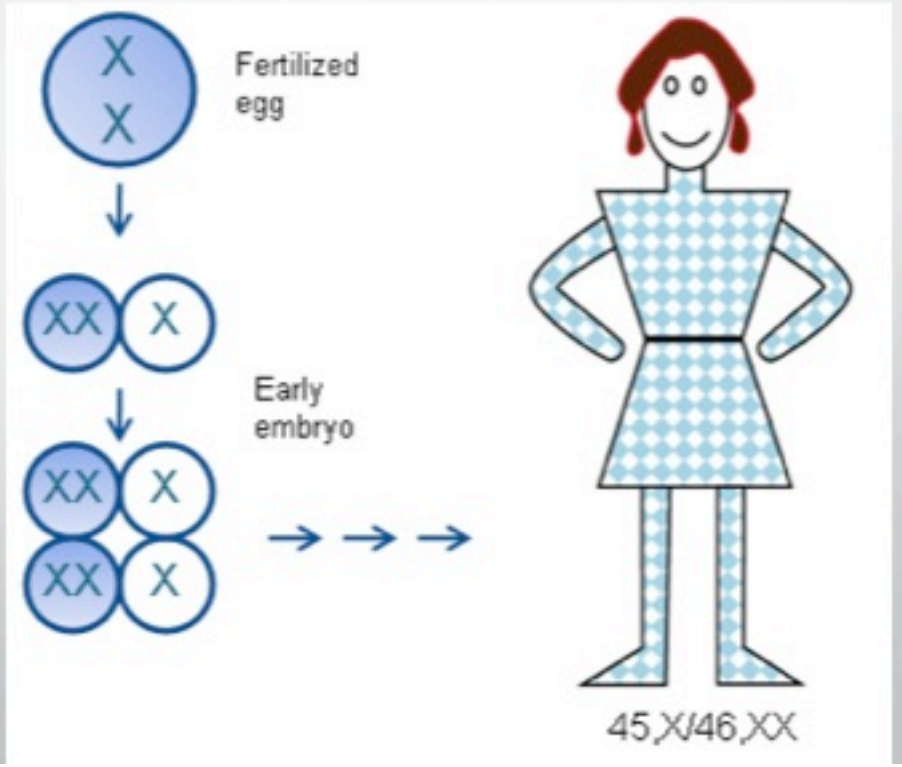
Steven Nim

Dr. Gorman

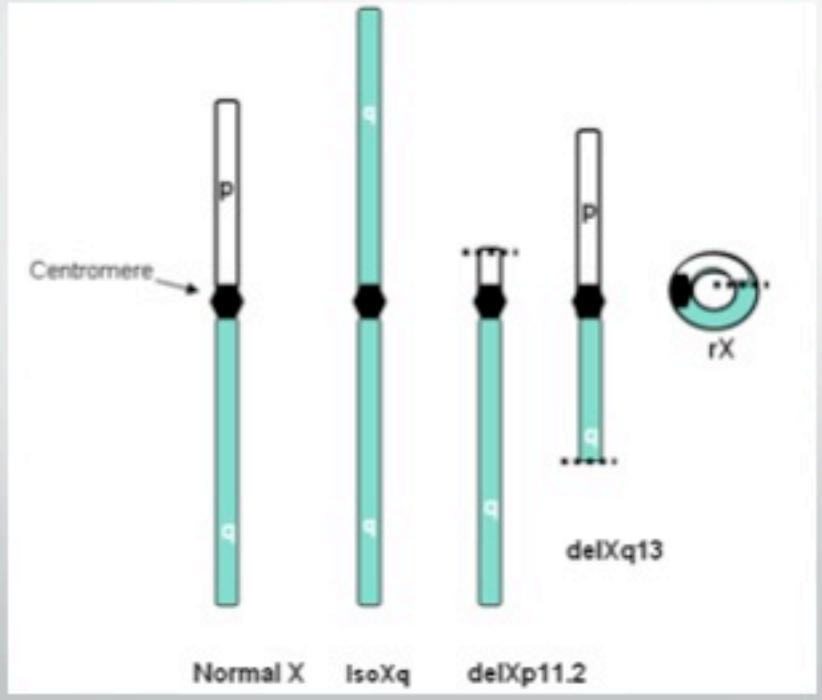
PYSC 132

Turner Syndrome: Causes





Turner Syndrome: Other Causes



Effects on Gender Identity and Gender Behavior

- Typically female phenotype and identity, but lacking the full features of females
- Short stature, premature ovarian failure, other physical deformities
- At risk of heart, kidney, thyroid problems

Treatment

- More of a health problem then gender problem
- Treatments involve growth hormone therapy (early on), estrogen injection, and in-vitro fertilization for those that desire having children

Reference

- Turner Syndrome Society of the United States. 2011. http://www.turnersyndorme.org/
- Bondy, Carolyn, M.D. Turner Syndrome. National Institutes of Health. http://turners.nichd.nih.gov/index.html

Timeframe

- Will hormones reverse your sex in adulthood? Any part of it?

- Permanent effects (organizational)
- Reversible effects (activational)

Organizational & Activational Effects

- Chapter 3
  - Pg. 140-167

Sex differentiation of…

Mating reflexes

Hormone regulation

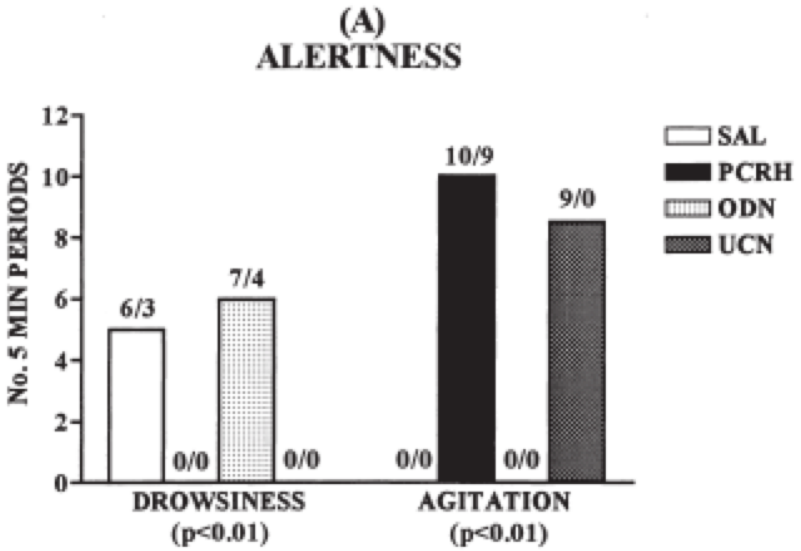
One particular brain structure

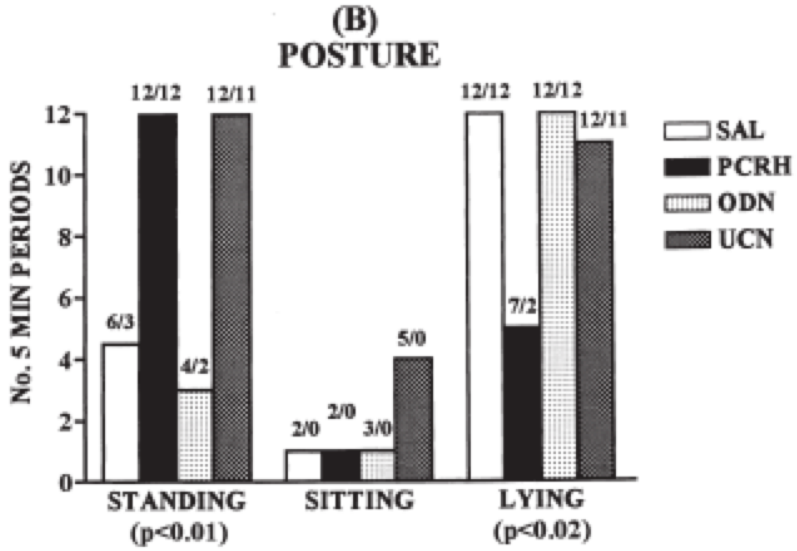
Activational effects

Transient, reversible, temporary effects of hormones

Example – stress hormone CRF/CRH

PCRH = pig's CRH
Saline = control
UCN = urocortin – brain peptide found to be similar to CRF
ODN = Ignore this!





ELSEVIER

Pharmacology Biochemistry and Behavior, Vol. 65, No. 1, pp. 123–129, 2000

0091-3057/00/$–see front matter

PII S0091-3057(99)00134-3

Behavioral and Hormonal Effects of Centrally Injected "Anxiogenic" Neuropeptides in Growing Pigs

R. F. PARROTT, S. V. VELLUCCI AND J. A. GOODE

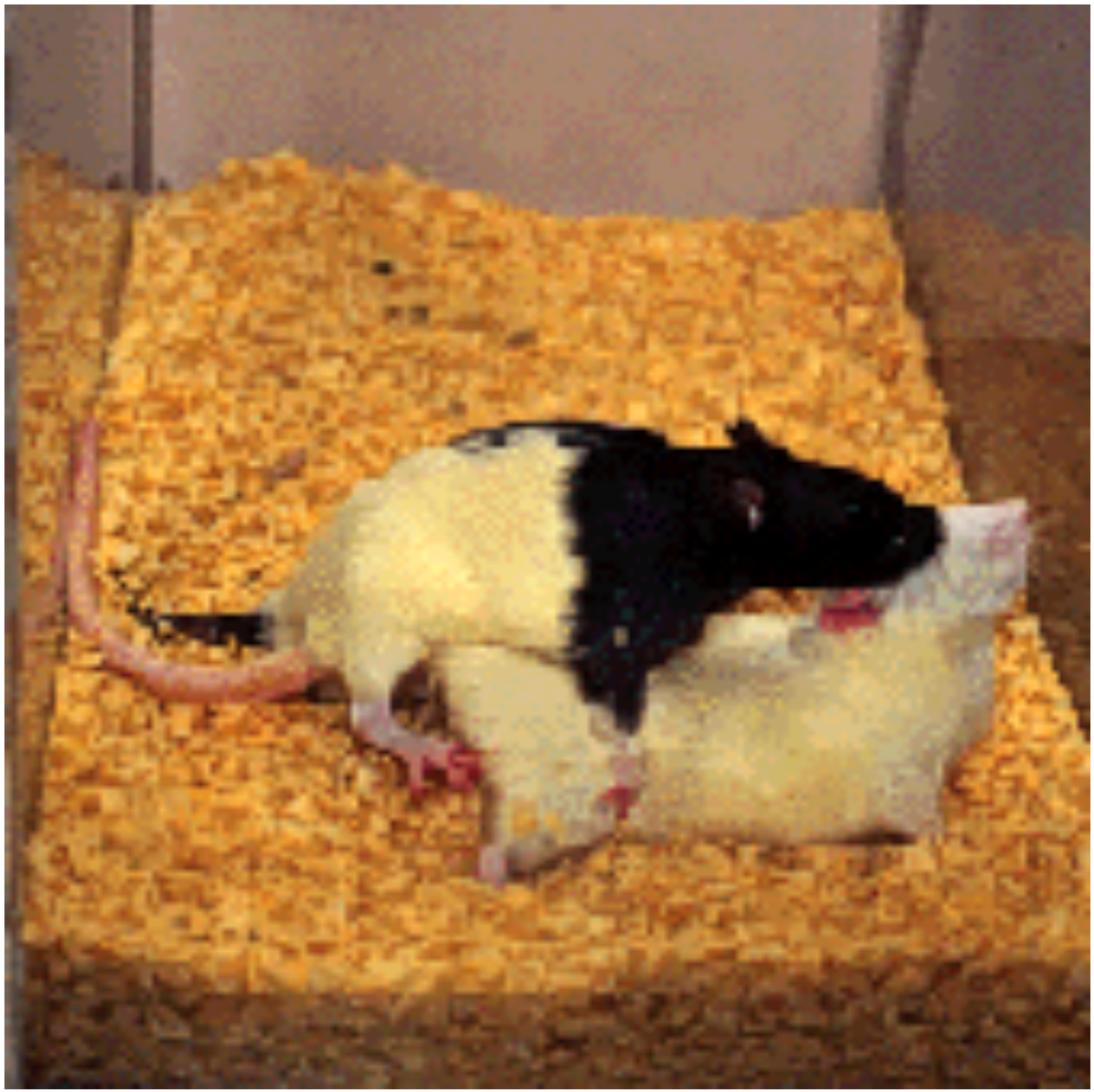
Activational effects

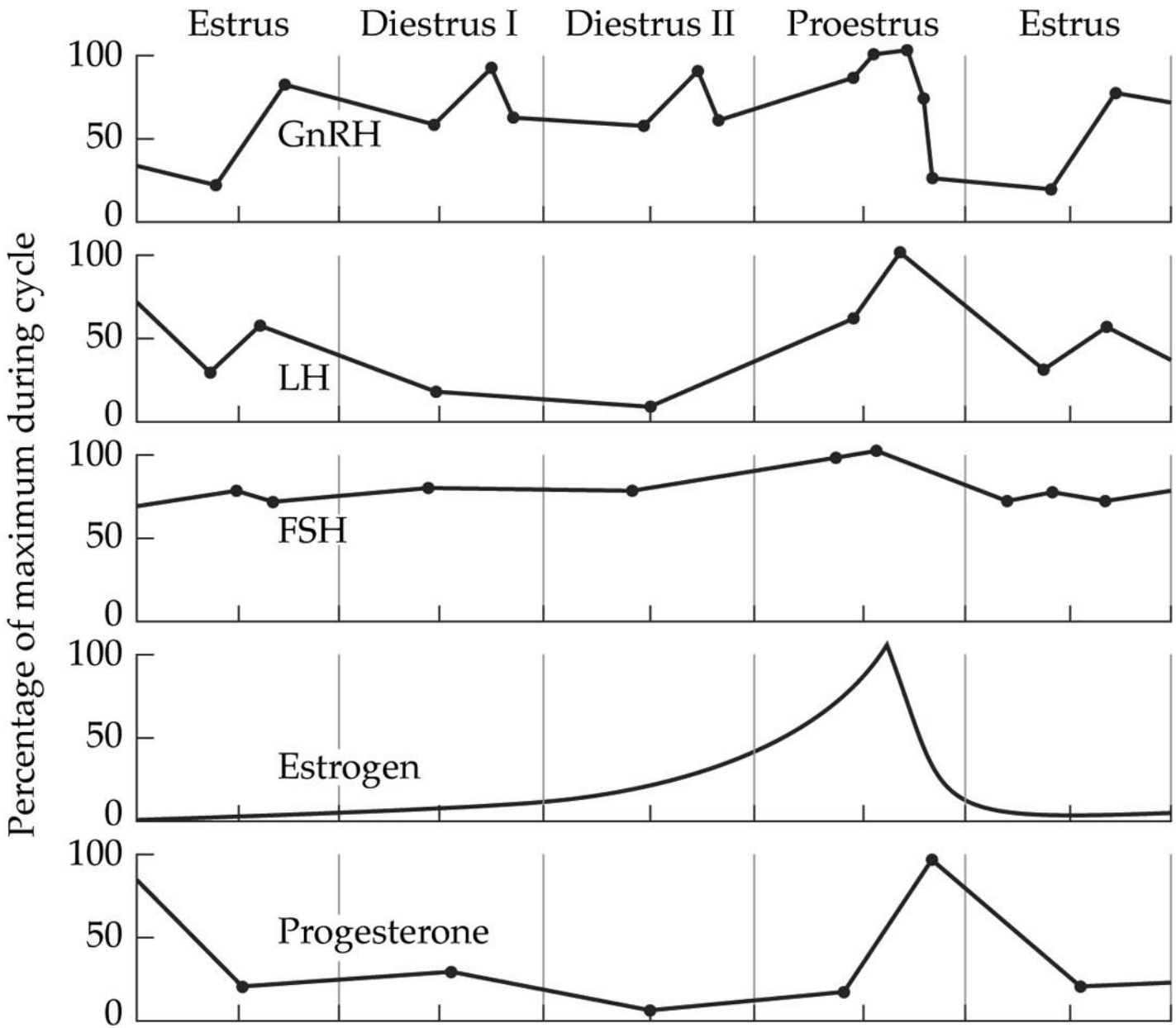
E.g.,Behaviors related to estrus/menstrual cycle

To test:

ablation/replacement study

For lordosis, E followed by P and sexual male
For mounting, T paired with receptive female





AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY, Third Edition, **Figure 6.21**

Are males and females the same besides current hormone levels?

- Certainly not always
- Implication?

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

ABSTRACT

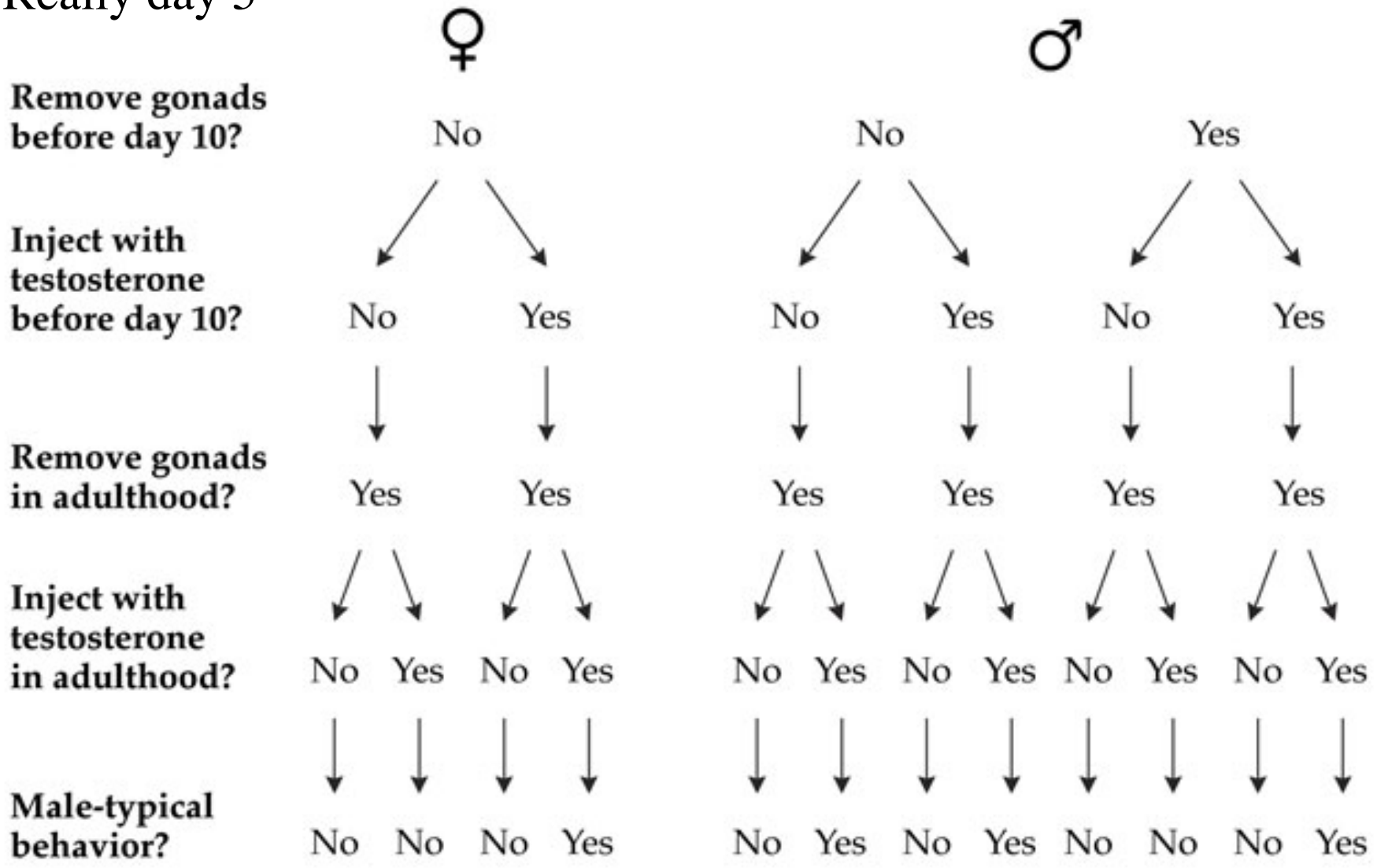
The sexual behavior of male and female guinea pigs from mothers receiving testosterone propionate during most of pregnancy was studied after the

	In pregnancy	Adulthood (OVX +E/P)	Adulthood (OVX + T)
	F + saline (Control)	lordosis	no mounting
	F + testosterone injections	No lordosis	mounting
	F + OVX	lordosis	no mounting

	Postnatal Rats (days 1-5)	Adulthood (Gx E/P)	Adulthood (Gx + T)
	M + saline (Control)	no lordosis	mounting
	M TestX	lordosis	no mounting
	M TestX + T	no lordosis	mounting
	F + saline (Control)	lordosis	no mounting
	F OVX	lordosis	no mounting
	F OVX + T	no lordosis	mounting
	M TestX (DAYS 10-15)	no lordosis	mounting
	F OVX + T (DAYS 10-15)	lordosis	no mounting

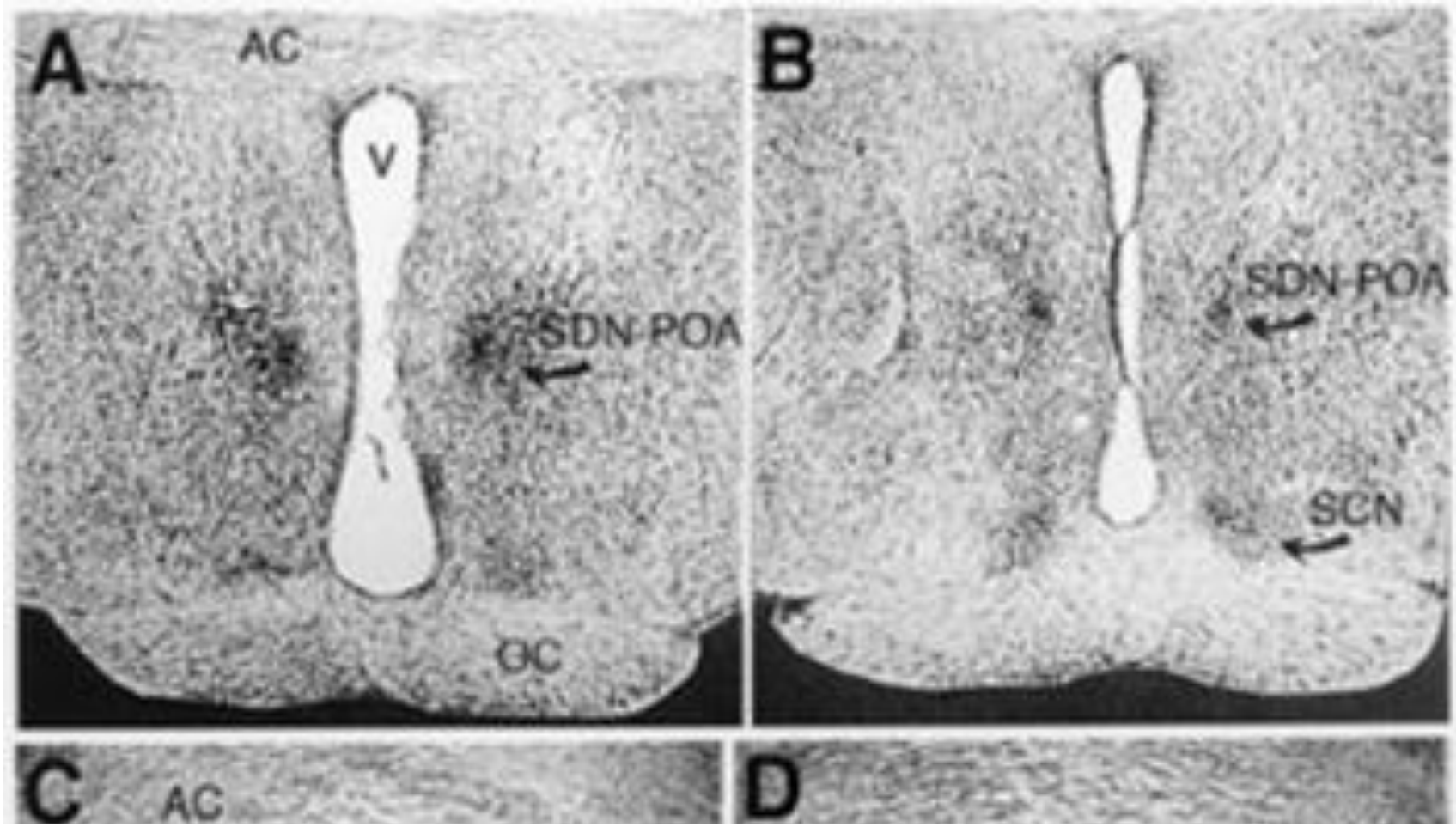
	Postnatal rats (days 1-5)	Adulthood (Gx +E/P)	Adulthood (Gx + T)
	M TestX +T	no lordosis	mounting
	M TestX + E2	no lordosis	mounting
	F + OVX + high E2	no lordosis	mounting

Really day 5



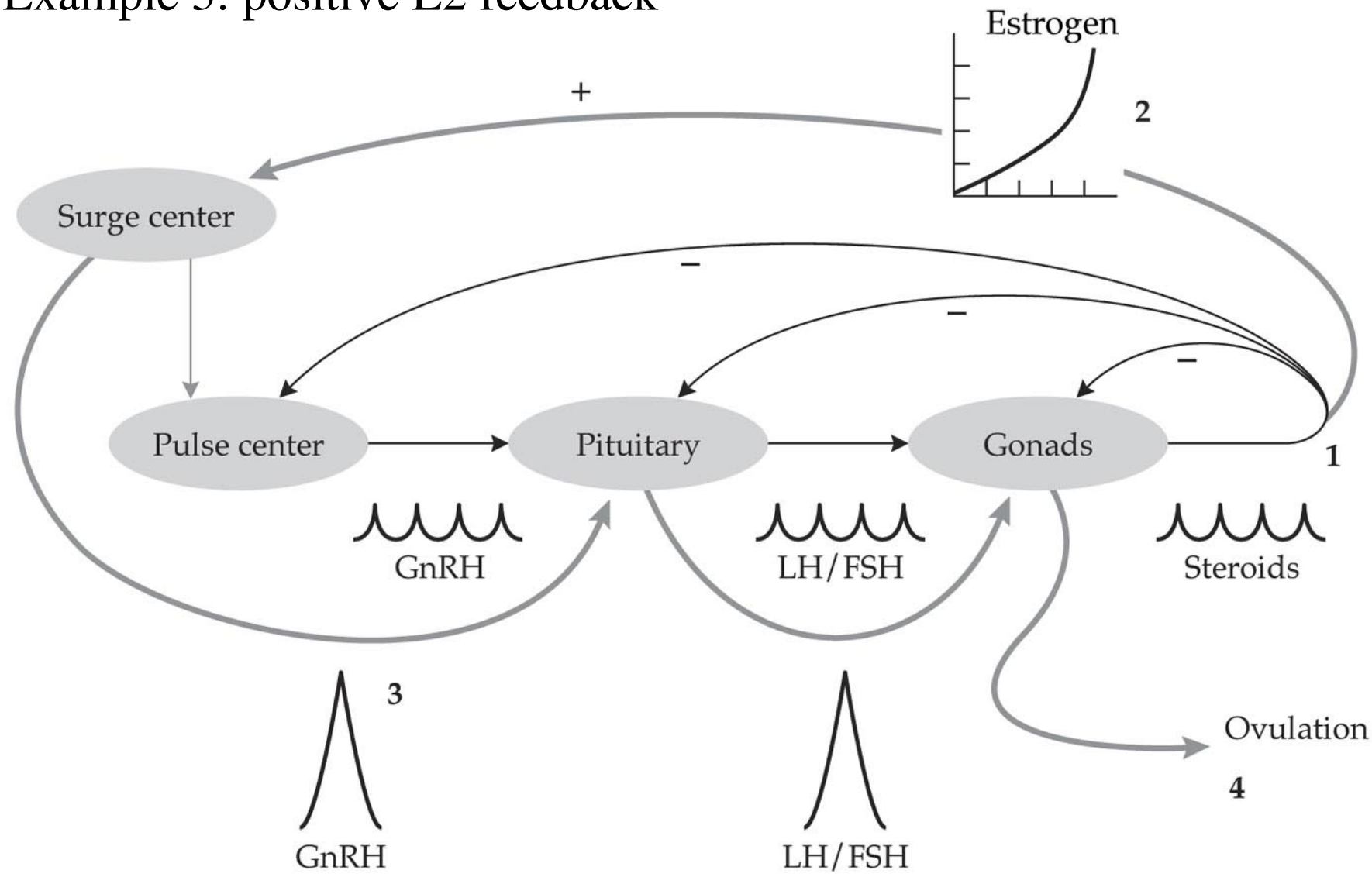
AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY, Third Edition, Figure 3.26

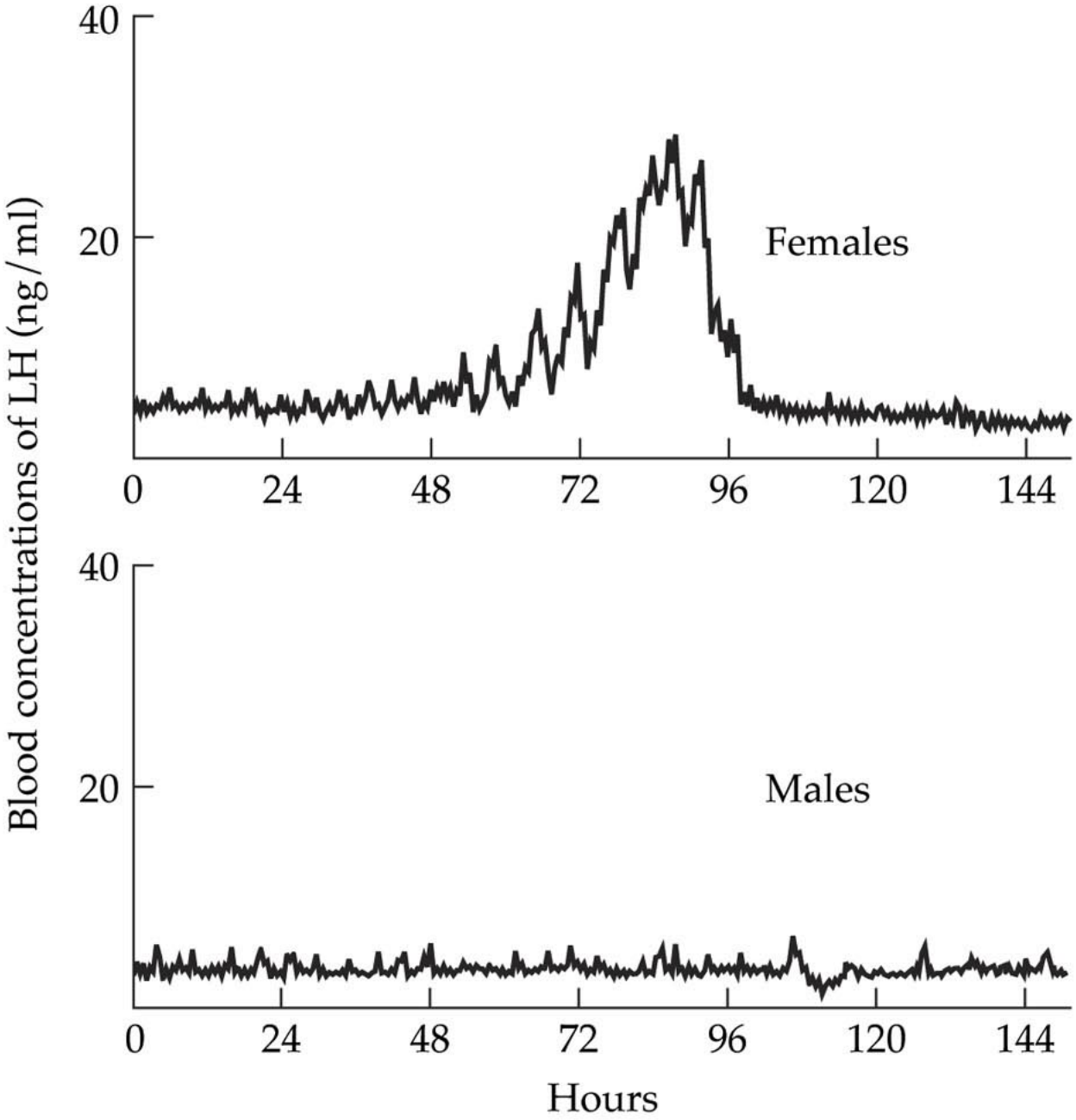
Example 2: SDN-POA



What does the SDN-POA do?

Example 3: positive E2 feedback





AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY, Third Edition, **Figure 3.23**

How generalizable are these examples?

SDN-POA in gerbils

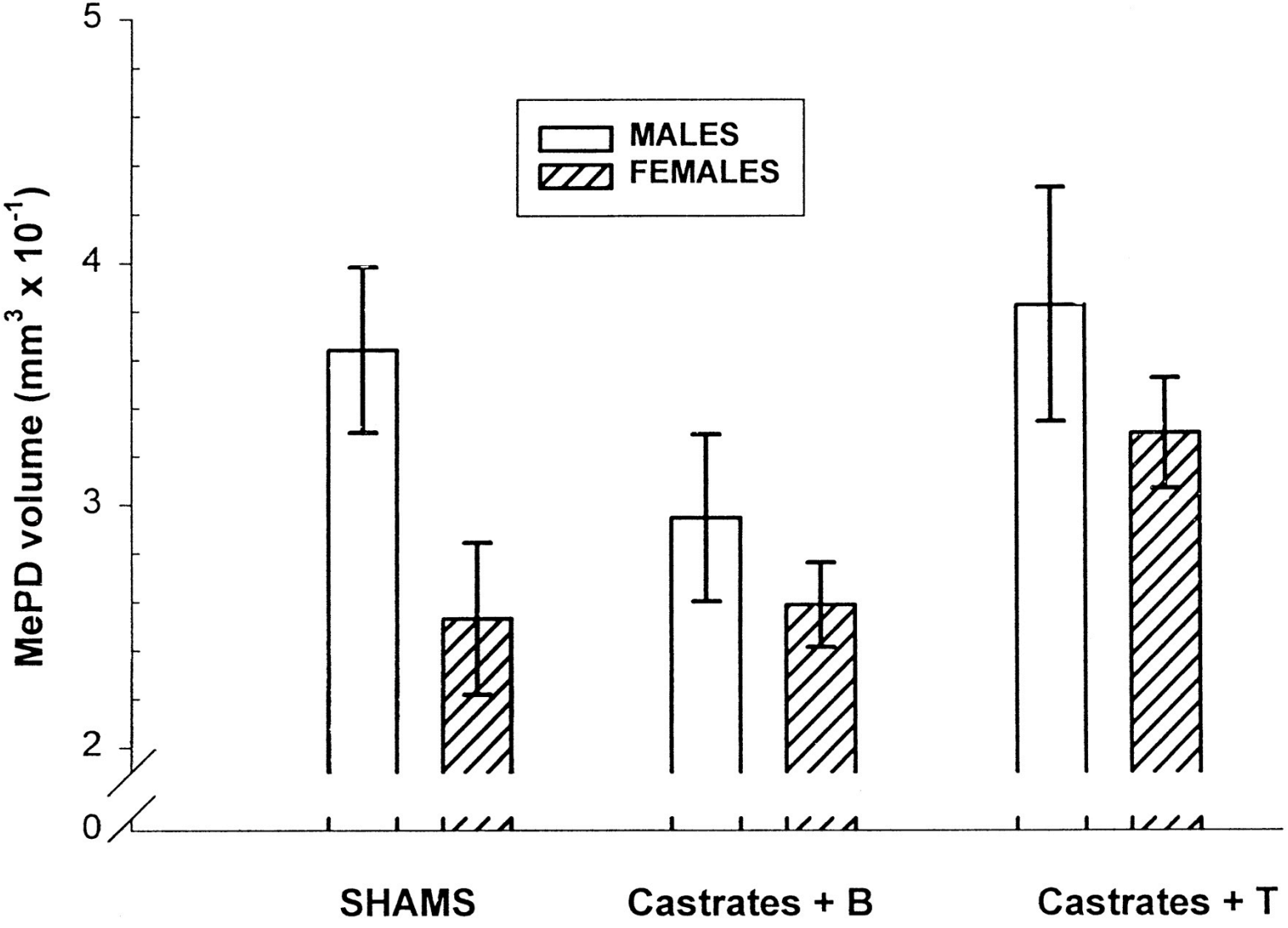
size sensitive to adult T

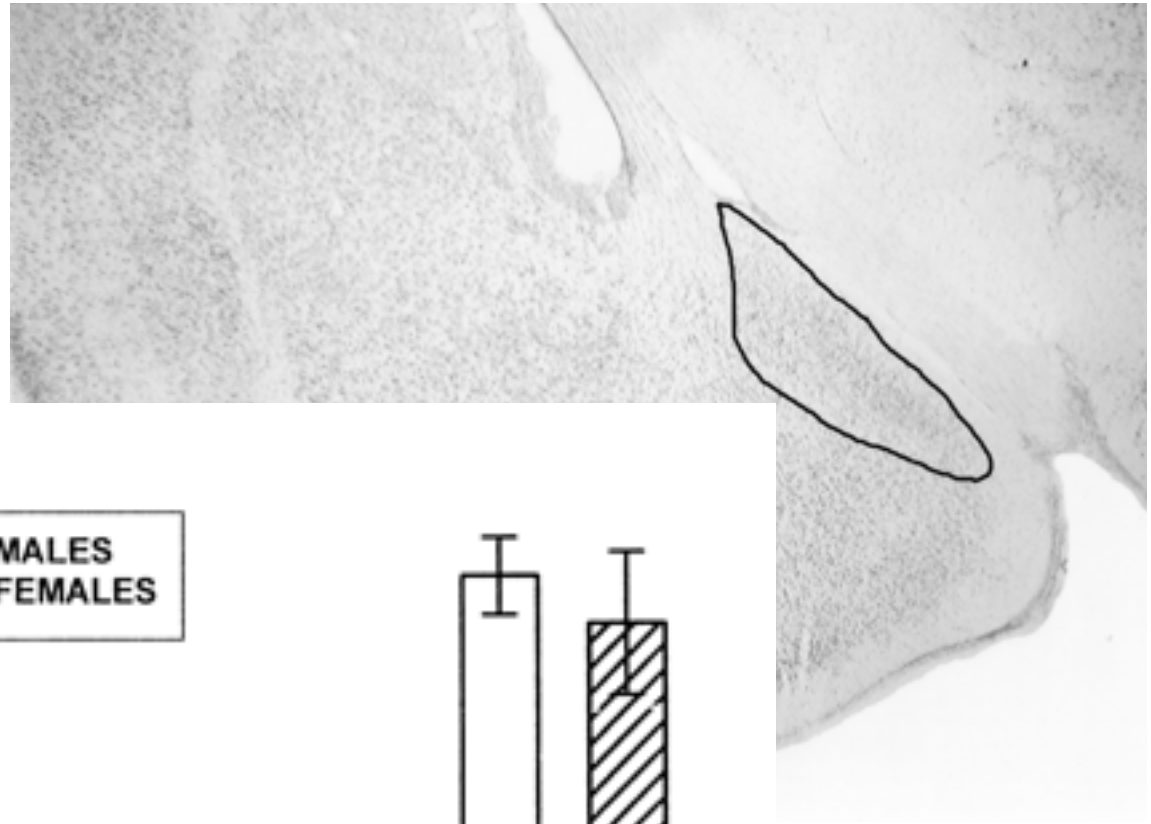
Aggressive behavior in monkeys

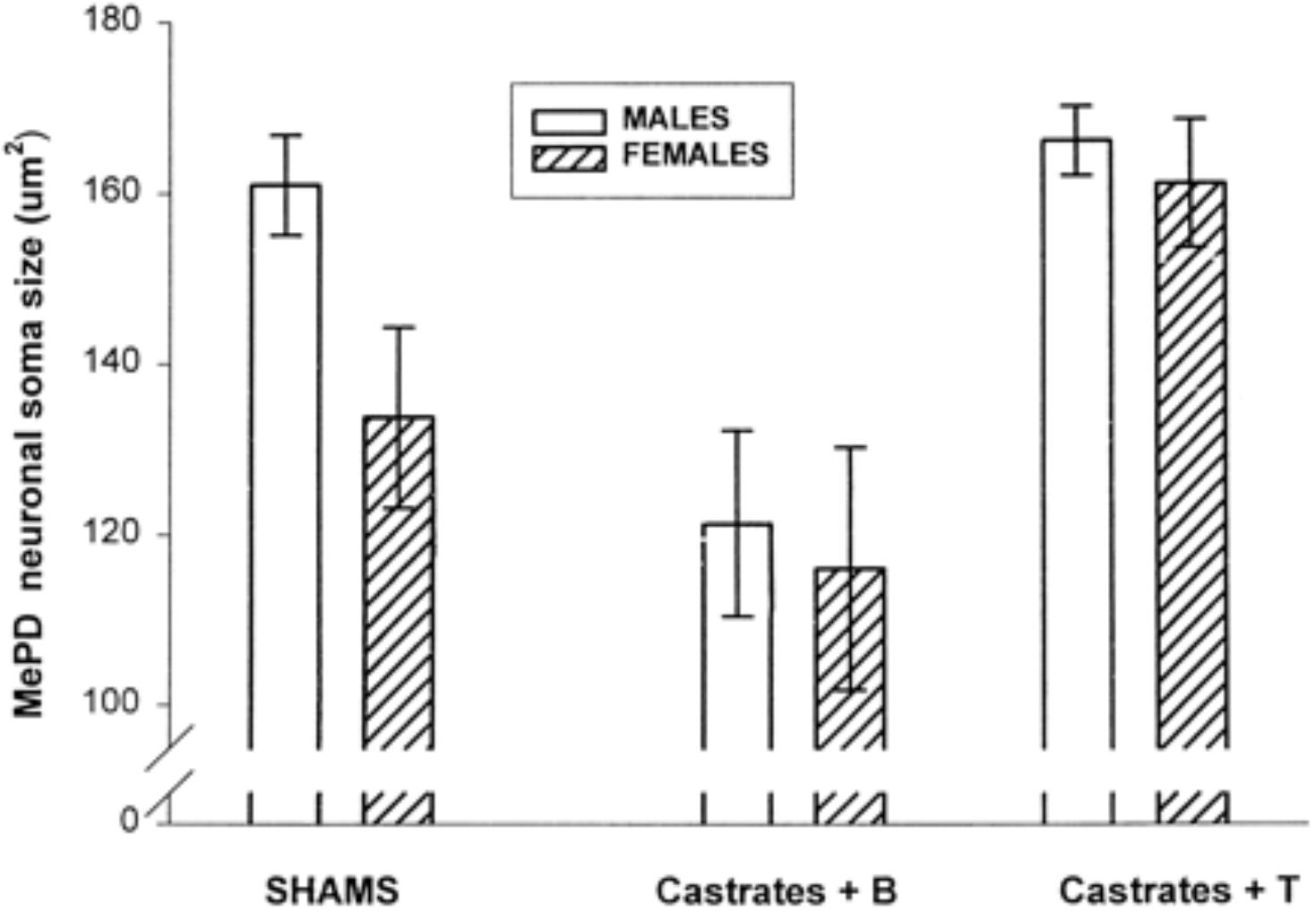
depends not on T==>E

Critical periods vary for different traits

Do Not ASSUME






MePD neuronal soma size (um²)
180
160
140
120
100
0
MALES
FEMALES
SHAMS
Castrates + B
Castrates + T

- Reports of structural differences between the brains of men and women, heterosexual and homosexual men, and male-to-female transsexuals and other men have been offered as evidence that the behavioral differences between these groups are likely caused by differences in the early development of the brain. However, a possible confounding variable is the concentration of circulating hormones seen in these groups in adulthood. Evaluation of this possibility hinges on the extent to which circulating hormones can alter the size of mammalian brain regions as revealed by Nissl stains. We now report a sexual dimorphism in the volume of a brain nucleus in rats that can be completely accounted for by adult sex differences in circulating androgen. The posterodorsal nucleus of the medial amygdala (MePD) has a greater volume in male rats than in females, but adult castration of males causes the volume to shrink to female values within four weeks, whereas androgen treatment of adult females for that period enlarges the MePD to levels equivalent to normal males. This report demonstrates that adult hormone manipulations can completely reverse a sexual dimorphism in brain regional volume in a mammalian species. The sex difference and androgen responsiveness of MePD volume is reflected in the soma size of neurons there.

Ovary Not Useless (don't memorize)

MEASURE	CHARACTERISTIC	SIGNIFICANT EFFECTS OF OVARIAN STEROIDS
Female Reproductive Behavior		
Receptive (lordosis)	F more than M	Neonatal Ovx + T lowered scores more than neonatal T alone
		Neonatal Ovx reduced scores more than postpuberal Ovx
"Proceptive (hopping, darting, ear wiggling)	F more than M	Neonatal Ovx reduced scores more than postpuberal Ovx
		Neonatal Gdx combined with E or ovarian transplant raised scores more than neonatal Gdx alone
Non-reproductive Behavior		
Open-field activity	F higher than M	Neonatal Ovx reduced activity
		Above restored by prepubertal low-dose E
		Neonatal Ovx + T lowered scores more than neonatal T alone
Plus maze	F higher than M	Neonatal TX or pubertal Ovx decreased time in open arms; neonatal TX + Ovx decreased time the most
Maze learning	F more errors than M	F errors increased after puberty
		Neonatal low-dose E increased M errors
Active avoidance learning	F fewer errors than M	Sex difference appeared after puberty
		Neonatal Ovx increased errors
		Postpubertal Ovx decreased errors
		Above reversed after 3 days of E
		Performance varied across estrus cycle; high E levels
	Increased errors	
AMPH induced locomotion	F more active than M	Prepubertal Ovx decreases activity as compared to adult Ovx

Morphology		
SDN-POA	F smaller than M	Neonatal TX to F reduced size, relative to control F
		Neonatal E mRNA antisense reduced size, relative to control F
		Postpubertal Gdx + E & P reduced size, relative to Gdx M
		Gdx alone had no effect on M
AVPv	F larger than M	Sex difference emerged at puberty with increase in F
		Postpubertal Gdx + E & P increased size, relative to Gdx M
		Gdx alone had no effect on M
Dendritic spine density		
Ventromedial hypothalamus	Varied across estrus cycle	Ovx reduced density; restored by low-dose E or E+P
Visual cortical pyramidal	After Day 20 M increased and F decreased	Day 30 Ovx prevented F-typical decrease in spines
Hippocampal pyramidal	Varied across estrus cycle	Ovx reduced density; restored by low-dose E&P
Dendritic branching		
Parietal cortical pyramidal	TP F more arbor than F	Day 150 Ovx increased arbor in oil treated F
Cortical thickness	M, R>L; F no asymmetry or trend to L>R	Neonatal Ovx increased cortical thickness
		Above reversed by E, days 40-90
		Above enhanced by P, days 40-90

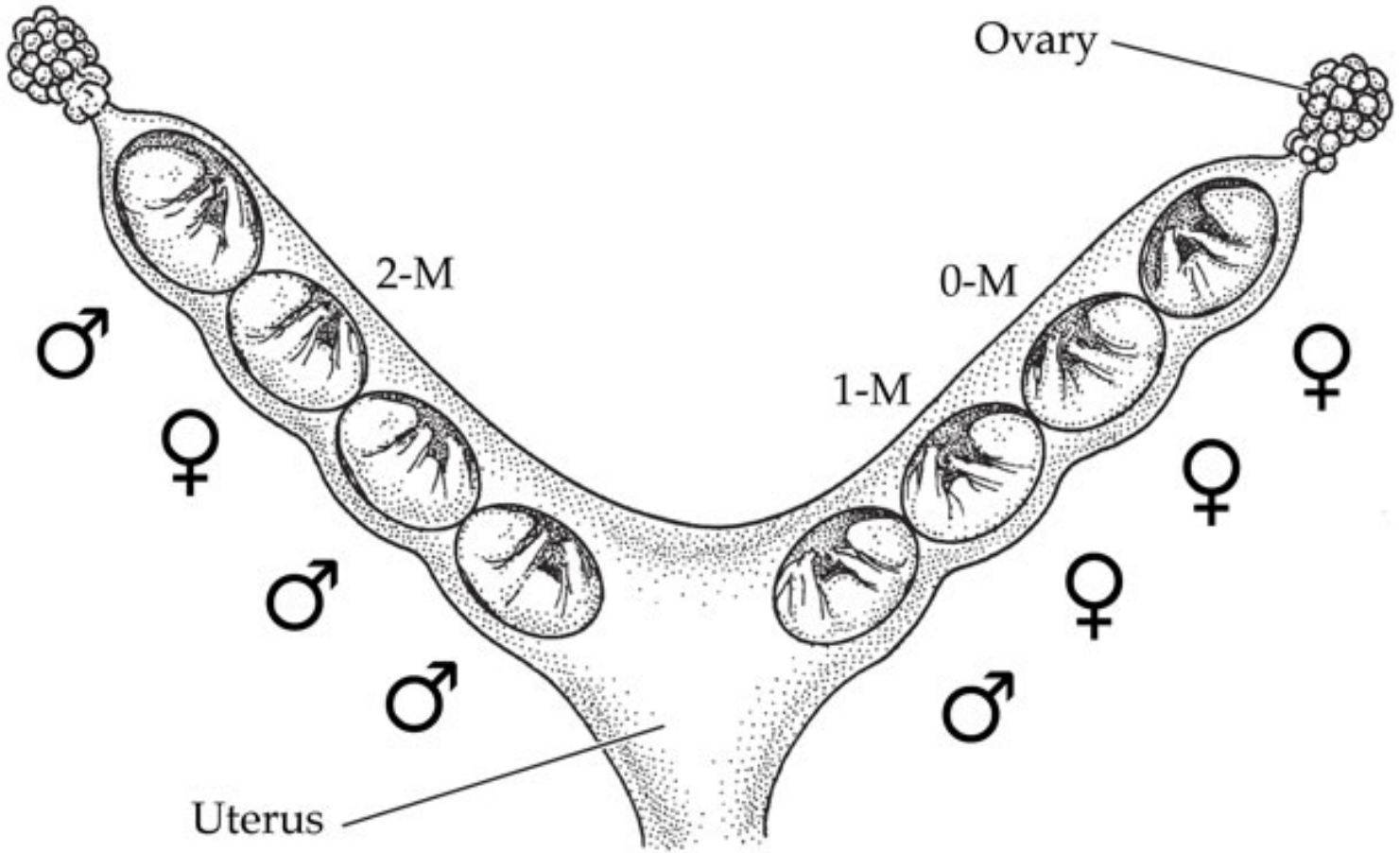
*Exclusive of corpus callosum

F: females; M: males; Ovx: ovariectomy; Gdx: male castration; T: testosterone; E: estrogen; P: progesterone; TX: tamoxifen

- http://www.bbsonline.org/Preprints/OldArchive/Figures/fitch.table.1.html

Uterine effects

- Natural variation in exposure rates



AN INTRODUCTION TO BEHAVIORAL ENDOCRINOLOGY, Third Edition, **Figure 3.28**

Variations in adult phenotype

Female rodents: 2M vs 0M

- longer ano-genital distance
- more mounting
- more aggressive

Main points

- Organizational effects on…
  - behavior
  - hormonal regulation
  - brain SDN-POA
- Alternatives/exceptions

Introduction

- Background
- What is already known? What is the burning question?

Methods

- How was the NEW experiment conducted?
  - Subjects?
  - Measures?
  - How analyzed?
- Enough detail for someone else to repeat

Results

- What was found in this new experiment?
  - Averages values
  - Statistical differences

Discussion

- What do the results mean?
  - Do they refute/support a hypothesis
  - Do they fit with previous research?
  - Do they raise new questions?
  - Were there problems with the experiment

Tissue preparation

- Grind up
- Leave structured
- Collect blood sample

Make something stick

Hormones stick to receptors

Antibodies stick to antigens

cDNA sticks to DNA, RNA

Make a sticky thing visible

Radioactive

Coloring Enzymes

Fluorescence

Methods and techniques

Main points

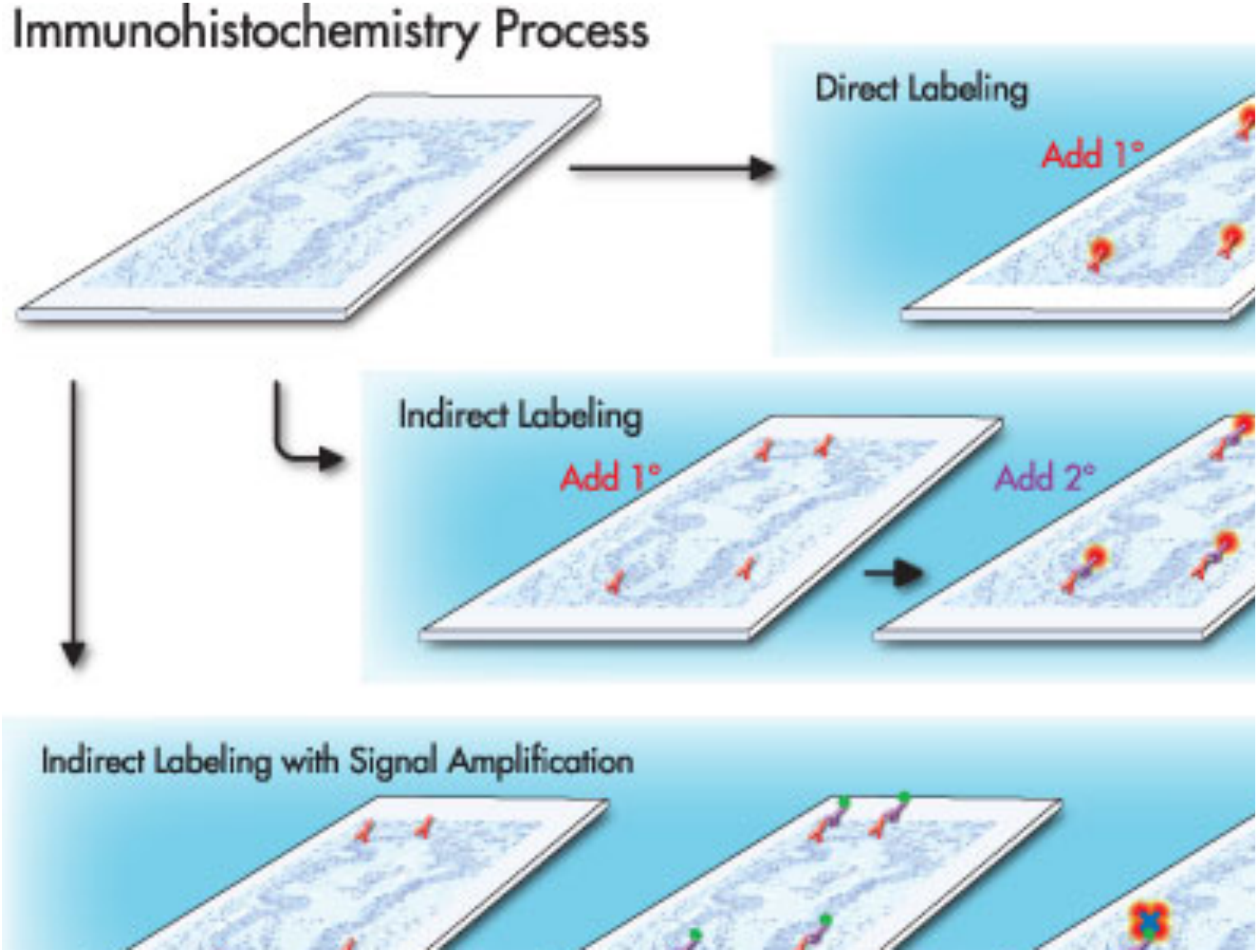
- Measuring hormones and receptors
- Behavioral methods/questions
- Each has strengths/weaknesses

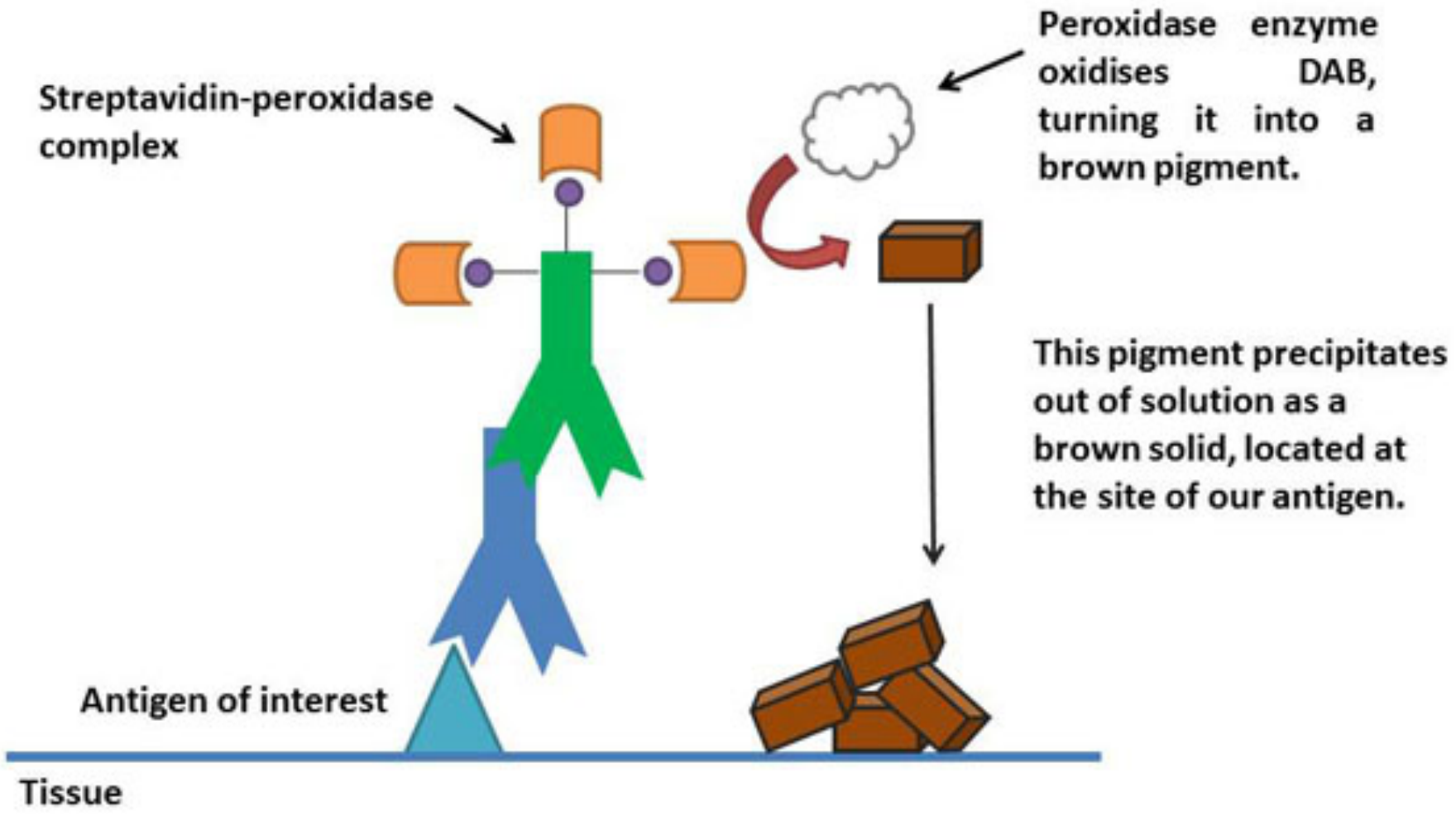
Preparing brains

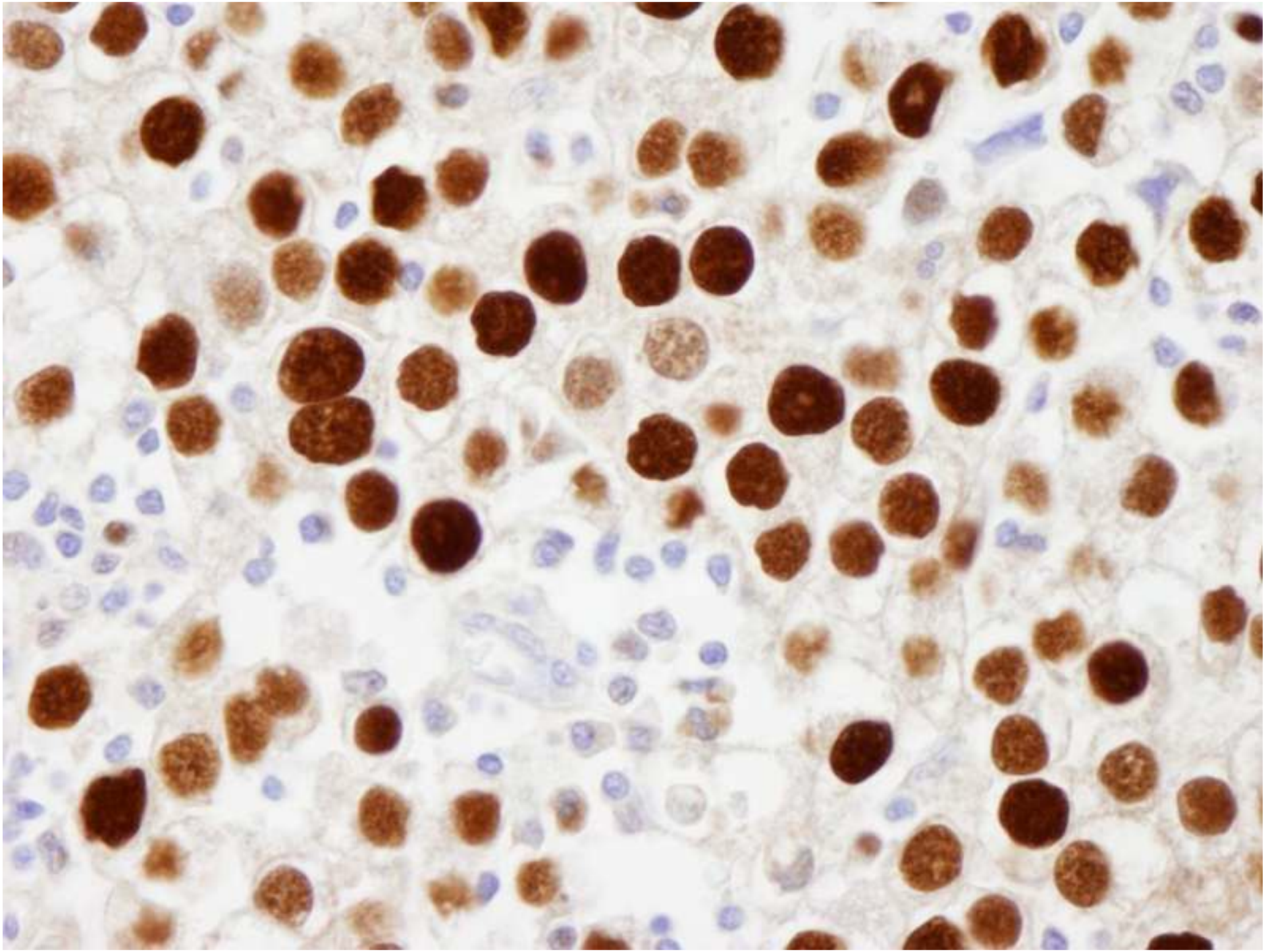
- Freeze or fix brain
- Slice it thinly

- Non-specific staining allows structure to be seen

- Expose it to sticking stuff
- Develop it
- Look under microscope


Immunohistochemistry Process
Direct Labeling
Add 1°
Indirect Labeling
Add 1°
Add 2°
Indirect Labeling with Signal Amplification


Streptavidin-peroxidase complex
Peroxidase enzyme oxidises DAB, turning it into a brown pigment.
This pigment precipitates out of solution as a brown solid, located at the site of our antigen.
Antigen of interest
Tissue



Kruijver article for Thursday

- Looks at androgen receptor in brains of humans

Techniques and Methods

- Chapter 1
  - Pg. 1-36