

# Hyperphagia

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# Our Family Story | 'The Why'

## A Mother's Instinct

Noticed persistent food-seeking behaviors and lack of satiety and satiation prior to 12 months old

## Clinical & Professional Lens

Registered Dietitian prior to Clara's birth with foundational knowledge of hyperphagia; proactively managing food environment and intake

## System Gaps in Care

Relocated across 4 states with access to major children's hospitals, yet no hyperphagia support without a Prader-Willi Syndrome diagnosis

## Profound Family Impact

Hyperphagia is the **greatest challenge to our family's quality of life** and the **largest barrier to Clara's independence**

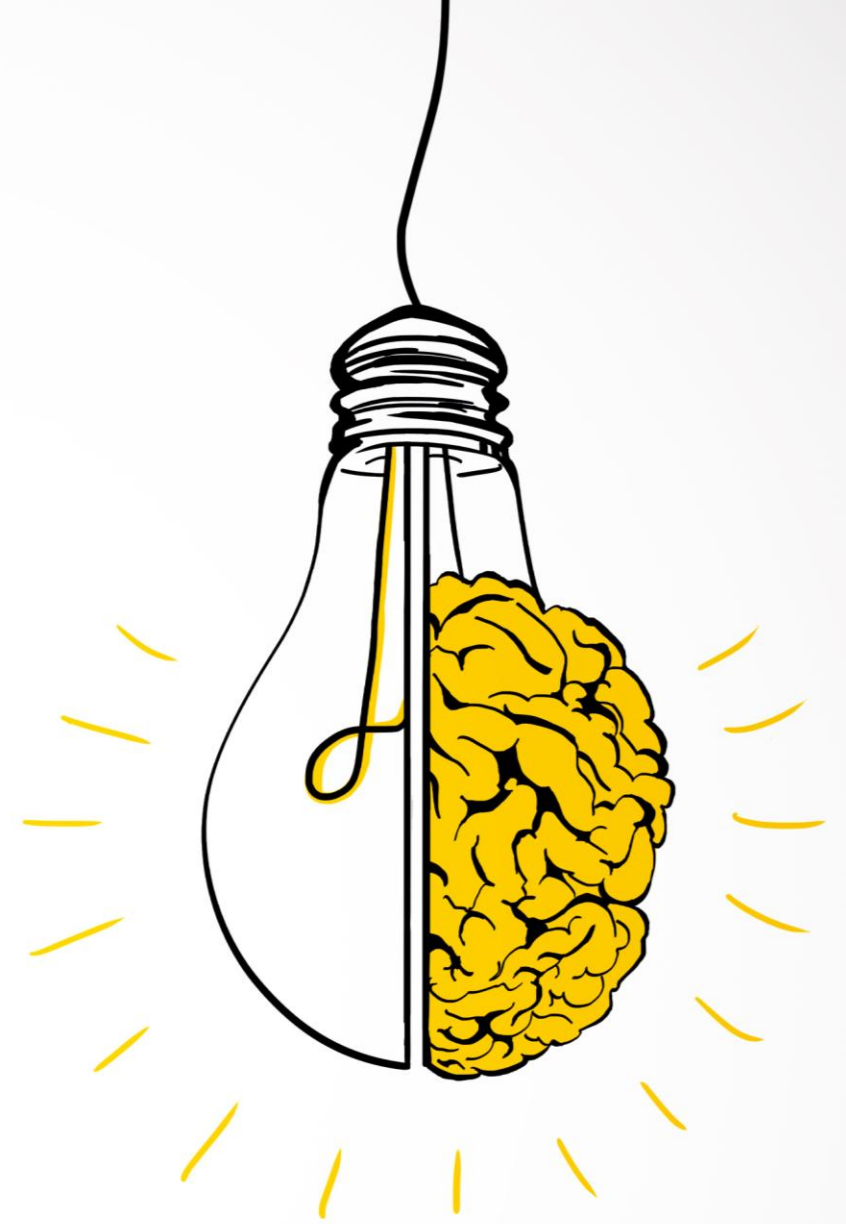
## Driving Purpose

Lived experience + clinical training + passion for prevention = commitment to **educate clinicians and empower parents/caregivers**

*(Continuing this work beyond LEND fellowship)*

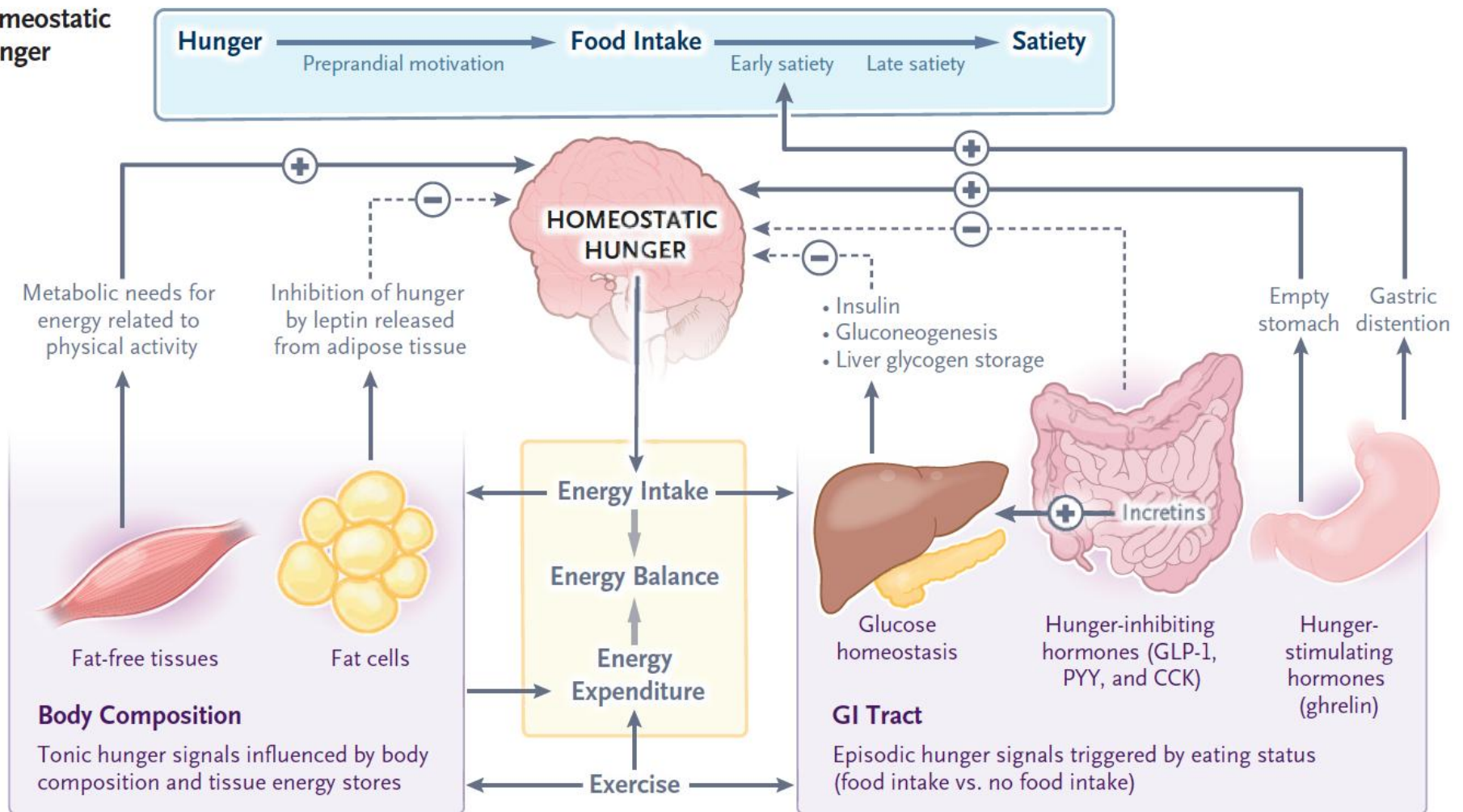
# Overview

- Mechanisms of Hunger
- Hyperphagia Defined
- Screening and Assessment
- Hyperphagia Conditions
- Patient + Caregiver Impact
- Clinician Recommendations
- Questions



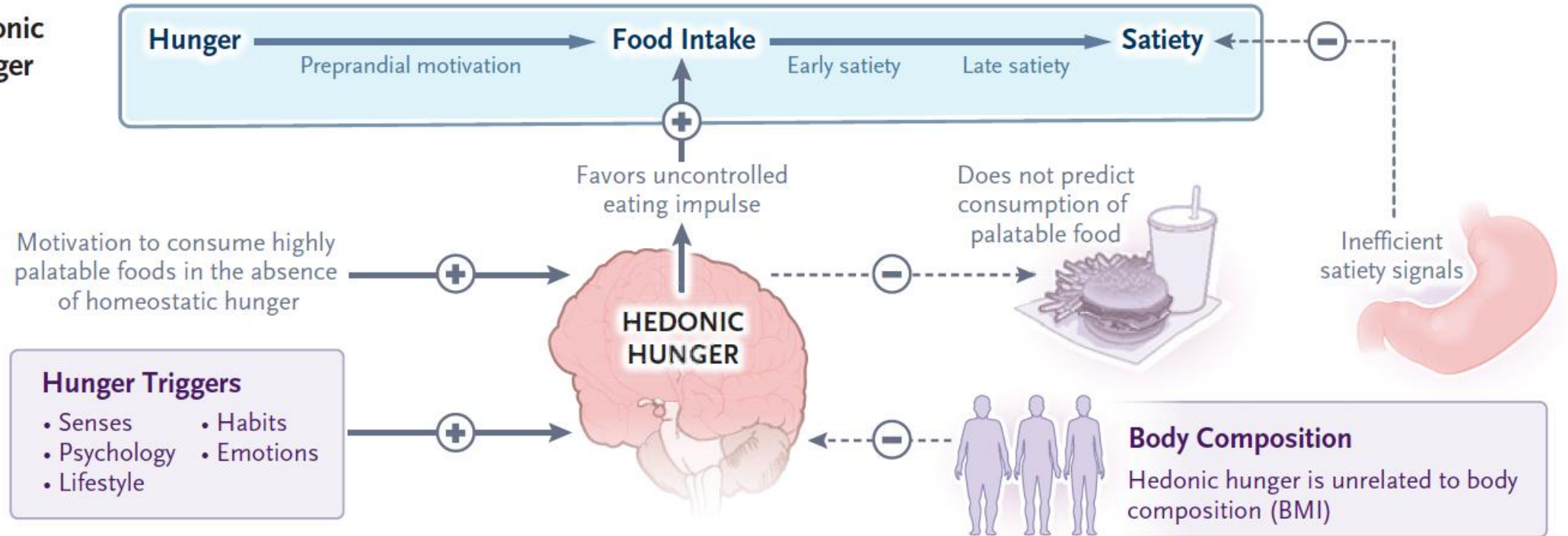
# Homeostatic Hunger

## A Homeostatic Hunger



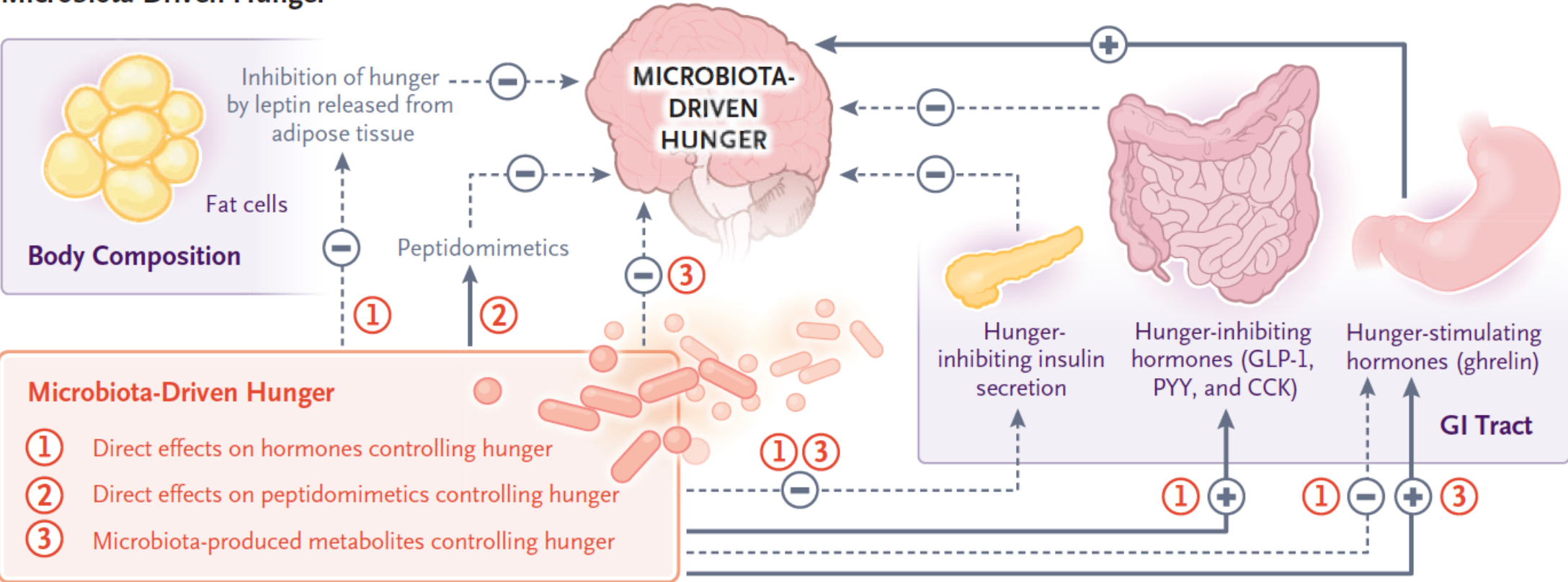
# Hedonic Hunger

## B Hedonic Hunger



# Microbiota Hunger

## C Microbiota-Driven Hunger



## Common Definitions



**Hunger:** physiological impulse to eat that is triggered by starvation (acute energy deprivation) to maintain energy balance



**Appetite (Hedonic Hunger):** food intake drive by pleasure rather than by metabolic necessity

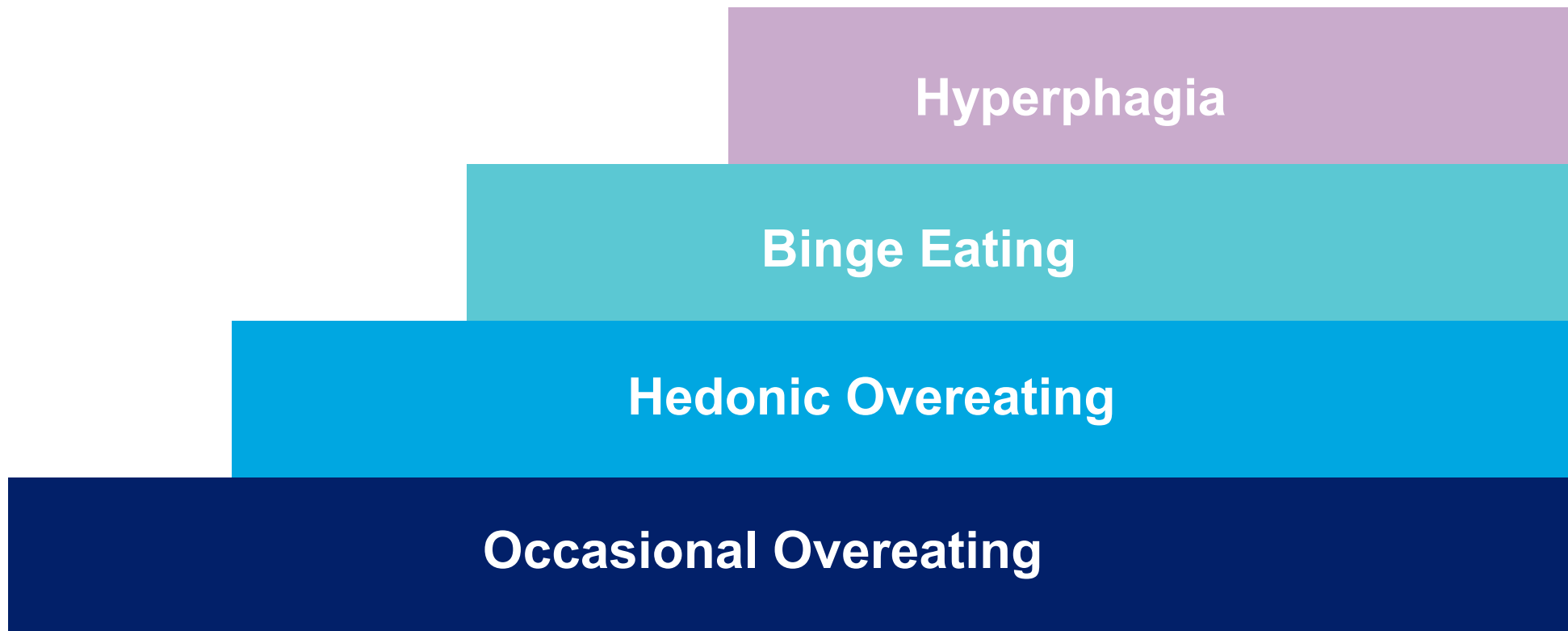


**Satiation:** feeling of fullness that occurs during a meal, causing you to stop eating (meal termination)



**Satiety:** suppression of hunger that lasts after a meal, determining the length of time until the next eating occasion

# Hunger Hierarchy



↑  
**SEVERITY**

***Obesity Week - Oct 2023  
Report Published 2025***

**“Defining Hyperphagia for  
Improved Diagnosis and  
Management of  
MC4R Pathway –  
Associated Disease:  
A Roundtable Summary”**

# **4 Key Deliverables**

- 1. Clear, standardized Definition**
- 2. Unified Underlying Pathology**
- 3. Previous Hyperphagia Assessments**
  - Questionnaires
- 4. Proposed Set of Questions for Hyperphagia screening**

## Definition | Symptoms

**Hyperphagia is an insatiable, pathologic desire to consume food that is accompanied by abnormal food seeking behaviors and impaired satiety.**

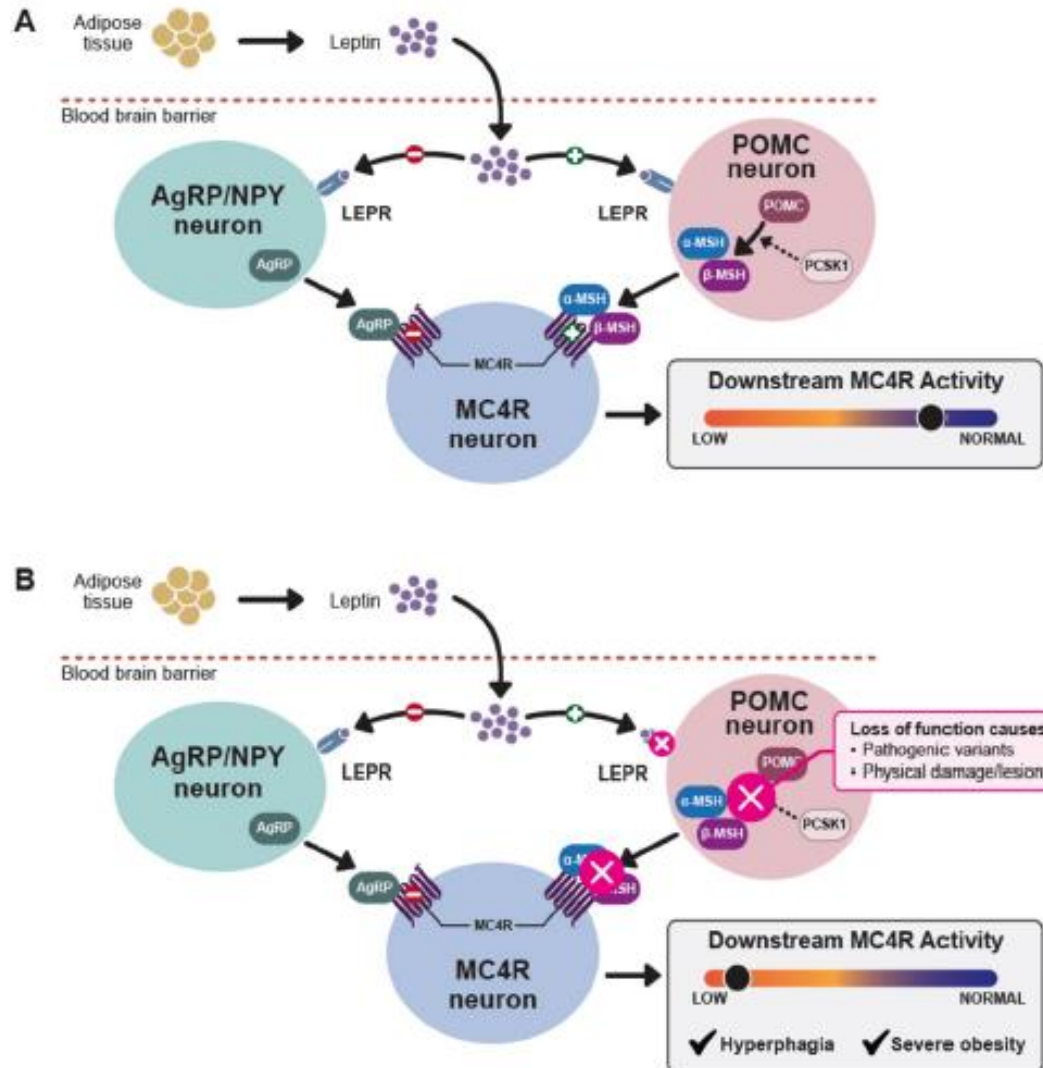
***\* Hyperphagia is a condition associated with rare obesity-related diseases***

- Severe preoccupation with food
- Lack of satiety or short duration to satiety
- Prolonged time to satiation
- Abnormal food-seeking behaviors (negotiating, perseverating, hoarding, hiding, sneaking)
- Lack of control with food consumption
- Waking at night (or very early morning) to eat
- Difficulty with work / school
- Tantrums, irritability, outburst over attempts at food restriction = “Food Anxiety”
- Rapid eating

**“It should be made clear that hyperphagia and its related behaviors cannot be willfully dismissed or overcome given they are driven by an underlying pathology.”**

# Unified Underlying Pathology

**Fig. 1** The hypothalamic melanocortin-4 receptor (MC4R) pathway. (A) MC4R signaling under physiological conditions. (B) Disruption of MC4R signaling



## (+) MC4R

- Decrease food intake (satiety)
- Increase energy expenditure

## (-) Constant Inhibition of MC4R

- Continuous food intake
- Decrease energy expenditure
- Severe Obesity

# Monogenetic Obesity

Caused by a single gene disorder

Typically, within or affecting the leptin signaling pathway

Presents as severe hyperphagia and obesity in early childhood

Non-Syndromic

## Syndromic Obesity

Single-gene disorders or contiguous gene deletions  
(subset of monogenic obesity)

Often includes intellectual disability, dysmorphic features, and multi-organ involvement, frequently presented hyperphasia or obesity onset

Early diagnosis enables anticipatory guidance, comorbidity screening and early obesity prevention counselling.

## Acquired Hypothalamic Obesity

Brain injury or damage to the hypothalamus

Can present with severe hyperphagia

Causes: trauma, tumors, surgery

Ex. Craniopharyngioma

# Hyperphagia Associated Obesity Gene Panel Sample | Not Comprehensive

Non-Syndromic versus Syndromic

## Non-Syndromic

Leptin (LEP)

Leptin Receptor (LEPR)

MC4R

POMC

PCSK1

CPE

BDNF

NTRK2

## Syndromic

Prader Willi syndrome

Prader Will like / Temple Syndrome (upd14, sim1, magel2)

16p11.2 deletion syndrome

Pseudohypoparathyroidism

Bardet Biedl syndrome

Alstrom syndrome

Cohen syndrome

WAGR(O)/11p deletion

Smith-Magenis syndrome

ADCY3

145 **Hyperphagia following childhood acute lymphoblastic leukemia: a symptom worth heeding.**

Cite Satyanarayana S, Cummings EA, Fernandez CV, Barnard D.  
Clin Pediatr (Phila). 2006 Apr;45(3):271-3. doi: 10.1177/00099  
PMID: 16708142 No abstract available.

8 **Hypothalamic Hyperphagia in the Hospice Patient: Case Report**

Cite Joseph P, Dixon J, Marks A.  
J Pain Symptom Manage. 2025 Feb;69(2):e147-e149. doi: 10.1016/j.jpainsym  
2024 Nov 2

85 **Two patients with chromosome 22q11.2 deletion presenting with childhood obesity and hyperphagia.**

Cite Bassett JK, Chandler KE, Douzgou S.  
Eur J Med Genet. 2016 Aug;59(8):401-3. doi:  
PMID: 27184501

143 **Prader-Willi-like phenotype** investigation of 1p36 deletion in 41 patients with delayed psychomotor development, hypotonia, obesity and/or hyperphagia, learning disabilities and behavioral problems.

Cite D'Angelo CS, Da Paz JA, Kim CA, Bertola DR, Castro CI, Varela MC, Koiffmann CP.

doi: 10.1016/j.ejmg.2006.02.001. Epub 2006 Mar 10.

110 **Hyperphagia** mild developmental delay but apparently no structural brain anomalies in a boy without SOX3 expression.

Cite Helle JR, Barøy T, Misceo D, Braaten Ø, Fannemel M, Frengen E.

136 **Detailed phenotype-genotype study in five patients with chromosome 6q16 deletion: narrowing the critical region for Prader-Willi-like phenotype.**

Cite Bonaglia MC, Ciccone R, Gimelli G, Gimelli S, Marelli S, Verheij J, Giorda R, Grasso R, Borgatti R, Pagone F, Rodríguez L, Martínez-Frias ML, van Ravenswaaij C, Zuffardi O.

“...hyperphagia remains underrecognized and as a result is underdiagnosed.”

# Screening & Assessment Challenges

## Caregiver / Parent + Patient

Parents of a single child / new parents may not recognize abnormal behaviors in their children because no basis for comparison.

Parents of caregivers have implemented compensatory lifestyle and dietary restrictions

Co-occurrence with genetic diagnosis with neurocognitive impairment, preventing ability to self report.

## Clinicians

Physicians and clinicians are often not familiar with or educated on hyperphagia

Pediatric Setting – mistaken by clinicians (and parents and caregivers) as an indication of a healthy appetite needed for growing child

Physicians who do recognize abnormal eating or food seeking behaviors are challenged by not understanding what questions to ask

**Improve hyperphagia identification through clinician and caregiver education, paired with standardized, efficient clinic-based screening**

# Screening | Questionnaires

**A Standard Questionnaire for screening hyperphagia has not been established.**

## 1. Proposed Screening Questions for Hyperphagia

- Developed by Obesity Society in 2023
- Designed to bridge screening gap between PWS and other MC4R pathway - associated diseases

## 2. Dykens Hyperphagia Questionnaire

- Validated for hyperphagia **diagnosis** in PWS
- Measures frequency and severity of hyperphagic behaviors
- Used (not validated) in other MC4R pathway - associated diseases
- Tool for screening - not diagnosis - when hyperphagia is suspected

**Table 3 A Proposed Set of Questions to Screen for Hyperphagia [15]<sup>a</sup>**

**Questions of satiety**

- Do you ever feel full and how long does this feeling last?
  - How long after a meal do you feel hungry again?
  - Do you eat past feeling full?
- What causes you to stop eating?
- How long do you usually go between meals?
- Can you skip meals?
- How often do you eat meals/snacks?

**Preoccupation with food**

- Are you anxious if food is restricted or withheld from you or if you cannot find or access food?
- Is food locked away from you by your spouse, parents, or roommates?
- Do you miss out on certain activities or hobbies you otherwise like because you are thinking of food or eating?

**Abnormal food behaviors**

- Have you ever eaten food out of the garbage or rotten food?
- Have you ever eaten things that are not usually considered food, like paper, crayons, or carpet?
- Have you hidden, hoarded, or eaten food in secret?
- Do you wake up at night to eat food?
- Have you ever stolen food or stolen money to buy food?
- How often is disturbed eating behavior present: always, sometimes, exceptionally, never?

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<sup>a</sup>Questions should be updated to accommodate “your child” for the case of parent’s and/or caregiver’s report

# Hyperphagia Questionnaire – Dykens (2007)

Hyperphagia and Impulsivity, Arnouk et al. - 2024

**Purpose:** Can help screen for severe hyperphagia in children with early-onset obesity

**Administered By:** A primary caregiver or parent

**Format:** 13 questions, each scored 0-5 (0-not present, 5=severe)

**Total Score:** A total score >19 indicates a diagnosis of hyperphagia

**Focus:** The HQ measures observable behaviors and food-related preoccupations, not just appetite

# Hyperphagia Questionnaire

## Hyperphagia in Prader-Willi Syndrome, Dykens et al. - 2007

Hyperphagia in Prader-Willi Syndrome, Dykens et al.

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### Appendix A. Hyperphagia Questionnaire

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- (1) How upset does your child generally become when denied a desired food?
- Not particularly upset at all
  - A little upset
  - Somewhat upset
  - Very upset
  - Extremely upset
- (2) How often does your child try to bargain or manipulate to get more food at meals?
- A few times a year
  - A few times a month
  - A few times a week
  - Several times a week
  - Several times a day
- (3) Once your child has food on their mind, how easy is it for you or others to re-direct your child away from food to other things?
- Extremely easy, takes minimal effort to do so
  - Very easy, takes just a little effort to do so
  - Somewhat hard, takes some effort to do so
  - Very hard, takes a lot of work to do so
  - Extremely hard, takes sustained and hard work to do so
- (4) How often does your child forage through the trash for food?
- Never
  - A few times a year
  - 1-2 times a month
  - 1-3 times a week
  - 4 to 7 times a week
- (5) How often does your child get up at night to food seek?
- Never
  - A few nights a year
  - 1-2 nights a month
  - 1-3 nights a week
  - 4 to 7 nights a week
- (6) How persistent is your child in asking or looking for food after being told "no" or "no more"?
- Lets go of food ideas quickly and easily
  - Lets go of food ideas pretty quickly and easily
  - Somewhat persistent with food ideas
  - Very persistent with food ideas
  - Extremely persistent with food ideas
- (7) Outside of normal meal times, how much time does your child spend talking about food or engaged in food-related behaviors?
- Less than 15 minutes a day
  - 15 to 30 minutes a day
  - 30 minutes to an hour
  - 1 to 3 hours a day
  - more than 3 hours a day
- (8) How often does your child try to steal food (that you are aware of)?
- A few times a year
  - A few times a month
  - A few times a week
- 

Hyperphagia in Prader-Willi Syndrome, Dykens et al.

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### Appendix A. Continued

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- Several times a week
  - Several times a day
- (9) When others try to stop your child from talking about food or engaging in food-related behaviors, it generally leads to:
- No distress or upset
  - Mild distress or upset
  - Moderate distress or upset
  - Severe distress or upset
  - Extreme distress, behaviors can't usually be stopped
- (10) How clever or fast is your child in obtaining food?
- Not particularly clever or fast
  - A little clever or fast
  - Somewhat clever or fast
  - Very clever or fast
  - Extremely clever or fast
- (11) To what extent to food-related thoughts, talk, or behavior interfere with your child's normal daily routines, self-care, school, or work?
- No interference
  - Mild interference; occasional food-related interference in completing school, work, or hygiene tasks
  - Moderate interference; frequent food-related interference in completing school, work, or hygiene tasks
  - Severe interference; almost daily food-related interference in completing school, work, or hygiene tasks
  - Extreme interference, often unable to participate in hygiene tasks or to get to school or work due to food-related difficulties
- Additional items:
- (12) How old was your child when they first showed an increased interest in food?
- (13) How variable is your child's preoccupation or interest in food?
- Hardly ever varies
  - Usually stays about the same
  - Goes up and down occasionally
  - Goes up and down quite a lot
  - Goes up and down all the time
-

# Assessment | Questionnaires

## 1. Dykens Hyperphagia Questionnaire

- Developed and validated for in PWS, previously reviewed as screening tool for MC4R diseases

## 2. Hyperphagia Questionnaire for Clinical Trials (HQ-CT)

- Developed for clinical trials of PWS
- Looks at treatment efficacy

## 3. **NEW (2025) – Proposed diagnostic tool for MC4R Pathway Diseases**

- Symptoms of Hyperphagia (SoH): Caregiver Version (Observer-Reported)
- Impacts of Hyperphagia (IoH): Caregiver Version (Observer-Reported)
- Impacts of Hyperphagia (IoH): Caregiver Version (Self-Reported)
- Validated in Bardet-Biedl Syndromes (BBS) as a model for MC4R pathway diseases

## Hyperphagia Questionnaire – Clinical Trials (HQ-CT)

**Purpose:** Measures the frequency and intensity of food-related behaviors in PWS patients

**Administered By:** A primary caregiver or parent, *past two weeks*

**Format:** 9 questions, each scored 0-4 (0-not present, 4=severe)

**Total Score:** Ranges from 0-36; higher scores indicate greater hyperphagia

**Focus:** Observable behaviors like food-seeking, talking about food, and emotional outburst related to food denial

# Symptoms of Hyperphagia (SoH) | Impacts of Hyperphagia (IoH)

Pomeroy et al. (2025)

**Table 1** Characteristics of Symptoms of Hyperphagia and Impacts of Hyperphagia – Caregiver version

	<b>Symptoms of Hyperphagia: Caregiver Version (Observer-Reported)</b>	<b>Impacts of Hyperphagia: Caregiver Version (Observer-Reported)</b>	<b>Impacts of Hyperphagia: Caregiver Version (Self-reported)</b>
<b>Items</b>	How often did the person in your care... 1. Try to negotiate or argue for more food than provided 2. Eat extremely quickly 3. Sneak or take food without permission 4. Wake up asking or looking for more food during the night 5. Ask for more food after just finishing a meal or snack	To what extent did the person in your care's hunger negatively affect his/her... 1. Sleep 2. Mood/emotion 3. School 4. Leisure or recreational activities 5. Relationships with family/friends	To what extent did the person in your care's hunger negatively affect your... 1. Sleep 2. Mood/emotion 3. Work 4. Leisure or recreational activities 5. Relationships with family/friends
<b>Recall period</b>	Past 24 h	Past 7 days	Past 7 days
<b>Response options</b>	0 = Never 1 = One to two times 2 = Three times or more	0 = Not at all 1 = A little 2 = Moderately 3 = A great deal	0 = Not at all 1 = A little 2 = Moderately 3 = A great deal
<b>Scoring<sup>a</sup></b>	Total score divided by the number of items answered; range: 0–2	Total score divided by the number of items answered; range: 0–3	Total score divided by the number of items answered; range: 0–3

<sup>a</sup>Higher scores indicate greater severity and impact

# Hyperphagia Clinical Complications

**Severe Obesity &  
Rapid Weight Gain**

**Metabolic  
Dysfunction:**  
Type 2 diabetes,  
insulin resistance,  
dyslipidemia

**Cardiovascular  
Disease:**  
Hypertension,  
increased cardiac risk

**Respiratory  
Complications:**  
Obstructive sleep  
apnea,  
hypoventilation

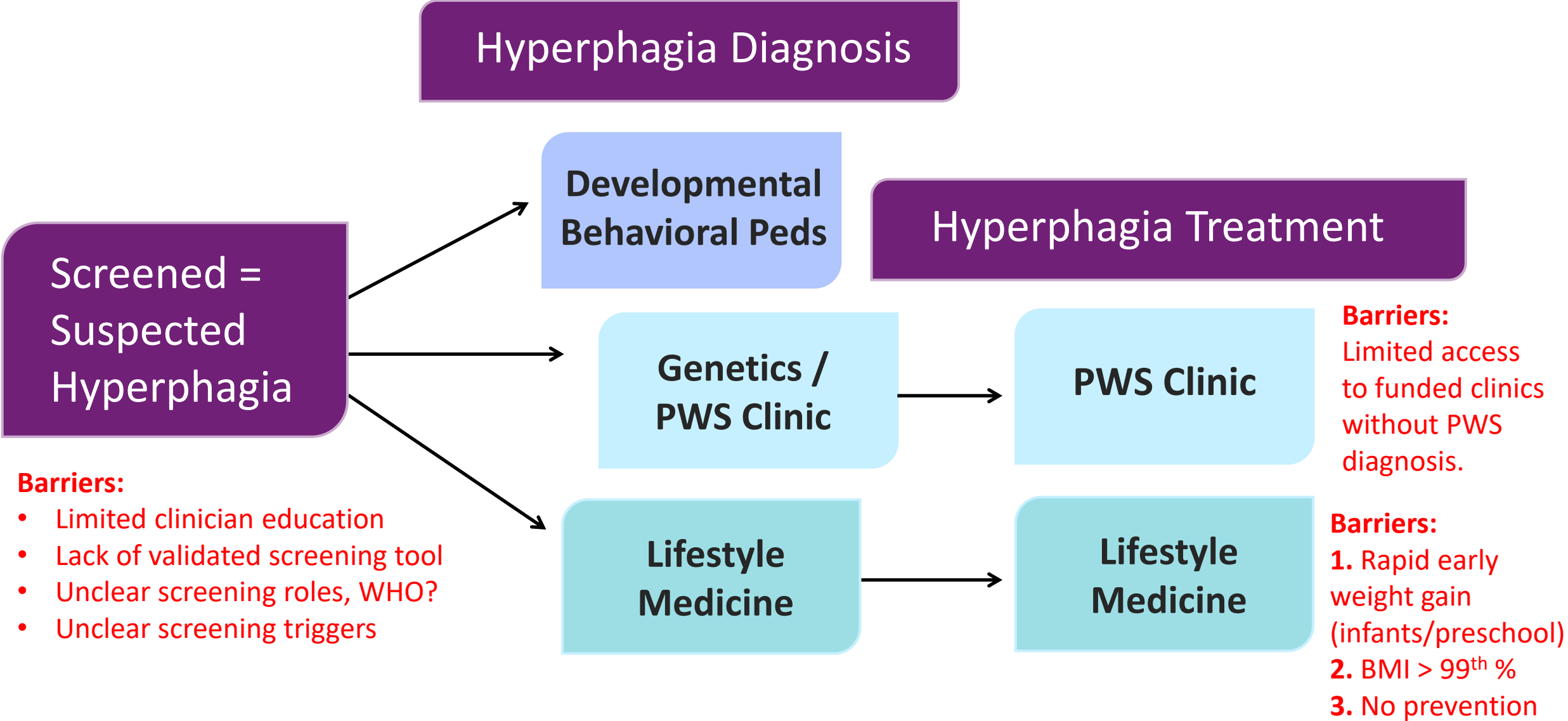
**Life-Threatening  
Complications  
(PWS):**

- Choking due to rapid eating
- Gastric rupture/perforation

**Endocrine  
Dysregulation:**  
Impaired satiety  
signaling, hormonal  
imbalance

**Musculoskeletal  
Impact:**  
Reduced mobility,  
joint stress

# Children's Hospital Current State



**BORN  
DIFFERENT**

**"It's hard feeling hungry all the time.  
It gives me anxiety"**



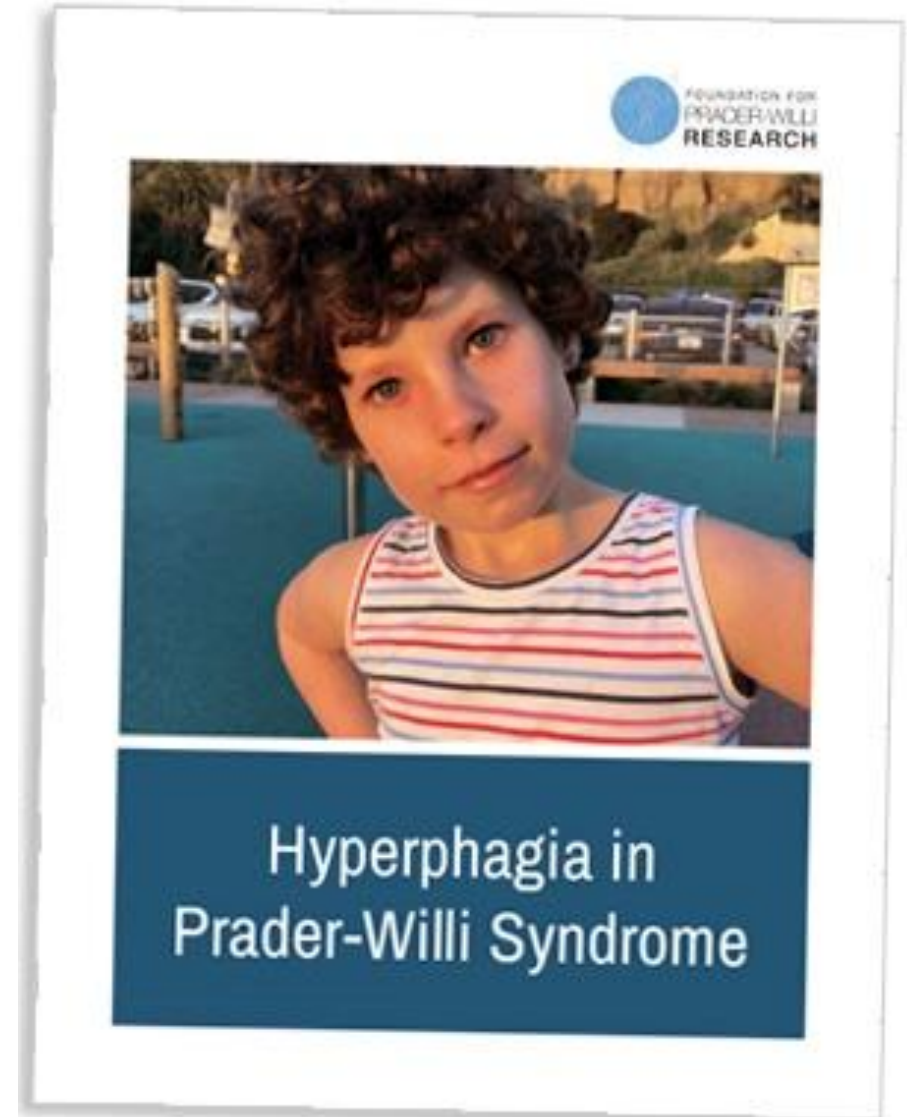
## Navigating Life with Prader-Willi Syndrome | Kelly & Clementine's Journey



[MORE VIDEOS](#)

## Impact on Patient Quality of Life

- Persistent Hunger & Food Preoccupation
- Emotional Distress
- Behavioral Dysregulation
- Social Challenges
- Reduced Autonomy
- Cognitive & Academic Impact



## Impact on Caregiver and Family Quality of Life

- Constant Vigilance & Environmental Control
- Emotional and Psychological Strain
- Behavioral Conflict & Relationship Strain
  - Marriage, Siblings, Child-Parent
- Social Isolation
- Financial & Occupational Impact
- Cognitive Load & Decision Fatigue
- Mental Health



## Impact on Caregiver and Family Quality of Life, Cont.

“The hard part is worrying about food. It is sickening. It is tiring. I hate it. I hate everything about food.”

“She is not compatible with the world. She is really smart, but she can't control the food behavior so that takes away all opportunity.”

“I am tired of living a separate life from my husband. One of us is always on duty and it's like we live two separate lives.”

“Hyperphagia is the relentless, overwhelming, life-threatening force, which sentences people with PWS [and other hyperphagia syndromes] to a frustrated lifetime of control and restricted lifestyle, denying them the possibility of achieving any independence or realization of hopes of fulfillment of capabilities, all common human instincts.”

# Managing Hyperphagia

## A Practical Guide for Parents

**Hyperphagia is an insatiable, pathologic desire to consume food that is accompanied by abnormal food seeking behaviors.** This means **structure** and **supervision** are essential to successfully navigate the food environment and to manage food safely.

### The Foundation: Food Security

**Food Security** is defined as the *ready availability of nutritionally adequate and safe foods with an assured ability to acquire acceptable foods in socially acceptable ways.*

**Food Security is the most important tool for managing hyperphagia.** When food is predictable and controlled, anxiety decreases, behavior improves, and weight is better managed.

#### The 3 Rules of Food Security:

1. **No Doubt:** when meals will occur and what foods to be served
2. **No Hope:** of getting anything different from what is planned
3. **No Disappointment:** related to false expectations

#### Main Benefits:

1. **Reduced Anxiety:** Knowing the food schedule lowers perseveration over food
2. **Physical Health:** Prevents rapid, dangerous weight gain and obesity
3. **Better Behavior:** Reduces frustration and behavioral issues related to food seeking

# Indirect Calorimetry (IC) in Hyperphagia-Related Syndromes

## Relevance

- Hyperphagia-related syndromes (e.g., PWS, BBS, hypothalamic obesity) often present with:
  - ↓ Resting Energy Expenditure (REE)
  - Altered body composition (↓ lean mass, ↑ fat mass)
- Standard predictive equations frequently **overestimate caloric needs**

## IC Provides

- Direct measurement of **Resting Energy Expenditure (REE)**
- Individualized metabolic data vs. population-based estimates
- Objective foundation for **precision nutrition planning**

## Clinical Benefits

- Prevents **overfeeding** - reduces excess weight gain
- Avoids **over-restriction** - may decrease food preoccupation and behavioral escalation
- **Supports prevention** - safe, sustainable weight management



# Potential Approaches for Managing Hyperphagia

	Environmental control	Lifestyle intervention	Pharmacotherapies	Surgical intervention	Neurostimulation
Approaches	<ul style="list-style-type: none"> <li>• Expectations management</li> <li>• Regular meal times</li> <li>• Pantry/Refrigerator locks</li> <li>• Supervision when eating</li> </ul>	<ul style="list-style-type: none"> <li>• Dietary modifications</li> <li>• Increased physical activity</li> </ul>	<ul style="list-style-type: none"> <li>• Leptin</li> <li>• Topiramate</li> <li>• Metformin</li> <li>• Psychomotor stimulants</li> <li>• Oxytocin</li> <li>• Diazoxide choline controlled-release</li> <li>• GLP-1R agonists</li> <li>• Setmelanotide</li> </ul>	<ul style="list-style-type: none"> <li>• Metabolic and bariatric surgery</li> </ul>	<ul style="list-style-type: none"> <li>• Neurostimulation</li> <li>• Deep brain stimulation</li> </ul>
Rationale	<ul style="list-style-type: none"> <li>• Primarily used/efficacy shown in PWS</li> </ul>	<ul style="list-style-type: none"> <li>• Clinical practice guideline recommended for obesity</li> </ul>	<ul style="list-style-type: none"> <li>• Can provide personalized or targeted therapy</li> <li>• Clinical trials in multiple MC4R pathway diseases (setmelanotide)</li> </ul>	<ul style="list-style-type: none"> <li>• Can lead to weight loss in MC4R pathway diseases</li> </ul>	<ul style="list-style-type: none"> <li>• Potential for use in treatment-refractory patients</li> </ul>
Limitations	<ul style="list-style-type: none"> <li>• Does not address underlying hyperphagia</li> <li>• Limited evidence outside of PWS</li> </ul>	<ul style="list-style-type: none"> <li>• Does not address underlying hyperphagia</li> <li>• Limited efficacy in MC4R pathway diseases</li> </ul>	<ul style="list-style-type: none"> <li>• Some only effective in certain diseases (eg, leptin)</li> <li>• Limited or conflicting evidence of efficacy for most MC4R pathway diseases</li> </ul>	<ul style="list-style-type: none"> <li>• Insufficient studies on the effect on hyperphagia</li> <li>• Varied outcomes with limited long-term efficacy in MC4R pathway disease</li> </ul>	<ul style="list-style-type: none"> <li>• Experimental in MC4R pathway diseases</li> <li>• Evidence primarily case reports</li> </ul>

# Key Clinical Challenges in Hyperphagia Syndromes

- **Limited awareness and education** among clinicians and caregivers
- **Narrow association with Prader-Willi Syndrome (PWS)**, leading to under-recognition in other hyperphagia syndromes
- **Misconception that hyperphagia requires obesity:** patients may exhibit hyperphagia without being obese
- **Lack of validated, standardized screening tools** for early identification
- **Minimal clinical and community support systems**, if available at all
- **Reactive rather than preventive care models** resulting in preventable obesity and complications

# Hyperphagia: Key Clinical Takeaways

Hyperphagia Does Not Equal Obesity

Beyond Prader-Willi Syndrome (PWS)

Distinct Characteristics of Hyperphagia

- 1. Delayed satiation:** requires larger intake and prolonged eating to feel full
- 2. Impaired Satiety Signaling:** Short-lived fullness and rapid return of hunger
- 3. Persistent, Dysregulated Hunger:** Constant drive to eat, heightened response to food cues, food-seeking behaviors

# Thank You!

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