Are there Nutrients and Hormones that Alter Daily Food Intake as well as Body Weight and Obesity?

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Objectives:

• To determine the role of signals arising in the gut and other organs in the control of daily food intake, energy expenditure and body weight.

• To determine whether nutrients, nerves or hormones are involved in the observed changes in energy balance.
Satiety signals do exist!
Diet and Feeding:

• Rats were on a 17h feeding schedule

• Diet consisted of Ensure-plus (vanilla)
One-way Crossed Intestines Rats
Changes in Daily Food Intake
Conclusions

• The signals that control daily food intake do not arise at the level of the mouth or stomach.
• They do arise in the intestines or beyond.
• These signals appear to be related to the amount of food absorbed.
• There is little change in body weight.
Alternative Conclusion:

- The signal that controls daily intake could arise in the lower small intestine.
Hypothesis:

• The nutrients present in the blood stream control daily food intake
• or,
• in other words, endogenous gut signals (nerves or hormones) are not involved.
Test Procedure

• Bypass the gut by infusing nutrients intravenously and, then, measure the changes in daily intake and energy expenditure.

• Test each of the major macronutrients separately.
Glucose – 34 kcal/day

Fig. 2. Mean daily food intake (±SE) and body weight for 8 rats receiving infusions of glucose (34 kcal/day iv) on days 7–10.
Amino acids – 10 or 20 kcal/day
Fig. 4. Mean daily food intake (±SE) and body weight for 6 rats receiving infusions of lipid (Nutralipid, 20 kcal/day iv) on days 7–12.
Lipids – 40 kcal/day

Fig. 5. Mean daily food intake (±SE) and body weight for 8 rats receiving infusions of lipid (Nutralipid, 40 kcal/day iv) on days 7–12.
Strengths of these Studies

• The nutrients were infused slowly throughout the 17 hour feeding period.
• These infused nutrients supplement the rats’ own absorbed nutrients and endogenous signals from voluntary food intake.
• The amounts delivered were moderate in dose.
• The results were dose dependent.
Major weakness

• Infusing only one macronutrient made that macronutrient more prominent in the rats’ diet.

• Therefore, we need to infuse all three macronutrients in the same proportion that they are present in the diet.
I.V. Diet – 20 and 40 kcal/day
Comparison

![Graph showing comparison of food intake (% of baseline) for different conditions: saline, glucose, amino acids, lipid, IV diet. The graph includes bars with error bars for each condition, and the following data is provided:

- **KCAL INFUSED**
  - Saline: 34
  - Glucose: 10
  - Amino Acids: 20
  - Lipid: 20
  - IV Diet: 20

- **% OF BASELINE INTAKE INFUSED**
  - Saline: 52
  - Glucose: 14
  - Amino Acids: 28
  - Lipid: 58
  - IV Diet: 56]
Straight-forward Conclusions

• Food infused intravenously can alter energy balance.
• The presence of nutrients in the blood and in the body provide the major signals that alter daily food intake.
• Endogenous signals from the gut may provide about 25% of the overall signal that reduces daily food intake.
Strategy

• Try to determine where the iv nutrients are being sensed.
• Test the organs most likely to be involved.
  – The brain has known glucose and amino acid sensors in the LH (Oomura).
  – The liver has known glucoreceptors (Niijima) that send vagal messages to the brain and the liver controls metabolism.
Test of the Brain Hypothesis

• Infuse 10 or 20 kcal/day of the water-soluble nutrients into the carotid artery.

• Only 3% of cardiac output goes to the rat brain.

• The delta increase in brain blood glucose levels would be 44 mg% compared to 1.3 mg% in the control vena cava infusion.

• There was no change in daily intake.
Conclusions

• The brain does not sense plasma glucose levels in order to control daily food intake.
• There are brain glucoreceptors, but they serve other purposes, such as stimulation of counter-regulatory hormones.
Test the Liver Hypothesis

- Infuse 10 or 20 kcal/day of glucose or amino acid into the portal vein.
- About 20% of cardiac output flows to the liver, mostly through the gut.
- The delta increase in hepatic blood glucose would be 8 mg% above and beyond the increased levels due to absorption of food from voluntary intake.
- There was no change in daily intake.
Conclusions

• The liver does not sense plasma glucose or a.a. levels to control daily intake.
• There are hepatic gluco receptors, but they must serve other purposes.
Future Directions

• Test other organs that may be involved.
• The most likely possibilities are:
  – The organs that process the nutrients: the muscle and fat.
  – The gut itself stimulated by elevated iv nutrient levels.
Role of Insulin in Energy Balance

• The main hormone that causes nutrients to shift into tissues is insulin.

• Does the shift of nutrients into tissues alter food intake?
Food Intake in Diabetic Rats Infused with Insulin
24 Hour Blood Glucose Levels
Effect of Increased Insulin in Blood Flowing through Brain.
Conclusions

• Insulin causes increases in daily food intake.

• It doesn’t matter whether higher levels of insulin flow through the brain.

• The brain does not sense insulin to control daily food intake.
Final Conclusions

• Nutrients present in the bloodstream are the major causes of reduced food intake.
• Insulin which moves nutrients out of the blood causes increases in daily food intake.