PSYCH 260

Neurochem II

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Prelude (01:57)

Announcements

- Quiz 2 **this** Thursday
- Blog post 1 (of 3) due **this** Thursday

Today's Topics

- Warm-up
- Neurotransmitters
- Hormones

Warm-up

The presynaptic influx of which ion triggers the release of neurotransmitters from the axon terminal?

- Na+
- K+
- Ca++
- Cl-

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- Ionotropic
- Metabotropic
- Ligand-gated

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Which neurotransmitter is released at the largest number of synapses in the CNS?

- Glutamate
- GABA
- Acetylcholine
- Dopamine

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More on neurotransmitters

Monoamine neurotransmitters

Family	Neurotansmitter
Monoamines	Dopamine (DA)
	Norepinephrine (NE)/Noradrenaline (NAd)
	Epinephrine (Epi)/Adrenaline (Ad)
	Serotonin (5-HT)
	Melatonin
	Histamine

Monoamine Song

https://en.wikipedia.org/wiki/Mah_Nà_Mah_Nà

Monoamine Song

Monoamines, do-do do do-do
Monoamines, do do do-do
Monoamines, do do do do-do do do-do do do-do do do do do-do do

Monoamine Song

Monoamines, do-pa-mine is one
Monoamines, norepi, too
Monoamines, sero-tonin e-pinephrine, dop-a-mine, nor-epinephrine, melatonin, whoo!

Monoamine Song

Monoamines, mod-u-late neurons
Monoamines, throughout the brain
Monoamines, keep people happy, brains snappy, not sleepy, not sappy, do-do do-do do-do do

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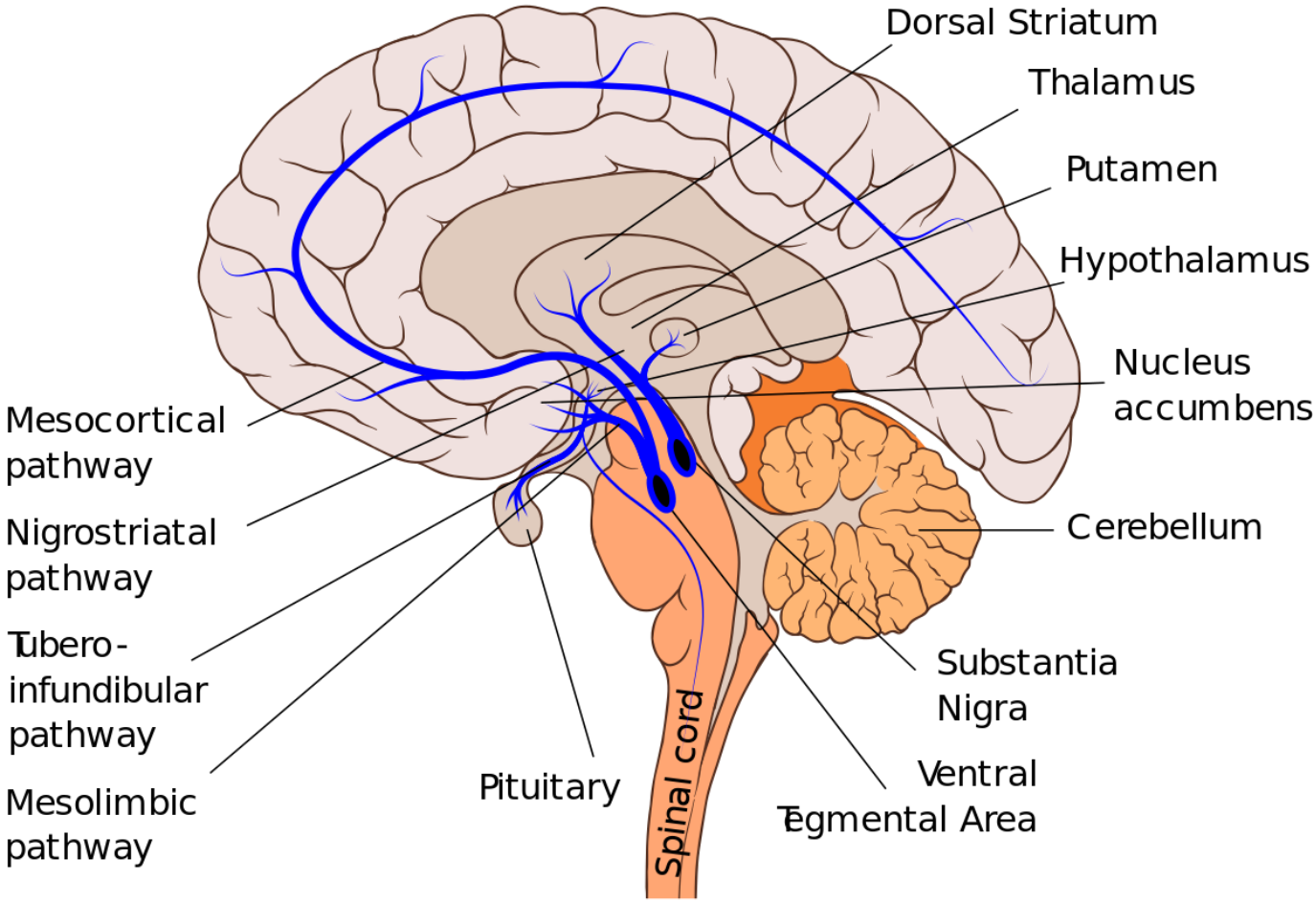
Dopamine (DA)

- Released by two pathways that originate in the midbrain tegmentum
  - Substantia nigra -> striatum, *meso-striatal projection*
  - Ventral tegmental area (VTA) -> nucleus accumbens, ventral striatum, hippocampus, amygdala, cortex; *meso-limbo-cortical projection*

DA pathways

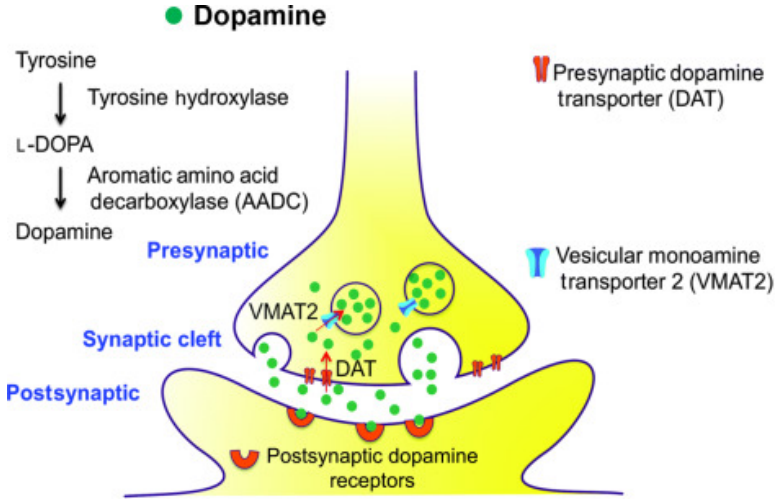

Dorsal Striatum
Thalamus
Putamen
Hypothalamus
Nucleus accumbens
Cerebellum
Substantia Nigra
Ventral Tegmental Area
Spinal cord
Pituitary
Mesocortical pathway
Nigrostriatal pathway
Tubero-infundibular pathway
Mesolimbic pathway

DA Disruption linked to

- Parkinson's Disease (mesostriatal)
  - DA agonists treat (agonists facilitate/increase transmission)
- ADHD (mesolimbocortical)
- Schizophrenia (mesolimbocortical)
  - DA antagonists treat
- Addiction (mesolimbocortical)

DA Inactivated by

- Dopamine transporter (DAT)



https://doi.org/10.1016/bs.vh.2014.12.009

- Chemical breakdown

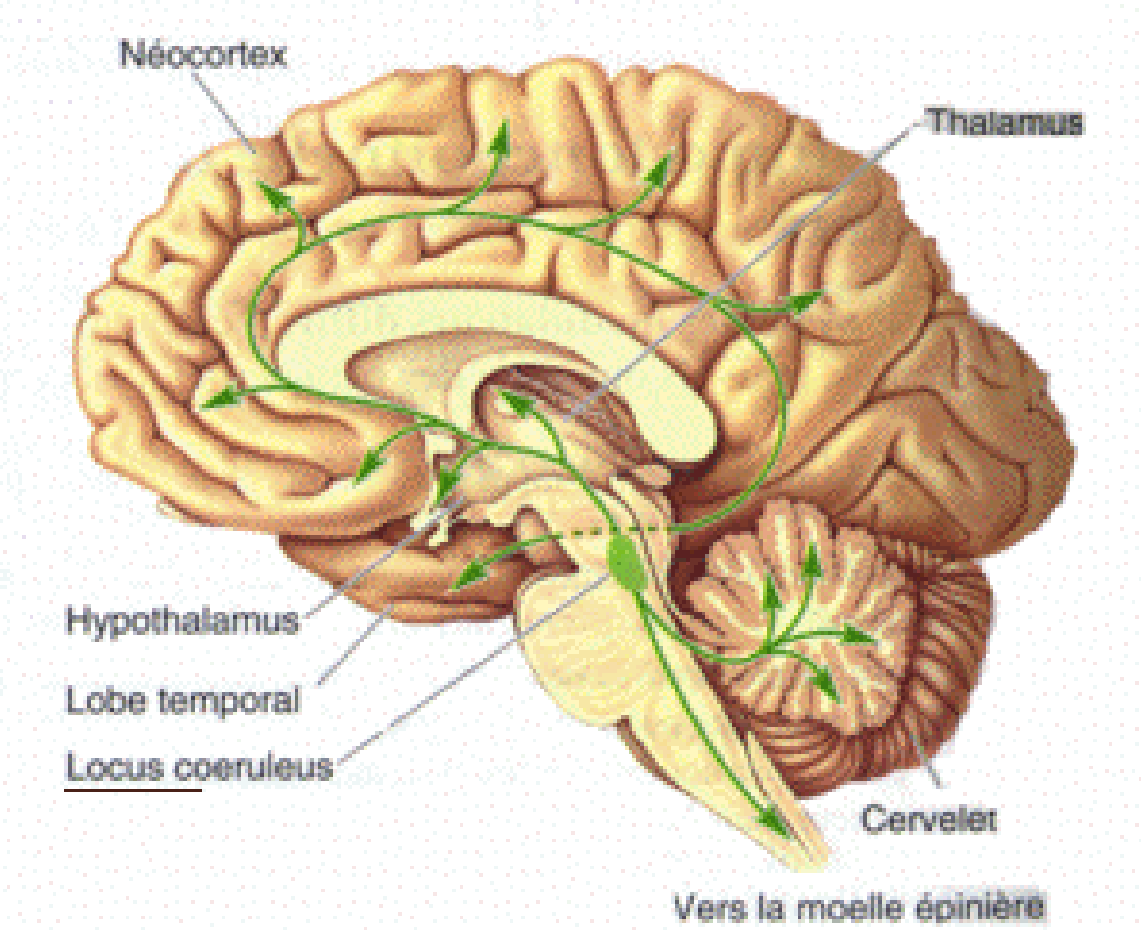
Dopamine receptors

Type	Receptor	Comments
Metabotropic	*D1-like (D1 and D5)*	more prevalent
	D2-like (D2, D3, D4)	target of many antipsychotics (drugs that treat schizophrenia symptoms)

Norepinephrine (NE)

- Role in arousal, mood, eating, sexual behavior
- Released by
  - *locus coeruleus* in pons/caudal tegmentum

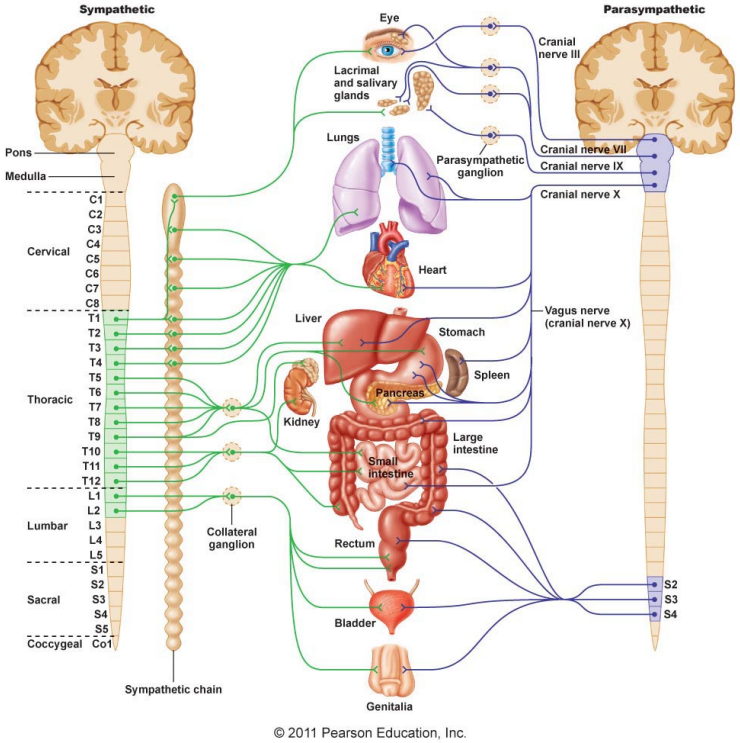
Locus coeruleus



https://upload.wikimedia.org/wikipedia/commons/6/6d/Locus-coeruleus.gif

Sympathetic Nervous System

- NE released onto target tissues

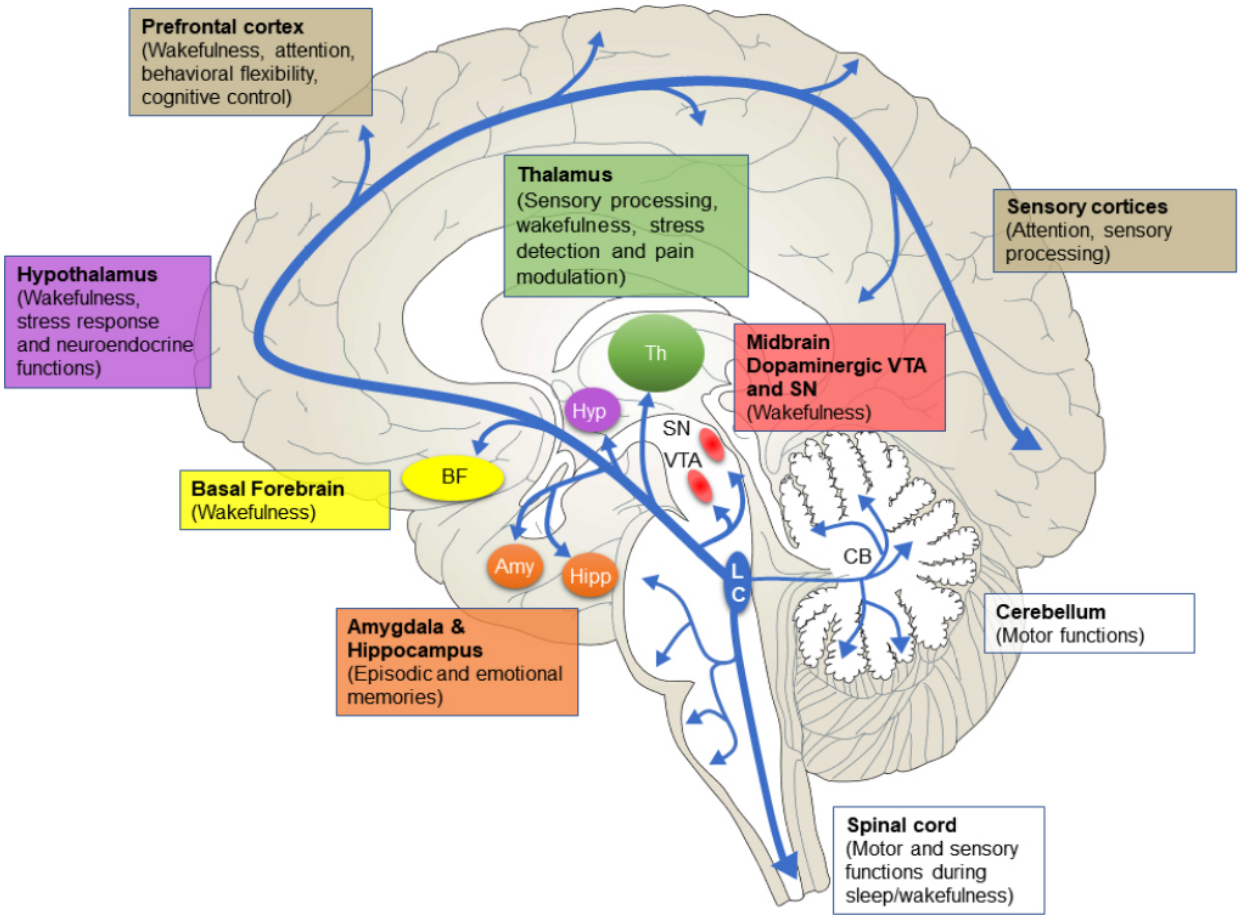


http://myzone.hrvfitltd.netdna-cdn.com/wp-content/uploads/2014/09/Image-1.jpg

NE and monoamine oxidase

- Monoamine oxidase inactivates monoamines in neurons, glial cells
- Monoamine oxidase inhibitors (MAOIs) *increase* NE, DA
  - Inhibiting inactivation ~ $-(-1) = +1$
- Treatment for depression, but side effects (dry mouth, nausea, headache, dizziness)

NE Anatomy



https://www.nrronline.org/article.asp?issn=1673-5374;year=2020;volume=15;issue=6;spage=1006;epage=1013;aulast=Bari

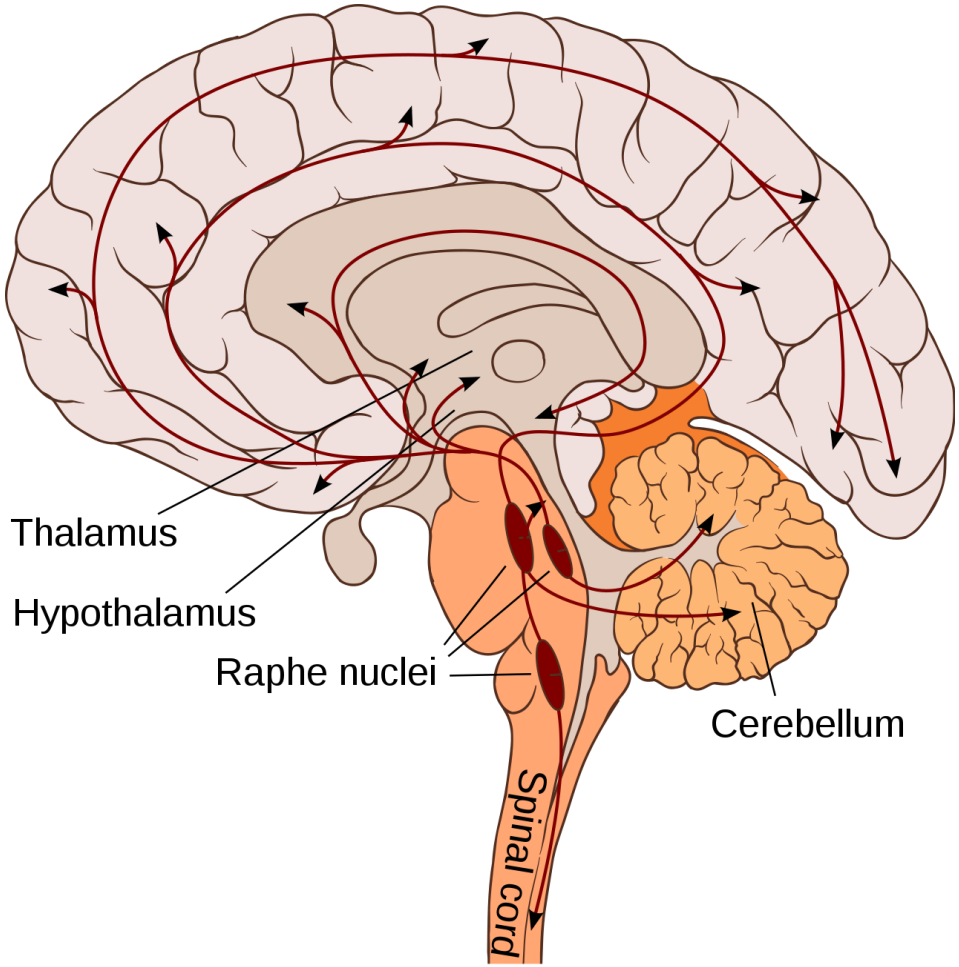
NE receptors

Type	Receptor	Comments
Metabotropic	α (1,2)	antagonists treat anxiety, panic
	β (1,2,3)	'beta blockers' in cardiac disease

Serotonin (5-HT)

- Released by *raphe nuclei* in brainstem
- Role in mood, sleep, eating, pain, nausea, cognition, memory
- Modulates release of other NTs
- Most of body's 5-HT regulates digestion
    - Enteric nervous system

5-HT anatomy



https://en.wikipedia.org/wiki/Serotonin_pathway

5-HT receptors

- Seven families (5-HT 1-7) with 14 types
- All but one metabotropic

5-HT clinical significance

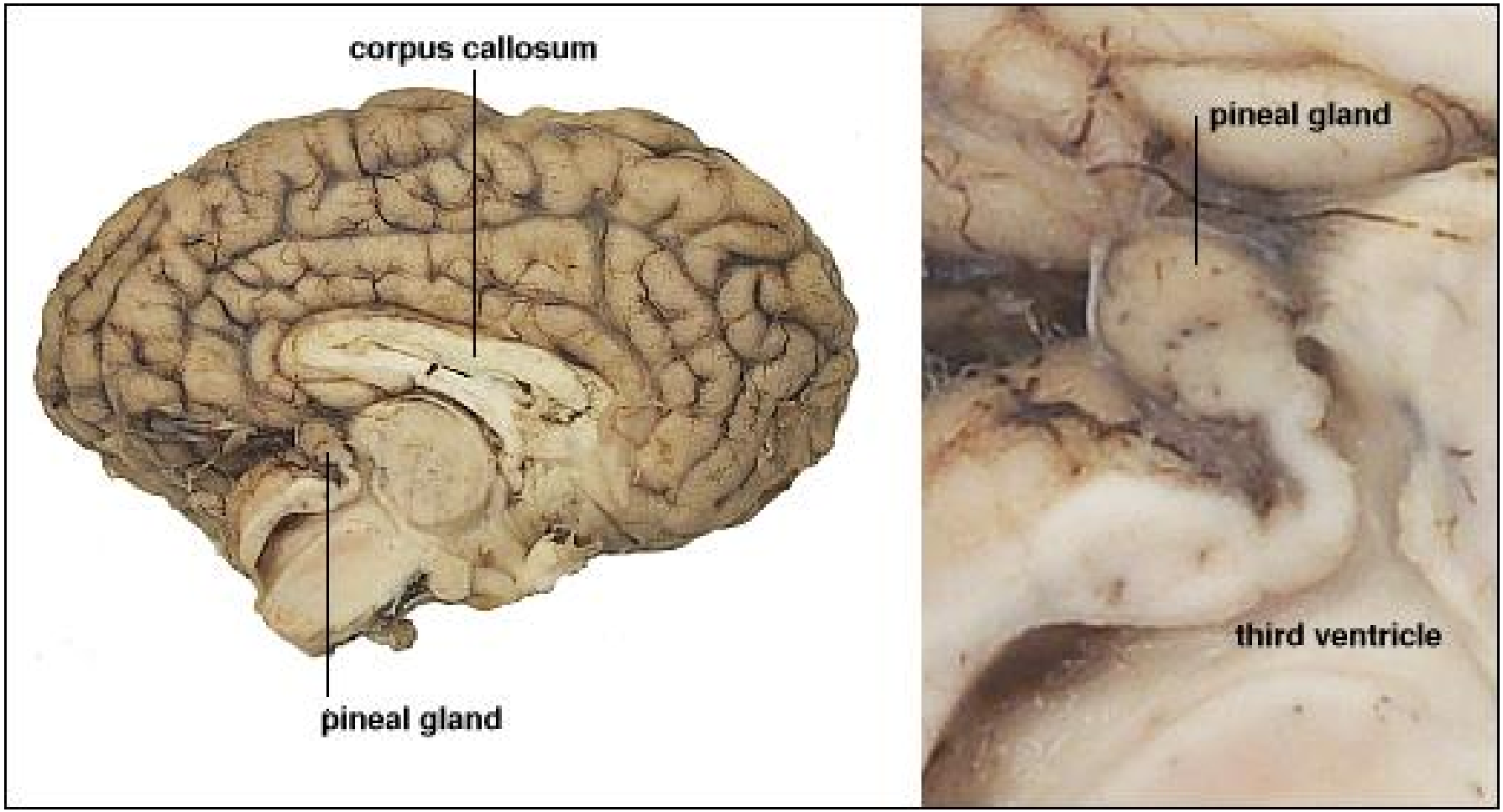
- Ecstasy (MDMA) disturbs serotonin
- So does LSD
- Fluoxetine (Prozac)
  - *Selective Serotonin Reuptake Inhibitor (SSRI)*
  - Inhibits reuptake -> increases extracellular concentration
  - Treats depression, panic, eating disorders, others

5-HT clinical significance

- 5-HT3 receptor antagonists are anti-mimetics used in treating nausea

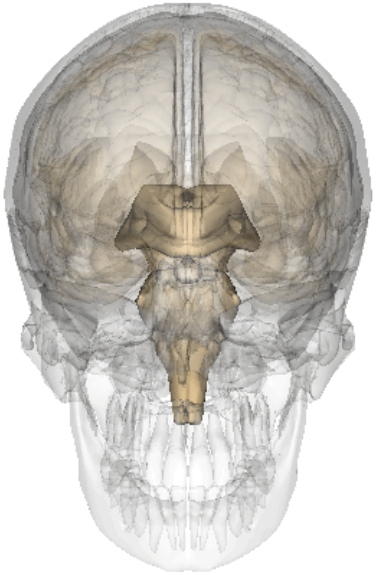
Melatonin

- Hormone released by pineal gland into bloodstream
- Concentrations vary over the day, peak near bedtime
- Release regulated by inputs from hypothalamus



http://www.vivo.colostate.edu/hbooks/pathphys/endocrine

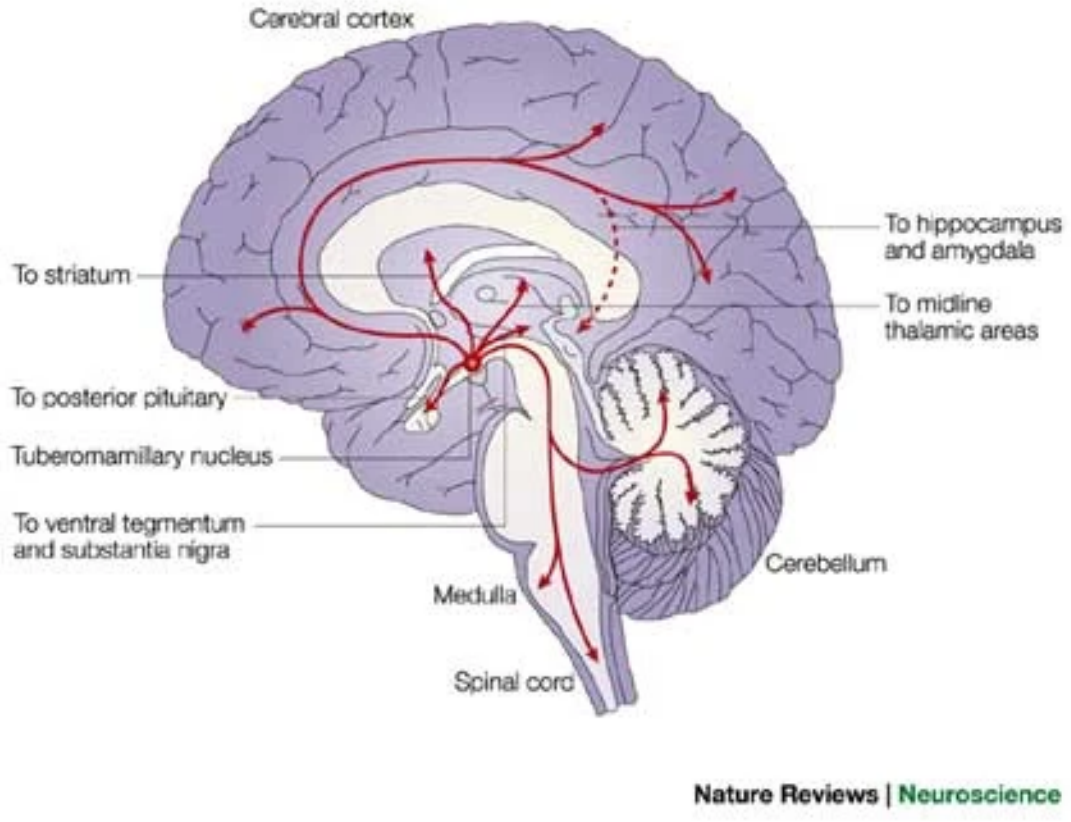
Pineal gland



Histamine

- In brain, released by hypothalamus, projects to whole brain
  - Metabotropic receptors
  - Role in arousal/sleep regulation
- In body, part of immune response

Histamine



https://www.nature.com/articles/nrn1034

Other NTs

- Gases
  - *Nitric Oxide (NO)*, *carbon monoxide (CO)*
- Neuropeptides
  - *Substance P* and *endorphins* (endogenous morphine-like compounds) have role in pain
  - *Orexin/hypocretin*, project from lateral hypothalamus across brain, regulate appetite, arousal

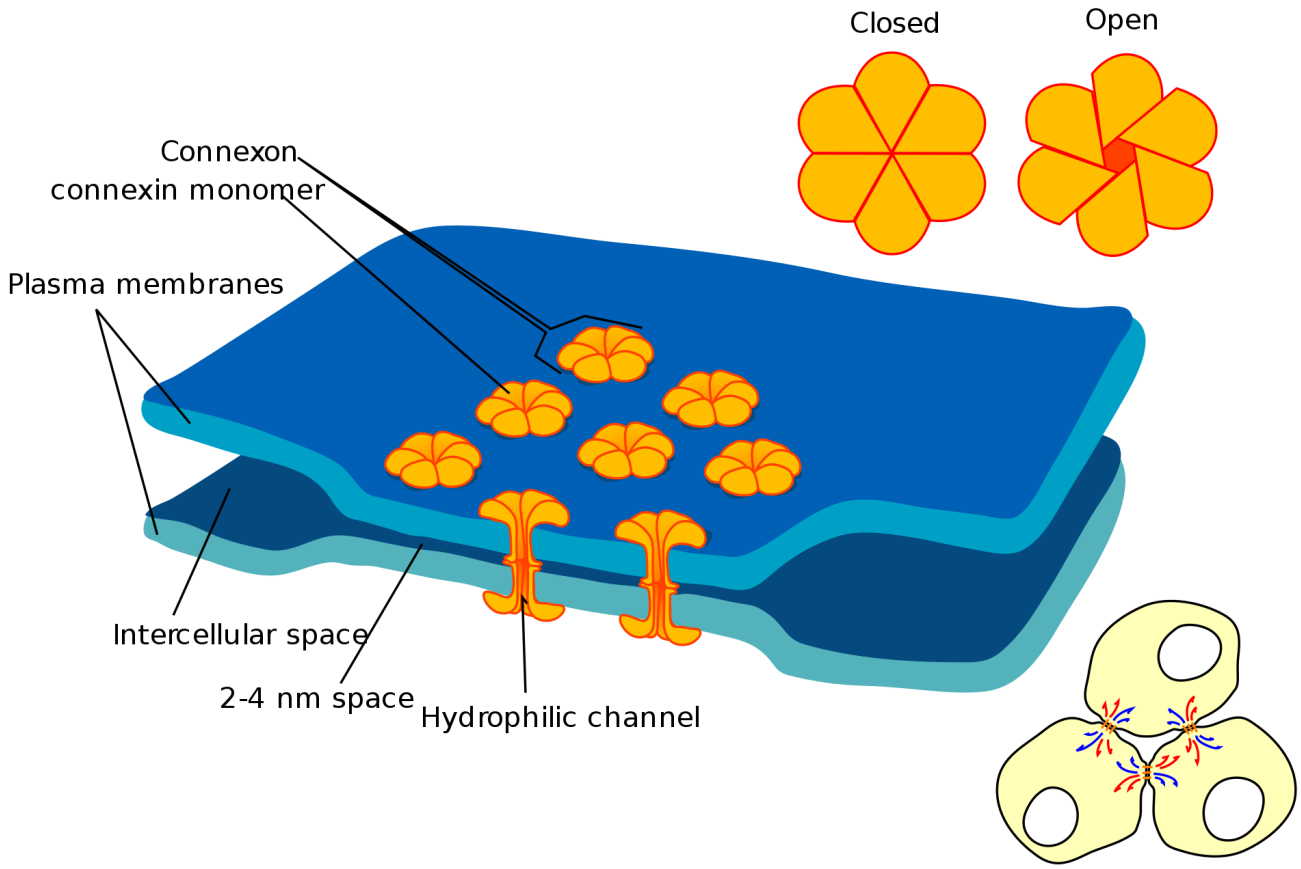
Other NTs

- Neuropeptides (continued)
  - *Cholecystokinin (CCK)* stimulates digestion
  - *Oxytocin* and *vasopressin* released by posterior hypothalamus onto posterior pituitary, regulate social behavior

Non-chemical communication between neurons

- Gap junctions
- Electrical coupling
- Connect cytoplasm directly
- Fast, but fixed, hard to modulate
- Examples, retina, cardiac muscle

Gap junctions



Ways to think about synaptic communication

- Specificity: point-to-point vs. broadcast
- Direct (immediate) action vs. (delayed, prolonged) modulatory
- Agonists vs. antagonists

Agonists vs. Antagonists

- *Agonists*
  - bind to receptor
  - mimic action of endogenous chemical
- *Antagonists*
  - bind to receptor
  - block/impede action of endogenous chemical

Valium is a GABA-A receptor agonist. This means:

- It decreases inhibition
- It activates a metabotropic Cl- channel
- It facilitates/increases inhibition
- It blocks an ionotropic channel

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2. It activates a metabotropic Cl- channel
3. It facilitates/increases inhibition
4. It blocks an ionotropic channel

Next time…

- Hormones

References