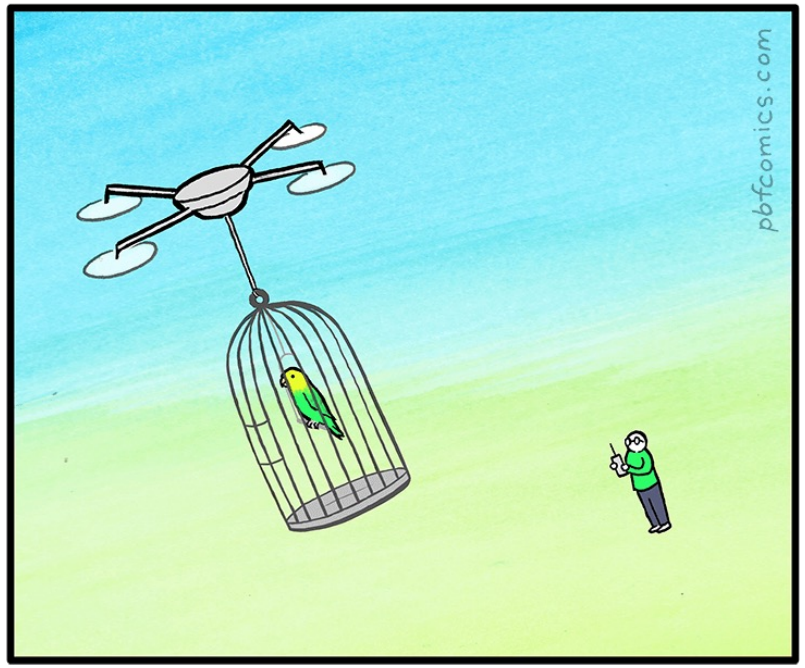
PSYC304: Introduction to hormones

Jay Hosking, PhD



Lecture outline

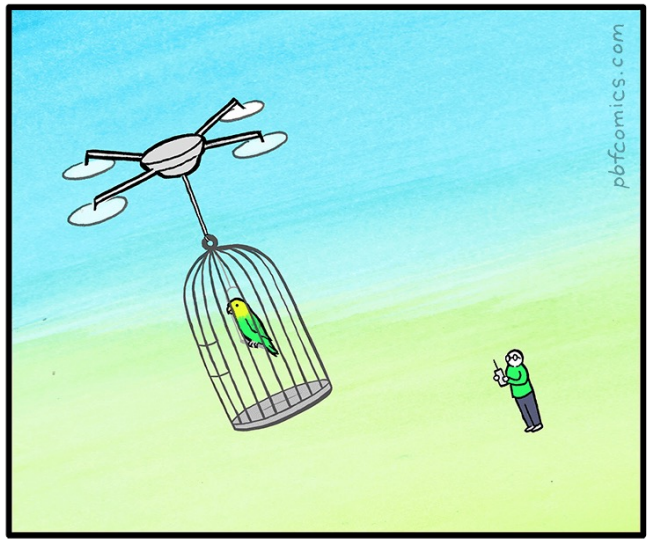
Principles of hormones

Hormone types and receptor types

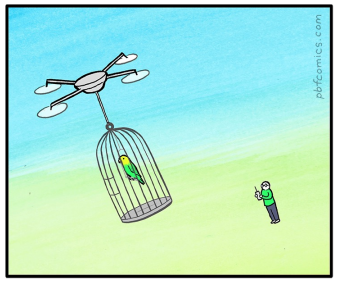
The hypothalamus and pituitary gland

Notable glands

Intro to hormones in behaviour



Learning objectives



1. Describe the methods, results, and implications of the first study of hormones.
2. Differentiate the following: exocrine vs. endocrine; endocrine vs. neurocrine vs. autocrine vs. paracrine, pheromone vs. allomone.
3. Describe the principles of hormone function, and note how they differ from neurotransmitter function.
4. Describe the role of the hypothalamus in controlling the endocrine system. What is a neuroendocrine cell?
5. Describe the three basic hormone types, including their size and plasma membrane permeability.
6. Describe hormone receptor types, including linking them to the hormone types. Be sure to appreciate their time course and effects.
7. Describe numerous methods for studying hormones and their receptors, including what each methodology brings that is different or valuable.
8. Describe the anatomy of the pituitary gland, including how that anatomy relates to function. Be sure to differentiate what hormones are released from what components of the pituitary.
9. Describe the pathway of transmission from hypothalamus to target cells, including all intermediary hormones.
10. Describe the following glands, including the hormones they release, and the function of these hormones: the adrenal gland, the thyroid gland, the pineal gland, the gonads.
11. Identify mechanisms through which oxytocin and vasopressin can influence behaviour, including multiple approaches to studying those hormones.
12. Are pheromones relevant to the human experience? Justify your answer with evidence.
13. Describe the dual pathways through which stress activates the adrenal gland. Do stress hormones mediate behaviour?

The “first” experiment on hormones: Berthold 1849

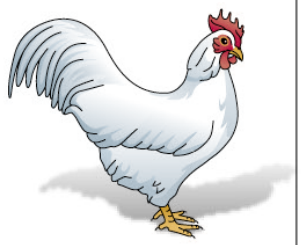
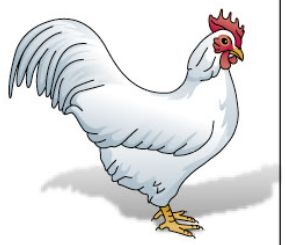
Loss of function experiment

Restoration of function with native or donor testes

Did not require innervation

Organizational (appearance) and activational (behavioural) effects

Testes make a “secretory blood-borne chemical”

	Group 1	Group 2	Group 3
			
	Left undisturbed, young roosters grow up to have large red wattles and combs, to mount and mate with hens readily, and to fight one another and crow loudly.	Animals whose testes were removed during development displayed neither the appearance nor the behavior of normal roosters as adults.	However, if one of the testes was reimplanted into the abdominal cavity immediately after its removal, the rooster developed normal wattles and normal behavior.
			
Comb and wattles:	Large	Small	Large
Mount hens?	Yes	No	Yes
Aggressive?	Yes	No	Yes
Crowing?	Normal	Weak	Normal

Conclusion
Because the reimplanted testis in group 3 was in an abnormal body site, disconnected from normal innervation, and yet still affected development, Berthold reasoned that the testes release a chemical signal, which we would call a hormone, that has widespread effects.

Behavioral Neuroscience 9e, Figure 5.2

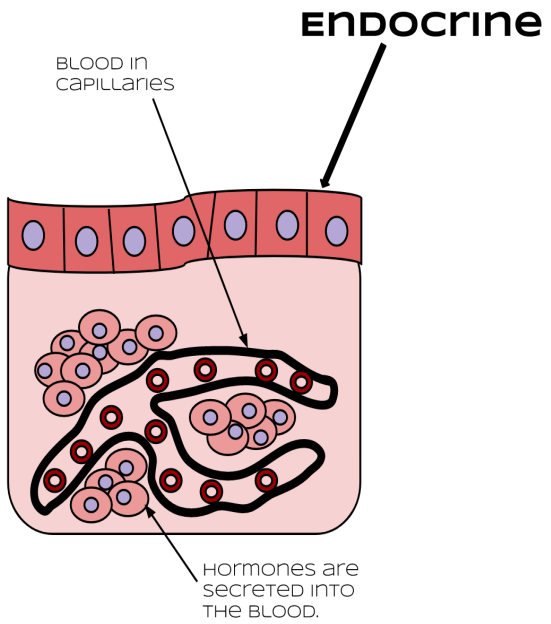
Many cells secrete chemicals (1)

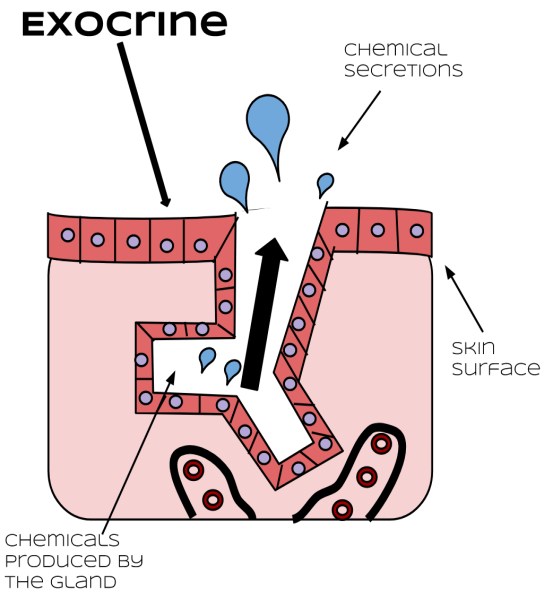
"Hormone" is quite a catch-all

- Released primarily by *glands* (but also other tissues)
- Released primarily into the bloodstream (but also locally)
- Released primarily by animals (but also plants?)

Exocrine vs. endocrine glands

- Endocrine glands release hormones





Many cells secrete chemicals (2)

Neurocrine

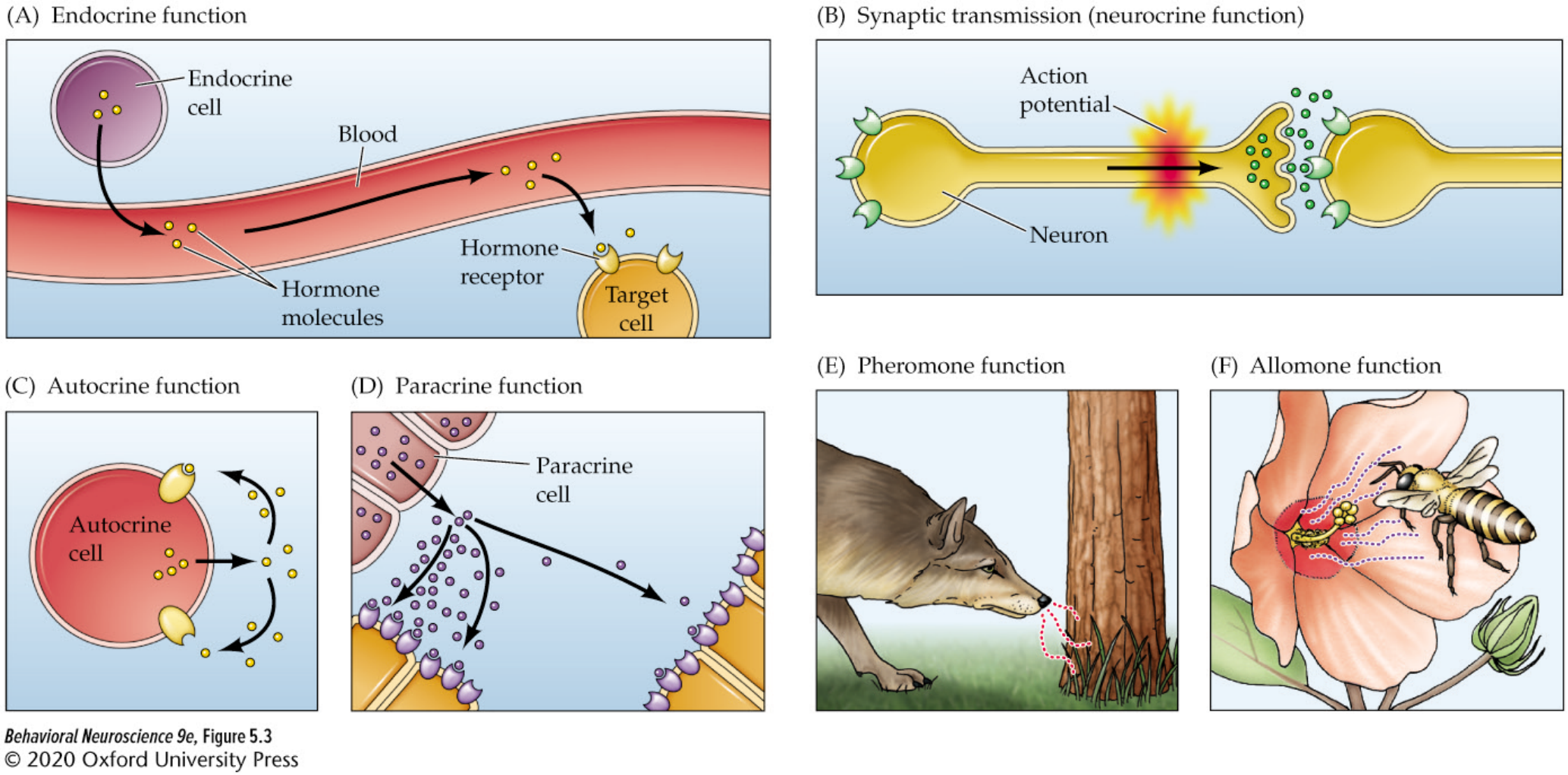
Endocrine

Autocrine

Paracrine

Pheromone

Allomone



Behavioral Neuroscience 9e, Figure 5.3

Principles of hormone function

Slow-acting, gradual effects

Behaviour changes in intensity/probability rather than polarity

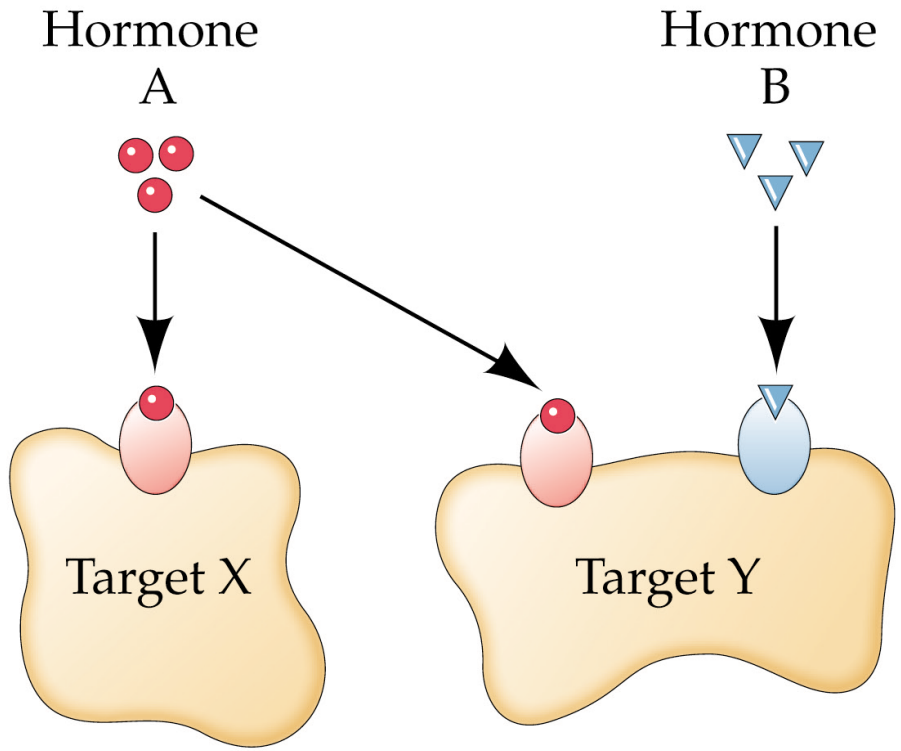
Behaviour and hormone release are reciprocal

Multiplicity of action

Secretion is often pulsatile and rhythmic

Hormones can interact

Hormones need receptors! (cf. neurotransmitters)



Behavioral Neuroscience 9e, Figure 5.5

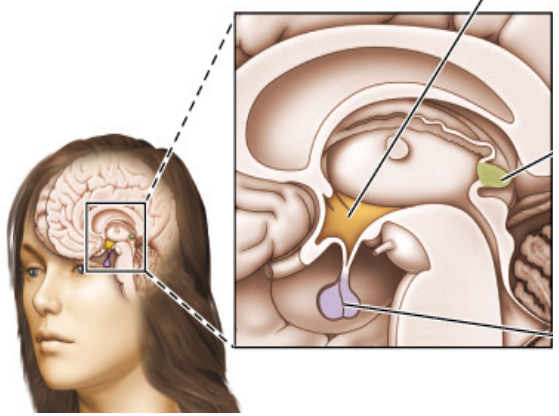
The hypothalamus and neuroendocrine cells

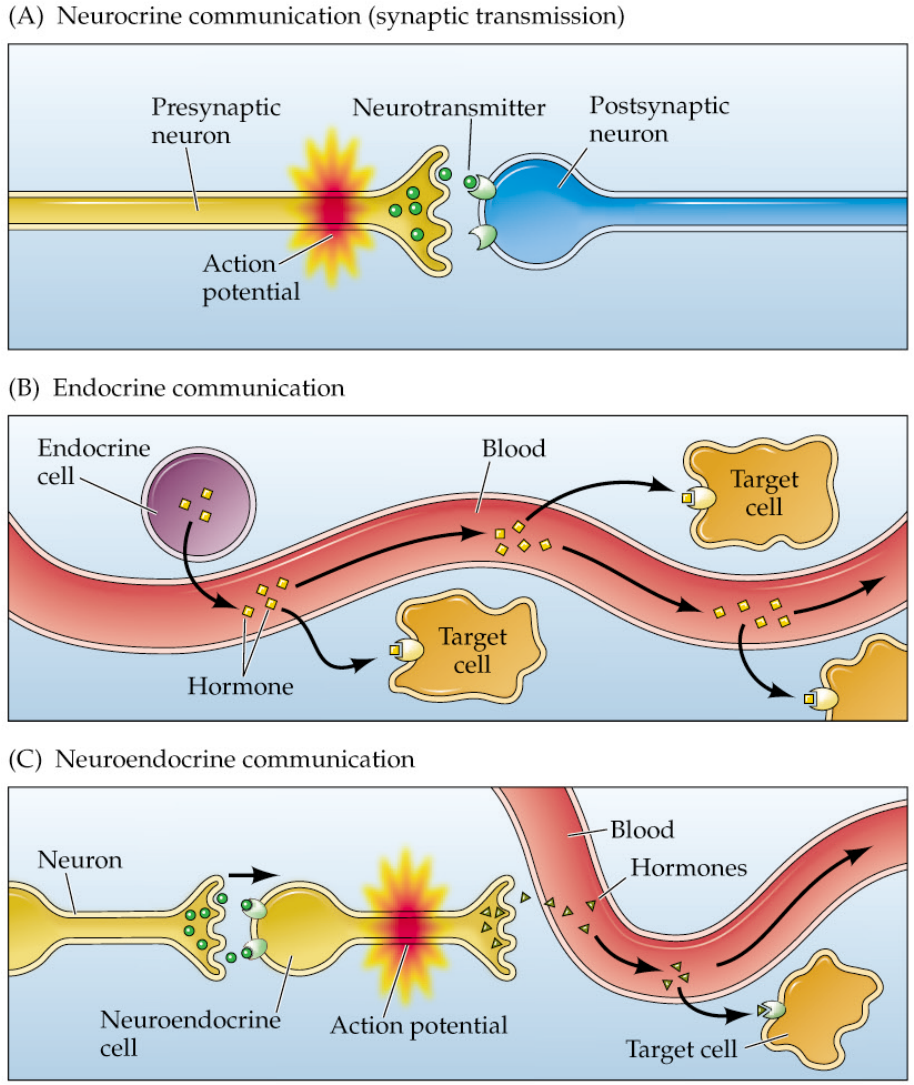
Hypothalamus (HTh): junction between NS and endocrine system

HTh contains neuroendocrine cells, aka neurosecretory cells

Some hormones are also neurotransmitters!

Major endocrine structures	Some main functions regulated by secretion
Hypothalamus	Control of hormone secretions





Behavioral Neuroscience 9e, Figure 5.6

Hormone types

Peptide

Amine

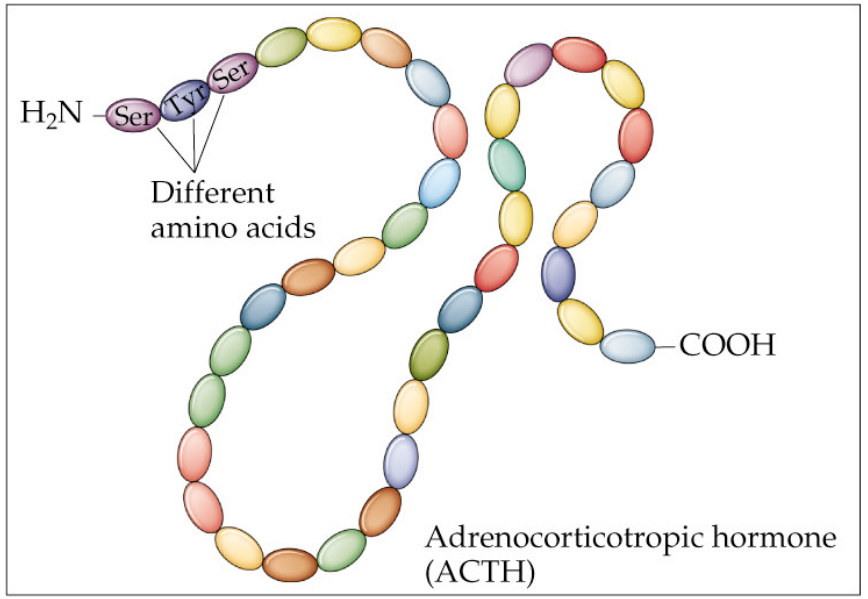
Steroid

TABLE 5.1 Examples of Major Classes of Hormones

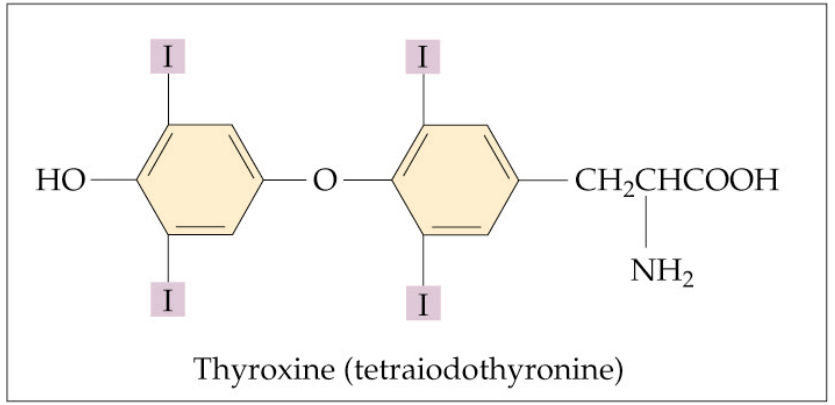
Class	Hormone
Peptide hormones	Adrenocorticotropic hormone (ACTH)
	Follicle-stimulating hormone (FSH)
	Luteinizing hormone (LH)
	Thyroid-stimulating hormone (TSH)
	Growth hormone (GH)
	Prolactin
	Insulin
	Glucagon
	Oxytocin
	Vasopressin (arginine vasopressin, AVP; antidiuretic hormone, ADH)
	Releasing hormones, such as:
	Corticotropin-releasing hormone (CRH)
	Gonadotropin-releasing hormone (GnRH)
Amine hormones	Epinephrine (adrenaline)
	Norepinephrine (NE)
	Thyroid hormones
	Melatonin
Steroid hormones	Estrogens (e.g., estradiol)
	Progestins (e.g., progesterone)
	Androgens (e.g., testosterone, dihydrotestosterone)
	Glucocorticoids (e.g., cortisol)
	Mineralocorticoids (e.g., aldosterone)

Behavioral Neuroscience 9e, Table 5.1

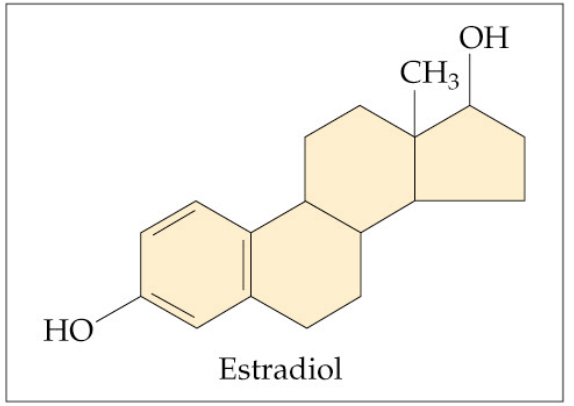
(A) Peptide hormone



(B) Amine hormone



(C) Steroid hormone



Behavioral Neuroscience 9e, Figure 5.7

Hormone receptor types

At the membrane

i.e. GPCRs

faster

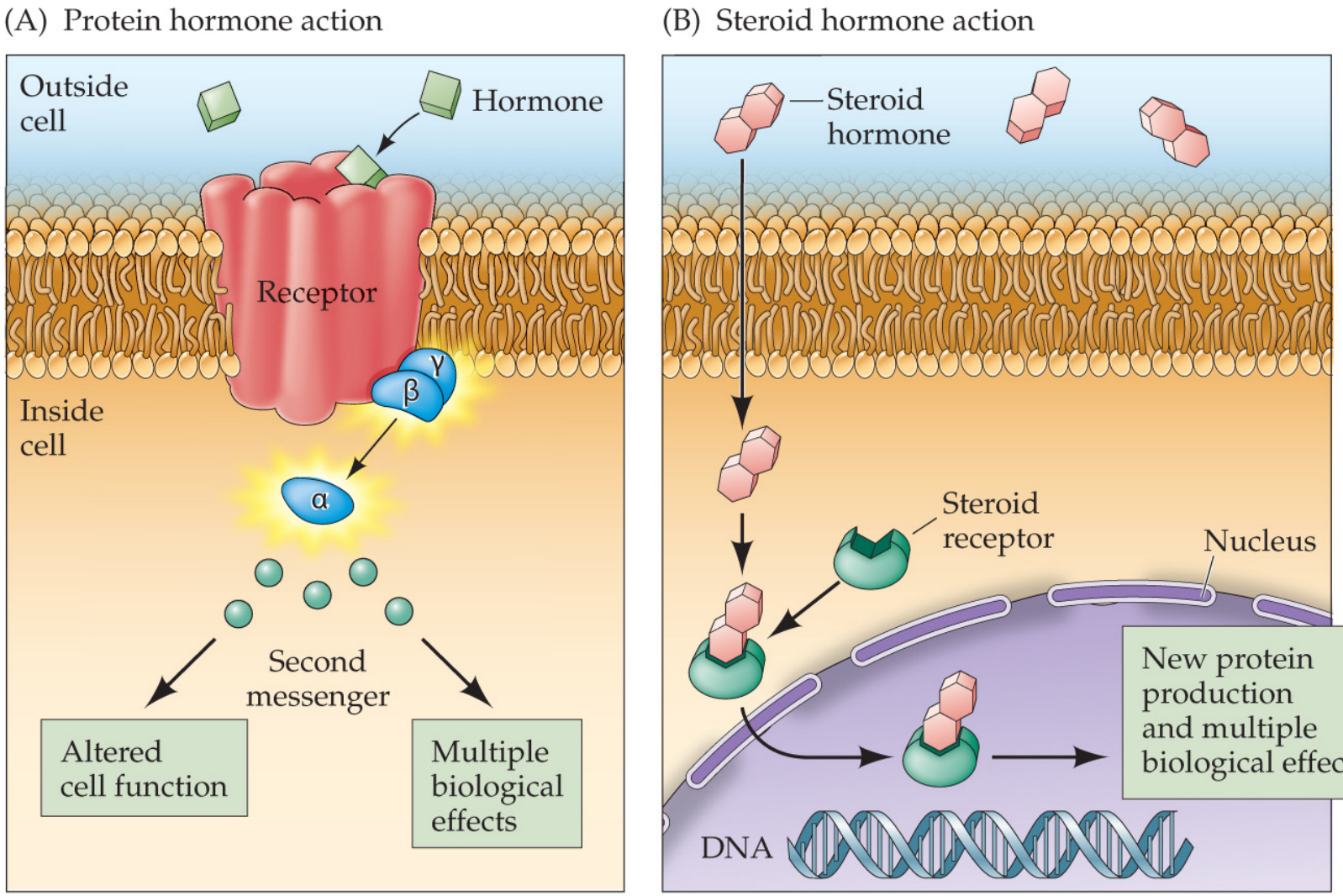
Intracellular

usually near nucleus

i.e. transcription factor

slower

Note: steroid hormones can have GPCRs, too!



Behavioral Neuroscience 9e, Figure 5.8

Methods in measuring hormones and receptors

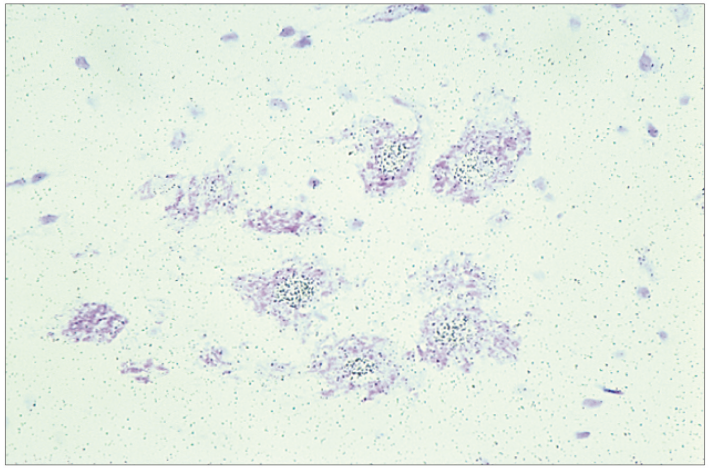
Radioimmunoassay

Autoradiography

Immunohistochemistry/immunocytochemistry

In situ hybridization

(B) Autoradiogram



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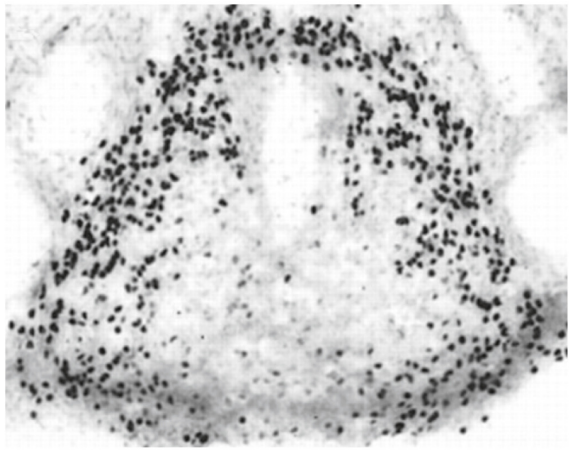
(C) Expression of *c-fos* in activated cells



From N. Sunn et al., 2002. *Proc Natl Acad Sci* 99: 1701–1706. © 2002 National Academy of Sciences, U.S.A.

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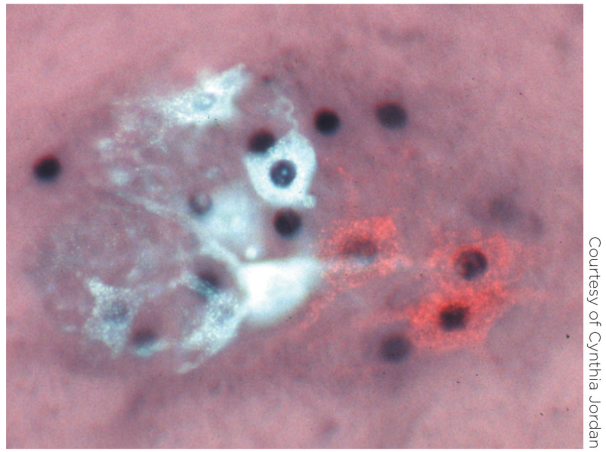
(D) Immunocytochemistry



Courtesy of Cynthia Jordan

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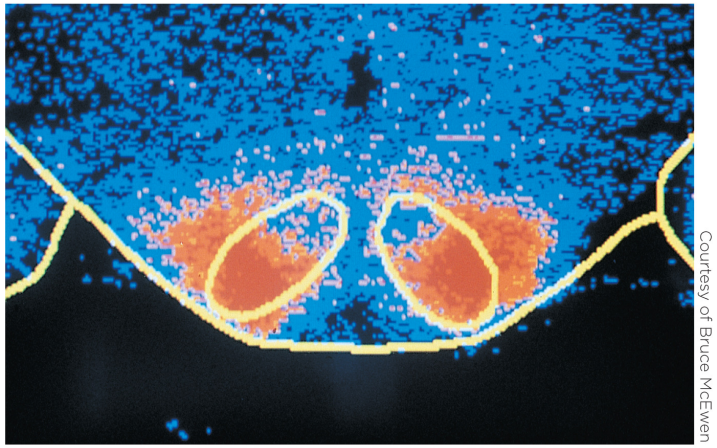
(C) Autoradiogram



Courtesy of Bruce McEwen

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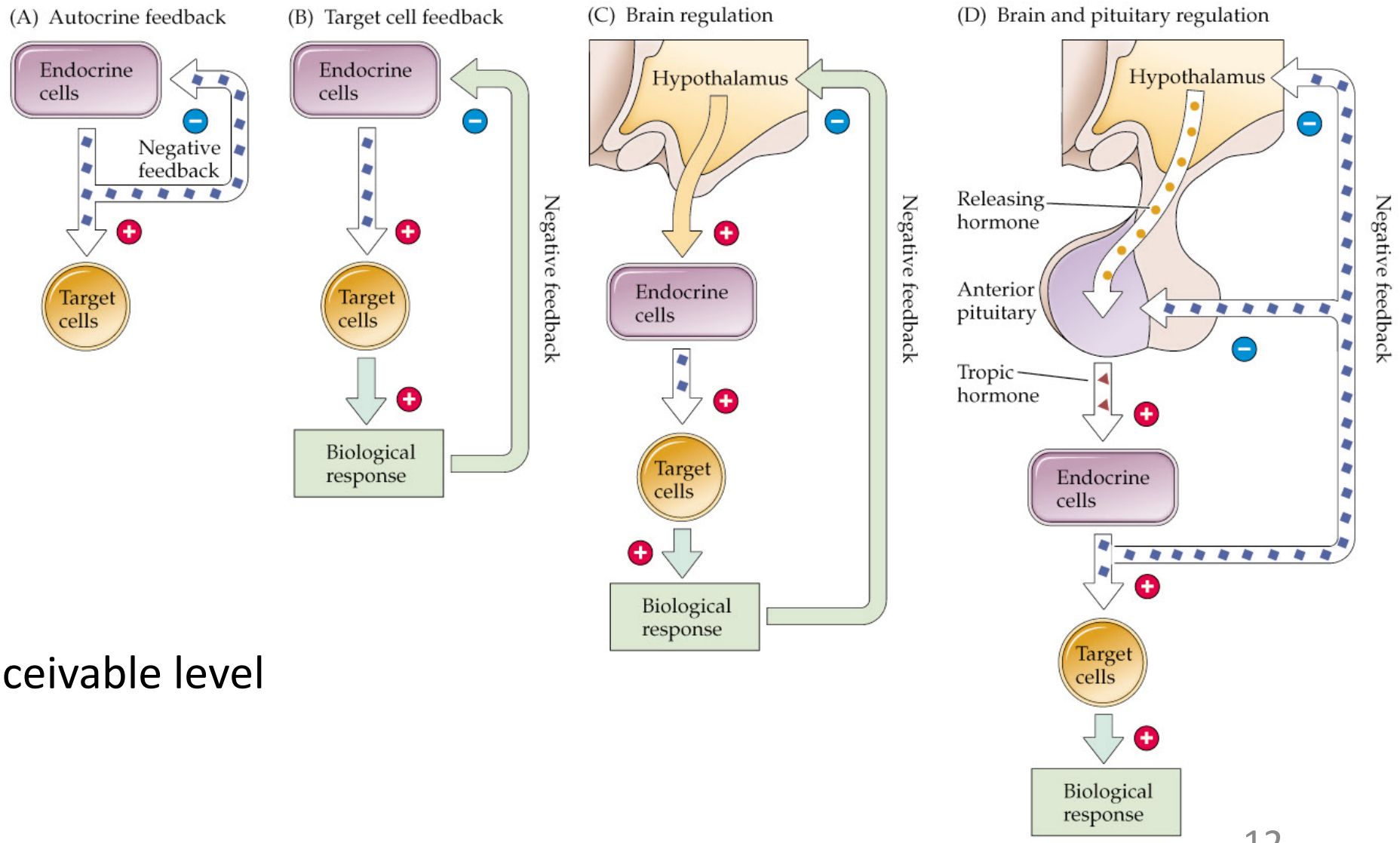
Negative feedback mechanisms



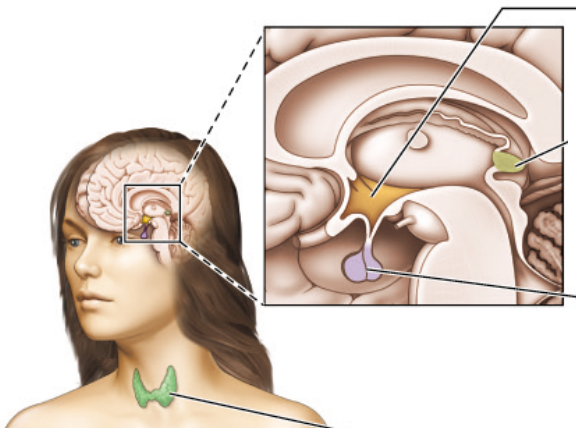
Happen at every conceivable level

The pituitary gland

The other side of the NS/endocrine intersection

Connected via *infundibulum*, aka pituitary stalk

Anterior and posterior divisions



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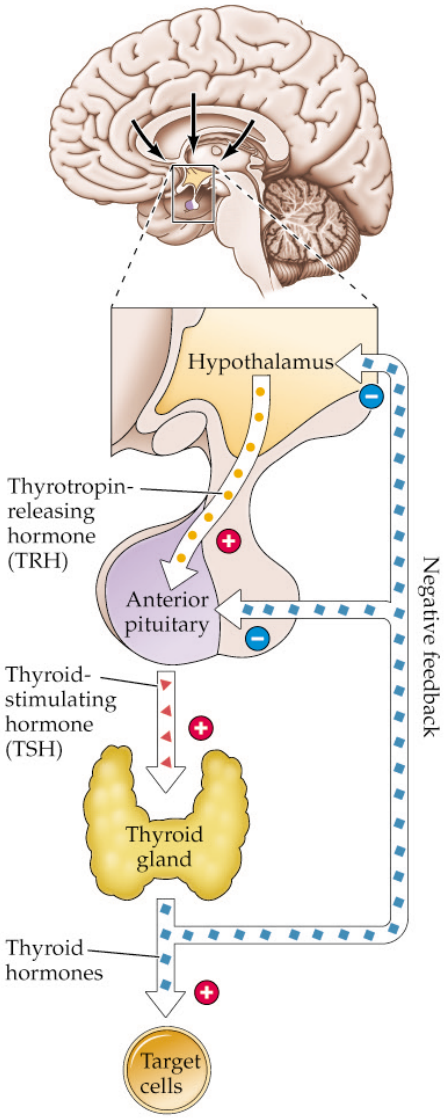
Hypothalamus	Control of hormone secretions
Pituitary gland:	
Anterior pituitary	Hormone secretion by thyroid, adrenal cortex, and gonads; growth
Posterior pituitary	Water balance; salt balance



The posterior pituitary

HTh has neuroendocrine cells in paraventricular and supraoptic nuclei

Axons travel down infundibulum to posterior pituitary

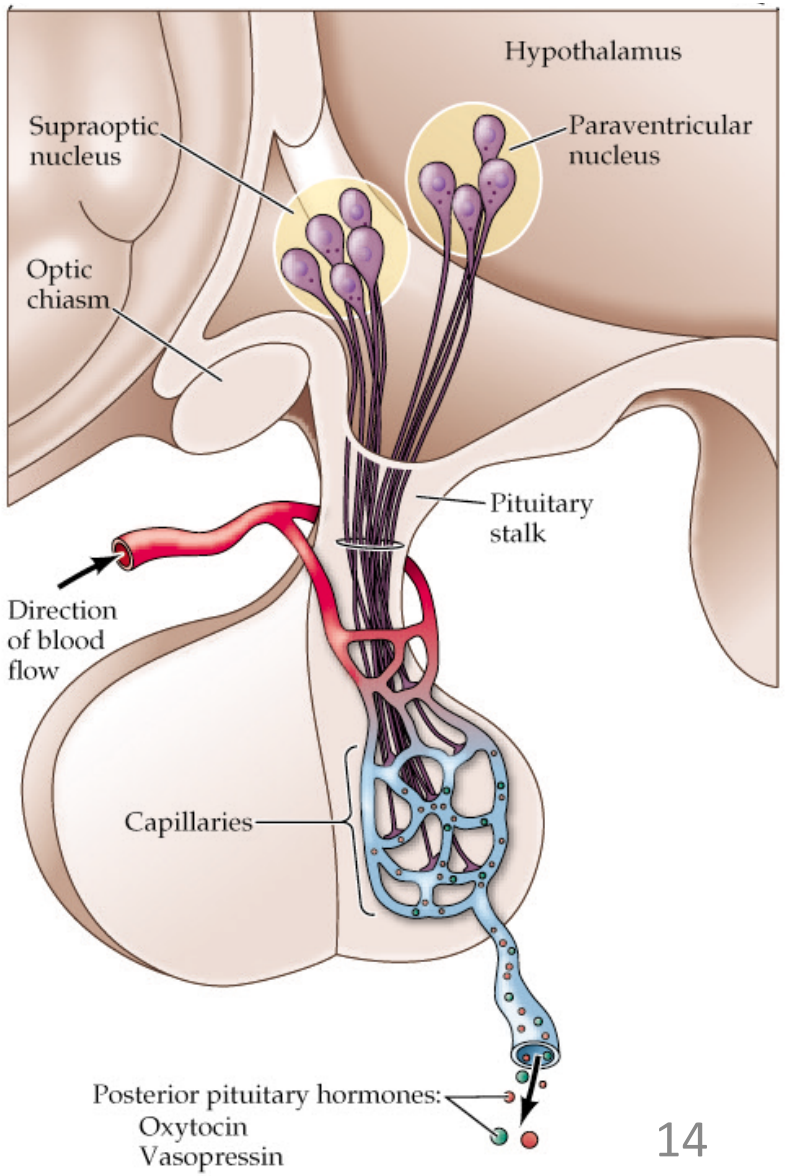
These HTh axons terminate on capillaries

These axons release **oxytocin** and **vasopressin/anti-diuretic hormone (ADH)** into blood

Oxytocin: stimulate uterine contractions in pregnancy; milk letdown reflex (cf. pitocin)

ADH: conservation of water; blood vessel constriction

Alcohol inhibits L-type calcium channels, which inhibits ADH release (effect?)



The anterior pituitary

HTh neuroendocrine cells terminate at **median eminence**

HTh release **releasing hormones**

Releasing hormones carried (only a few mm) via **hypophyseal portal veins**

Anterior pituitary has its own hormone-producing cells

When releasing hormones arrive, anterior pituitary cells release **tropic hormones**

Tropic hormones travel to **glands** and cause further hormone release

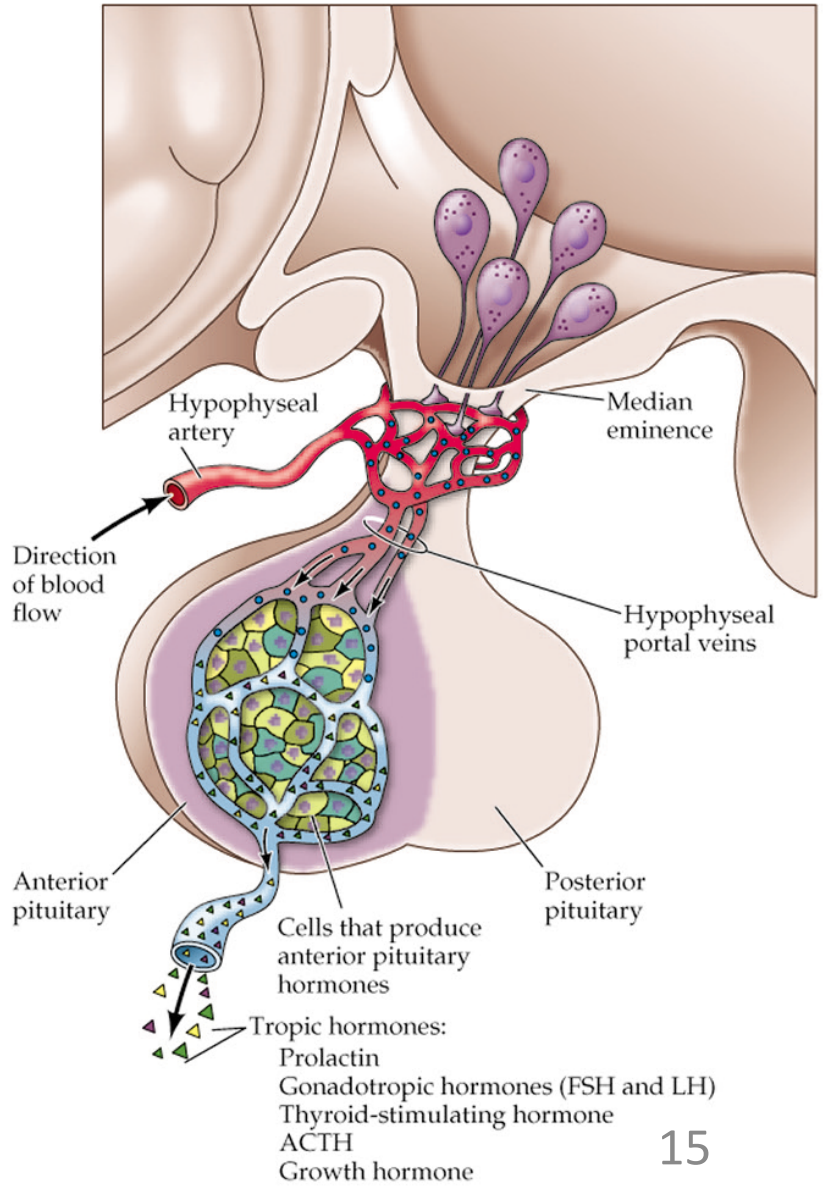
The common motif:

Releasing hormones (HTh)

→ *tropic hormones (anterior pituitary gland)*

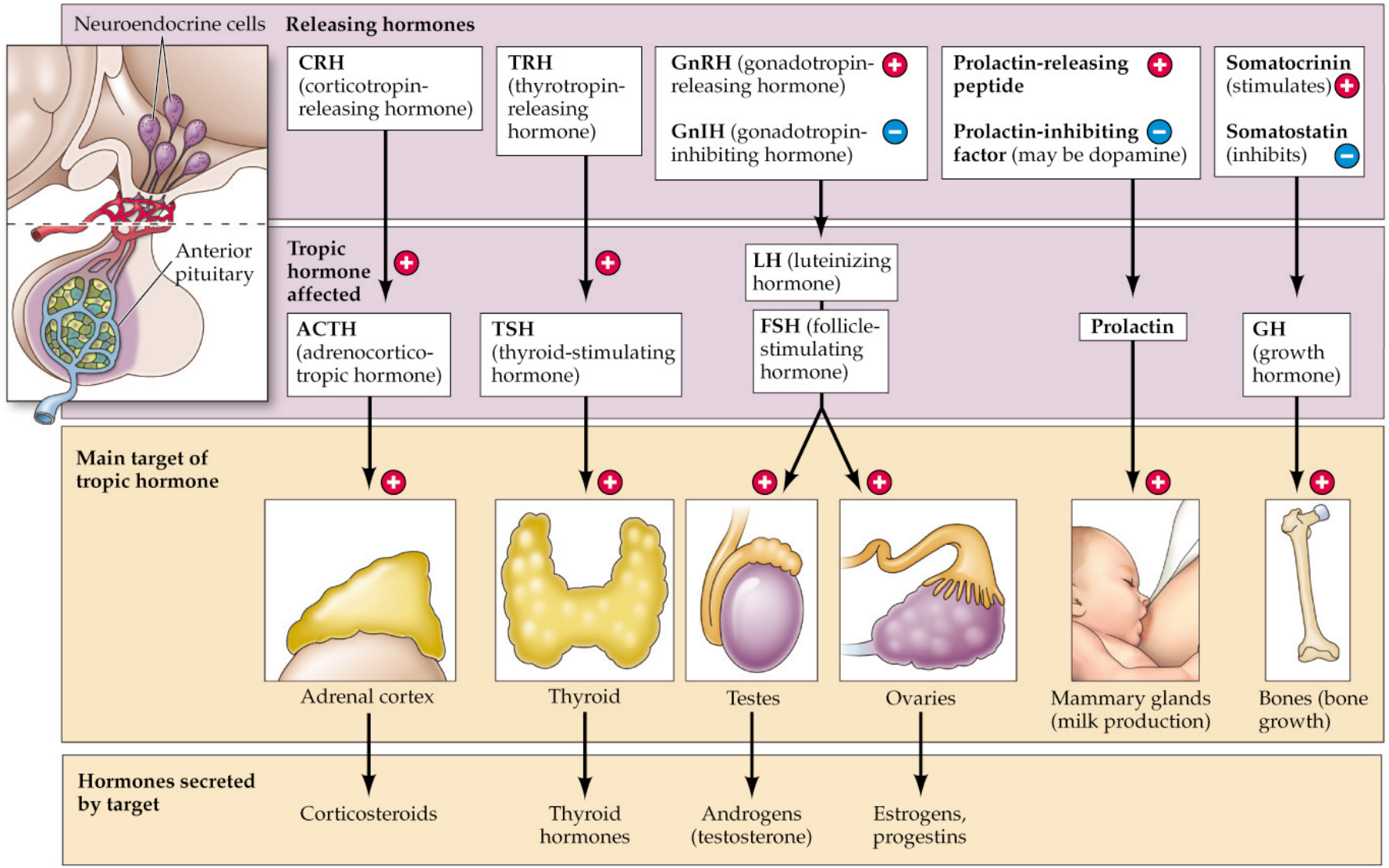
→ *hormones (gland)*

→ *target*



Hormones of the anterior pituitary

Six main ones (again, these are tropic hormones):



Notable glands (1): the adrenal gland

Adrenal cortex vs. adrenal medulla

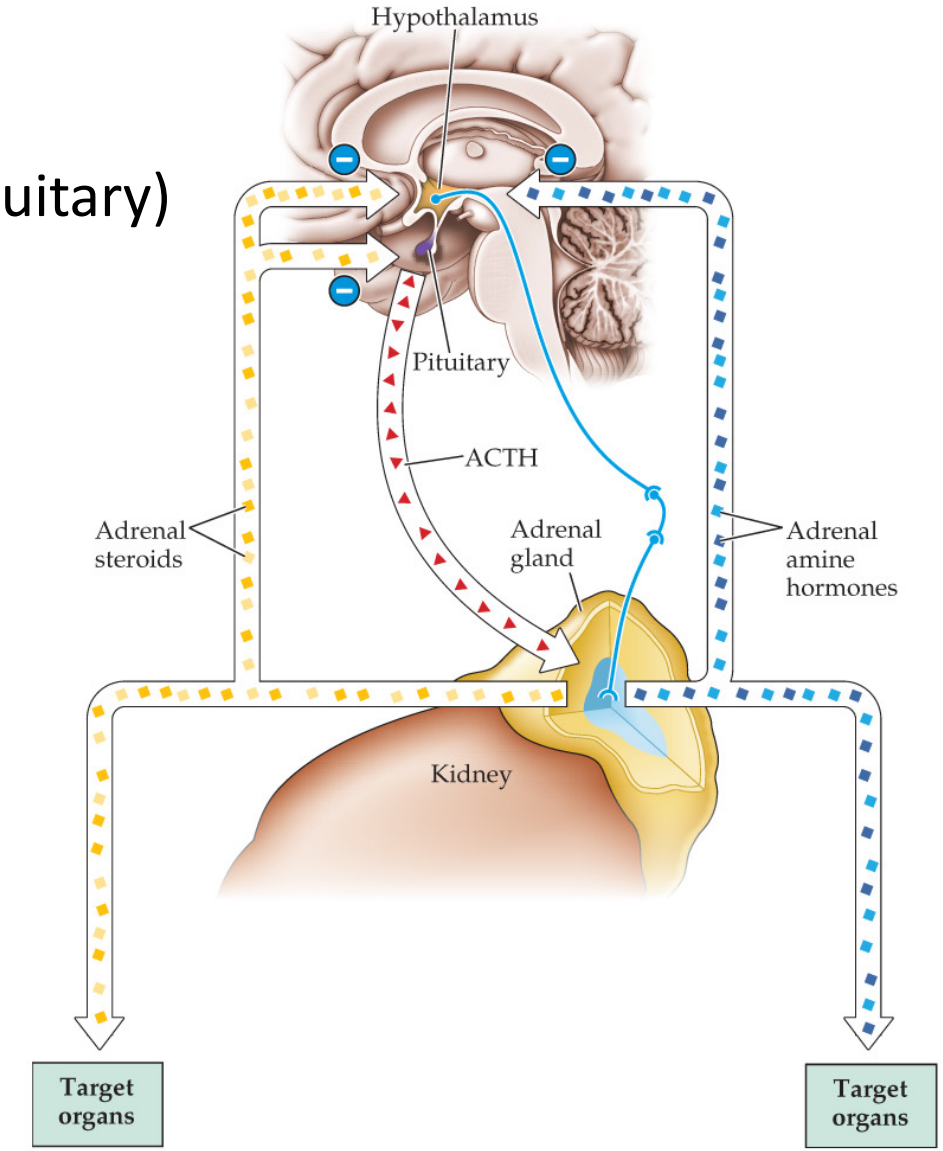
Different inputs to adrenal cortex (anterior pituitary) vs. adrenal medulla (ANS)

Adrenal cortex releases steroid hormones:

- Glucocorticoids (e.g. cortisol)
- Mineralocorticoids (e.g. aldosterone)
- Sex steroids (e.g. androstenedione)
- **Synthesized on demand** via ACTH

Adrenal medulla releases amine hormones:

- Epinephrine
- Norepinephrine



Notable glands (2): the thyroid gland

Releases thyroid hormones:
thyroxine, triiodothyronine

These are amines but act like steroids (meaning?)

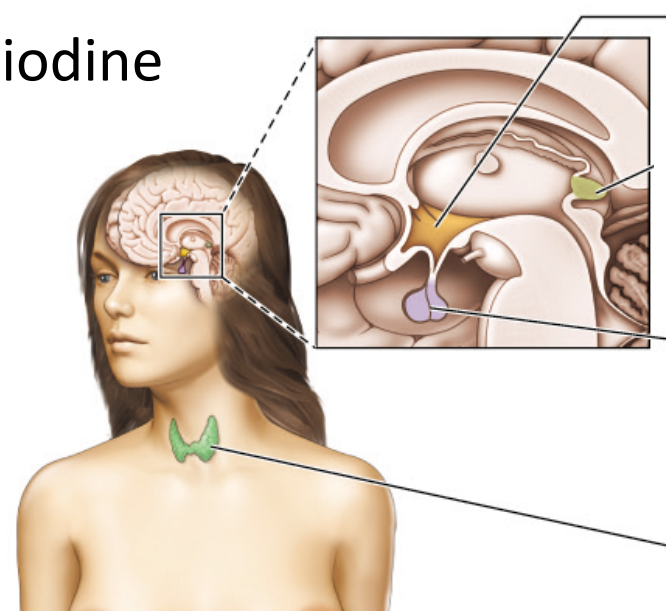
Generally, regulate growth and metabolism

Also has a general activating effect on NS

Only substance in body that needs iodine

Hypothyroidism

Thyroid also releases calcitonin



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Hypothalamus	Control of hormone secretions
Pituitary gland:	
Anterior pituitary	Hormone secretion by thyroid, adrenal cortex, and gonads; growth
Posterior pituitary	Water balance; salt balance
Thyroid	Growth and development; metabolic rate

Notable glands (3): the pineal gland

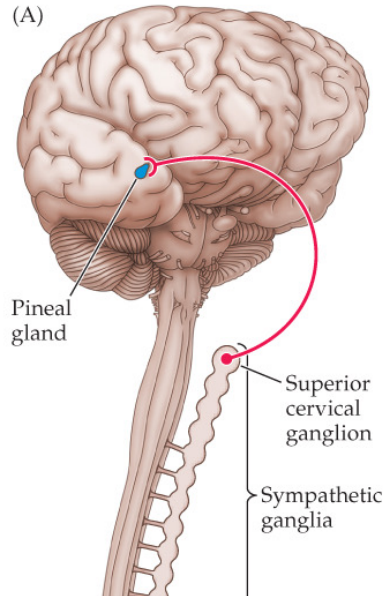
aka Your third eye! (Not really)

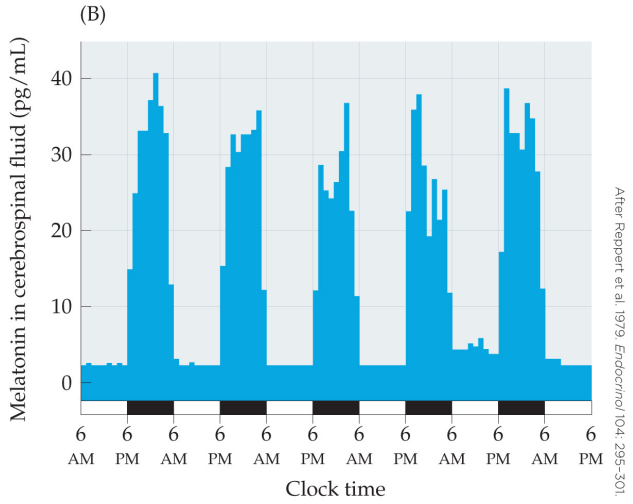
The seat of the soul? (Also no)

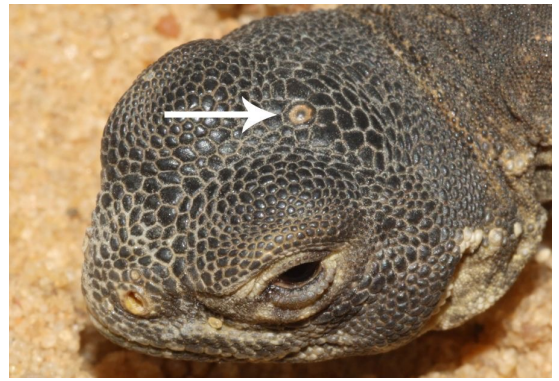
Releases melatonin

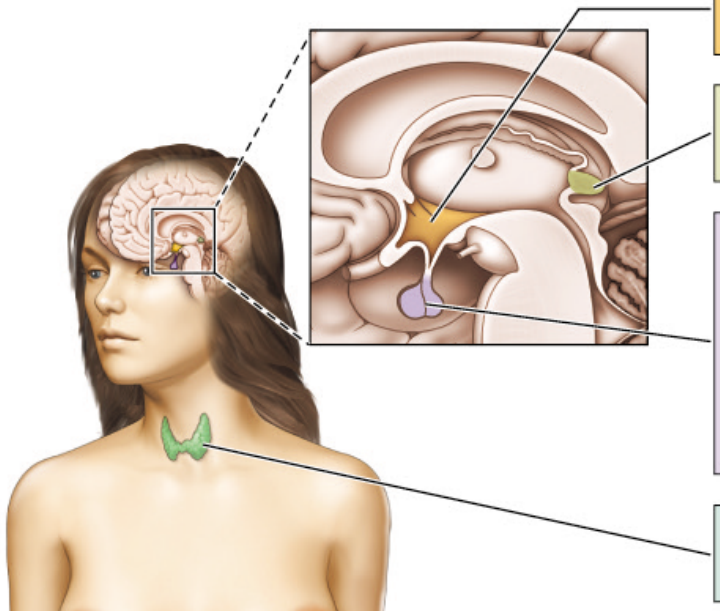
Melatonin released at night

Inputs: from sympathetic NS!









Major endocrine structures	Some main functions regulated by secretion
Hypothalamus	Control of hormone secretions
Pineal gland	Reproductive maturation; body rhythms
Pituitary gland:	
Anterior pituitary	Hormone secretion by thyroid, adrenal cortex, and gonads; growth
Posterior pituitary	Water balance; salt balance
Thyroid	Growth and development; metabolic rate

Notable glands (4): the gonads

Two compartments in male and female gonads:
one for sex hormone production,
one for gametes production

GnRH and/or GnIH (HTh)

→ FSH & LH (anterior pituitary)

→ gonads

And kisspeptin (peptide nt) stimulates GnRH

Testes:

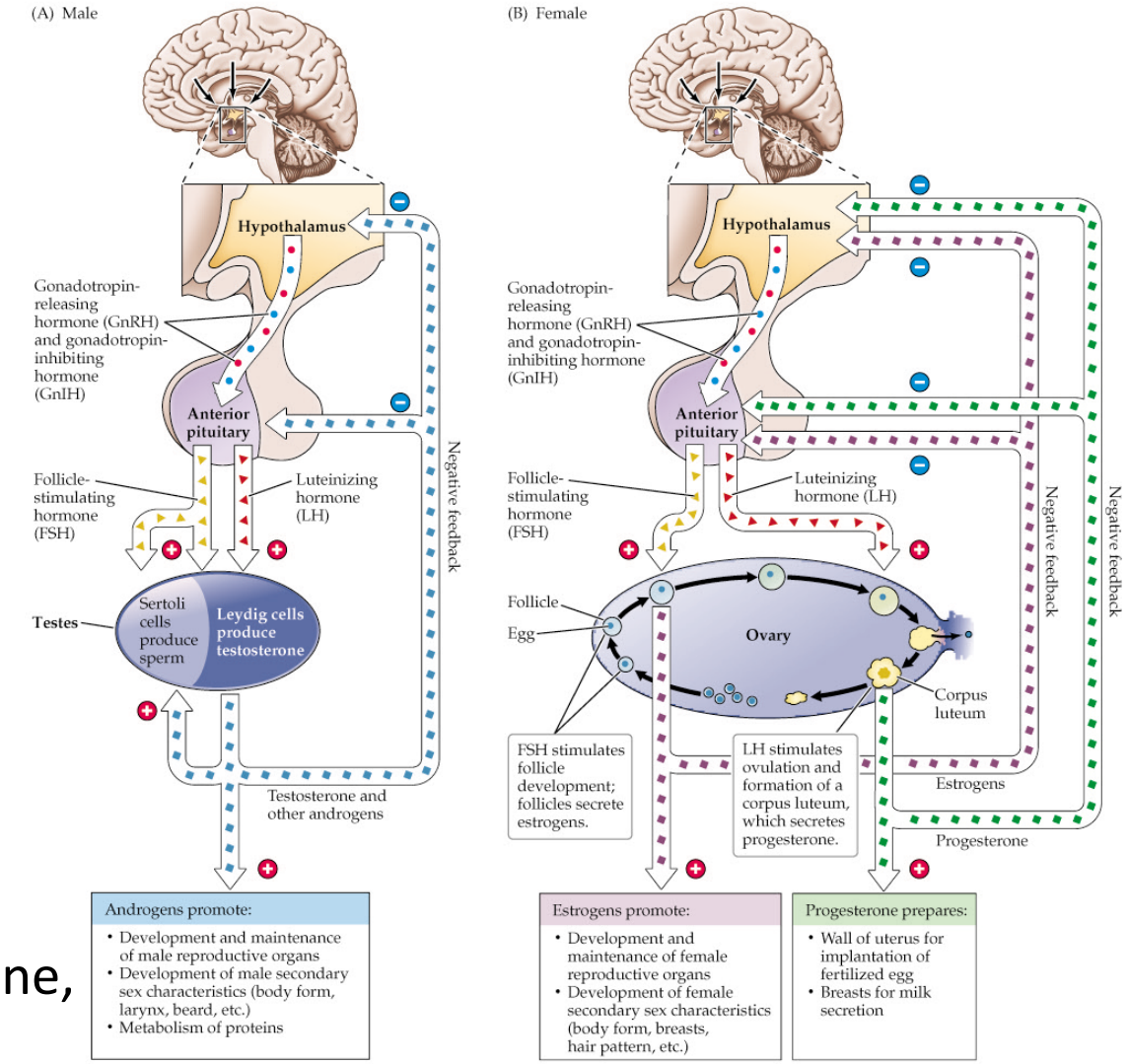
Sertoli cells (sperm)

Leydig cells (androgens, e.g. testosterone)

Ovaries:

Ova (mature gametes)

Steroid hormones (progestins, e.g. progesterone, and estrogens, e.g. estradiol)



Hormones in behaviour?

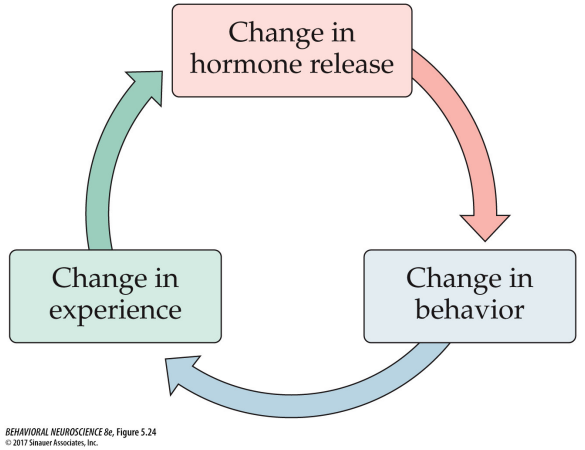
Yes, BUT with notable limitations in humans

i.e. Cortex often supersedes many older controls for behaviour

The most vigorous responses are observed in animal models

And the converse is true: behaviour influences hormones

e.g. Psychosocial dwarfism



BEHAVIORAL NEUROSCIENCE 8e, Figure 5.24
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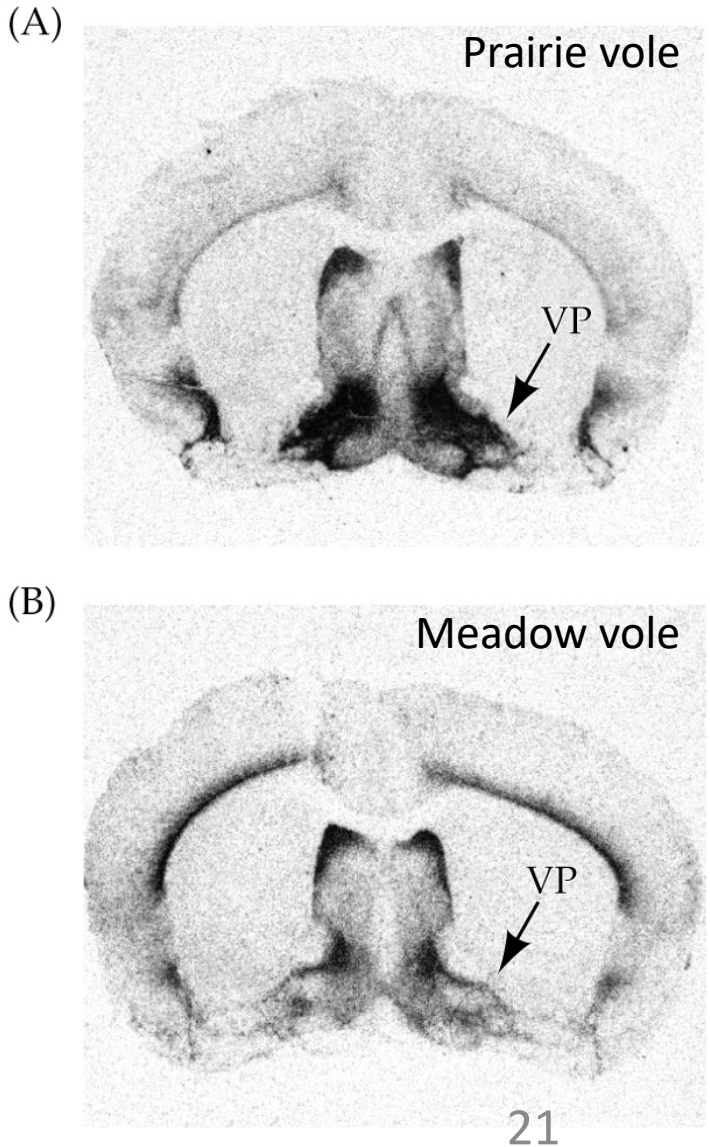
e.g. Oxytocin and vasopressin/ADH

Exogenous oxytocin in rats

Oxytocin knock-outs in mice

Oxytocin & vasopressin receptors: ventral pallidum (VP)

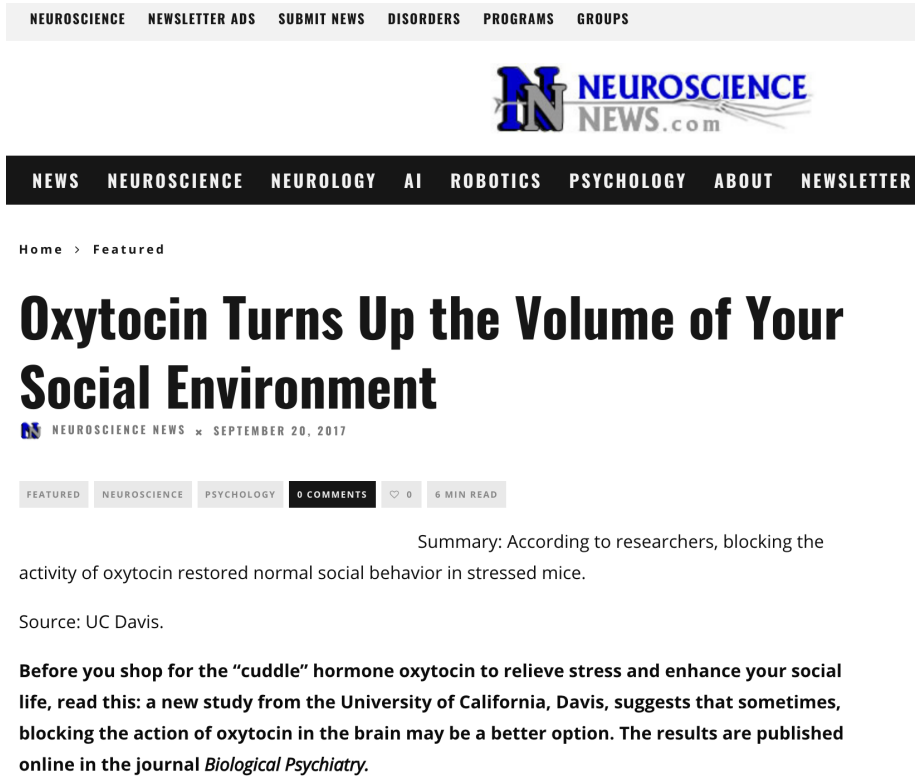
Prairie voles vs. meadow voles



Courtesy of Miranda Lim and Larry Young

The “love molecule”? The “cuddle chemical”?

The promise of oxytocin is alluring, but the data show (as per usual) that the story is more complicated than we initially thought



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Oxytocin Turns Up the Volume of Your Social Environment

NEUROSCIENCE NEWS × SEPTEMBER 20, 2017

FEATURED NEUROSCIENCE PSYCHOLOGY 0 COMMENTS ♡ 0 6 MIN READ

Summary: According to researchers, blocking the activity of oxytocin restored normal social behavior in stressed mice.

Source: UC Davis.

Before you shop for the “cuddle” hormone oxytocin to relieve stress and enhance your social life, read this: a new study from the University of California, Davis, suggests that sometimes, blocking the action of oxytocin in the brain may be a better option. The results are published online in the journal *Biological Psychiatry.*

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Surprising effects of oxytocin on cocaine addiction

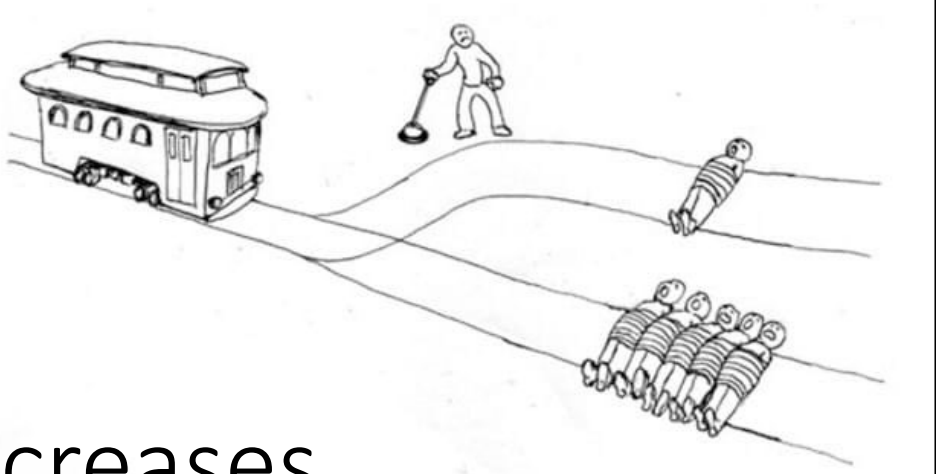
NEUROSCIENCE NEWS × JANUARY 15, 2020

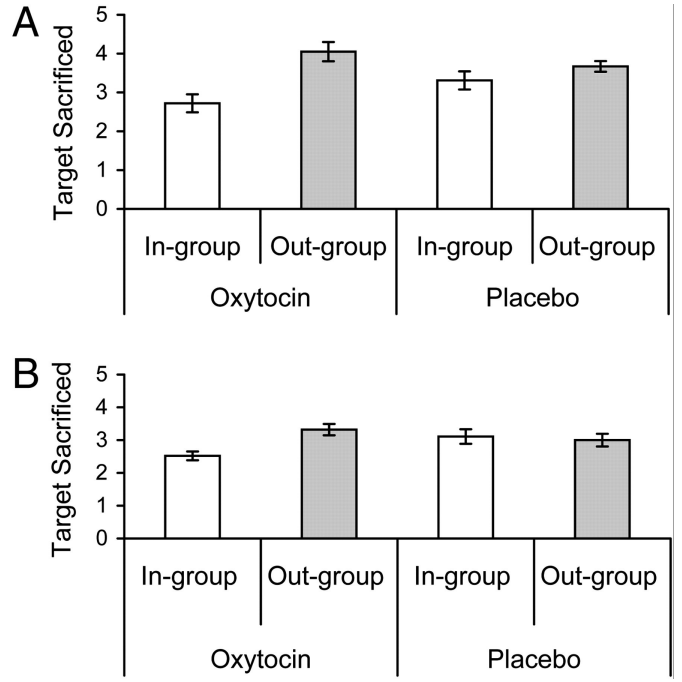
FEATURED NEUROSCIENCE 0 COMMENTS ♡ 0 7 MIN READ

Summary: *In men with a history of childhood trauma, oxytocin reduced the activity within the amygdala and cravings for cocaine. Women who were addicted to cocaine and had experienced childhood trauma showed an increase in amygdala activity following exposure to oxytocin.*

Source: *Medicial University of South Carolina*

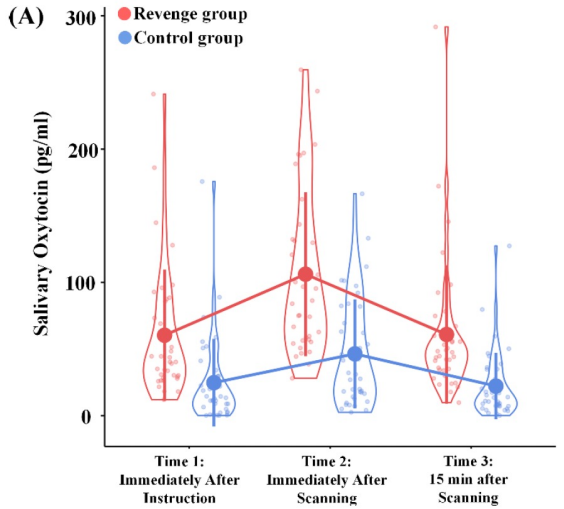
A team of addiction researchers at the Medical University of South Carolina (MUSC) report in *Psychopharmacology* that oxytocin, a hormone produced naturally in the hypothalamus, has significant gender differences when used as a treatment for cocaine-addicted individuals with a history of childhood trauma.

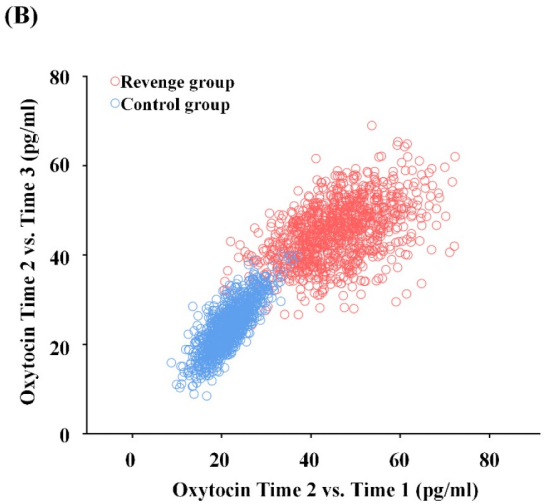




De Dreu et al. 2011

Oxytocin increases in-group bias (and increases revenge against out groups!)





Han *et al*. 2020

How about pheromones? Do they mediate behaviour?

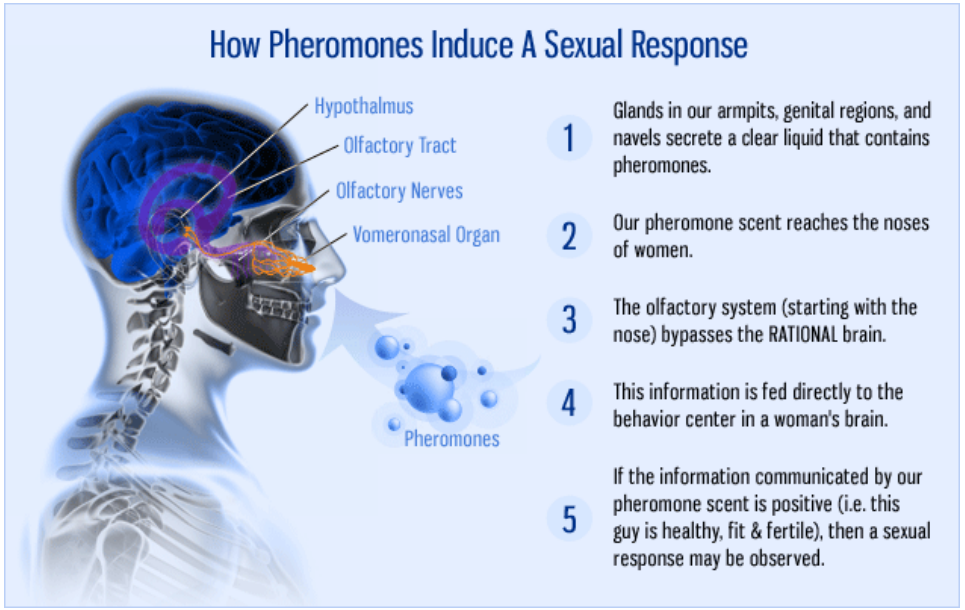
The power of pseudoscience (and marketing)

NO GIRLFRIEND?

Attract Women with New Pheromone Cologne

Try it Absolutely Risk FREE!

Click Here ▶▶

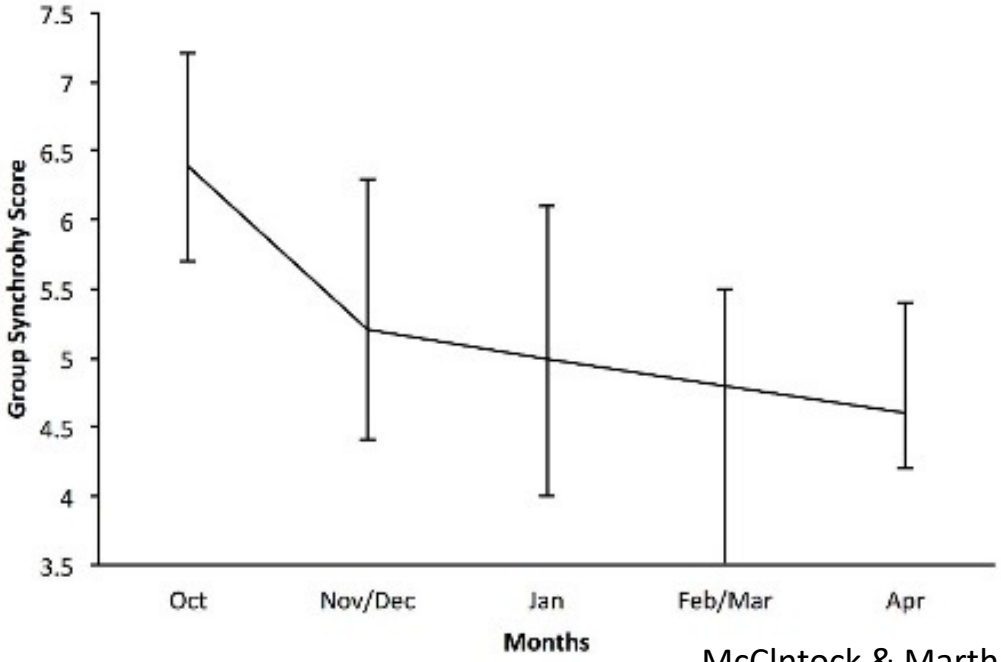


How about pheromones? Do they mediate behaviour?

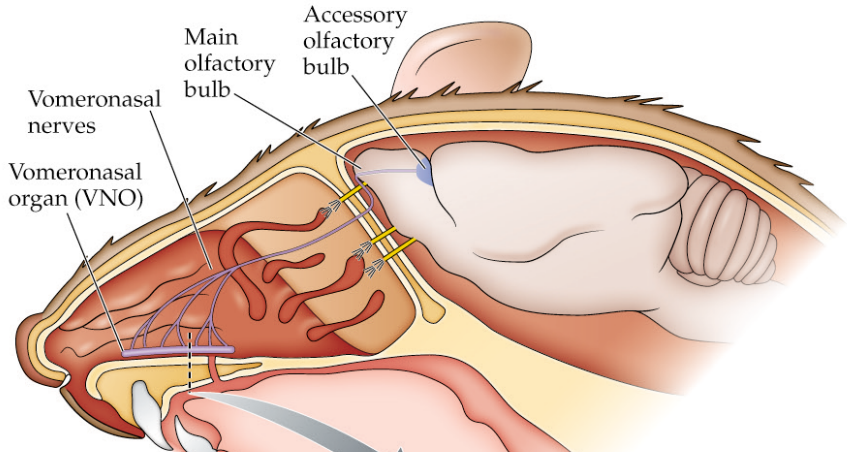
Non-human animals: yes, definitely, via the vomeronasal organ (VNO)

Humans: Not so much. Our VNO and its related genes are basically non-existent

Putative human pheromone effects (McClintock effect, men's sweat) often don't replicate



McClntock & Martha 1971



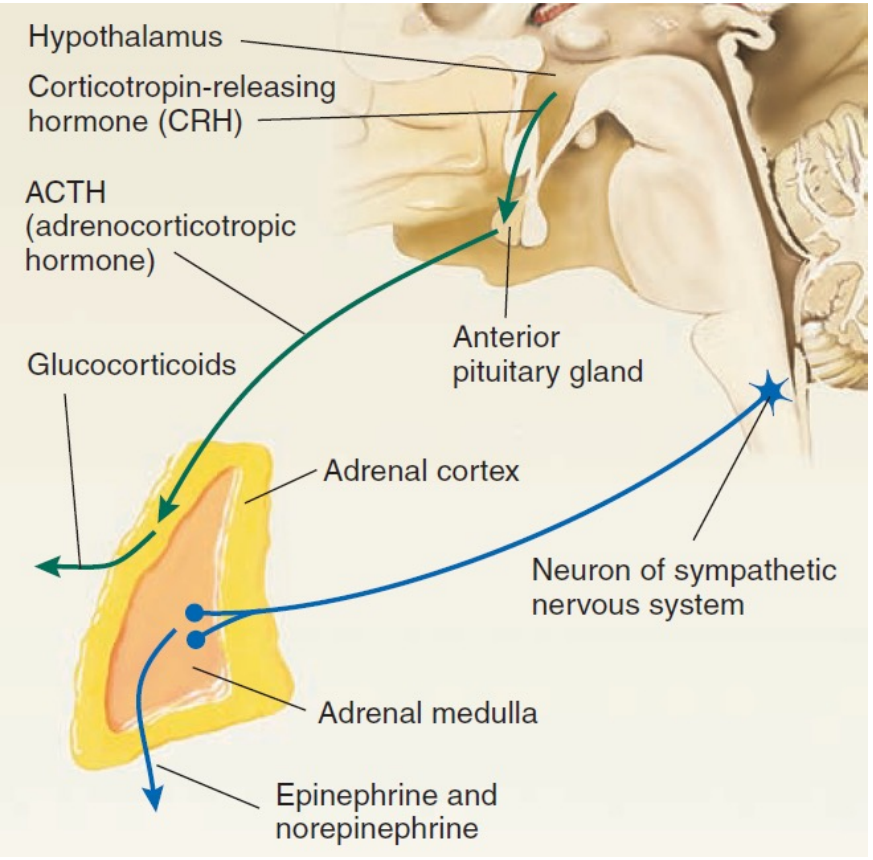
How about stress hormones? Do they mediate behaviour?

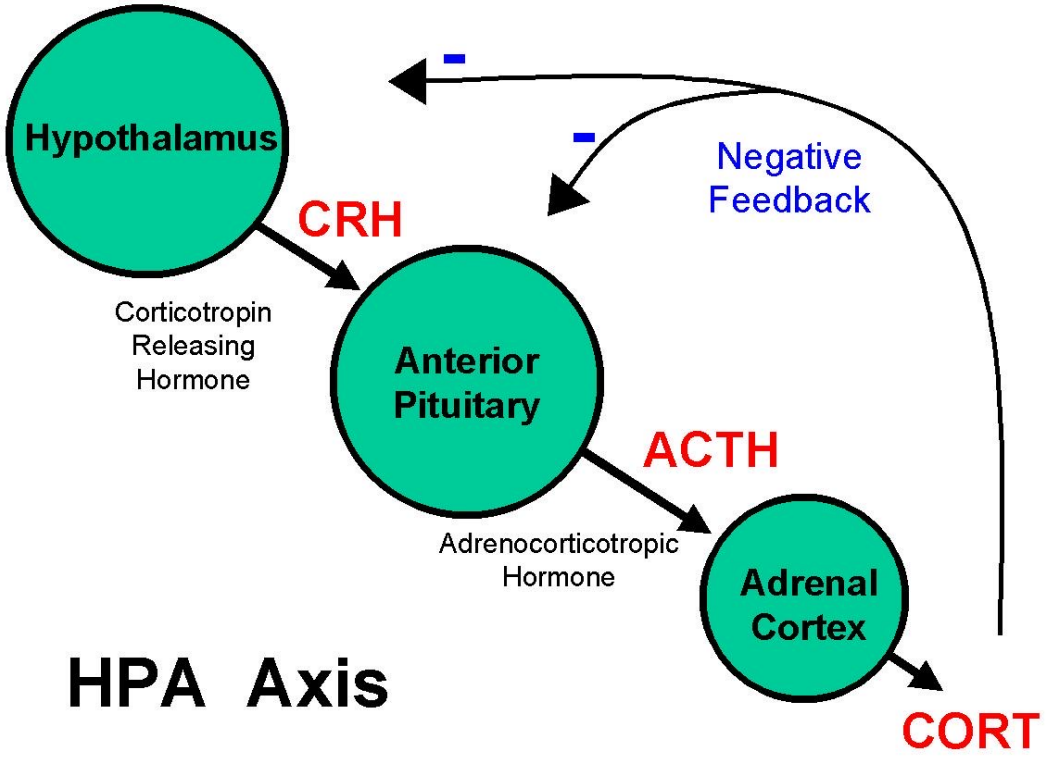
All animals (including humans): yes, definitely
BUT part of stress response is central (i.e. in the brain)

Dual pathways

HPA axis

Sympathetic NS



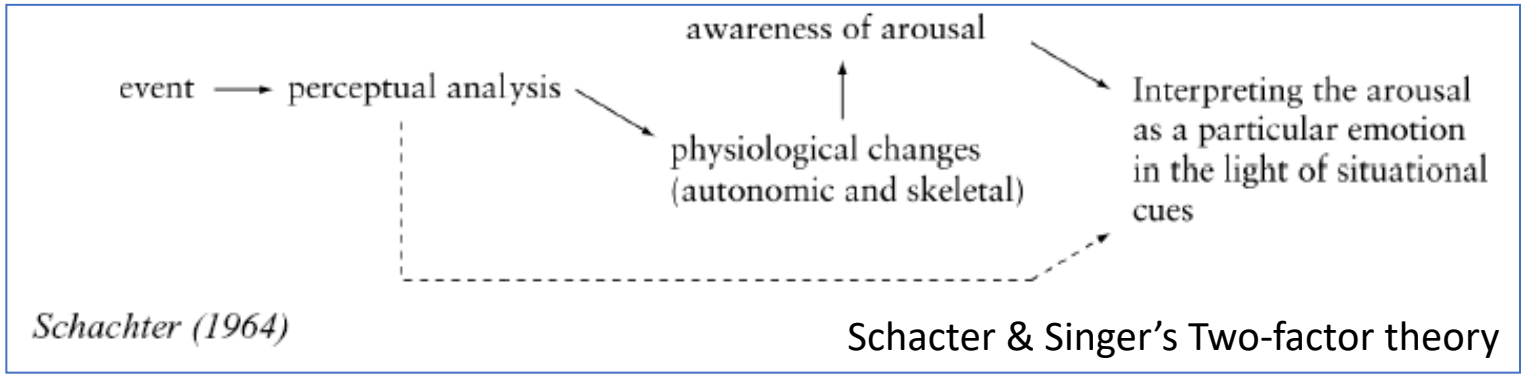


How about stress hormones? Do they mediate behaviour?

All animals (including humans): yes, definitely
BUT part of stress response is central (i.e. in the brain)

Schacter & Singer 1962: stress response is interpreted

Experiment to test “new vitamin” (epinephrine)



Schacter & Singer’s Two-factor theory

Stay tuned for this in semester 2! (I think)

Sex, gender, and sexuality are complicated topics

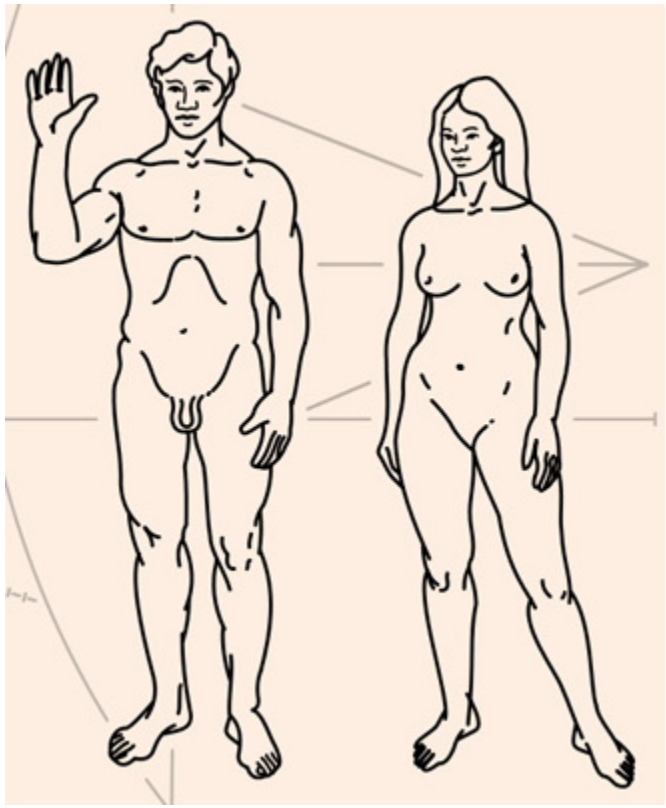
Biological sex — not just genes!

Gender identity — typically aligns with sex, but not always

Sexual behaviour

Sexual orientation — typically heterosexual, but not always

(includes asexuality, which is common; Wellings 1994)



Intersex births are also common (*a la* Blackless *et al.* 2000)

Sexual dimorphism in brains? Not as much as you might think

ELSEVIER

Neuroscience & Biobehavioral Reviews

Volume 125, June 2021, Pages 667-697

Dump the "dimorphism": Comprehensive synthesis of human brain studies reveals few male-female differences beyond size

Lise Eliot [a, b], Adnan Ahmed [b], Hiba Khan [b], Julie Patel [b]

If you want to read more:

https://www.sciencedaily.com/releases/2021/03/210325115316.htm

https://www.sciencedirect.com/science/article/pii/S0149763421000804?via%

9. Conclusion

Scholarly interest in brain sex difference is as old as Aristotle (Deslauriers, 2009). Despite clear behavioral differences between men and women, s/g differences in the brain are small and inconsistent, once individual brain size is accounted for. Most neuroscientists assume this ambiguity will be solved through technical improvements: that larger studies, using higher resolution imaging and better processing pipelines will uncover the "real," or species-wide differences between male and female brain structure and connectivity patterns. However, the present synthesis indicates that such "real" or universal sex-related difference do not exist. Or at best, they are so small as to be buried under other sources of individual variance arising from countless genetic, epigenetic, and experiential factors. Thus, s/g differences in brain architecture may be similar to sex effects in gene-phenotype architecture; while statistically discernable in a very large (>100,000) sample, such effects contributed only 1.4 % to the accuracy of genotype-phenotype prediction (Rawlik et al., 2016).

In layperson's terms, these findings can be interpreted as rebutting popular discourse about the "male brain" and "female brain" as distinct organs. They also have relevance to research on the many neuro-behavioral disorders that differ in prevalence between men and women, such as autism, ADHD, dyslexia, depression, anxiety, dementia and eating disorders. Although studies of s/g brain difference often begin from the premise that they will lead to a better understanding of these health disparities, their actual data seem unlikely to advance the aims of precision medicine.

Sex hormones have potent organizational effects

i.e. Your chromosomes are not your sex!

Y chromosome: SRY gene

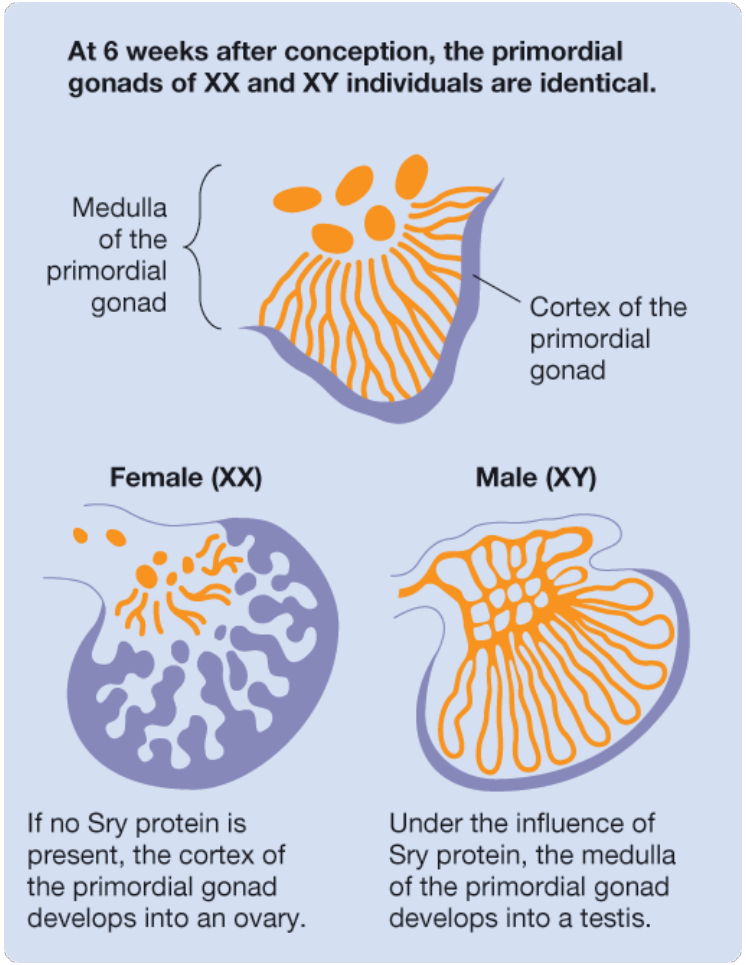
SRY protein: causes testes formation

Testes: release testosterone and anti-Müllerian hormone (AMH)

T + AMH: cause male phenotype

In other words: female pattern is the default

Importantly: changes with SRY/T/AMH/other can influence development of phenotype…



Development can vary dramatically despite your X & Y chromosomes

Thanks to (you guessed it) changes in hormone function

Androgen-insensitivity syndrome in genetic males (XY)

Androgen receptor mutations

Women of an androgen-insensitivity support group

Sry mutations?

Sry “hopping” from Y to X?

(XX male syndrome)

AMH (or receptor) mutations?

High exposure to androgens?

(congenital adrenal hyperplasia, CAH)

Differences in sex are related to meaningful differences in biology, physiology, pathology

Ambien (Zolpidem) doses for men vs. women (2013)

Metabolism, in general, seems to be a major difference

Sex differences in pain and response to pain medication

Estrogen/progesterone and opioid system interactions

Sex differences in acute and chronic stress (Liisa Galea's work!)

Women are more likely to develop depression, Alzheimer's disease, lung cancers;
Men are more likely to have addiction, commit suicide, or develop Parkinson's disease

Do androgens and estrogens mediate behaviour? (1)

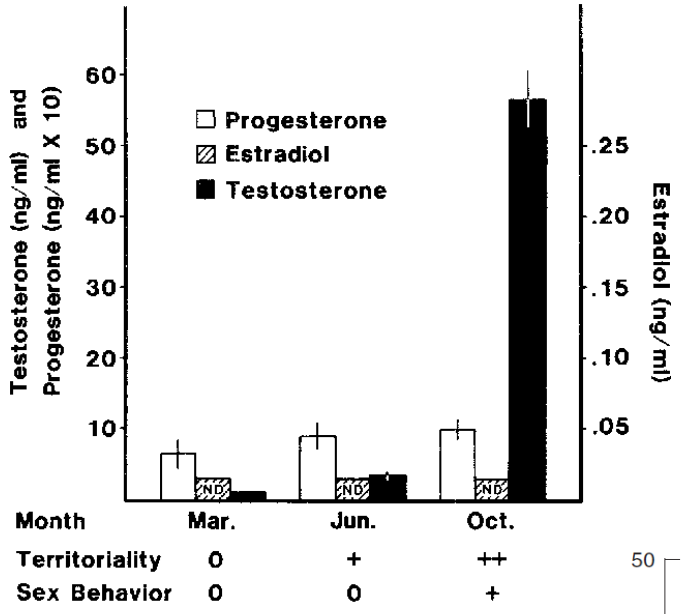
Non-human animals (e.g. reptiles): yes

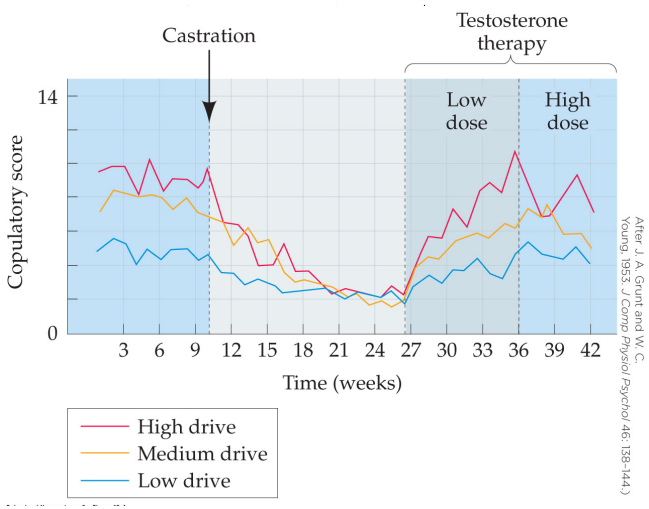
Humans: at least somewhat

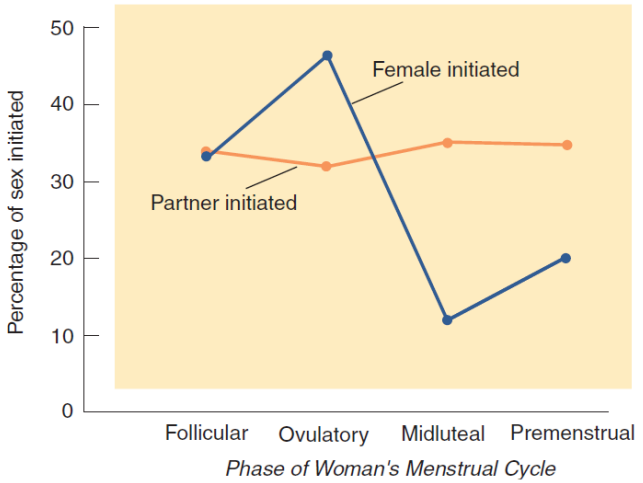
Rats and humans: Individual differences in male sexual activity are not determined by differences in androgen levels

Some testosterone needed for men's sexual interest

(e.g. loss of function case studies)







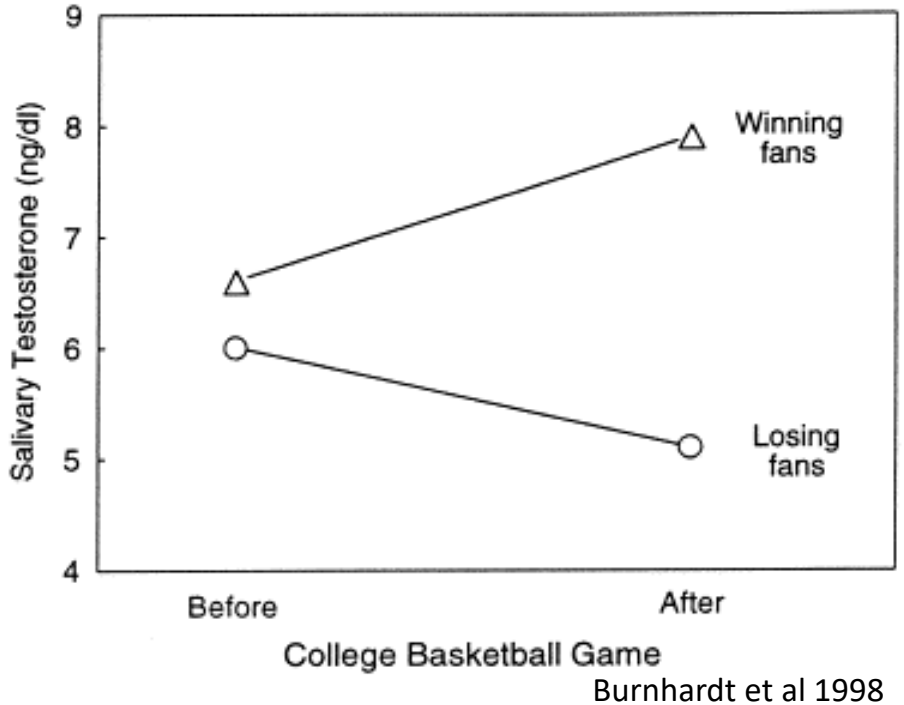
Wallen, 2001

Do androgens and estrogens mediate behaviour? (2)

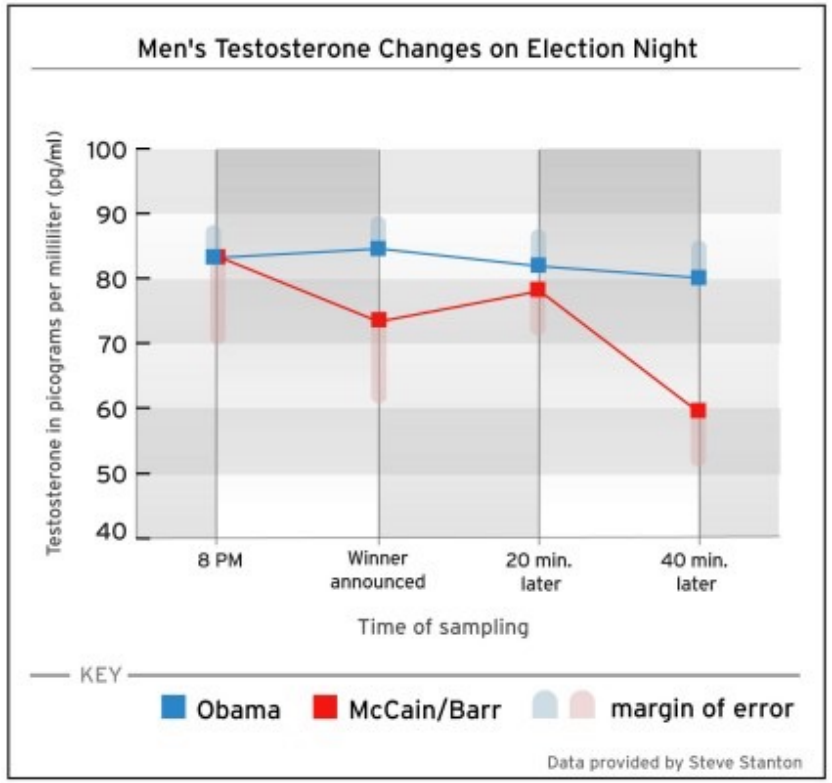
Non-human animals (e.g. reptiles): yes

Humans: at least somewhat

Testosterone levels track aggression in animals, vicarious victory in human males



Burnhardt et al 1998



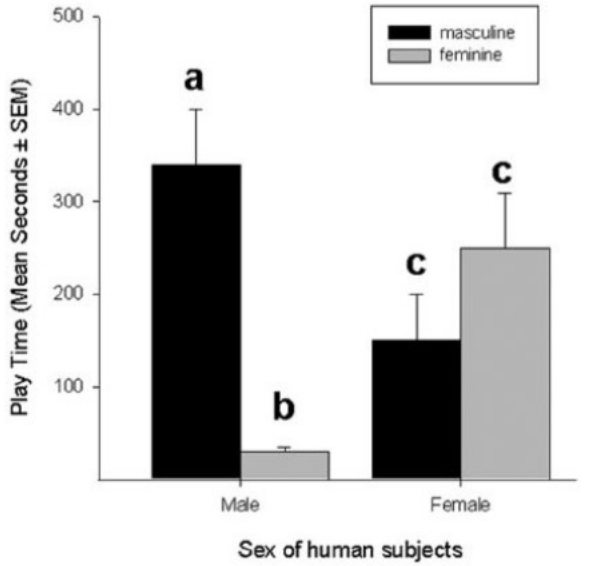
Stanton et al 2009

Do androgens and estrogens mediate behaviour? (3)

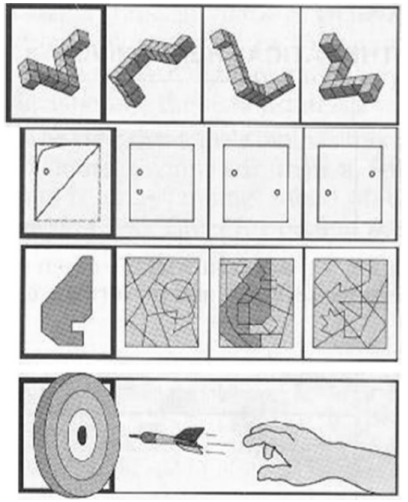
Non-human animals (e.g. reptiles): yes

Humans: at least somewhat

Gendered behaviours are certainly present, BUT
differentiating social from biological influences on behaviour is challenging

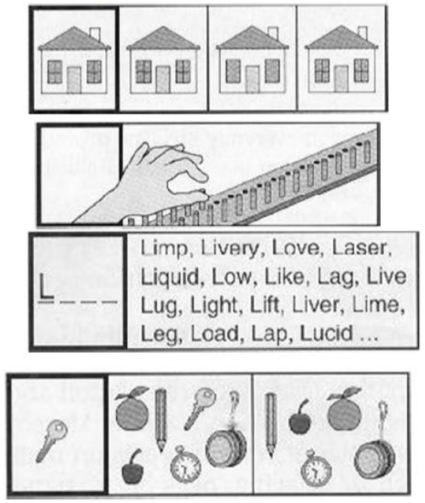


Berenbaum and Hines 1992



Observable differences in cognitive abilities

Some of these (e.g. math ability) are vanishing



https://www.youtube.com/watch?v=nWu44AqF0iI

Sexual orientation and hormones

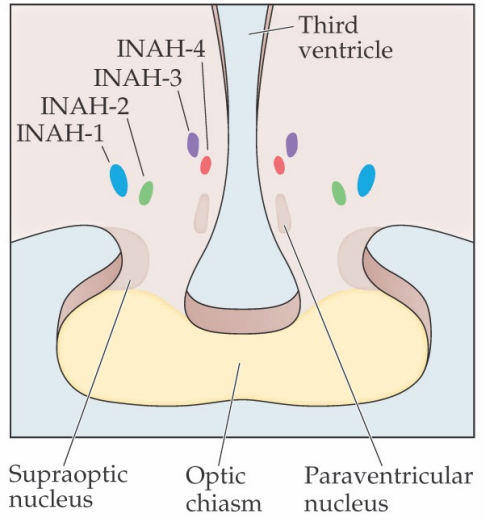
Homosexuality is reported in hundreds of species

Men: some evidence for hypothalamic differences in homosexuality

Rams: the preoptic area

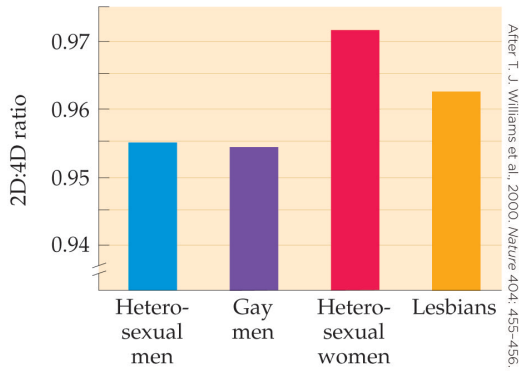
Humans: INAH-3 of the preoptic area

Homosexuality in men also related to *fraternal birth order effect*



Women: some indirect evidence for higher fetal androgen exposure in homosexuality

Often reported: 2D:4D finger digit ratio



BUT effect sizes are small, and impossible to discern at the level of the individual