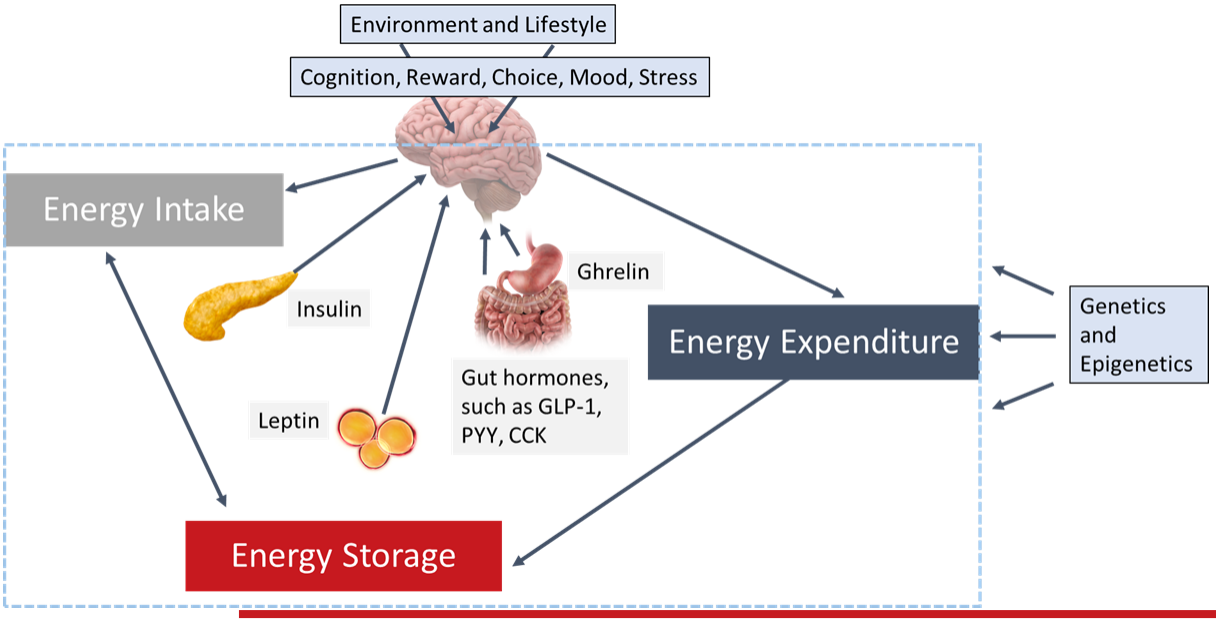
OBESITY PATHOPHYSIOLOGY

Obesity is a chronic disease with a multifactorial origin

Obesity is a chronic, relapsing and progressive disease driven by the interaction of multiple factors beyond food intake and physical activity, many of which are beyond an individual's control. These include biologic factors, genetic factors, environmental influences, and social determinants of health. The heritability of body weight has been estimated at 40-77%.

The brain plays a central role in body weight regulation

The central nervous system (CNS) plays a major role in regulating food intake, energy expenditure and body weight in response to peripheral signals, such as leptin, insulin, glucagon-like peptide 1 [GLP-1], peptide YY [PYY], cholecystokinin [CCK] and ghrelin. Emerging data suggests that the neuroendocrine regulation of CNS pathways involved with food intake and body weight may be disrupted in obesity.



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UCONN RUDD CENTER FOR FOOD POLICY AND HEALTH

Lilly

Weight reduction can improve obesity-related complications

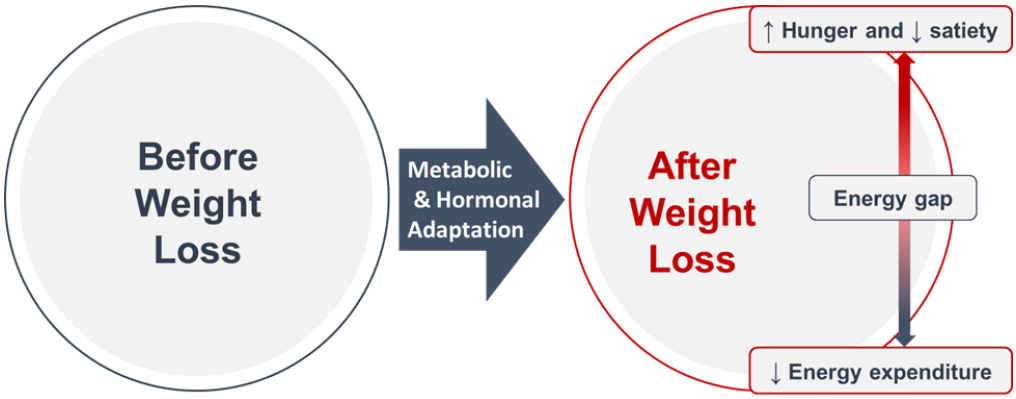
Obesity affects all organ systems, contributing to over 200 complications including type 2 diabetes (T2D), hypertension, hyperlipidemia, cardiovascular disease, obstructive sleep apnea, and certain types of cancer. In obesity, adipose tissue dysfunction can lead to elevated circulating lipids, ectopic fat deposition (in organs like the pancreas, liver, kidney, heart, and skeletal muscle), local and systemic inflammation, and insulin resistance. Weight loss of ≥ 5-10% improves lipids, blood pressure, and glycemic control and reduces risk of T2D. Weight loss of ≥10-15% has additional benefits, improving certain complications such as osteoarthiritis, gastroesophageal reflux disease, hepatic steatosis, and obstructive sleep apnea.

Lifestyle modification can produce meaningful weight reduction for some patients, but weight regain is common

Although lifestyle interventions can result in clinically meaningful weight reduction for some patients, most are do not achieve and maintain a ≥5-10% weight reduction over time. For example, a meta-analysis of 29 dietary interventions for obesity indicated that by 4 to 5 years after initial weight reduction, the average individual had regained most of the lost weight, maintaining an average weight reduction of just 3% below initial weight. Even with intensive lifestyle interventions and ongoing support, studies suggest that less than one-third of individuals maintain weight reductions of ≥10% at 5-8 years.

Hormonal and metabolic changes that occur with weight loss favor weight regain

Weight reduction triggers adaptive changes in hunger and satiety hormones (such as ghrelin, leptin, insulin, GLP-1, PYY, CCK, and amylin) which favor weight regain. At the same time, there is a decrease in energy expenditure (often called metabolic adaptation), which is out of proportion to the amount of weight lost. This creates a gap between desired energy intake and actual energy expenditure (i.e. an energy gap). These hormonal and metabolic changes may persist over time, making maintenance of weight loss more challenging.



Obesity is a complex disease, with multiple contributing factors, many of which are outside of an individual's control. Understanding and acknowledging this is essential to promoting a supportive and collaborative health care environment.

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