PRE-RELEASE RESOURCE FOR SNACK TWO OF FOUR
RELEASING [DATE TBD]

Amylin at a Glance

The Satiety Current: Amylin Biology as a Systems Signal

CME OUTFITTERS

Amylin isn't a new hormone — but it's a promising therapeutic current. Co-secreted with insulin, it signals satiety through the brainstem and even reaches reward circuits. Here's the mechanism mapped in four steps.

THE STORY IN FOUR STEPS

1 One cell, two signals

β-cell → Insulin + Amylin (fixed 1:100)

Released **together** from the β-cell. As β-cell function falls, **both** decline.

2 One receptor, many forms

Calcitonin receptor (CTR) + receptor activity-modifying protein (RAMP) 1/2/3 → **amylin receptor** $(AMY)_1$ / AMY_2 / AMY_3.

AMY_1 & AMY_3 are the weight-relevant complexes.

Receptor complexity **shapes each drug's unique effects on physiology and behavior**.

3 Where it acts

Brainstem — dorsal vagal complex (area postrema/nucleus of the solitary tract [AP/NTS]): satiation · ↓ gastric emptying · ↓ glucagon.

A brainstem satiety hub — the **same region** that drives nausea.

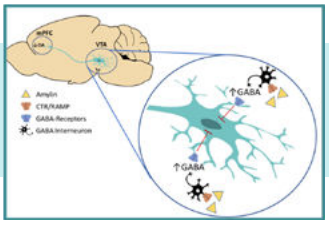
Mesolimbic Reward Nuclei → ↓ impulsive eating.

4 Two drug classes

Selective amylin analog ↔ dual amylin and calcitonin receptor agonists (DACRA)

Selective = better tolerated. DACRA = ↑ weight loss, but ↑ nausea, emesis, fatigue.

A question of balance: **efficacy vs. tolerability**.



THE REWARD ANGLE [PRECLINICAL]

BEYOND APPETITE: As an example, in the brain's reward center (VTA), amylin activates receptors on **gamma-aminobutyric acid (GABA) interneurons**, which turn **down** dopamine output to the striatum and prefrontal cortex — blunting **impulsive, food-directed** behavior, not just hunger.

Geisler CE, et al. *Biol Psychiatry*. 2024;95(10):938-950. Figure from Geisler CE, et al. *Biol Psychiatry*. 2024;95(10):938-950.

BEYOND "EAT LESS"

Meal-ending satiety	Acts as a satiation signal to the brain to terminate a meal (satiety).
Slowed gastric emptying	Prolonged fullness; flatter post-meal glucose curve.
Glucagon suppression	Glucose-dependent — dampens inappropriate post-meal glucagon.
Insulin sensitization	Improves insulin action at skeletal muscle.
Restored leptin sensitivity	Re-opens the brain's leptin response — the durability link.

> *"It's fortuitous that the amylin and GLP-1 systems are not the same — which means you can get combinatorial effects from the two together."*
>
> — Matthew R. Hayes, PhD
>
> ALBERT J. STUNKARD PROFESSOR IN PSYCHIATRY
> UNIVERSITY OF PENNSYLVANIA

PROGRAM COMING YOUR WAY...

FORMAT	~30 min video CME "Snack" — a moderated expert conversation
FACULTY	Matthew R. Hayes, PhD, with chair Robert F. Kushner, MD
AUDIENCE	Obesity-medicine, endocrinology, primary care & cardiometabolic clinicians (MD, NP, PA, PharmD)

LEARNING OBJECTIVES

Evaluate amylin's physiologic role in energy and glucose regulation, and assess how its receptor biology supports complementary therapeutic strategies.

THE SERIES AHEAD — FOUR SNACKS, ONE ARC

SNACK ONE
The multi-pathway rationale
Lee M. Kaplan, MD, PhD

SNACK TWO (NOW)
The biology of amylin
Matthew R. Hayes, PhD

SNACK THREE
Phenotypes & who benefits
Andres Acosta, MD, PhD

SNACK FOUR
Emerging therapies & the data
W. Timothy Garvey, MD

Chaired throughout by **Robert F. Kushner, MD** *— Northwestern University Feinberg School of Medicine. Emerging amylin agents are investigational; data are presented fair-balanced in later Snacks.*

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Key references: Chung CW, et al. *J Obes Metab Syndr*. 2026;35(1):38-48 · Geisler CE, et al. *Biol Psychiatry*. 2024;95(10):938-950 · Secher A, et al. *Nat Metab*. 2026;8(2):299-312 · Walker CS, et al. *Nat Rev Endocrinol*. 2025;21(8):482-494.