Physiologic and Neural Controls of Eating

Timothy H. Moran, PhD[a,b,*], Ellen E. Ladenheim, PhD[a]

KEYWORDS

• Nutrient availability • Adiposity signaling • Satiety signals • Reward processing • Eating

KEY POINTS

- Multiple physiologic and neural systems contribute to the controls over what and how much we eat.
- These systems include signaling involved in the detection and signaling of nutrient availability, signals arising from consumed nutrients that provide feedback information during a meal to induce satiation, and signals related to the rewarding properties of eating.
- Each of these has a separate neural representation but important interactions among these systems are critical to the overall controls of food intake.

What and how much we choose to eat are influenced by a variety of factors. These include the palatability or taste of particular foods, what we have learned about specific foods through experience, social and cultural influences on what foods and what amounts of food are appropriate to consume, the relative availability and the cost of specific foods, and an interacting system of physiologic controls that serve to both maintain adequate nutrition and limit intake to maximize our use of consumed nutrients. The recent obesity epidemic makes it clear that environmental influences can have a tremendous effect on overall energy balance. Obesity rates began to increase in the United States in the 1970s and this can all be attributed to changes in the food environment. However, the changing food environment interacts with a set of physiologic controls that are important in the meal-to-meal controls of eating.

In this review, we concentrate on the roles of 3 interacting physiologic and neural systems important in feeding control (**Fig. 1**). These are systems that mediate (1) signals related to metabolic state and nutrient availability, (2) signals that arise during a

Disclosures: T.H. Moran is a consultant for Healthways and Novo Nordisk. E.E. Ladenheim has nothing to declare.

[a] Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, 720 Rutland Avenue, Baltimore, MD 21205, USA; [b] Global Obesity Prevention Center at Johns Hopkins, Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Baltimore, MD 21205, USA

* Corresponding author. Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Ross 618, 720 Rutland Avenue, Baltimore, MD 21205.
E-mail address: tmoran@jhmi.edu

Gastroenterol Clin N Am ■ (2016) ■–■
http://dx.doi.org/10.1016/j.gtc.2016.07.009 **gastro.theclinics.com**

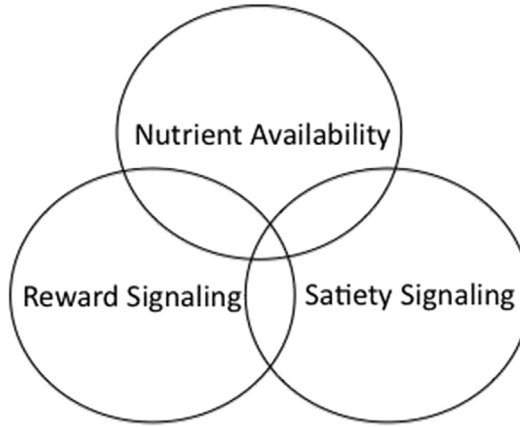

Fig. 1. Overall physiologic controls of eating behavior.

meal that serve to end that meal and maintain as state of satiety, and (3) affective signals related to taste and nutritional consequences that serve to reinforce aspects of eating. We will also identify how these systems interact in the defense of overall energy balance.

NUTRIENT AVAILABILITY SIGNALING

Studies of rodent genetic obesity models had long suggested the importance of circulating factors in overall body weight control. Having identified 2 different mutations in mice that led to obesity,[1] led to parabiosis experiments involving 2 strains of obese (obese [ob/ob] and diabetic [db/db]) and normal mice in which the blood supply between 2 mice in a parabiotic pair was shared. The results led to the conclusion that ob/ob mice lacked a circulating satiety factor that, in its absence, results in greatly increased food intake and obesity, whereas the db/db mouse produced the factor but lacked the ability to appropriately respond to that factor. Twenty years later, Friedman and colleagues[2] cloned the ob gene and named the protein that it produced "leptin" from the Greek "leptos" meaning thin, because this was a factor that helped maintain a normal body weight. Shortly thereafter, the leptin receptor protein was identified as the product of the db gene.[3,4] Leptin is produced primarily in white fat and circulating leptin levels correlate positively with the fat mass, increasing in circulation as animals or humans become obese.[5] Thus, leptin serves as a signal of the available stored energy.

The study of leptin's actions has illuminated many of the brain circuits that contribute critically to the control of energy balance and provided a basis for understanding earlier lesion work demonstrating a role for hypothalamic nuclei in energy balance. Leptin receptors are expressed throughout the brain with a particularly high expression within hypothalamic nuclei and other brain regions with identified roles in energy balance.[6] Interactions of leptin with its receptors within these hypothalamic nuclei result in the activation or inactivation of hypothalamic pathways containing various peptides that when administered into the brain either stimulate or stop eating.[7,8]

A major hypothalamic site of leptin's actions is the arcuate nucleus. The arcuate contains 2 distinct neuronal populations that express leptin receptors. The first are