The Hypothalamic–Pituitary Axis

BCH 120 — Metabolic & Endocrine Biochemistry · Dr. Radi

By the end of this unit, you can…

- Contrast the posterior pituitary (a neural extension releasing oxytocin and ADH) with the anterior pituitary (a portal-fed endocrine gland), and explain ADH's control of water balance and diabetes insipidus
- Map the hypothalamic releasing/inhibiting factors (TRH, GnRH, CRH, GHRH, somatostatin, dopamine) to their target cells and pituitary hormones, and the peptide end-modifications that protect them
- Describe growth-hormone control (GHRH/somatostatin, sleep pulse) and prolactin (dopamine brake, suckling/estrogen/TRH)
- Explain the glycoprotein hormones (shared α + unique β; FSH/LH/TSH/hCG), ACTH from the POMC precursor, and somatostatin as a broad paracrine inhibitor

Today's route

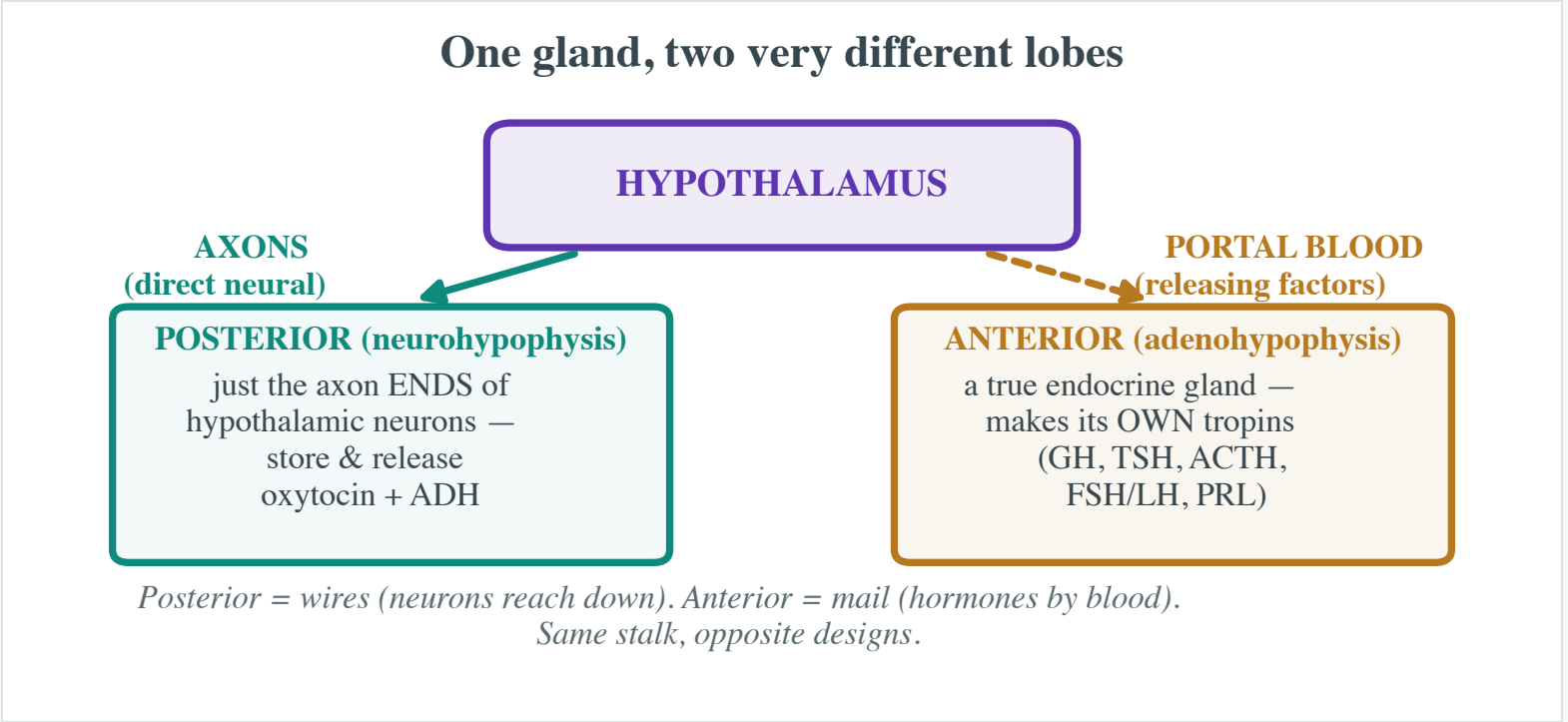
1. **The Posterior Pituitary – Oxytocin & ADH**
2. **Hypothalamic Releasing Factors**
3. **Growth Hormone & Prolactin**
4. **Glycoprotein Hormones, ACTH & Somatostatin**

1 · The Posterior Pituitary — Oxytocin & ADH

"The pituitary is the body's master gland — but it's really two glands in one. Start with the back half, which is just the hypothalamus reaching down: two small peptides, oxytocin and vasopressin, that run labor, milk, and your entire water balance."

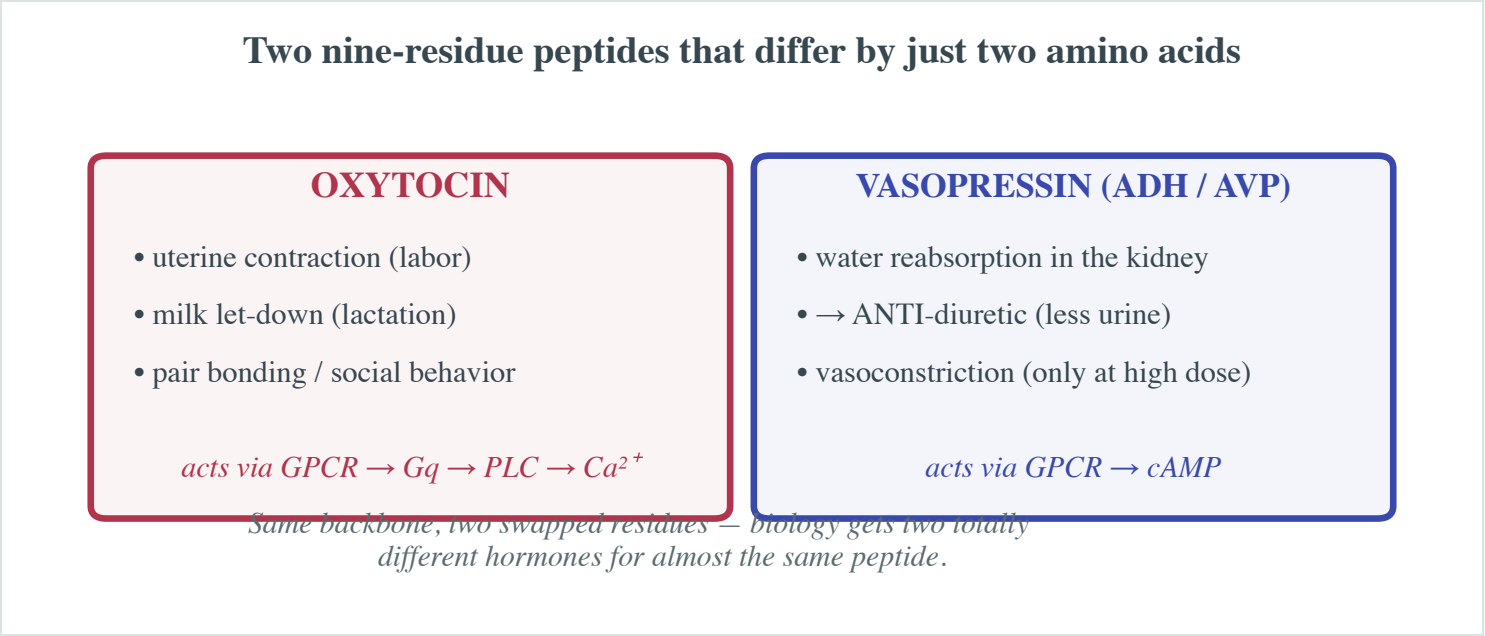
One gland, two very different lobes

The **pituitary** hangs off the **hypothalamus** — and it's two glands wearing one coat. The **posterior lobe** (neurohypophysis) is **not really a gland at all**: it's just the **axon endings** of hypothalamic neurons reaching down, storing and releasing their peptides directly. The **anterior lobe** (adenohypophysis) is a **true endocrine gland** that makes its own hormones on command from the hypothalamus. **Posterior = wires. Anterior = mail.** Today, the wires.



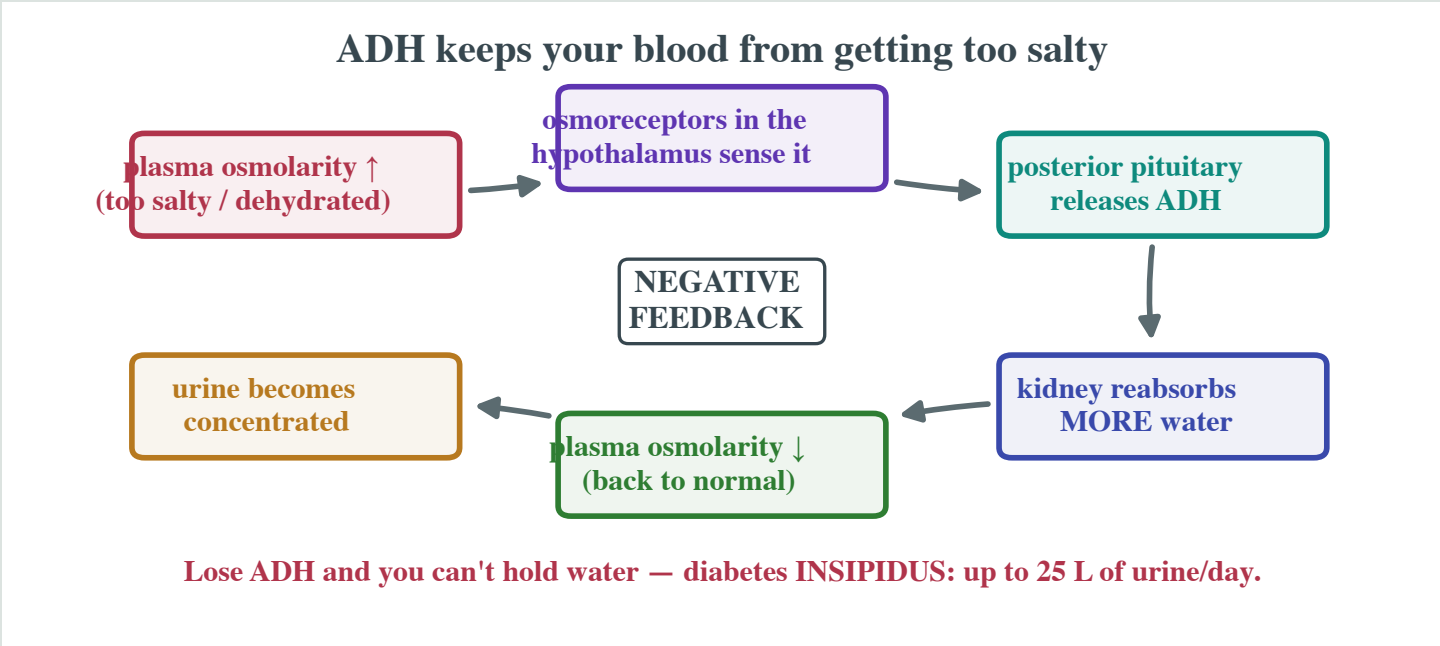
Two peptides, two amino acids apart

The posterior pituitary releases just **two** hormones, almost the same molecule — **nine residues each, differing by only two**. **Oxytocin** drives **uterine contraction** and **milk let-down** (and bonding). **Vasopressin** — **ADH, antidiuretic hormone** — makes the kidney **reabsorb water** (and constricts vessels at high dose). Both are **made in hypothalamic neurons**, shipped down the axons bound to **neurophysin**, and released from the posterior lobe. Nearly identical peptides, opposite jobs.



ADH runs your water balance

Here's the loop you have to know. When your blood gets **too salty** (high osmolarity — you're dehydrated), **osmoreceptors** in the hypothalamus sense it and fire **ADH** from the posterior pituitary. ADH tells the **kidney to reabsorb water**, which **dilutes the blood back down** and concentrates the urine — classic **negative feedback**. Lose ADH and you can't hold water: **diabetes insipidus**, up to **25 liters** of dilute urine a day. (Totally different from diabetes **mellitus** — they just share the thirst.)

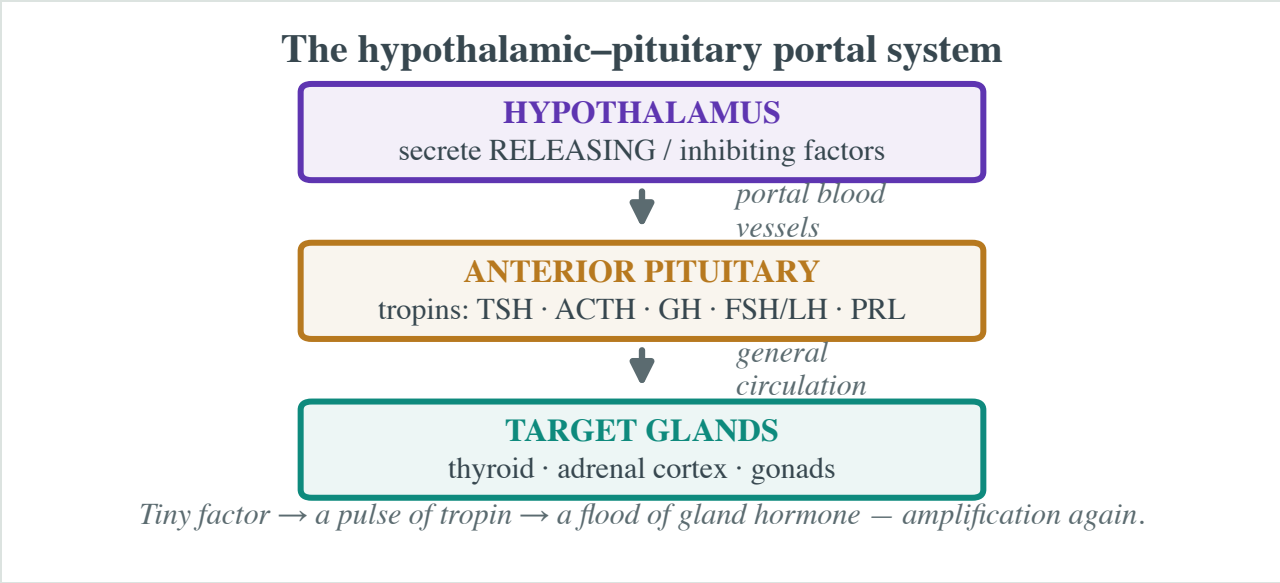


2 · Hypothalamic Releasing Factors

"The anterior pituitary can't see the brain — so the hypothalamus talks to it by a private bloodstream, the portal system, sending tiny 'releasing' and 'inhibiting' peptides. Learn this roster and you can predict the whole endocrine cascade."

How the anterior lobe gets its orders

The anterior pituitary isn't wired to the brain like the back lobe — so the hypothalamus reaches it by a **private plumbing loop**, the **hypothalamic–pituitary portal system**. Hypothalamic neurons dump **releasing** (or **inhibiting**) **factors** into these portal vessels; the anterior pituitary reads them and pumps out its **tropins** — **TSH, ACTH, GH, FSH/LH, PRL** — into the general circulation to hit **target glands**. It's a **three-tier relay**: hypothalamus → pituitary → gland.



The control roster

Memorize this table and endocrinology gets easy. **TRH** → releases **TSH**. **GnRH** → releases **LH and FSH**. **CRH** → releases **ACTH**. **GHRH** → releases **GH**. Those are the "go" signals. Two are brakes: **somatostatin** shuts down **GH and TSH**, and **dopamine** holds back **prolactin**. Each hypothalamic factor hits one pituitary cell type and flips one hormone — a clean set of levers.

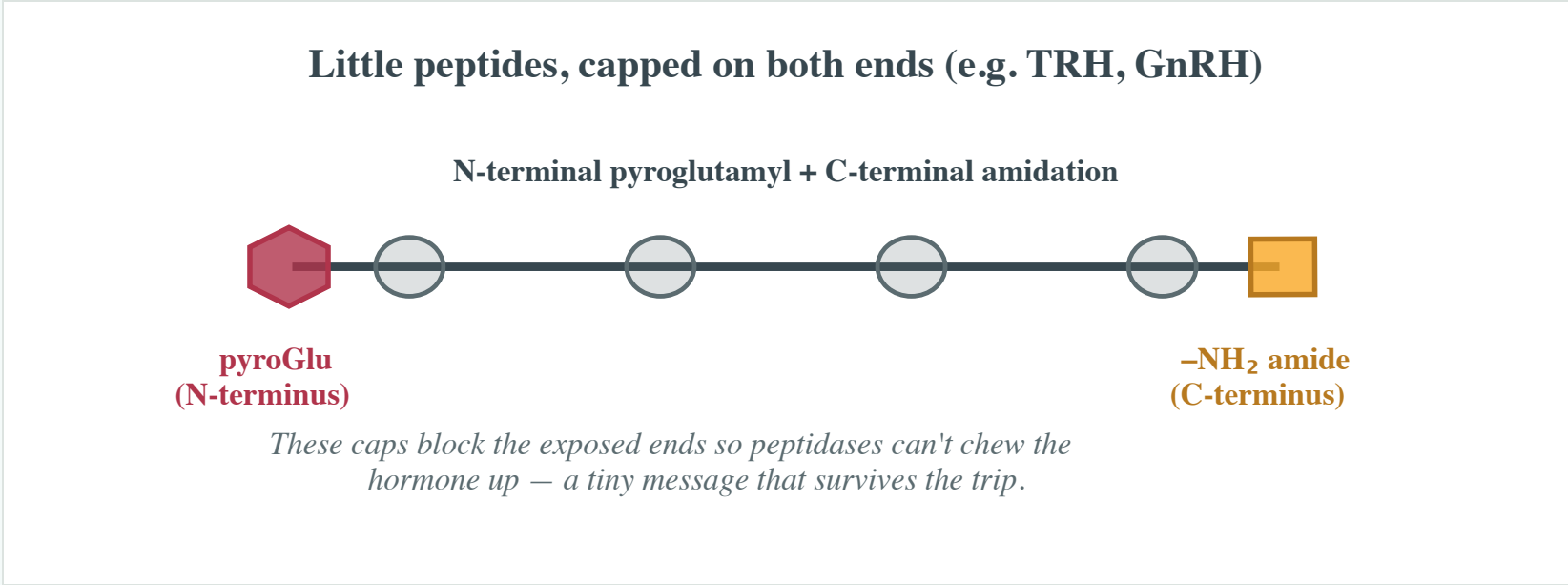
The hypothalamic control roster

TRH	→ thyrotrope	→ **release TSH**
GnRH	→ gonadotrope	→ **release LH + FSH**
CRH	→ corticotrope	→ **release ACTH**
GHRH	→ somatotrope	→ **release GH**
Somatostatin	→ somatotrope +	⊣ **INHIBIT GH, TSH…**
Dopamine	→ lactotrope	⊣ **INHIBIT prolactin**

Green = 'go' (releasing); red = 'stop' (inhibiting) — dopamine's brake on prolactin can cause milk flow.

Tiny peptides, capped for the trip

These hypothalamic factors are **very short peptides** — TRH is only three residues — so how do they survive the journey without being chewed up? They're **capped on both ends**. The **N-terminus** carries a **pyroglutamyl** group; the **C-terminus** is **amidated** (–NH_2). Those caps block the exposed ends where peptidases would attack. A tiny message, armored just enough to reach its target intact.

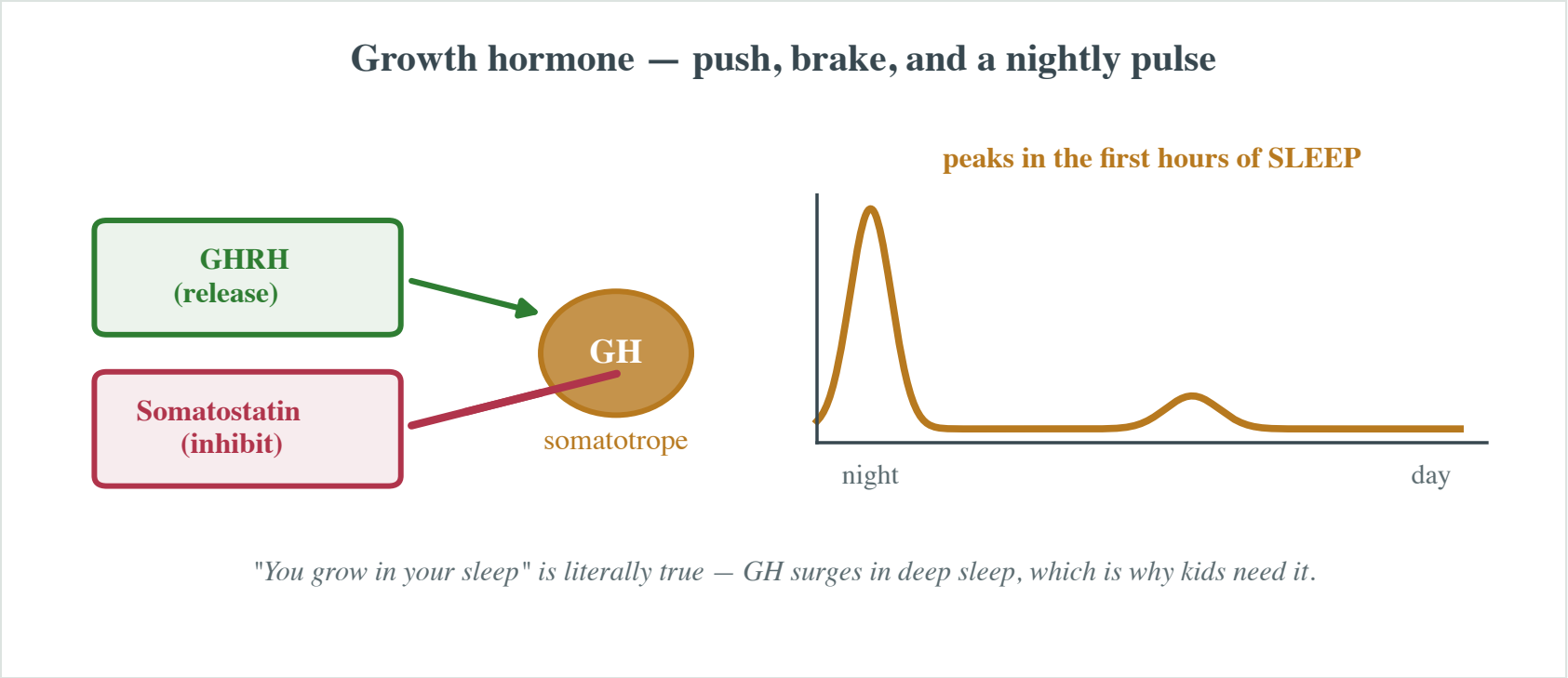


3 · Growth Hormone & Prolactin

"Two anterior-pituitary hormones act directly on the body rather than on another gland. Growth hormone builds you — and surges while you sleep. Prolactin makes milk — and is unique because its default setting is ON."

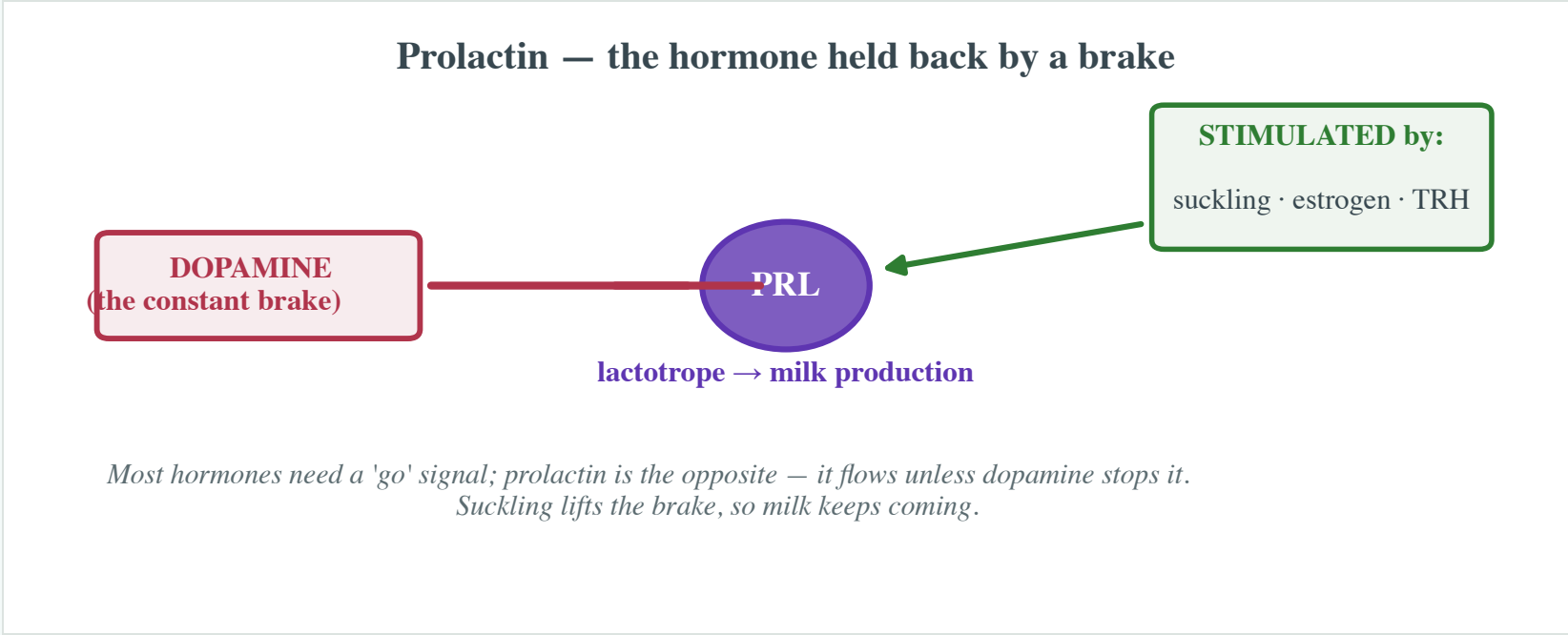
Growth hormone: push, brake, and a nightly pulse

Growth hormone (GH) is controlled by a **push–pull** pair from the hypothalamus: **GHRH** stimulates its release, **somatostatin** shuts it off. And its output isn't steady — it comes in **pulses**, with the biggest surge in the **first hours of deep sleep**. So "you grow in your sleep" is literally true: skimp on sleep and you blunt the GH pulse. That's why growth and repair really do depend on rest.



Prolactin: the hormone on a brake

Prolactin (PRL) drives **milk production**, and it's the endocrine oddball: **its default is ON**. Most hormones need a "go" signal to be released — prolactin flows **unless** something stops it, and that constant stop signal is **dopamine** from the hypothalamus. **Suckling, estrogen, and TRH** push it up (suckling by **lifting the dopamine brake**). Fun consequence: drugs that block dopamine can cause unexpected **milk production**.

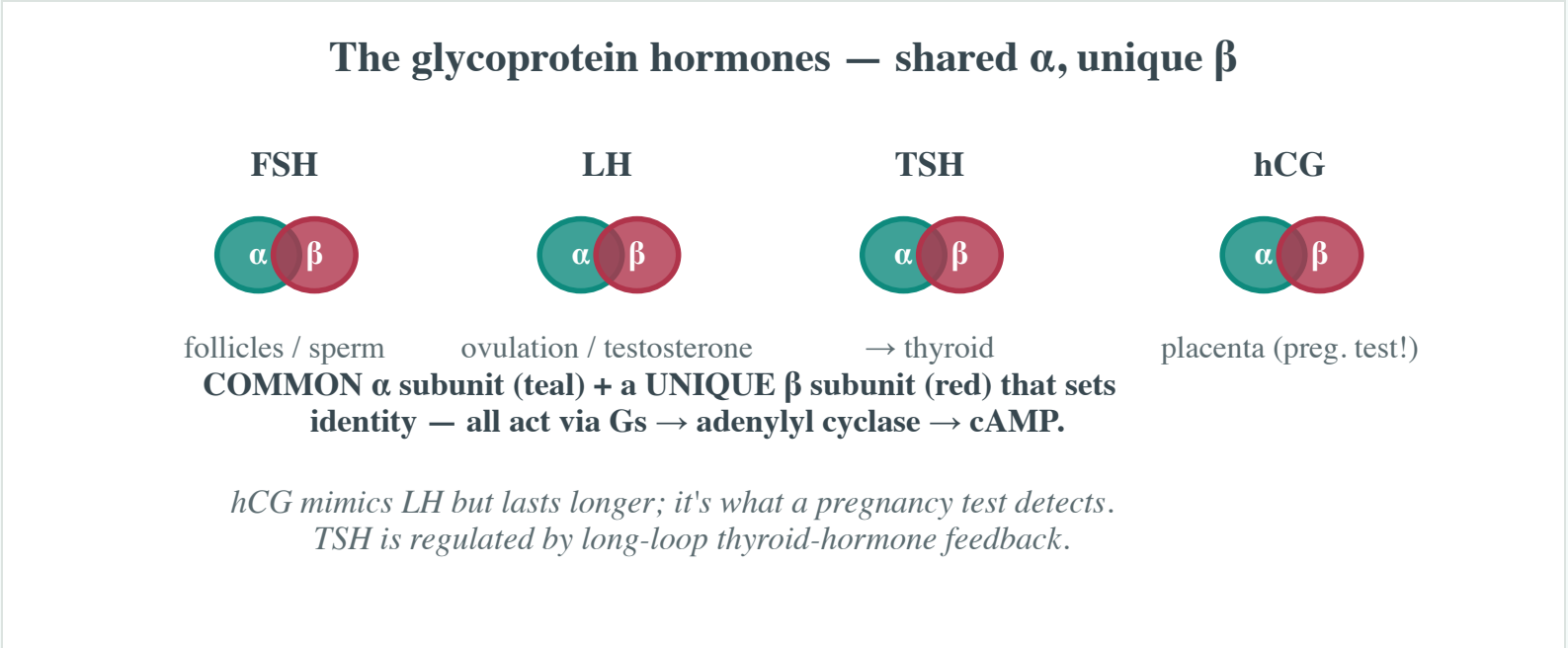


4 · Glycoprotein Hormones, ACTH & Somatostatin

"Finish the anterior pituitary with the hormones that command other glands: the glycoprotein family that share one subunit, ACTH cut from a remarkable multi-hormone precursor, and somatostatin — the body's universal 'quiet down' switch."

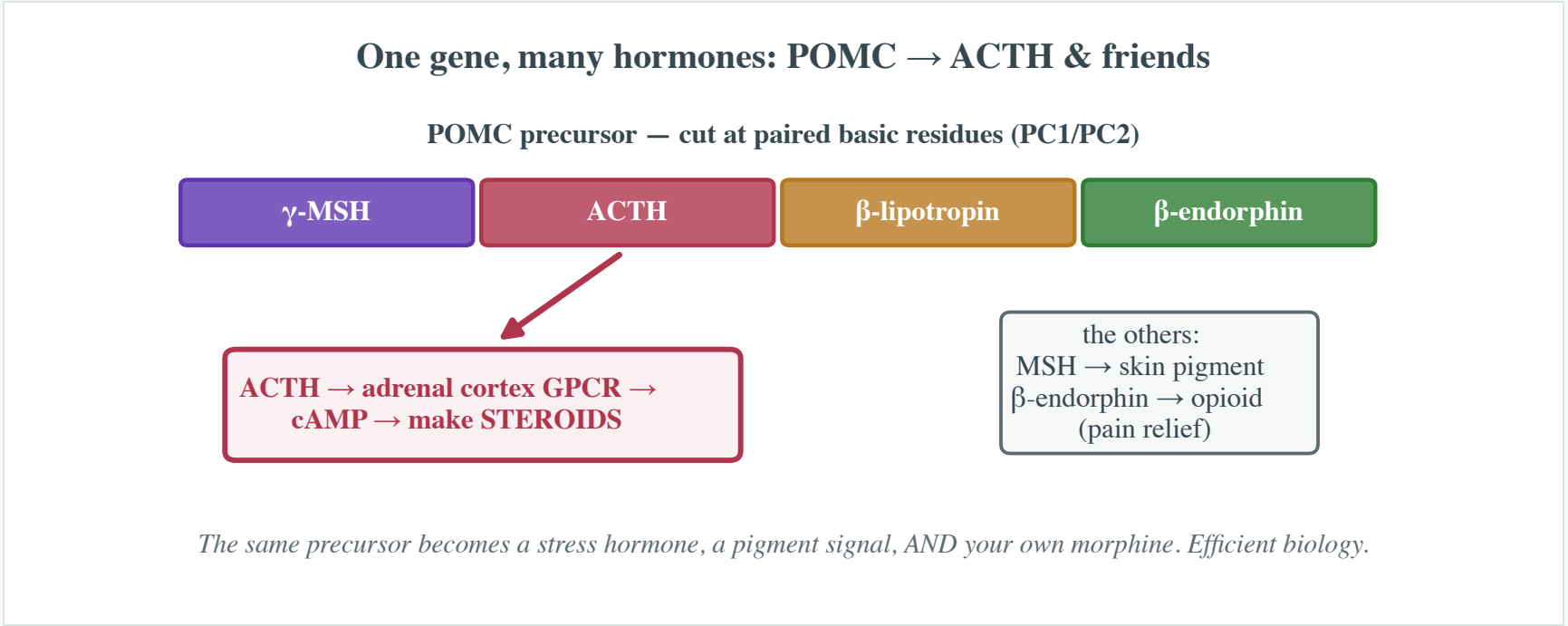
The glycoprotein hormones — shared α, unique β

Four hormones — **FSH, LH, TSH, and hCG** — are built on a **shared blueprint**: every one is a **common α subunit** paired with a **unique β subunit** that gives it its identity. All four signal through **Gs → adenylyl cyclase → cAMP**. **FSH and LH** run the gonads; **TSH** drives the thyroid to take up iodide and build thyroglobulin; and **hCG** mimics LH but lasts longer — it's made by the placenta, which is exactly what a **pregnancy test** detects. **TSH** is reined in by long-loop feedback from thyroid hormones.



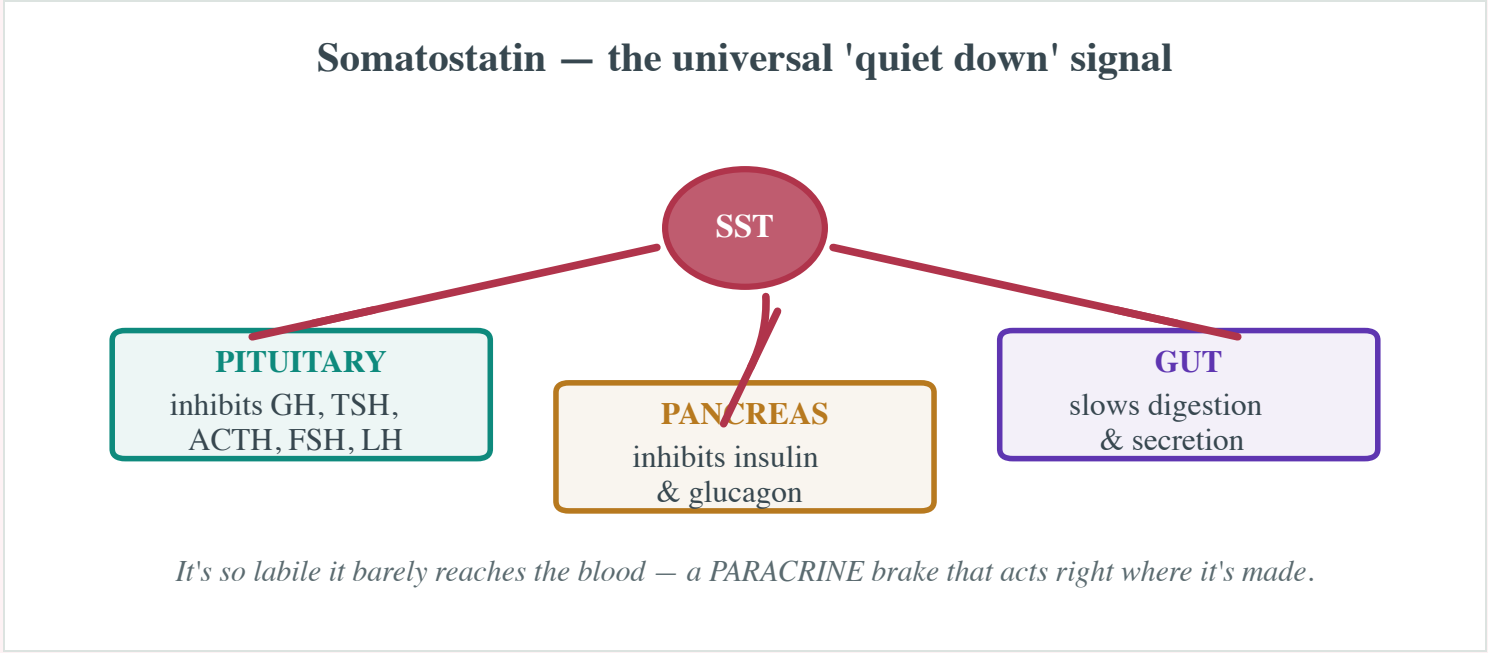
ACTH: one precursor, many hormones

ACTH comes from a beautiful piece of biology — a single precursor called **POMC** (pro-opiomelanocortin) that gets **cut at paired basic residues** into **several** hormones at once. Out of one chain come **ACTH**, **MSH** (skin pigment), **β-endorphin** (your own opioid), and more. **ACTH** is the one you can't live without: it hits **adrenal-cortex GPCRs → cAMP → steroid synthesis**, the stress-hormone axis we'll open next unit. One gene, a whole toolkit.



Somatostatin: the universal brake

We keep meeting **somatostatin (SST)**, and now the full picture: it's the body's general **"quiet down"** signal. In the **pituitary** it inhibits **GH, TSH, ACTH, FSH, and LH**. But it's also made in the **pancreas** (where it dampens insulin and glucagon) and the **gut** (slowing digestion). It's so **labile** it barely reaches the bloodstream — a **paracrine** brake that acts right where it's released. When in doubt, somatostatin says **less**.



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