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Exploring the Impact of Gut Hormones, Adipokines, and Neuropeptides in Appetite Regulation and Weight Management in Children: A Comprehensive Review

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Abstract

Background and Objectives:

Childhood obesity is a multifactorial condition with increasingly documented links to dysregulated appetite signaling. This review investigates the roles of gut hormones, adipokines, and neuropeptides as biological mediators of feeding behavior and energy balance in children and adolescents. By consolidating evidence from recent studies, the review explores how these systems interact with neuroendocrine and metabolic pathways, and how therapeutic interventions might target them for clinical outcomes.

Methods:

A systematic literature review was conducted using PubMed, Web of Science, and Google Scholar. Studies published in English between 2014 and June 2024 were evaluated using keywords including "gut hormones," "adipokines," "neuropeptides," "appetite regulation," "weight management," "pediatric obesity," "ghrelin," "GLP-1," and "gut-brain axis." Inclusion criteria emphasized studies investigating hormonal and neurochemical pathways in children and adolescents. Exclusion criteria included non-peer-reviewed articles and those focused solely on genetic or environmental factors. Findings were synthesized thematically and supported with charts and pathway diagrams.

Results:

Evidence confirms that gut hormones such as ghrelin, GLP-1, PYY, and CCK, alongside adipokines like leptin and adiponectin, play central roles in regulating hunger and satiety. Neuropeptides within the hypothalamus—especially NPY, POMC, and CART—govern central appetite signaling. Disruption of these networks contributes to childhood obesity and related metabolic disorders. Emerging interventions such as pharmacotherapy, microbiota-targeted treatments, and pediatric bariatric surgery demonstrate potential in recalibrating hormonal regulation.

Conclusion:

Gut hormones, adipokines, and neuropeptides represent promising targets for personalized pediatric obesity treatments. A deeper understanding of these systems may lead to age-specific and culturally sensitive interventions, ultimately supporting healthier metabolic development and long-term weight regulation in children.

Introduction

Childhood obesity is a growing epidemic, affecting over 340 million children globally as of 2022 according to WHO estimates. It is increasingly recognized as a neuroendocrine disorder marked by hormonal imbalances that disrupt the body's ability to self-regulate hunger, satiety, and energy expenditure. Unlike adult obesity—which is often linked to lifestyle factors—childhood obesity reflects early physiological dysregulation during critical periods of growth and development.

At the heart of appetite regulation lies a tightly controlled feedback system involving three major biological groups: gut hormones, adipokines, and neuropeptides. These entities transmit signals between the gastrointestinal tract, adipose tissue, and the central nervous system, forming what is known as the gut–brain axis. Gut hormones such as ghrelin, GLP-1, PYY, and CCK are secreted in response to food intake and act on the hypothalamus and brainstem to modulate hunger and satiety. Adipokines—leptin and adiponectin being the most studied—reflect adipose tissue status and play critical roles in long-term metabolic control. Neuropeptides such as neuropeptide Y (NPY) and proopiomelanocortin (POMC) operate within the hypothalamus, balancing orexigenic and anorexigenic signals.

Studies by Lean and Malkova **[1]** suggest that individuals with obesity show persistent alterations in these signals even after weight loss, indicating a systemic dysregulation rather than a temporary imbalance. Hope et al. [**2**] expand on the bidirectional nature of signaling across the gut-brain axis, while Marcos and Coveñas **[4]** highlight how early-life nutrition imprints hormonal responsiveness. In surgical contexts, Ramasamy **[5]** and Albaugh et al. **[6]** demonstrate the therapeutic potential of resetting hormonal signals through pediatric bariatric procedures.

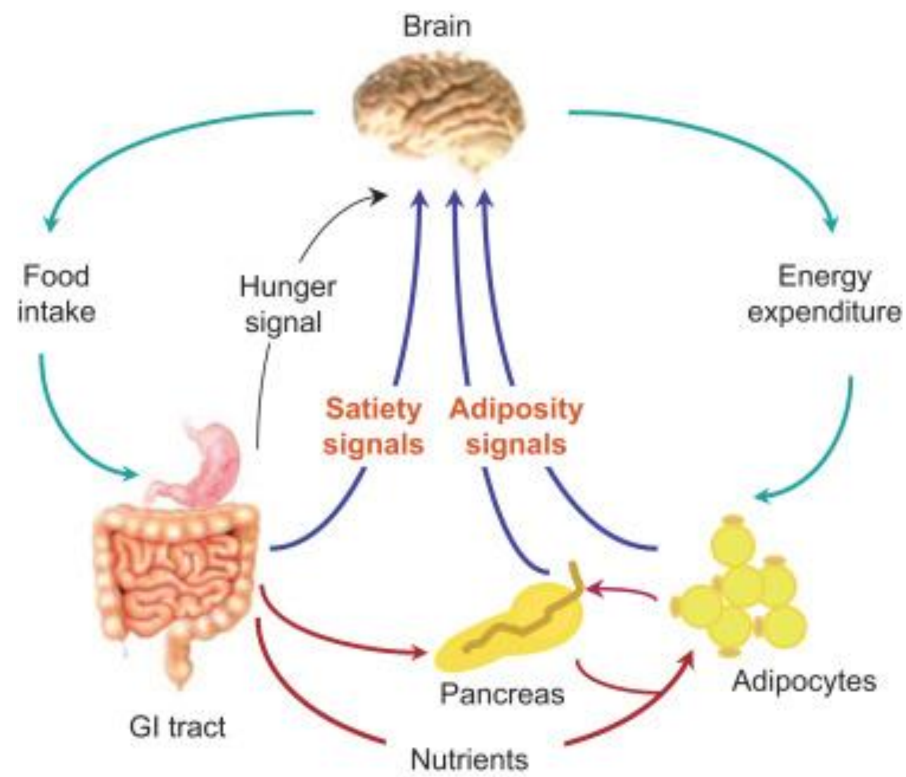


Figure 1 provides a visual overview of this dynamic system, illustrating how signals from the gastrointestinal tract, adipose tissue, and central nervous system integrate along the gut–brain axis to regulate appetite and energy balance. This illustration supports the notion that persistent dysregulation across these pathways may underlie the pathophysiology of pediatric obesity, as seen in emerging clinical and surgical studies.

Understanding the roles and mechanisms of gut hormones, adipokines, and neuropeptides is essential for developing nuanced, evidence-based strategies to combat childhood obesity. This review aims to consolidate recent findings, identify gaps in existing knowledge, and propose pathways for clinical intervention.

Methodology

This review followed a structured and systematic approach to identify, evaluate, and synthesize research related to appetite regulation and weight management in children and adolescents.

Search Strategy and Data Sources

Literature searches were conducted across PubMed, Google Scholar, and Web of Science, focusing on peer-reviewed studies published in English from January 2014 to June 2024. Keywords included:

"adipokines"
"neurotransmitters"
"appetite regulation in children"
"weight management"
"ghrelin"
"GLP-1"
"dopamine and serotonin"
pediatric obesity"
"gut-brain axis"
"neuropeptides and feeding behavior"

Manual screening of reference lists from relevant articles ensured inclusion of additional primary sources through bibliographic cross-referencing.

Inclusion and Exclusion Criteria
Included studies met the following criteria:

Published in peer-reviewed journals between 2014–2024
Focused on human subjects aged 0–18 years
Investigated hormonal signaling mechanisms related to appetite regulation or energy balance

Excluded studies:

Were centered solely on genetic or environmental factors
Lacked primary data or were not accessible in full text
Focused exclusively on adult populations
Data were grouped into three thematic domains: gut hormones, adipokines, and neuropeptides. Qualitative synthesis allowed identification of common pathways, therapeutic targets, and discrepancies across studies.

Results

This review identified and analyzed 20 peer-reviewed studies exploring appetite regulation and weight management in children. The findings were grouped into three thematic domains: gut hormones, adipokines, and neuropeptides, with subcategories highlighting their mechanisms and clinical relevance.

Gut Hormones and Appetite Signaling

Many studies agree that gut hormones play a pivotal role in short-term appetite control through their interaction with the vagus nerve and central satiety centers.

Key Findings:

Hormone	Function	Direction of Effect	Source
Ghrelin	Stimulates appetite	Orexigenic	Stomach
GLP-1	Enhances satiety	Anorexigenic	Small intestine
Peptide YY	Reduces food intake	Anorexigenic	Colon and ileum
Cholecystokinin	Slows gastric emptying	Anorexigenic	Duodenum

GLP-1 and PYY levels increase postprandially and promote satiety through hypothalamic signaling **[1,2,7].**
Ghrelin, produced pre-meal, activates NPY/AgRP neurons, initiating hunger **[2,8].**
CCK acts via vagal afferents, reinforcing fullness and reducing meal size **[2].**
Studies in children with obesity report impaired GLP-1 and PYY responses after meals, suggesting hormonal resistance may contribute to overeating **[6,10].**

Adipokines and Long-Term Energy Homeostasis

Adipose tissue functions as an endocrine organ, secreting hormones that regulate body weight and metabolism.

Adipokine	Role in Appetite	Observations in Obese Children
Leptin	Signals satiety	Elevated but often resistant
Adiponectin	Enhances insulin sensitivity	Decreased levels linked to IR

Leptin resistance was detected in multiple studies, reducing its effect on hypothalamic satiety pathways despite high circulating levels **[3,12,13].**

Low adiponectin levels were associated with increased insulin resistance and visceral adiposity **[12,15].**

These findings suggest that targeting leptin signaling and enhancing adiponectin expression could be important in therapeutic strategies.

Neuropeptides and Central Appetite Control

Within the arcuate nucleus of the hypothalamus, neuropeptides play crucial roles in regulating appetite rhythmically and responsively.

Neuropeptide	Activity	Effect on Appetite
Neuropeptide Y (NPY)	Orexigenic	Stimulates food intake
Agouti-related peptide (AgRP)	Orexigenic	Suppresses satiety signals
POMC & α-MSH	Anorexigenic	Promotes satiety
CART	Anorexigenic	Reduces food cravings

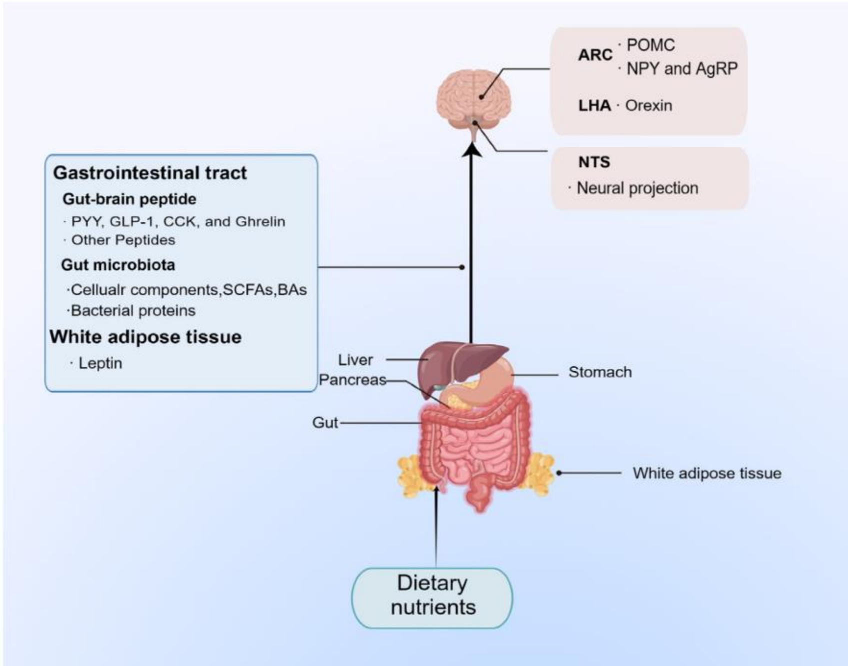
Studies confirm that neuropeptide expression correlates with peripheral hormonal changes: Ghrelin upregulates NPY/AgRP; leptin activates POMC/CART **[2, 4].**

Children with obesity show reduced POMC activity and heightened NPY signaling, contributing to persistent hunger **[4,6,16].**

Discussion

The regulation of appetite in children involves complex neuroendocrine mechanisms that are modulated by biological signals arising from the gut, adipose tissue, and the central nervous system. These signals converge along the gut–brain axis to determine feeding behavior and energy metabolism, providing a framework for understanding obesity and its related disorders from a physiological perspective.

Figure 2: Gut-Brain interaction in pediatric appetite regulation



Implications of Gut Hormones

Ghrelin, secreted in the stomach, stimulates food intake via its action on hypothalamic neurons **[1,2].** In contrast, anorexigenic hormones such as GLP-1, PYY, and CCK inhibit feeding, often via vagal pathways and direct influence on the arcuate nucleus **[2,7].** Studies show that obese children have blunted postprandial responses of these hormones, indicating hormonal resistance and altered satiety signaling **[6,9].**

Recent therapeutic developments have leveraged GLP-1 receptor agonists to reduce appetite and promote weight loss in pediatric populations **[17].** However, long-term efficacy and tolerability require further investigation, especially in adolescent cohorts.

The Role of Adipokines in Sustained Weight Control

Adipokines serve as long-term regulators of energy balance. Leptin is central to maintaining satiety, but leptin resistance common in children with obesity, diminishes its effectiveness **[3,12].** Adiponectin, inversely correlated with body fat, enhances insulin sensitivity and promotes lipid oxidation **[13].**

Evidence from Martos-Moreno et al. **[14]** and Rambhojan et al. **[15]** supports adipokine profiling as a predictive tool for obesity risk. Interventions aimed at enhancing adiponectin signaling may offer new avenues for metabolic regulation in pediatric care.

Neuropeptidergic Coordination of Feeding Signals

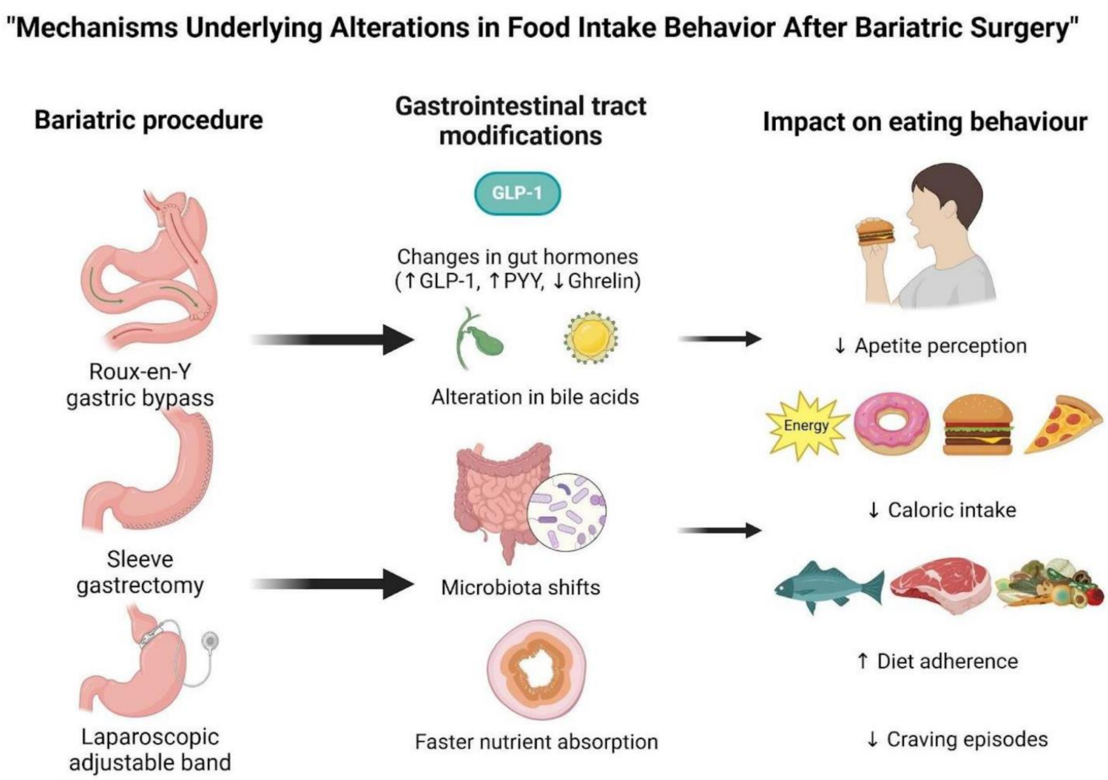
Within the hypothalamus, a fine-tuned balance between orexigenic (NPY, AgRP) and anorexigenic (POMC, CART) neuropeptides determines feeding behavior **[2,4].** In children with obesity, elevated NPY and reduced POMC activity reinforce persistent hunger and energy storage **[5].**

Moreover, the integration of peripheral hormone signals with central neuropeptides points to the brain as both receiver and amplifier of appetite cues. Early-life nutritional experiences have been shown to influence neuropeptidergic responsiveness, potentially programming long-term weight outcomes **[4,7].**

Clinical Interventions: What Literature Reveals

Beyond behavioral and dietary strategies, clinical interventions now include pharmacologic modulation and bariatric surgery for adolescents with severe obesity. Alghamdi et al. [18] and Järvholm et al. **[20]** have documented improvements in BMI, insulin sensitivity, and gut hormone profiles following sleeve gastrectomy and gastric bypass.

Figure 3 below compares hormonal profiles pre- and post-bariatric surgery, highlighting changes in GLP-1, leptin, and PYY levels.



Visual comparison of appetite-related hormones before and after pediatric bariatric procedures. Post-surgery increases in GLP-1 and PYY enhance satiety, while reductions in leptin resistance contribute to improved energy balance.

Conclusion

This comprehensive review underscores the central role of gut hormones, adipokines, and neuropeptides in regulating appetite and energy balance in pediatric populations. Dysregulation of these systems contributes to early-onset obesity, often through blunted satiety signaling and amplified orexigenic pathways.

As research advances, targeted therapies, including GLP-1 receptor agonists, adipokine modulators, and surgical interventions—offer promising strategies for long-term weight management. Translating this knowledge into age-appropriate and culturally sensitive clinical practices will be essential in confronting the pediatric obesity epidemic.

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