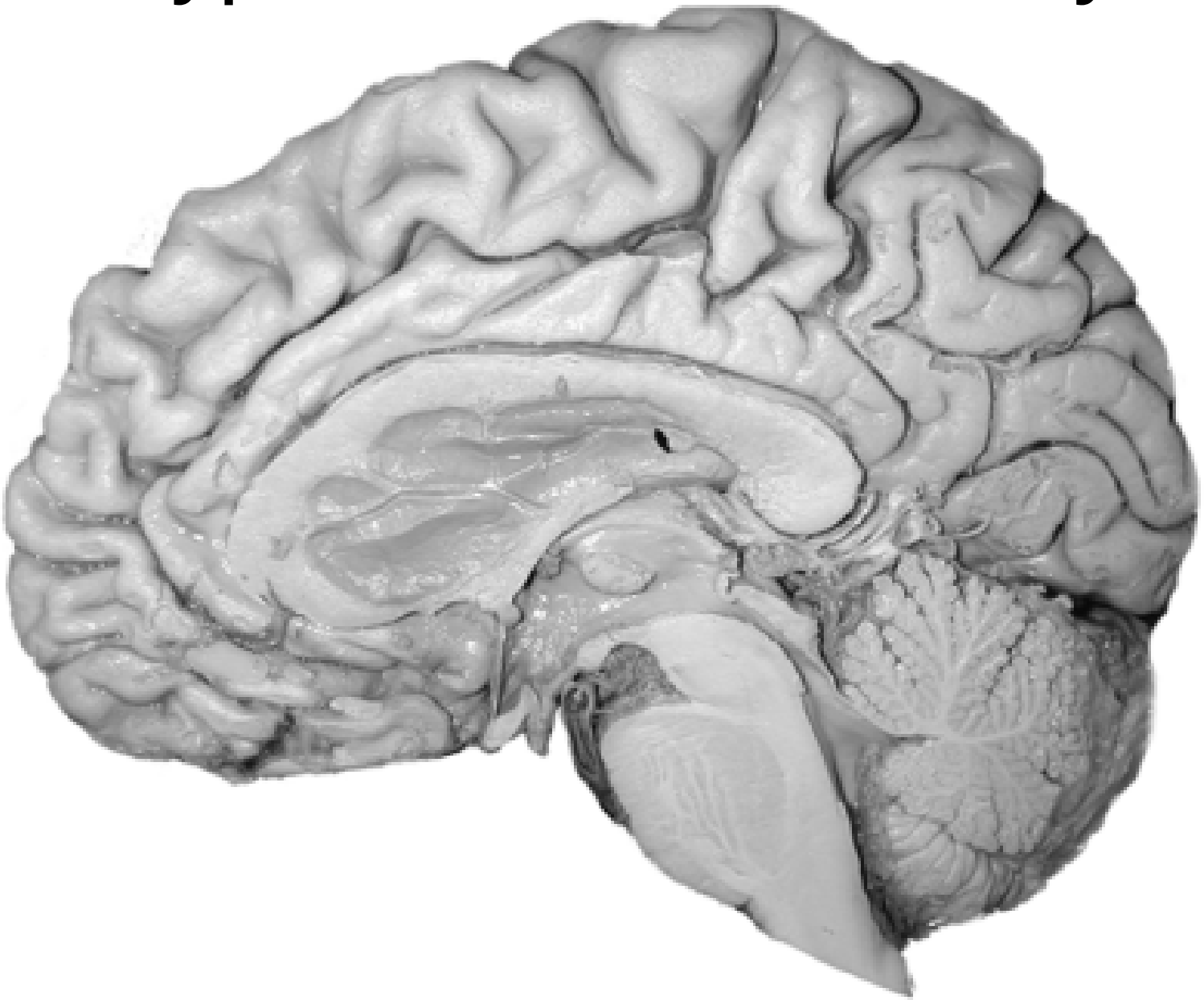
Hypothalamus

Small, central, & essential.

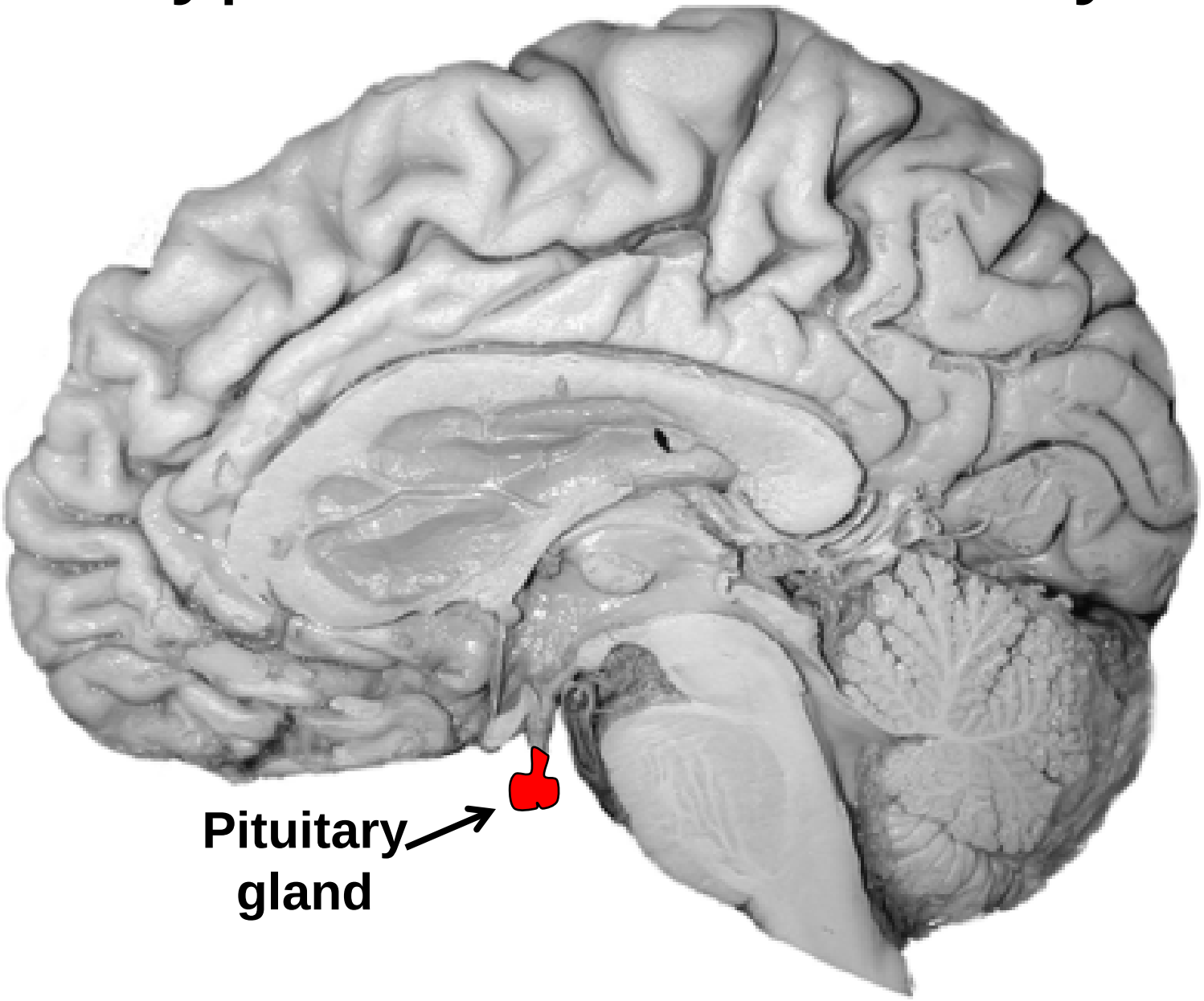
Summary: You can’t live without a hypothalamus.

- Located at the junction between the brain stem and the forebrain
- Medial hypothalamus: interface between the brain and the endocrine system
  - Blood volume
  - Metabolic rate
  - Lactation
  - Stress
- Hypothalamus: major interface between the limbic system & the autonomic nervous system
  - Eating
  - Thermoregulation
  - Blood pressure
- Hypothalamus also sets our biological clock
  - Sleep/wakefulness

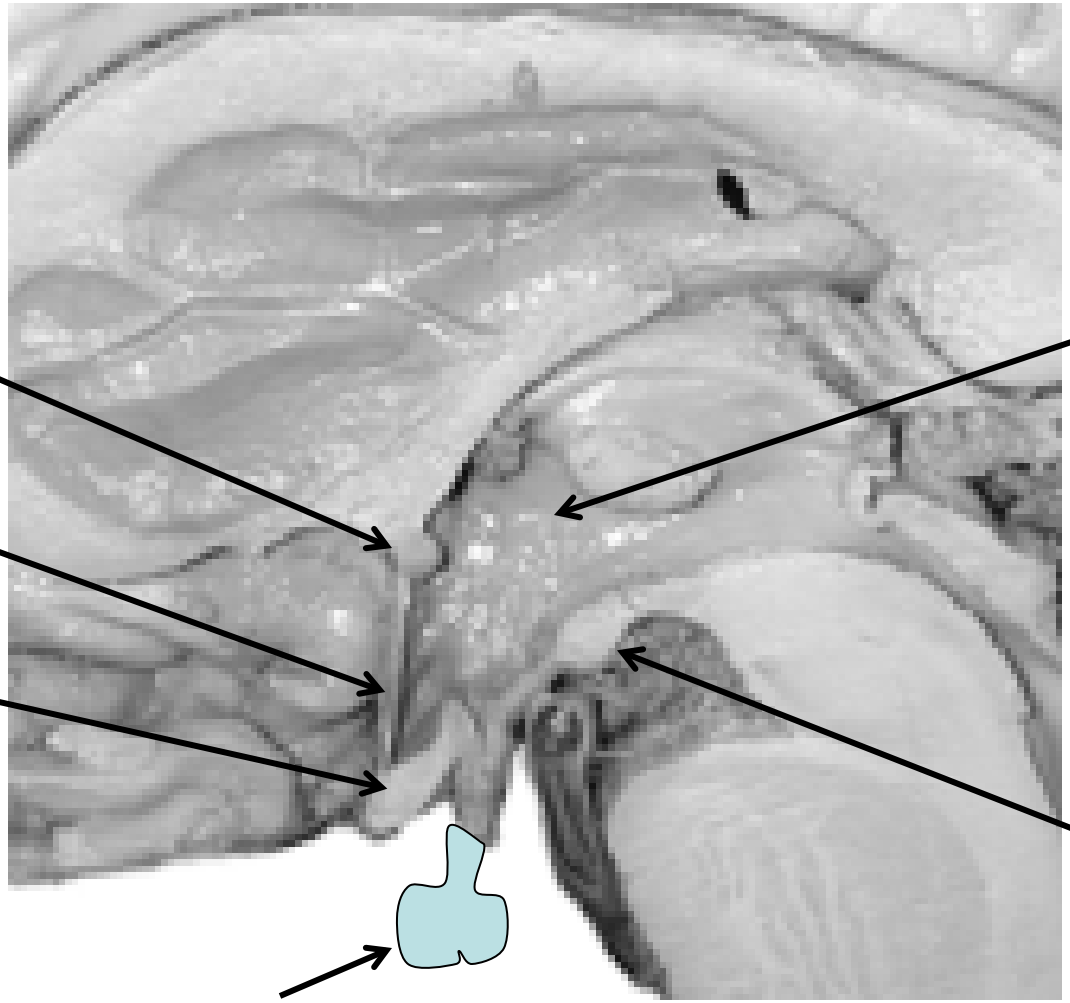
Hypothalamus: anatomy



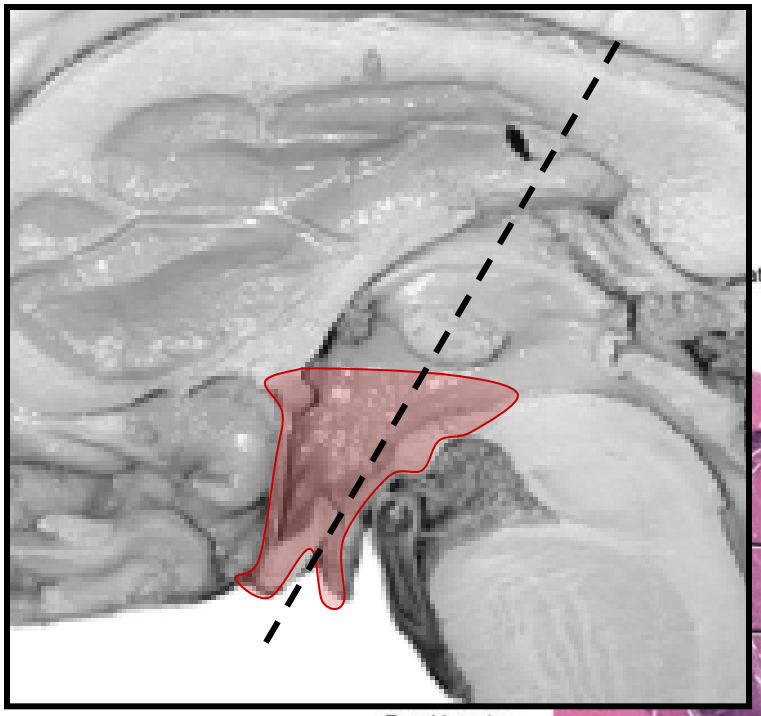
Hypothalamus: anatomy

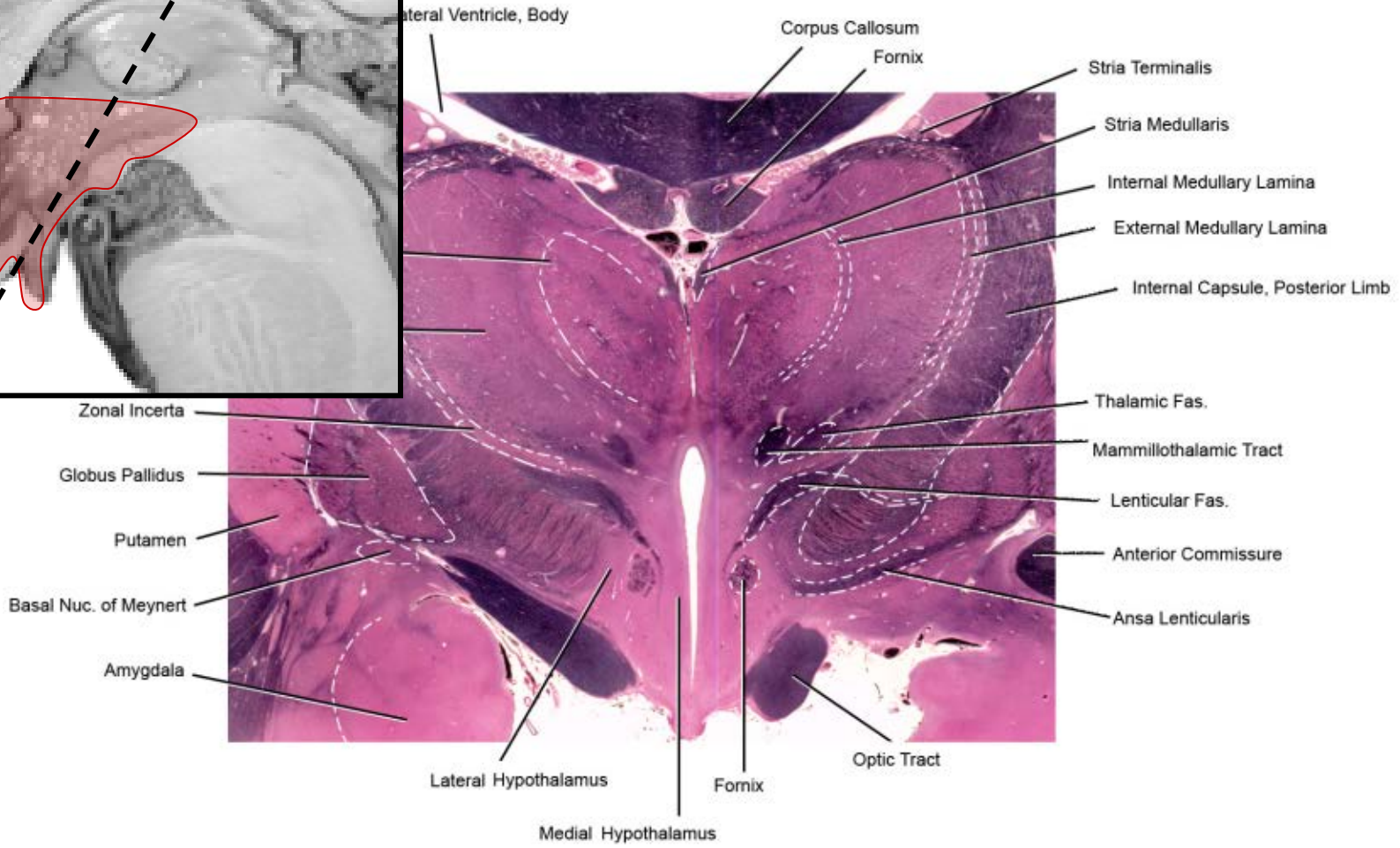


Hypothalamus: anatomy



Hypothalamus: anatomy

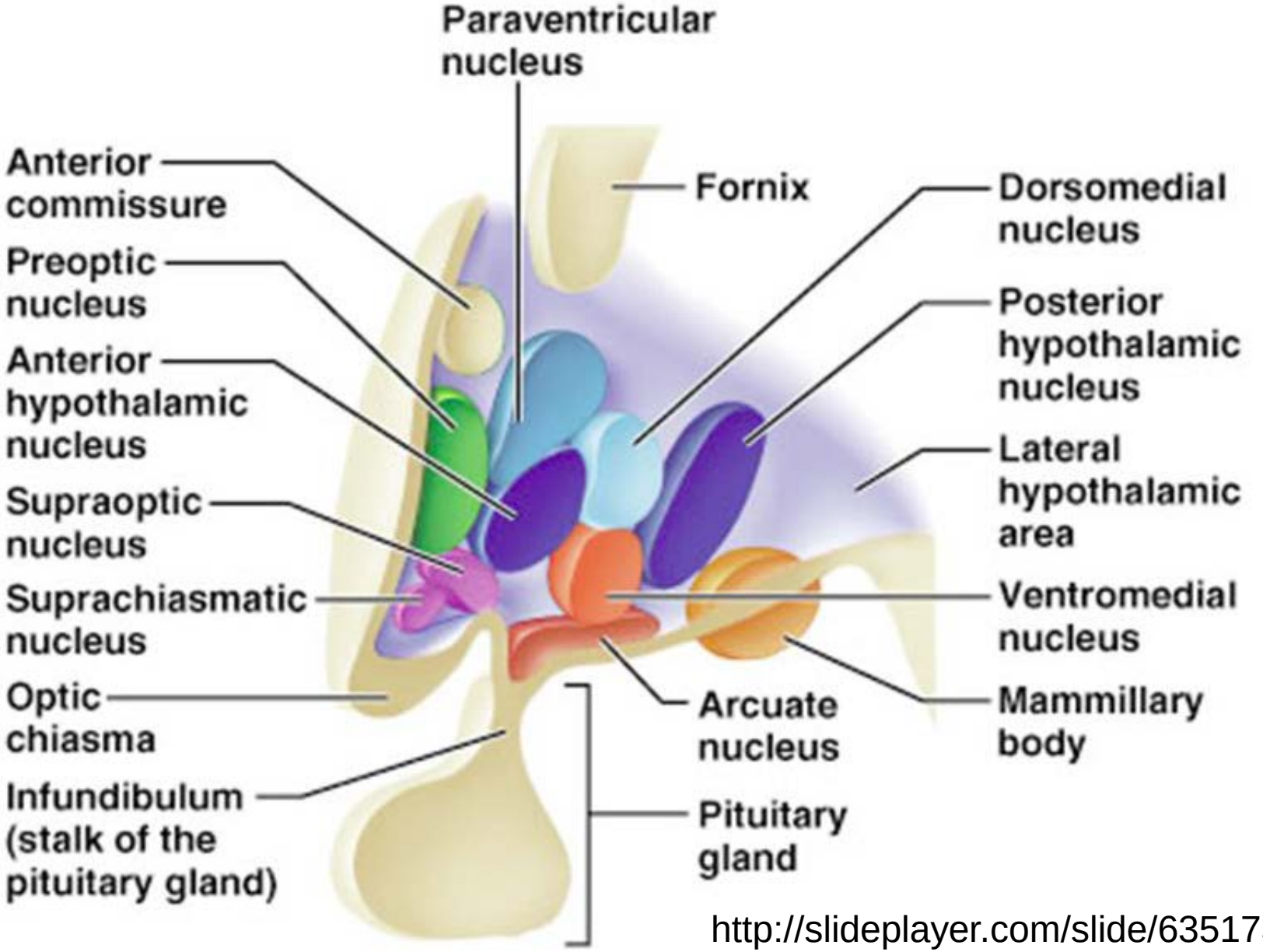




Fornix: medial vs. lateral hypothalamus

Inputs & outputs

Hypothalamus: anatomy



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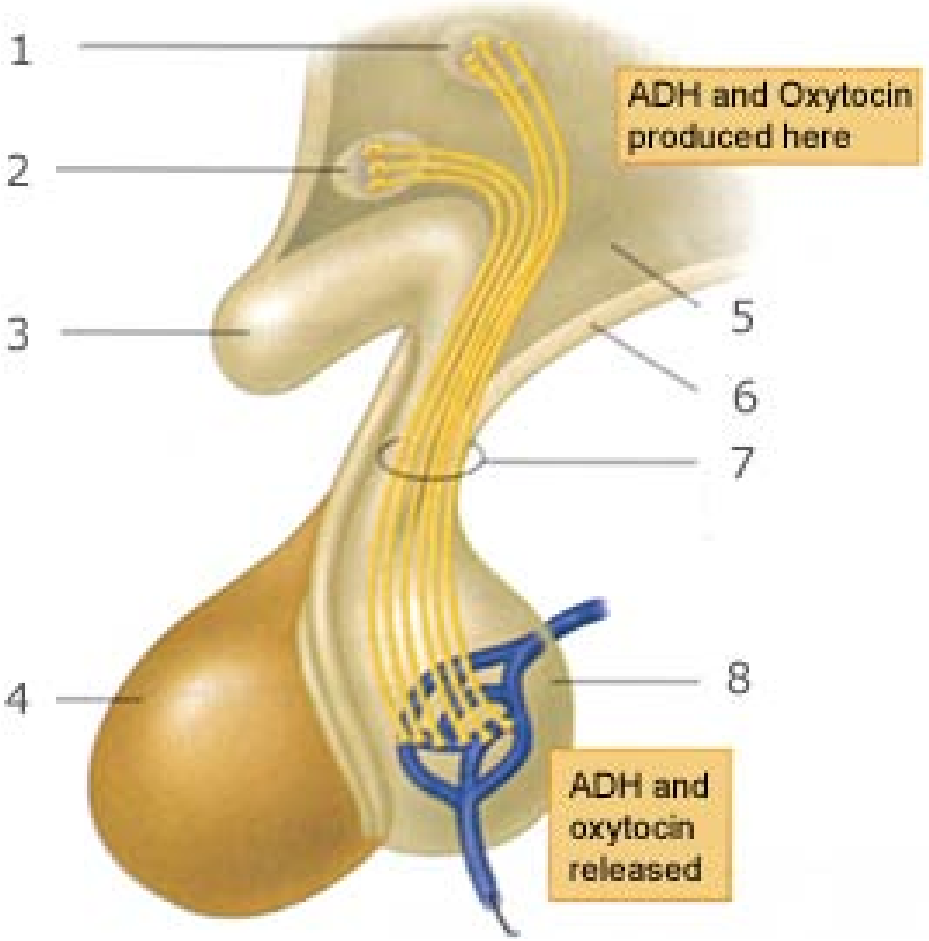
Hypothalamus as an endocrine organ

- ***Hypothalamus directly projects*** to posterior pituitary
  - Vasopressin
  - Oxytocin

- Cells in supraoptic n. & paraventricular n.
- Axons release these hormones into blood in posterior pituitary



http://homepage.smc.edu/wissmann_paul/intranetstuff/dept/scienceLRC/wissmann_site/pituitary.htm

Vasopressin (antidiuretic hormone; ADH)

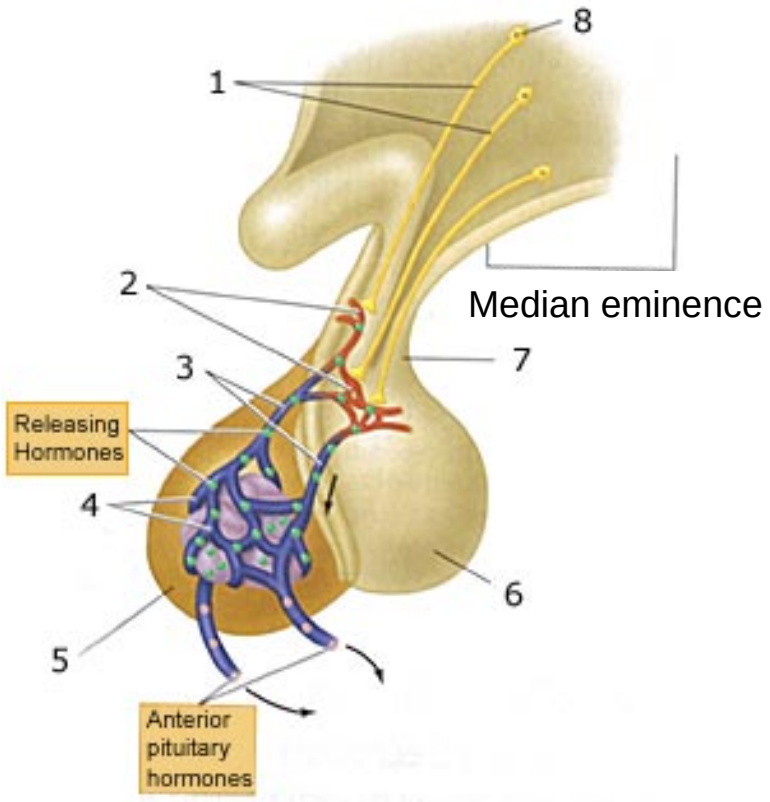
- Increases blood volume
  - Decreases urine production by increasing reabsorption of water into bloodstream
- Increases blood pressure (--constricts arterioles)
- Made by magnocellular (i.e. big) neurons in supraoptic n. (***not*** suprachiasmatic n. or preoptic n.) and also paraventricular n.
- Cells sense osmolarity (i.e. concentration of salt in blood): increased salt → increased firing
- *Release inhibited by ethanol*

Oxytocin

- Reproduction: acts on uterus & breasts
  - Uterine contraction during birth
  - Milk ejection reflex
- “Love hormone”?
- More social bonding & empathy *within one’s group*
  - Increases trust; decreases fear; increases generosity
  - Promotes monogamous behavior in males
- Magnocellular neurons in supraoptic n. and also paraventricular n.

Hypothalamus as an endocrine organ

- ***Indirect connection*** to anterior pituitary
  - Hormone in neurons in arcuate n. & paraventricular n. (ventromedial hypothalamus)
  - Hormones released into *hypothalamic-hypophyseal portal system*
  - Blood carries hormones to pituitary → modulate release of pituitary hormones



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--What is a “portal circulation”?

- Normal circulation passes through only one organ: arteries → arterioles → capillaries in organ → venules → veins

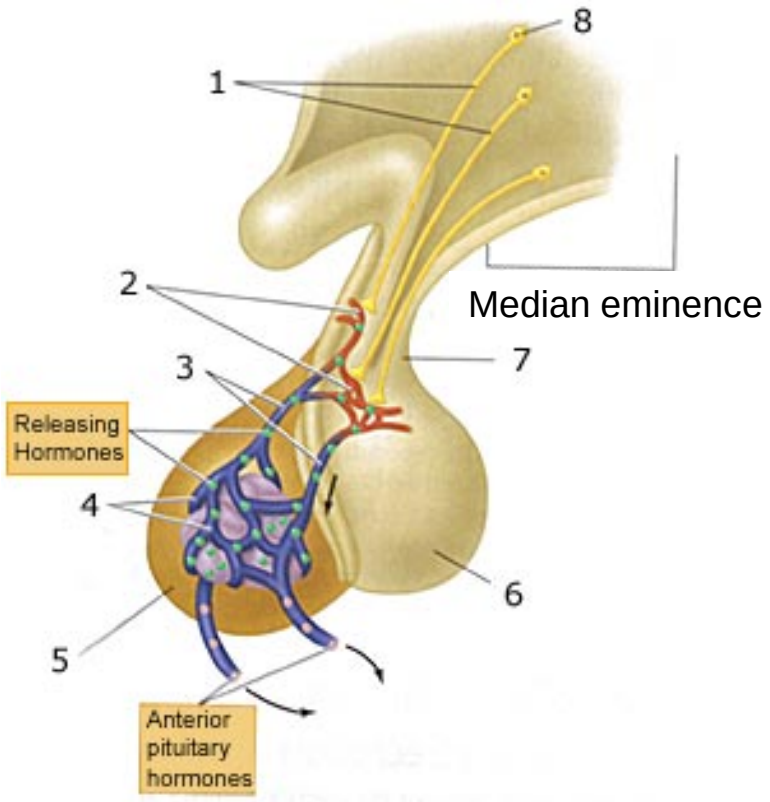
- Portal circulation goes through two organs: arteries → arterioles → capillaries in organ #1 → portal veins → capillaries in organ #2 → venules → veins

Hypothalamic-hypophyseal portal system

- arteries → arterioles → ventral hypothalamus (capillaries of median eminence) → portal veins (pituitary stalk) → capillaries of anterior pituitary → venules → veins

Thyrotropin-releasing hormone (TRH): release into portal system

- ***Indirect connection*** to anterior pituitary
- Portal circulation carries TRH to **anterior** pituitary
- Causes release of thyroid-stimulating hormone
- Thyroid stimulating hormone→ general circulation to thyroid
- Causes release of thyroid hormone→ sets basal metabolic rate



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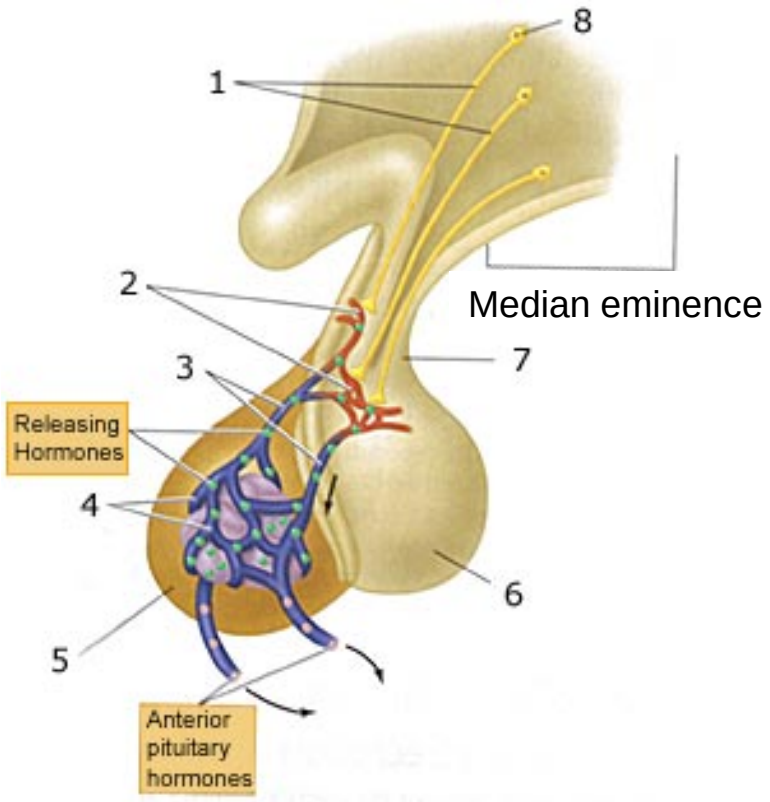
Corticotropin-releasing hormone (CRH)

- Portal circulation to pituitary
- Causes release of adrenocorticotropic hormone (ACTH) in response to stress
- ACTH → general circulation to adrenal cortex
- Causes release of cortisol



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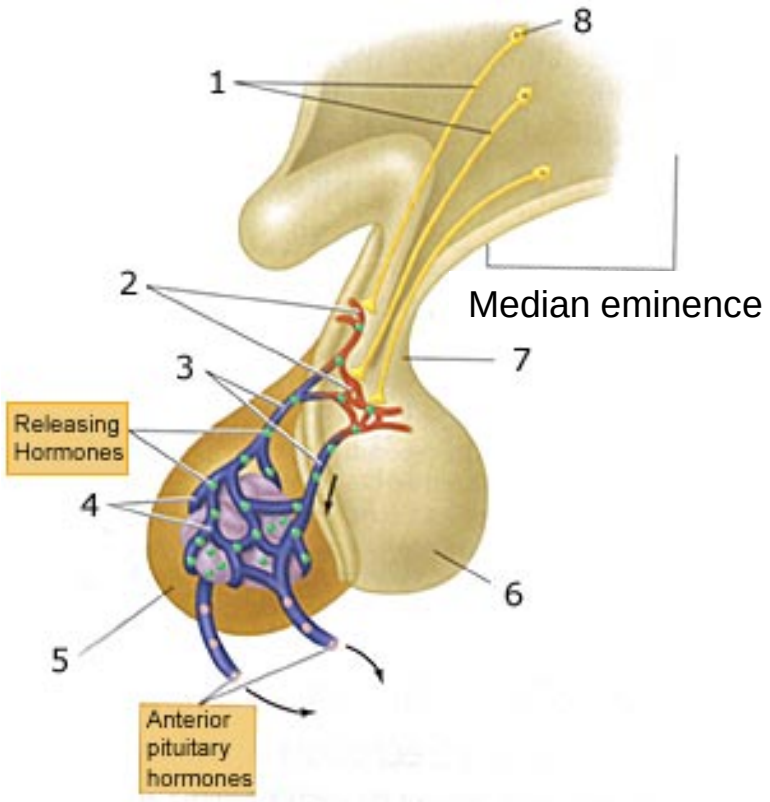
Growth hormone-releasing hormone (GHRH)

- Released from median eminence into portal circulation → anterior pituitary
- Promotes release of growth hormone from pituitary
- Growth hormone → liver→ release of insulin-like growth factor 1 → cell proliferation



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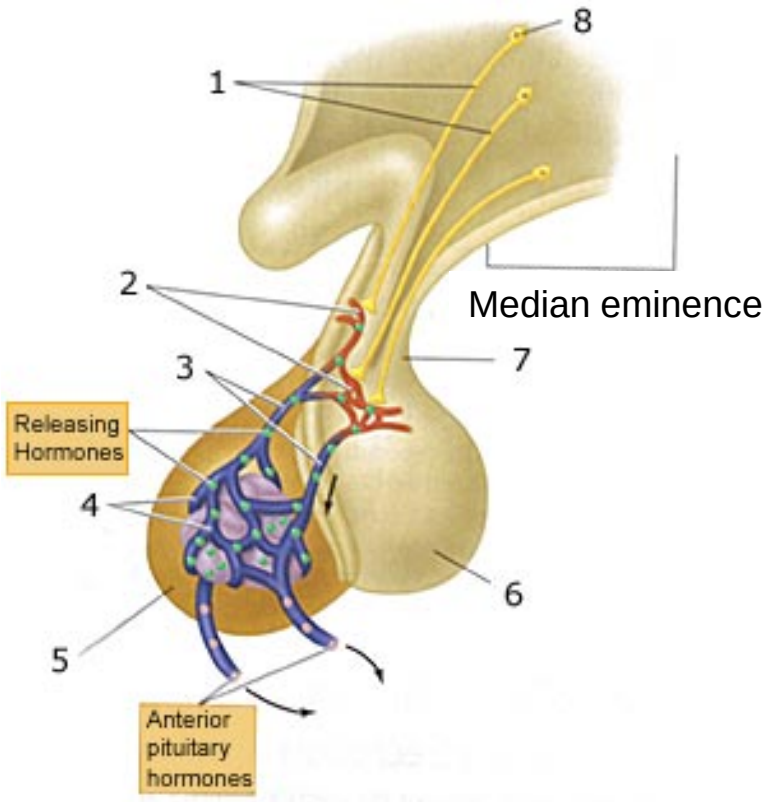
Somatostatin

- Released from median eminence; portal circulation to anterior pituitary
- Inhibits release of growth hormone from pituitary
- Opposes action of growth hormone-releasing hormone



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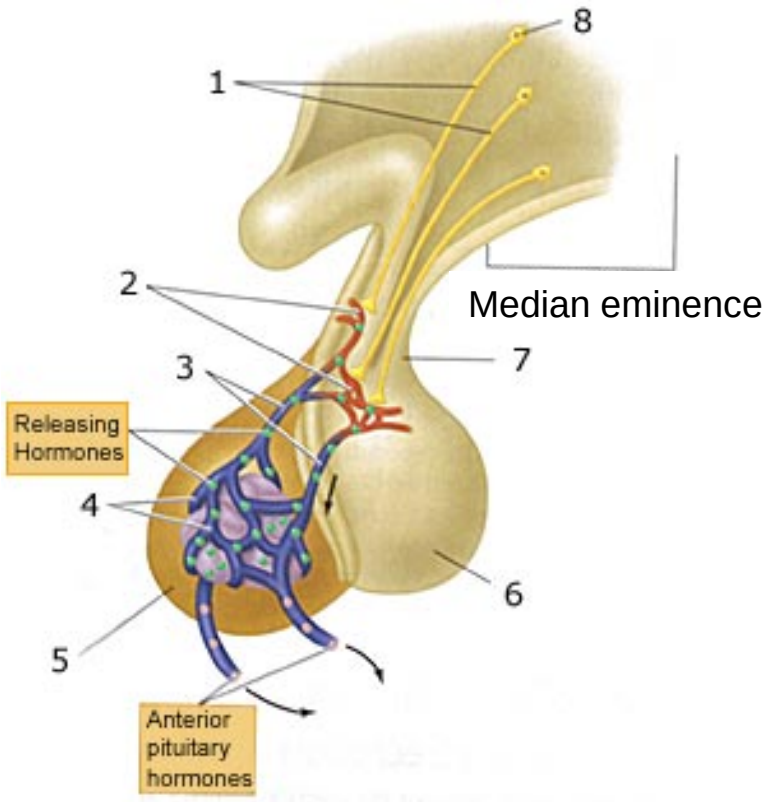
Gonadotropin-releasing hormone (GRH)

- Released into portal circulation→ pituitary
- Promotes release of follicle-stimulating hormone (FSH) & lutenizing hormone (LH) into general circulation
- FSH→ maturation of reproductive cells (eggs; sperm)
- LH→
  - females: ovulation
  - males: synthesis of testosterone



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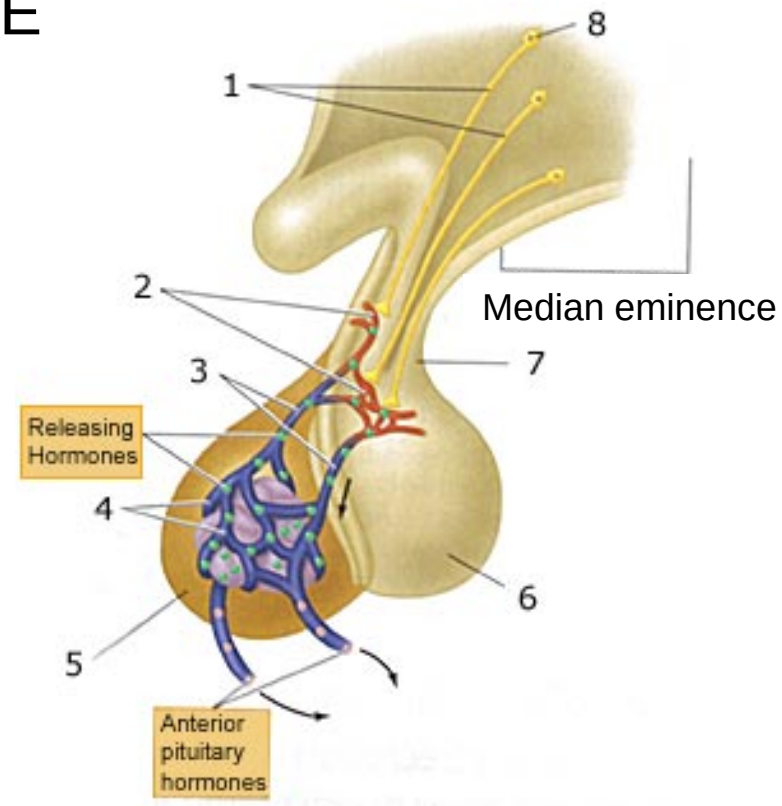
Control of prolactin by dopamine

- Prolactin = PITUITARY HORMONE
- Prolactin increased by elevated levels of estrogen and progesterone (e.g., in pregnancy)
- Prolactin *promotes lactation*
  - Increased breast mass
- Dopamine → portal circulation→ inhibition of prolactin release—i.e. acts as prolactin-inhibitory hormone



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Regulation of endocrine function

- Feedback control of hormone synthesis:
  - Hormones may directly inhibit the synthesis or release of hypothalamic releasing hormones
  - Thyroid hormone decreases TRH
  - Cortisol decreases ACTH
  - Etc.

Hypothalamus vs. pituitary: Keeping hormones straight

- Pituitary hormones
  - Adrenocorticotropic hormone (ACTH)
  - Thyroid stimulating hormone (TSH)
  - Growth hormone (GH)
  - Etc.

- Hypothalamic hormones: ***hyphenated*** (mostly)
  - Corticotropin-releasing hormone (CRH)
  - Thyrotropin-releasing hormone (TRH)
  - Growth hormone-releasing hormone (GH-RH)
  - **Exception**: somatostatin

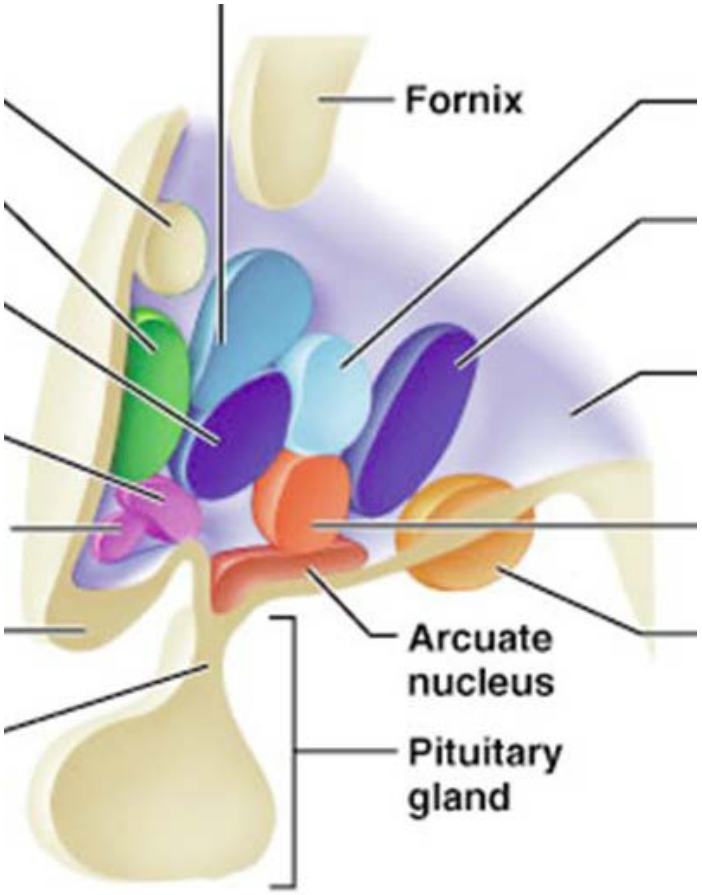
Hypothalamus & the autonomic nervous system

- Classical autonomic effects
  - Blood pressure
  - Thermoregulation
  - Urination
- Autonomic effects not mediated directly through sympathetic or parasympathetic nervous systems
  - Feeding
  - Circadian rhythms

Blood pressure

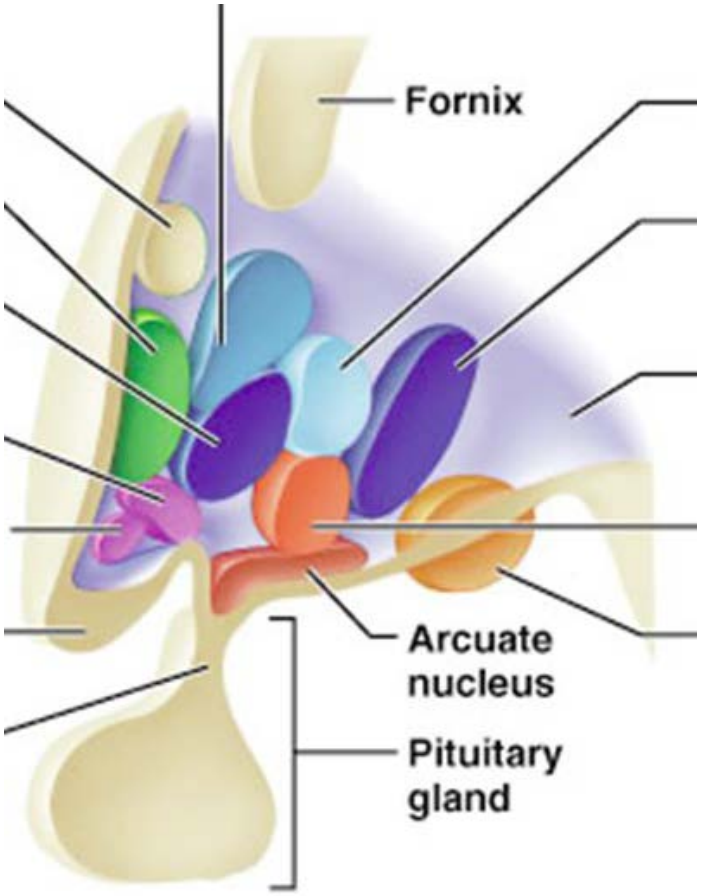
- Paraventricular n. of hypothalamus *reduces long-term increases in BP*

- Dorsomedial n. of hypothalamus *increases BP and heart rate to stress*: classic sympathetic effects



Thermoregulation

- Preoptic nucleus of hypothalamus
  - 20% of preoptic neurons activated by warmth
    - Directly sensitive
    - Also receive input from skin
  - Firing reduces body heat
    - Activates vasodilation
    - Inhibits vasoconstriction
    - Ultimately activates sweating



Thermoregulation

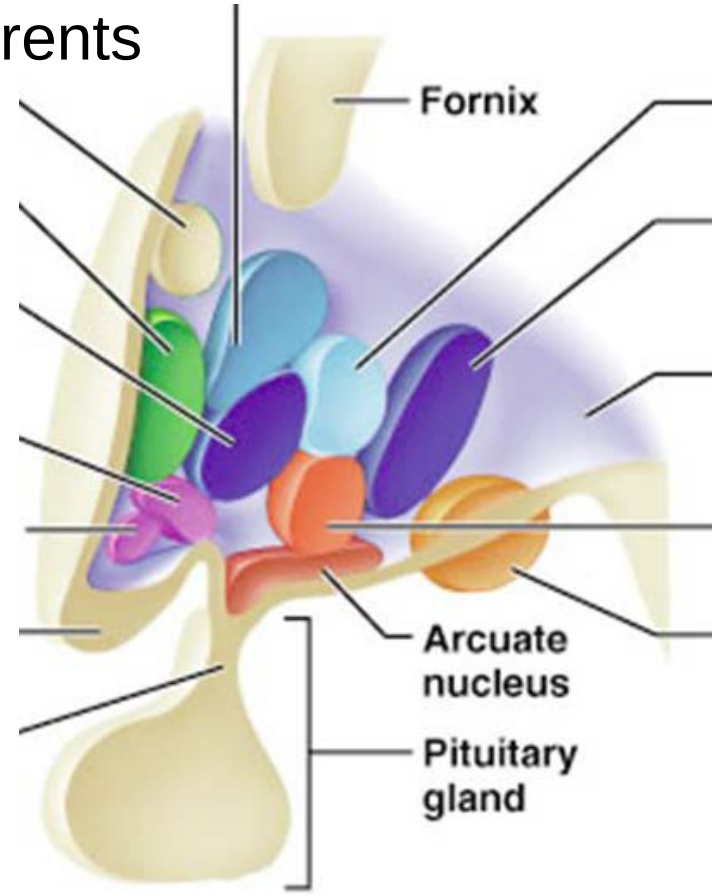
- Exposure to cold → activation by hypothalamus of descending excitatory systems
  - Skeletal muscle activity → heat : shivering
  - Activation of sympathetic nervous system
    - brown adipose tissue (brown fat) → heat
    - “Non-shivering thermogenesis”

Feeding

- Stimulation of lateral hypothalamus → eating
  - Lesions → aphagia (lack of eating)
- Stimulation of medial hypothalamus → decreased eating
  - Lesions → hyperphagia (excessive eating)

Feeding

- Arcuate nucleus of hypothalamus responds to caloric intake
  - Receives input from visceral afferents
  - Responds to glucose; fatty acids
- Also responds to hormones
  - Leptin
  - Ghrelin
  - Orexin

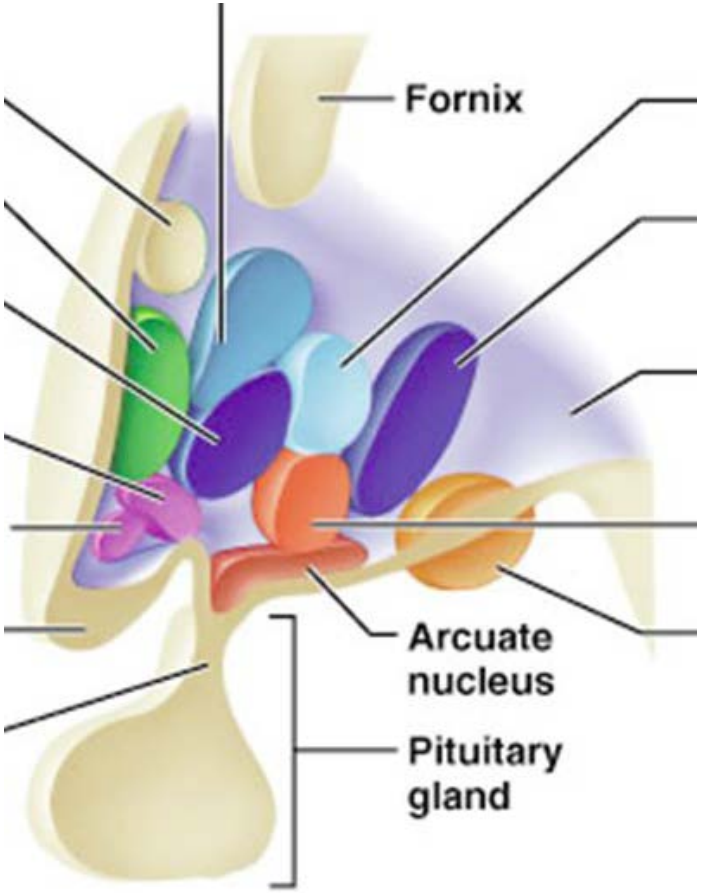


Eating

- Arcuate nucleus: receptors for leptin, ghrelin, & orexin
  - Leptin: hormone secreted by white fat cells
    - Leptin levels = measure of stored energy
    - Inhibits hunger
    - Mutations → obese mice & humans + hyperphagia
  - Ghrelin: secreted by stomach when empty
    - Secretion increases with time after meal
    - Stomach filling inhibits secretion
  - Orexin: promotes food intake but may be effect of general arousal

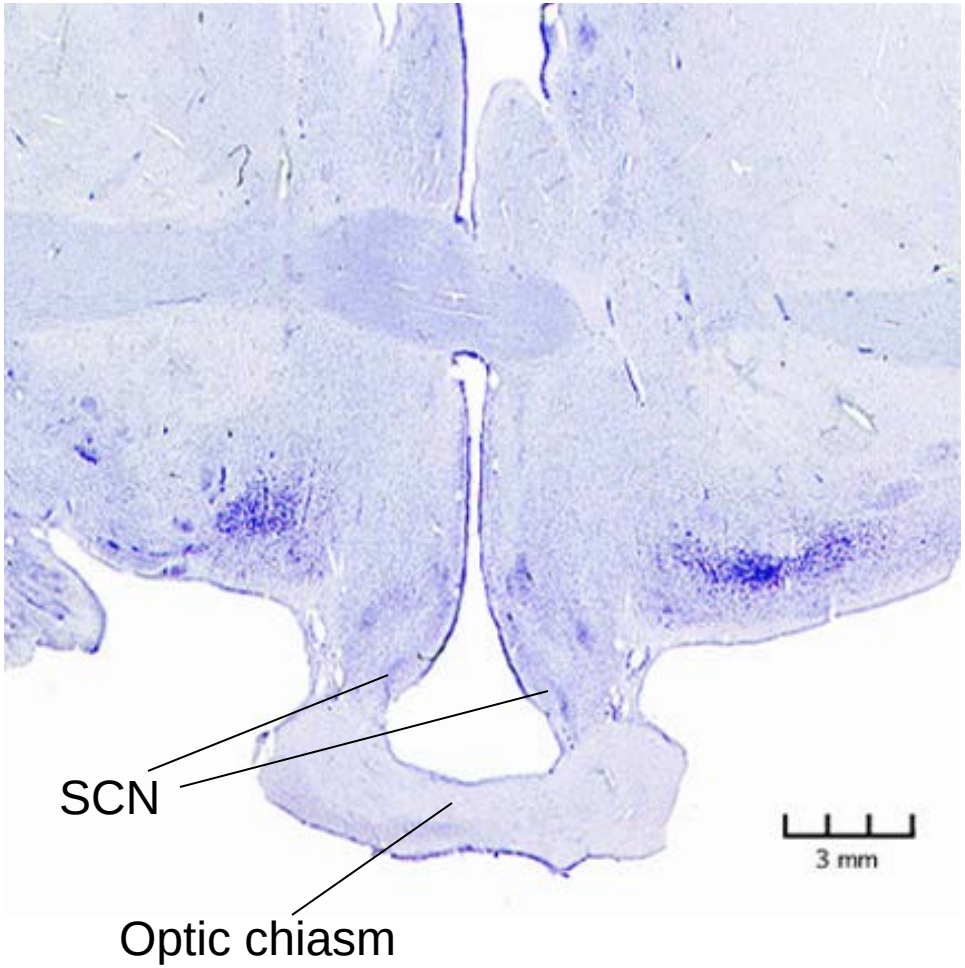
Circadian rhythms (Latin, “approximately a day”)

- Regulation of our daily rhythm
  - Eating
  - Sleeping
  - Defecating
  - Periods of activity
- Suprachiasmatic n.



Circadian pattern generation

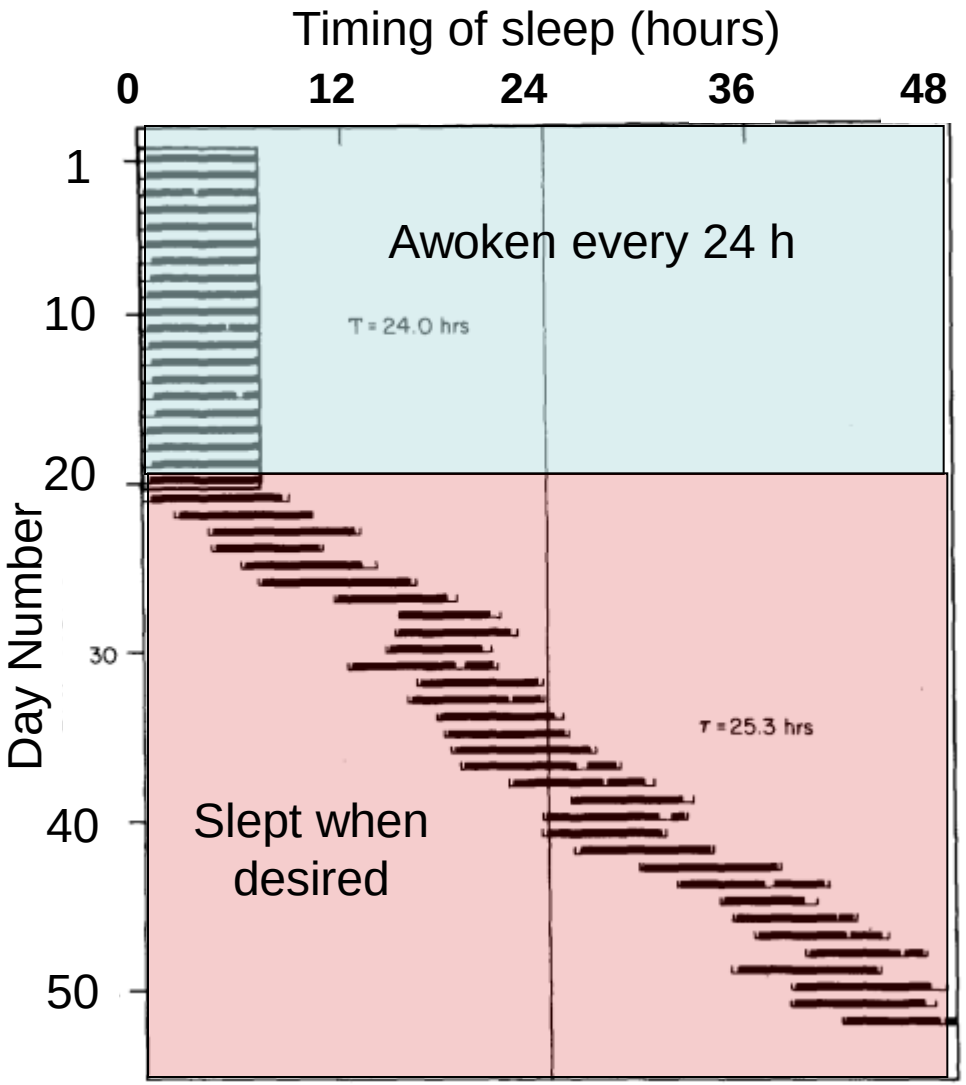
- Suprachiasmatic nucleus (SCN)
- SMALL: only 10,000 neurons
- “master clock”



https://msu.edu/~brains/brains/human/hypothalamus/1c.html

Intrinsic circadian rhythm runs slow

- Laboratory experiment; 20- y.o. male
- With no light cues, 25.3 hr sleep cycle
- Similar intrinsic rhythm also seen in SCN tissue slices



Czeisler CA; Sleep. 4(1):1-21, 1981.

Setting the circadian beat

- Light sets the circadian clock
  - Input from eyes: retino-hypothalamic pathway
  - Light-sensitive retinal ganglion neurons
- SCN expresses melatonin receptors
  - Melatonin is secreted by pineal
  - Secretion increases at night