

Concurrent Session 3: Regulation of Protein Metabolism

The protein leverage hypothesis in human obesity

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Background – The role of protein in the obesity crisis has, until recently, been largely ignored. This is for two reasons. First, protein provides the minor part of the human energy budget. Second, protein intake has remained far more constant over time and across populations than either fat or carbohydrate, both as a percentage of energy in the diet and in terms of absolute amounts eaten. Hence, while the obesity epidemic has spread, protein intake has remained relatively unchanged – giving the impression that protein cannot be responsible.

Method – We use state-space models (the Geometric Framework) developed from extensive animal studies to postulate a key role for protein appetite in the obesity epidemic, and provide supporting evidence from experimental, nutritional survey, and animal studies.

Results – Protein is the most satiating macronutrient group for humans and is the most tightly regulated post-absorptively. Results from comparative studies of other vertebrates, human experiments, and population-level data strongly suggest that the response of humans when faced with imbalanced diets is to prioritise protein intake. Hence, when the percent protein in the diet is low, non-protein energy is overeaten, whereas when dietary % protein is high, energy intake is limited: in both cases, absolute intake of protein is maintained near constant.

Conclusion – We show how, paradoxically, it may be because protein comprises a relatively small component of the human diet and is tightly regulated that it has sufficient leverage over human ingestive behavior to explain obesity. Focusing on this leverage over intake clarifies the role of dietary protein in the development of obesity, provides a possible means of ameliorating the problem, and explains the effectiveness of high-protein diets as weight loss regimes.

Detecting variations in dietary protein intake: the roles of molecular sensors for amino acids

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Background: Dietary protein promotes growth and regulates appetite. In the gut, protein elicits digestive, absorptive and hormonal responses that facilitate nutrient disposal and the control of growth. In bone, dietary protein promotes bone density and resistance to fracture. The molecular and cellular mechanisms that underlie these effects of protein, however, have been poorly understood.

Review: As dietary protein intake changes, serum and intracellular amino acid levels also change and recent research indicates that the body is equipped with sophisticated amino acid sensing mechanisms for detecting and responding to states of feast - and famine. The molecular mechanisms that are emerging are predominantly intracellular in the case of amino acid famine and predominantly extracellular in the case of amino acid plenty. Mechanisms for amino acid depletion are based on the generation of amino acid-free forms of transfer RNA and operate, for example, to regulate appetite, perhaps even the appetites for specific types of foods. Two basic mechanisms appear to operate in the case of amino acid plenty. One is based on amino acid transporters and the other on class 3 G-protein coupled receptors, some of which bind multiple amino acids in their extracellular bilobed “Venus FlyTrap” domains. Expression of these receptors in the gut provides mechanisms by which amino acids contribute to the control of digestion and absorption. Expression in endocrine cells, on the other hand, provides mechanisms by which the synthesis and/or secretion of growth-regulating hormones can be regulated. Finally, amino acid modulation of calcium-sensing receptors provides a mechanism by which protein and calcium metabolism are linked providing insights into the molecular control of bone homeostasis.

Conclusions: The cellular and molecular mechanisms responsible for detecting and responding to changes in dietary protein intake are, at last, coming to light.

Reference

AD Conigrave and DR Hampson (2006) Broad-spectrum amino acid sensing by class 3 G-protein coupled receptors. Trends Endocrinology and Metabolism, in press.