Neuroendocrinology

BCH 120 – Metabolic & Endocrine Biochemistry · Dr. Radi

By the end of this unit, you can…

- Distinguish neurohormones from neurotransmitters and classic hormones, and describe the adrenal medulla's chromaffin cells and the catecholamine synthesis pathway (tyrosine → L-DOPA → dopamine → norepinephrine → epinephrine)
- Explain catecholamine reuptake and degradation (COMT, MAO; MAO inhibitors as antidepressants) and the four adrenergic receptor subtypes (α1/α2/β1/β2) with their G proteins and effects
- Describe the pineal gland and how it converts serotonin to melatonin in the dark to set circadian rhythm

Today's route

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1. **Neurohormones & Catecholamine Synthesis**
2. **Clearing Catecholamines & Adrenergic Receptors**
3. **The Pineal Gland, Melatonin & Your Clock**

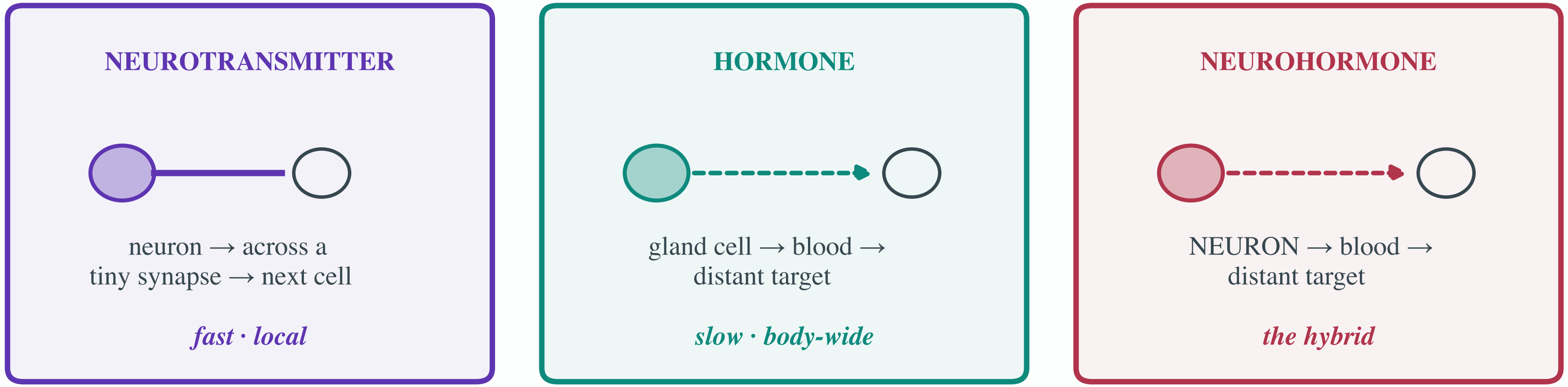
1 · Neurohormones & Catecholamine Synthesis

"Where does the nervous system end and the endocrine system begin? Right here – in cells that are half neuron, half gland. The adrenal medulla's chromaffin cells fire on nerve command and squirt adrenaline into the blood. And you need to know how they build it."

Neurotransmitter, hormone – or both?

First, a definition that ties the two control systems together. A **neurotransmitter** is released by a neuron across a **tiny synapse** to the very next cell – fast and local. A **hormone** is released by a gland into the **blood** to reach **distant** targets – slower, body-wide. A **neurohormone** is the **hybrid**: a **neuron** that dumps its messenger into the **bloodstream** to act far away. Two organs do exactly this – the **posterior pituitary** (you've met it) and the **adrenal medulla** (you're about to).

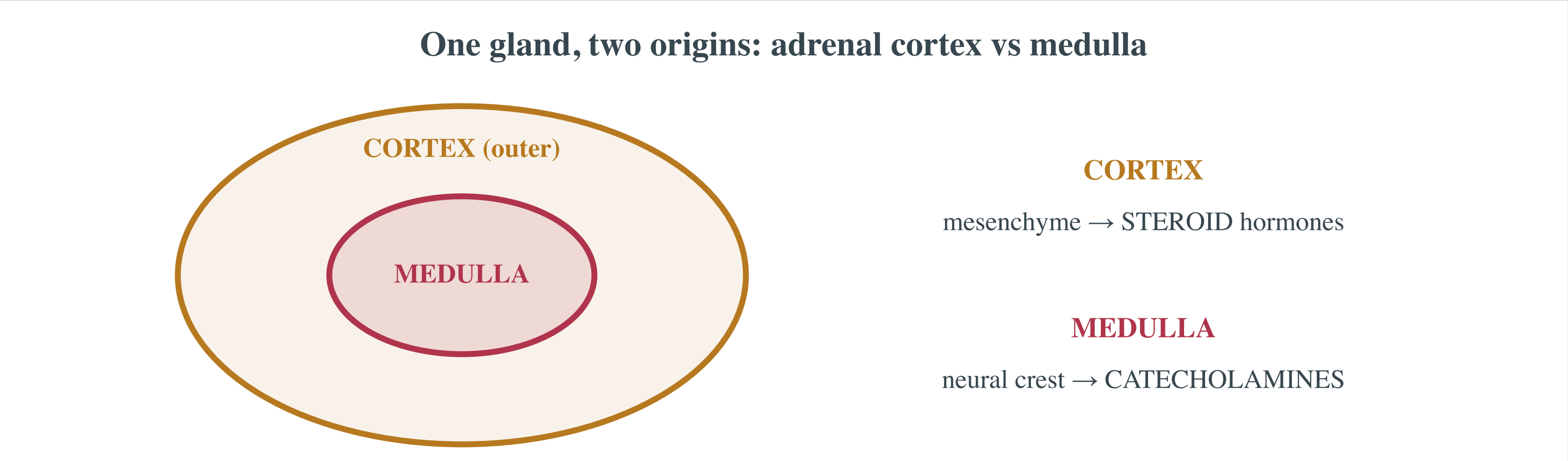
Neurotransmitter, hormone, or neurohormone?



A neurohormone is a NEURON acting like a gland — the posterior pituitary and adrenal medulla both do this.

The adrenal medulla: a gland run by nerves

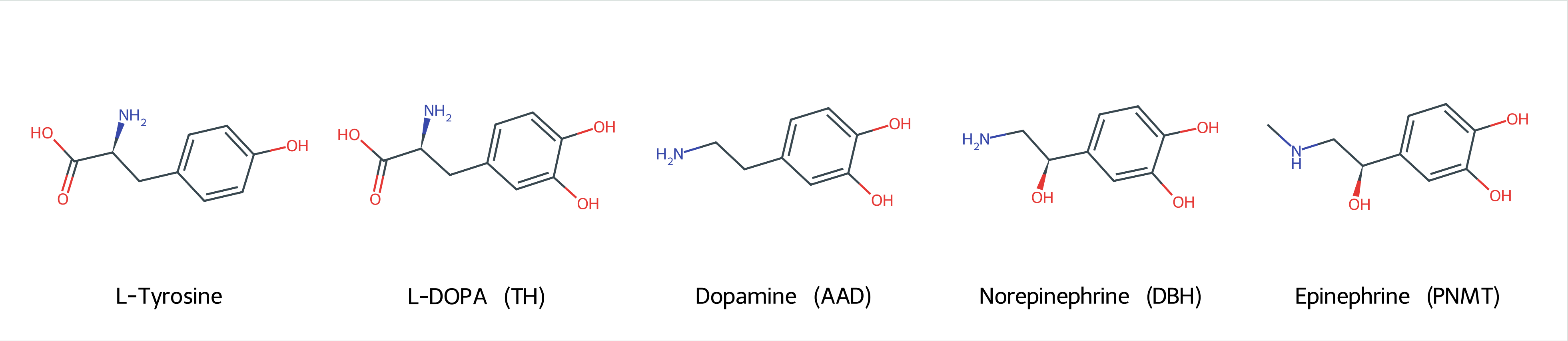
The **adrenal gland** is really two glands stacked together, from two different embryos. The outer **cortex** comes from mesenchyme and makes **steroids** (the next several units). The inner **medulla** comes from **neural-crest** cells – it's basically a **modified sympathetic ganglion**. Its **chromaffin cells** are fired by **spinal nerves**, and when they fire they release **catecholamines** – **epinephrine** and **norepinephrine** – straight into the blood. **Epinephrine is always a neurohormone**, never a neurotransmitter.



The medulla is a modified sympathetic ganglion that squirts adrenaline into the blood.

KNOW this pathway: how you build adrenaline

This is a "must-know" sequence, and it's a tidy one – start with an amino acid and add one change at a time. **Tyrosine** → (**tyrosine hydroxylase, TH** – the rate-limiter, adds the second ring-OH → a catechol) → **L-DOPA** → (**AAD**, decarboxylase – drops the –COOH) → **Dopamine** → (**DBH**, adds a β-OH) → **Norepinephrine** → (**PNMT**, adds an N-methyl) → **Epinephrine**. Four enzymes, four small edits. (Bonus: **L-DOPA** is the Parkinson's drug – it refills brain dopamine.)

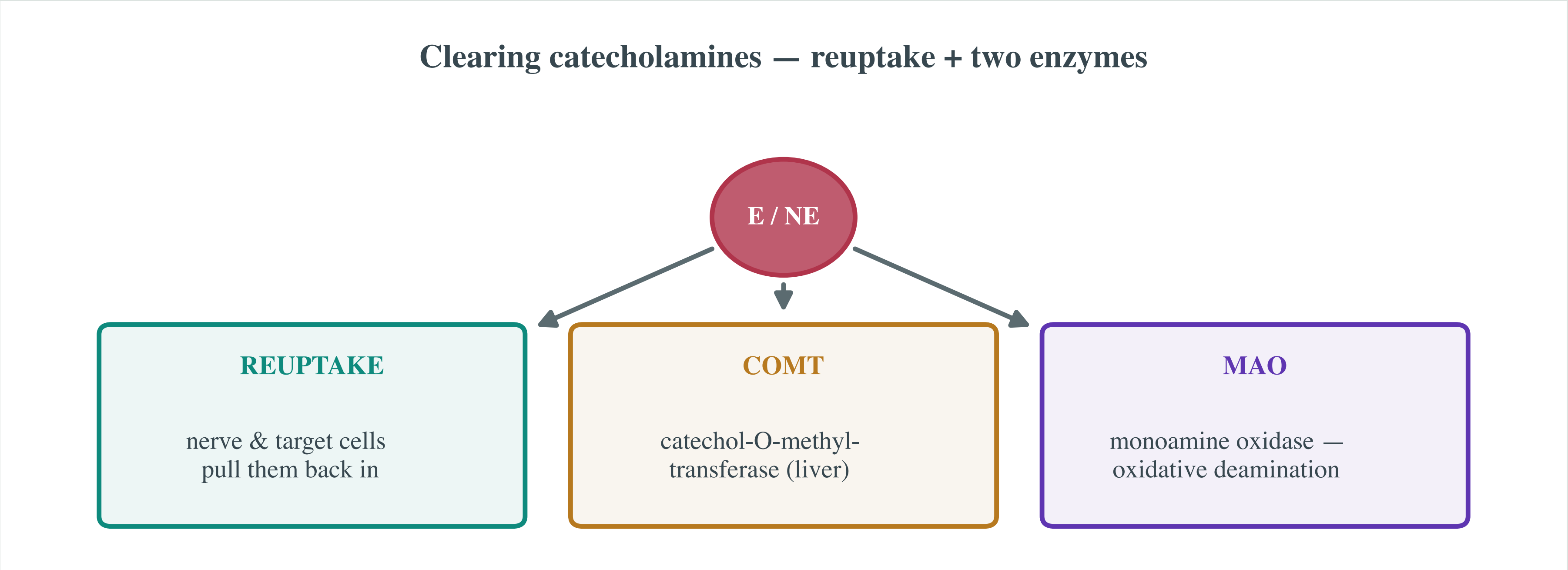


2 · Clearing Catecholamines & Adrenergic Receptors

"A fight-or-flight signal has to end fast – so catecholamines are cleared in seconds by reuptake and two enzymes you should know by name. Then the payoff: the SAME two hormones do opposite things depending on which adrenergic receptor they hit."

Turning the alarm off: reuptake, COMT, MAO

Adrenaline is meant to be **brief**, so the body clears it fast three ways. **Reuptake**: nerve and target cells rapidly **pull the catecholamines back in** (especially important at synapses). **COMT** (**catechol-O-methyltransferase**) **methylates** them, mainly in the **liver**. **MAO** (**monoamine oxidase**) **oxidatively deaminates** them. That last enzyme has a famous clinical hook: **MAO inhibitors were among the first antidepressants** – block the breakdown, and catecholamine (and serotonin) tone goes up.



Adrenergic receptors: same hormone, four switches

Here's why epinephrine can speed your heart **and** open your airways at once: there are **four adrenergic receptor subtypes**, all **GPCRs**, each wired to a different **G protein**. **α_1 → Gq** → IP_3/DAG/**Ca^{2+}** (vasoconstriction). **α_2 → Gi → ↓cAMP** (a presynaptic brake; ↓insulin). **β_1 → Gs → ↑cAMP** (the **heart** – rate and force). **β_2 → Gs → ↑cAMP** (bronchodilation, glycogenolysis). Same ligand, opposite outputs – it all depends on the receptor. (That's why a **β-blocker** slows the heart while an **α-agonist** clears your nose.)

Adrenergic receptors — same hormone, four different switches

receptor	G protein	2^{nd} messenger	signature effect
α_1	**Gq**	IP_3 / DAG → ↑Ca^{2+}	**vasoconstriction (E>NE)**
α_2	**Gi**	↓ cAMP	**↓insulin · presynaptic brake**
β_1	**Gs**	↑ cAMP	**HEART: ↑rate & force (E=NE)**
β_2	**Gs**	↑ cAMP	**bronchodilation · glycogenolysis**

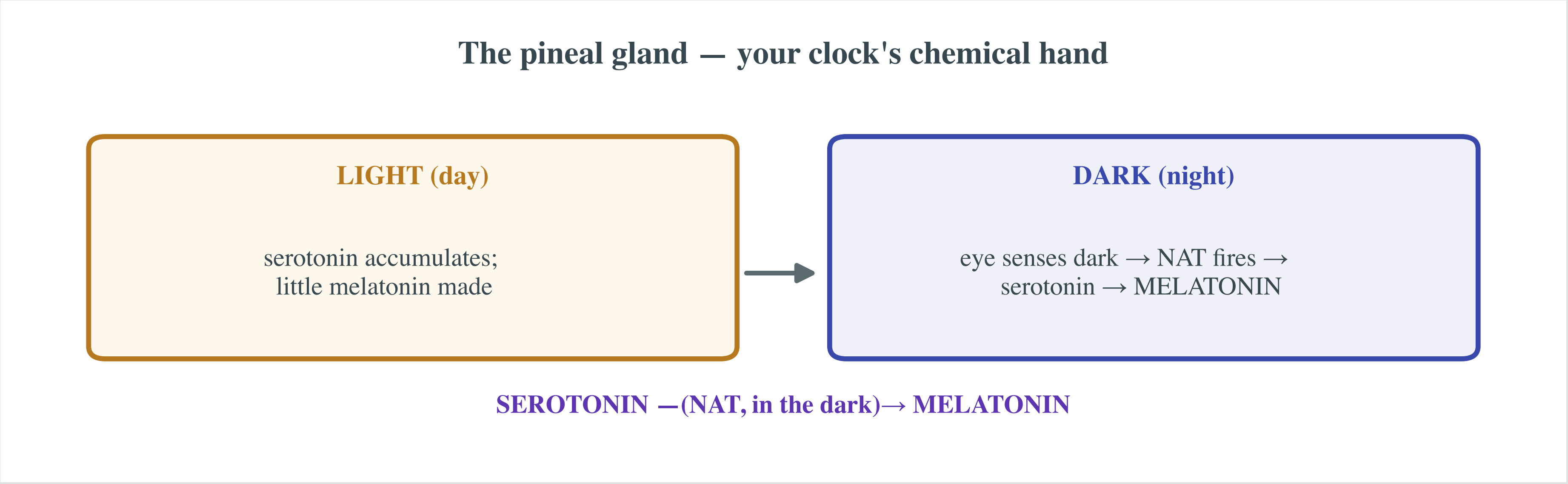
All are GPCRs — only the G protein differs. β-blockers hit β; α-agonists are decongestants.

3 · The Pineal Gland, Melatonin & Your Clock

"One more neuroendocrine organ, and it's the one that keeps time. The pineal gland reads light and dark and turns it into a chemical signal – melatonin – that sets the rhythm of your whole day."

The pineal gland keeps time

The **pineal gland** is your **circadian clock** – an evolutionary leftover that once sensed light directly and still runs on it (via **neural** day/night signals). It makes **melatonin** from **serotonin** (which the gland builds from the amino acid **tryptophan**), switched by **darkness**: in the **light**, serotonin builds up; when the eye senses **dark**, the enzyme **NAT** converts it to **melatonin**, secreted at night. Melatonin acts on the brain's master clock, the **suprachiasmatic nucleus**, to set your ~24-hour rhythm and normal sleep. Sleep aids like **ramelteon** are melatonin-receptor agonists working through this very pathway.



Can you…?

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If any box stays empty, the practice site has a drill for it.
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