Comment on: Vila et al. B-Type Natriuretic Peptide Modulates Ghrelin, Hunger, and Satiety in Healthy Men. Diabetes 2012;61:2592–2596

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Vila et al. (1) reported that brain natriuretic peptide (BNP) infusions reduce total and acylated-ghrelin levels while increasing satiety. Since ghrelin acts orexigenic, the authors conclude that BNP might indirectly regulate food intake in conditions associated with excessive BNP levels, such as in heart failure. The hypothesis is provocative but ignores the complex metabolic actions of natriuretic peptides.

Because ghrelin stimulates hypothalamic AMP-activated protein kinase (AMPK) activity, reduced ghrelin promotes satiety, attenuating food intake. However, other factors could be involved as well. Insulin, glucose, and specific fatty acids inhibit central AMPK activity, also promoting satiety. Atrial natriuretic peptide and BNP potently stimulate human adipose tissue lipolysis (2–4). Resulting fatty acid release is associated with increased circulating insulin concentrations (5–7). Furthermore, natriuretic peptides induce lipid oxidation and energy expenditure in mice (8,9) and men (5). Increased hepatic lipid oxidation generates β-hydroxybutyrate (5), which also affects food intake. Thus, natriuretic peptides affect several important mechanisms involved in the regulation of food intake independently of ghrelin. Moreover, natriuretic peptide–induced changes in insulin could indirectly regulate ghrelin (10).

Besides, the hypothesis that BNP has a crucial role in the regulation of food intake is challenged by observations in mice transgenically overexpressing BNP. These animals show chronically elevated BNP plasma concentrations comparable to levels attained with BNP infusions in clinical studies. Yet, feeding behavior and food intake are completely normal (8). Therefore, it is premature to conclude that natriuretic peptides regulate satiety and food intake through ghrelin. Integrative human studies are required that take into account the wide spectrum of metabolic actions elicited by natriuretic peptides.

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