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

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**The Obesity Conundrum**

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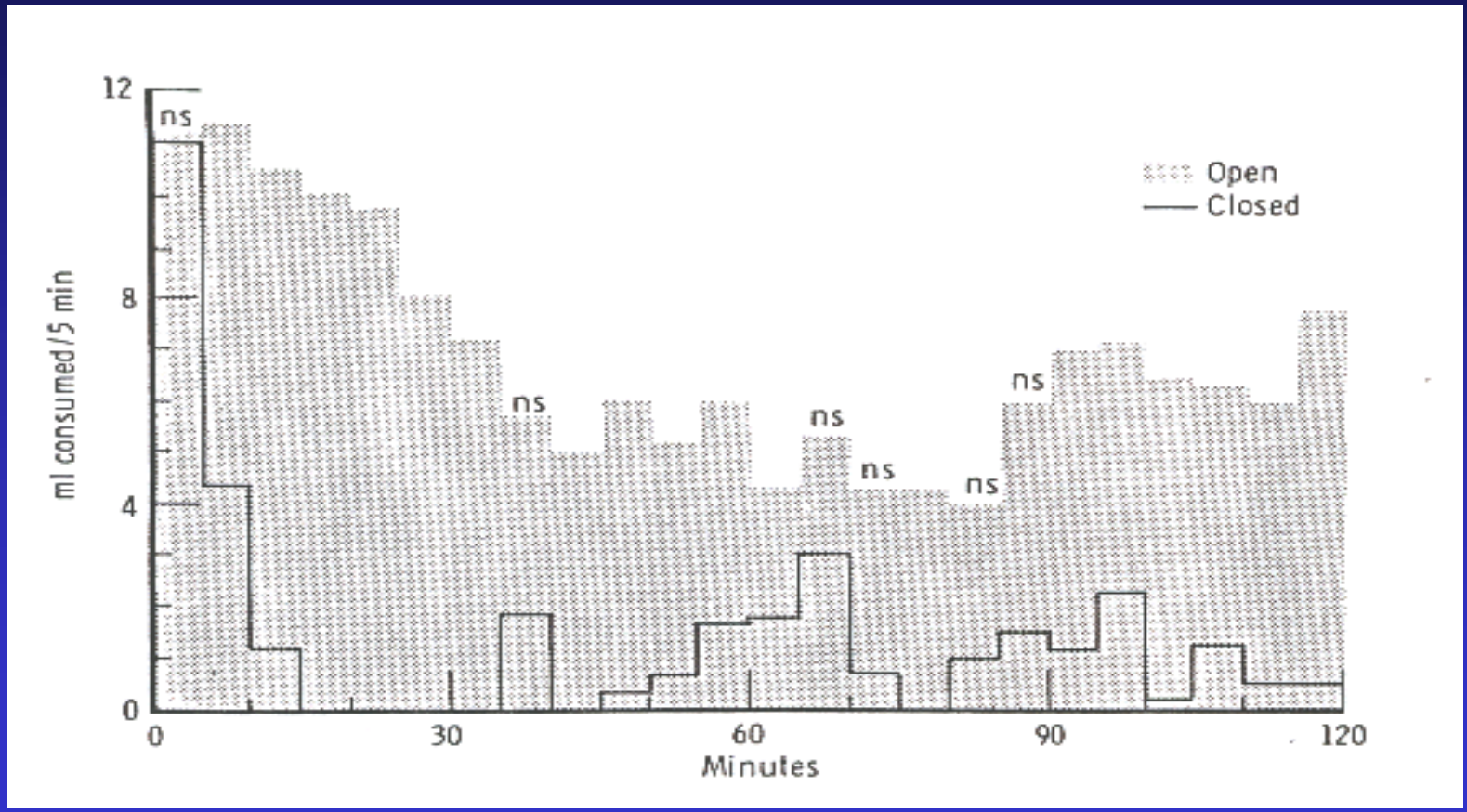
# Objectives :

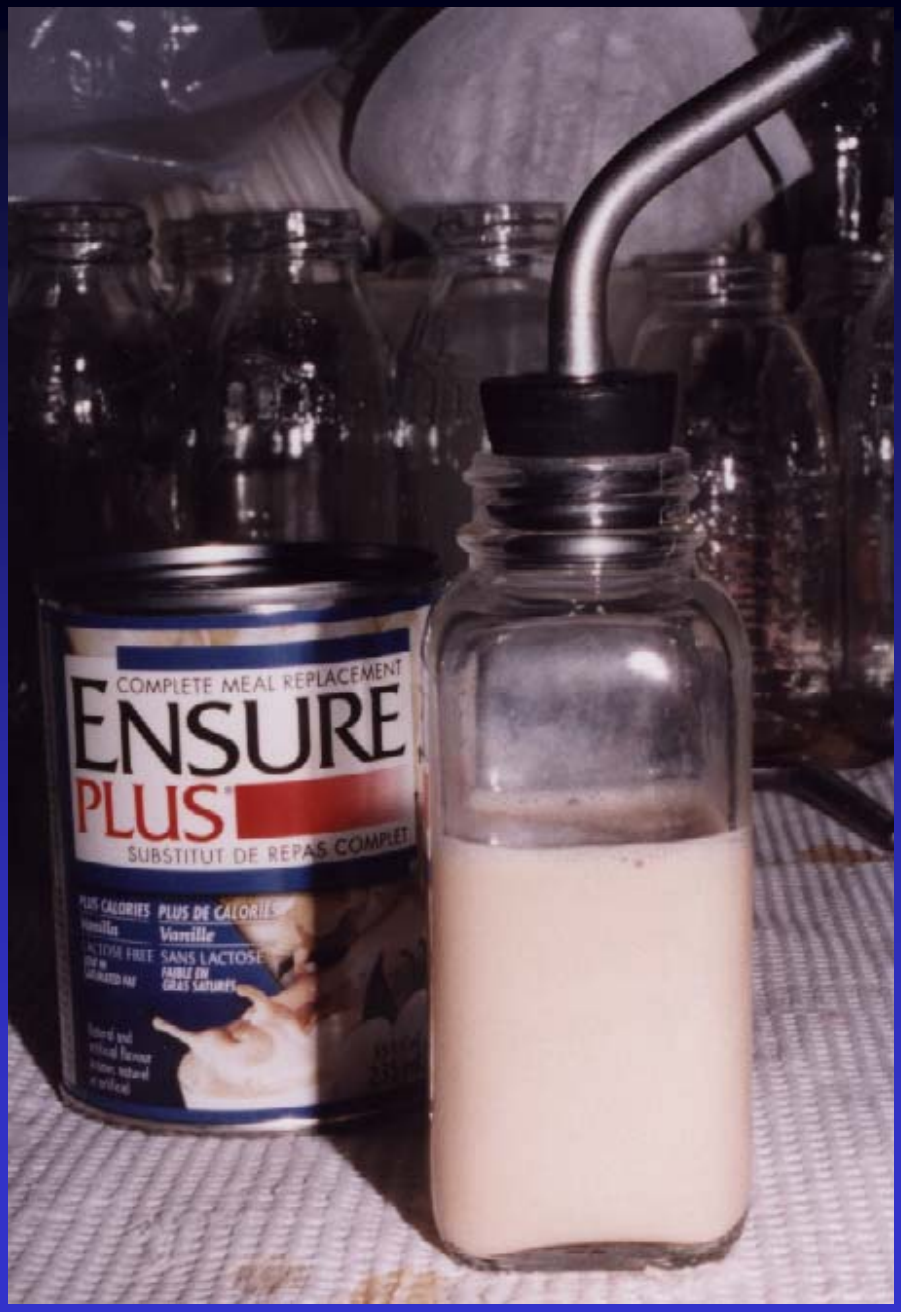
- **To determine the role of signals arising in the gut and other organs in the control of daily food intake, energy expenditure and body weight.**
- **To determine whether nutrients, nerves or hormones are involved in the observed changes in energy balance.**

# Satiety signals do exist !

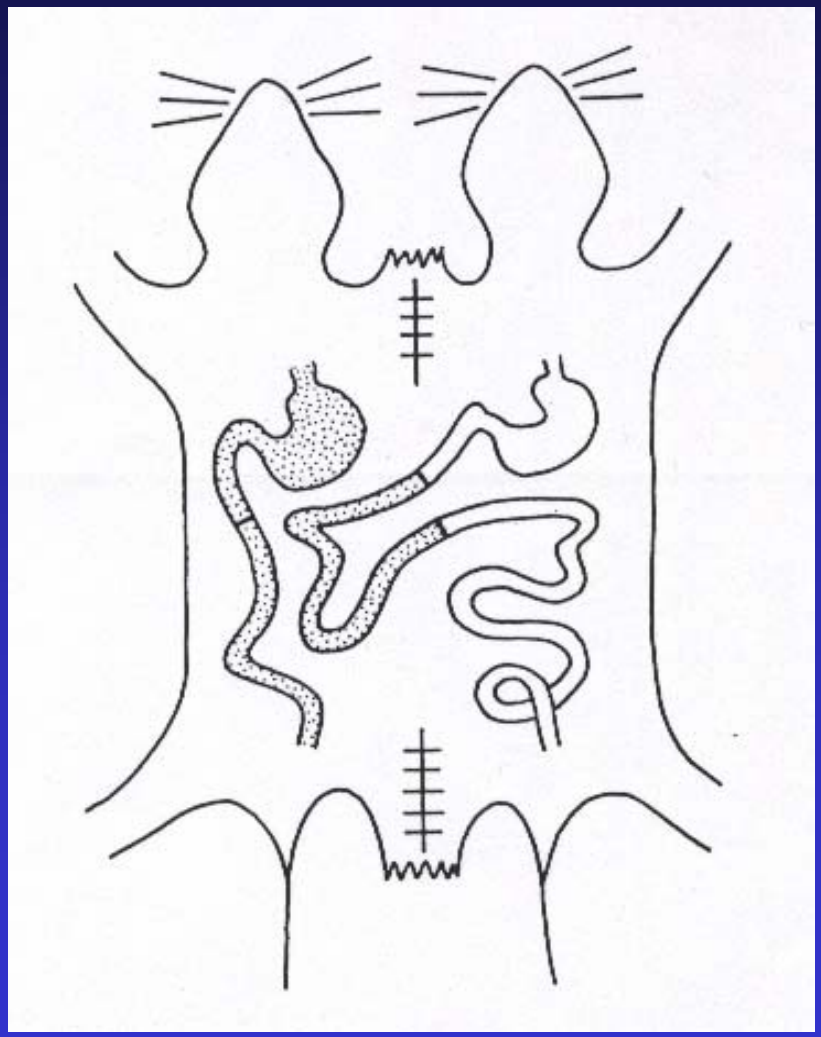


# Diet and Feeding:

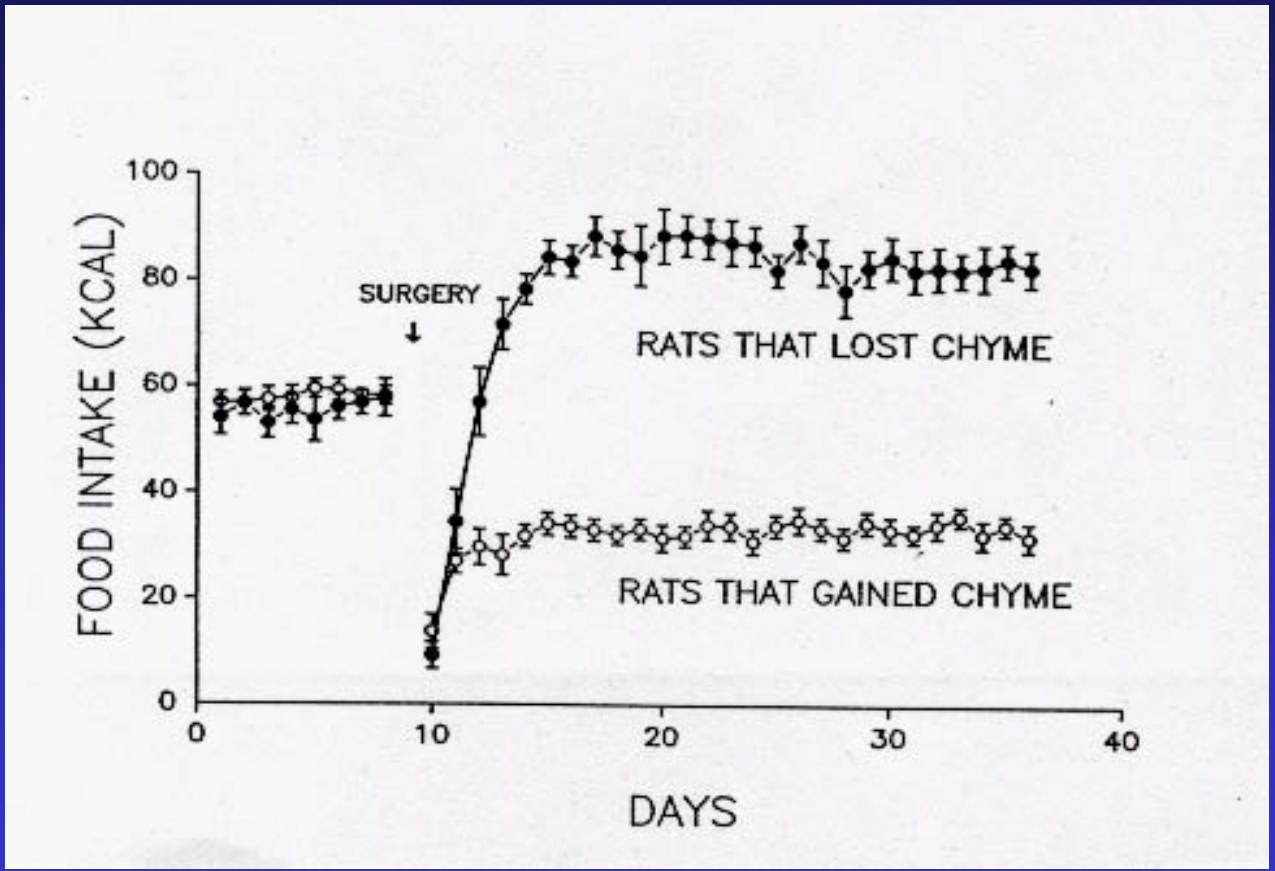
- Rats were on a 17h feeding schedule
- Diet consisted of Ensure-plus (vanilla)


COMPLETE MEAL REPLACEMENT
ENSURE
PLUS
SUBSTITUT DE REPAS COMPLET
PLUS CALORIES
PLUS DE CALORIES
Vanilla
Vanille
LACTOSE FREE
SANS LACTOSE
LOW IN SATURATED FAT
FAIBLE EN GRAS SATURÉS

# One-way Crossed Intestines Rats



# Changes in Daily Food Intake

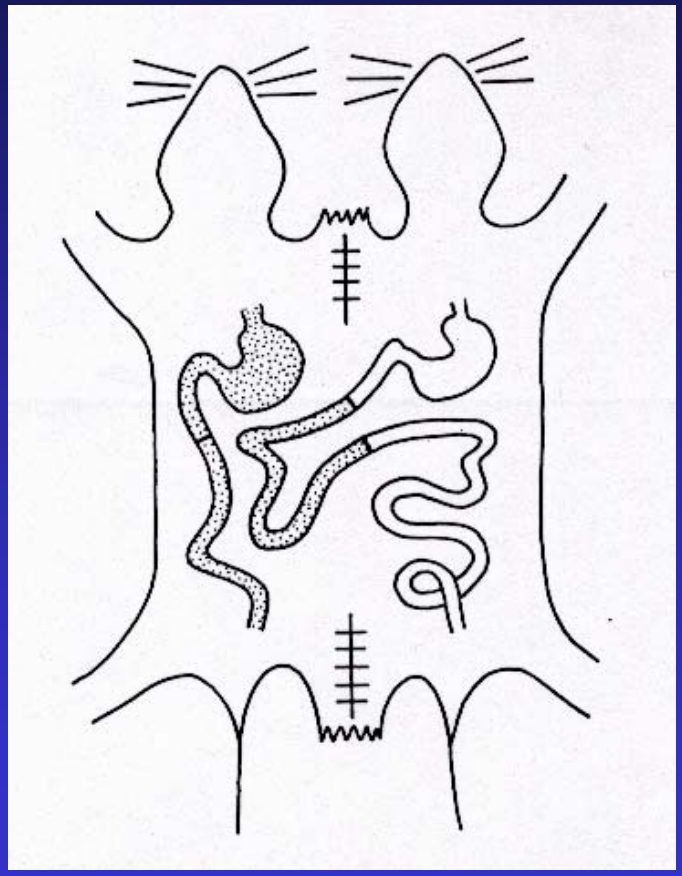


# Conclusions

- **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

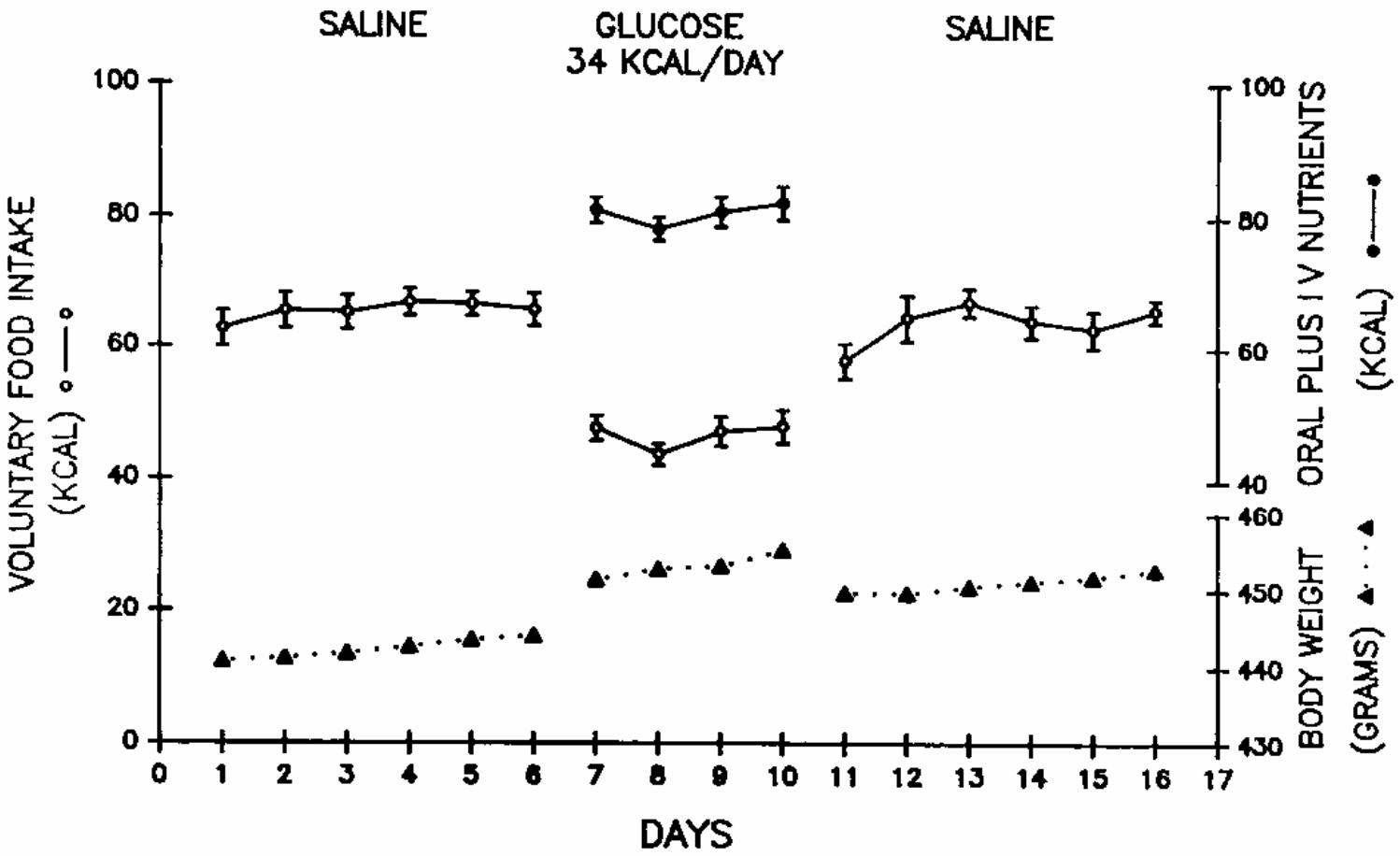
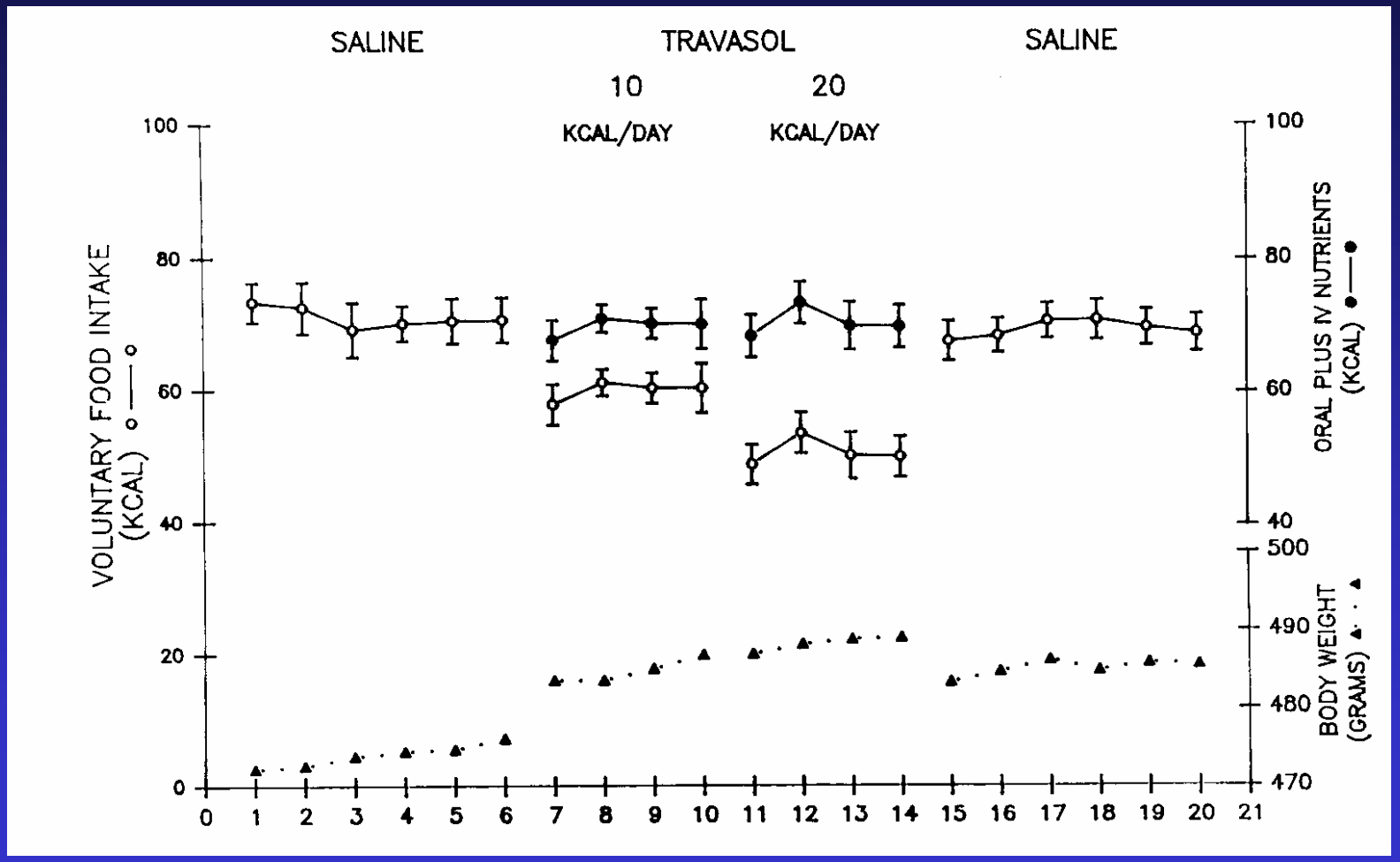



Fig. 2. Mean daily food intake (±SE) and body weight for 8 rats receiving infusions of glucose (34 kcal/day iv) on *days 7–10*.

# Amino acids – 10 or 20 kcal/day



# Lipids – 20 kcal/day

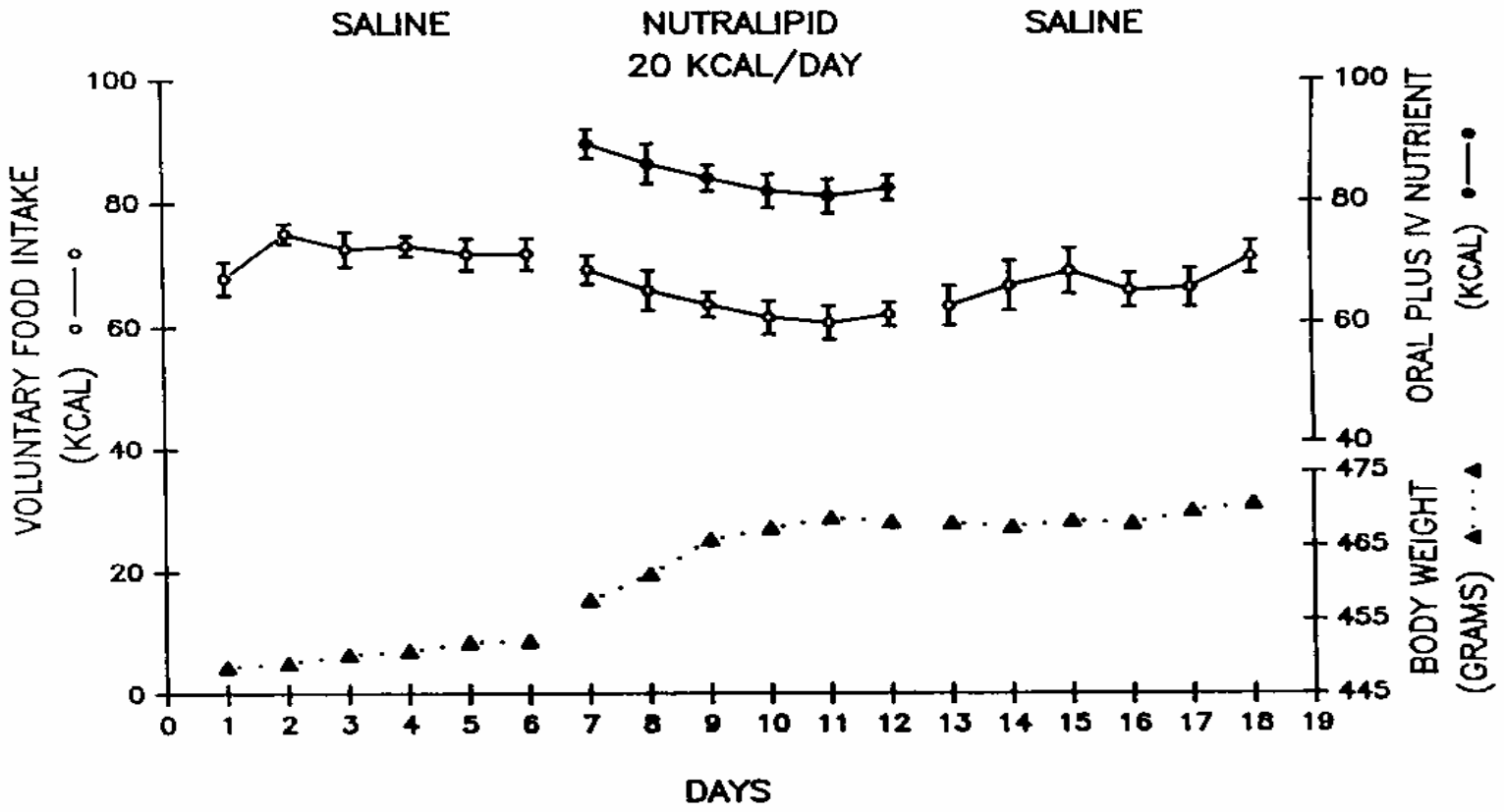



Fig. 4. Mean daily food intake (±SE) and body weight for 6 rats receiving infusions of lipid (Nutralipid, 20 kcal/day iv) on *days 7–12*.

# Lipids – 40 kcal/day

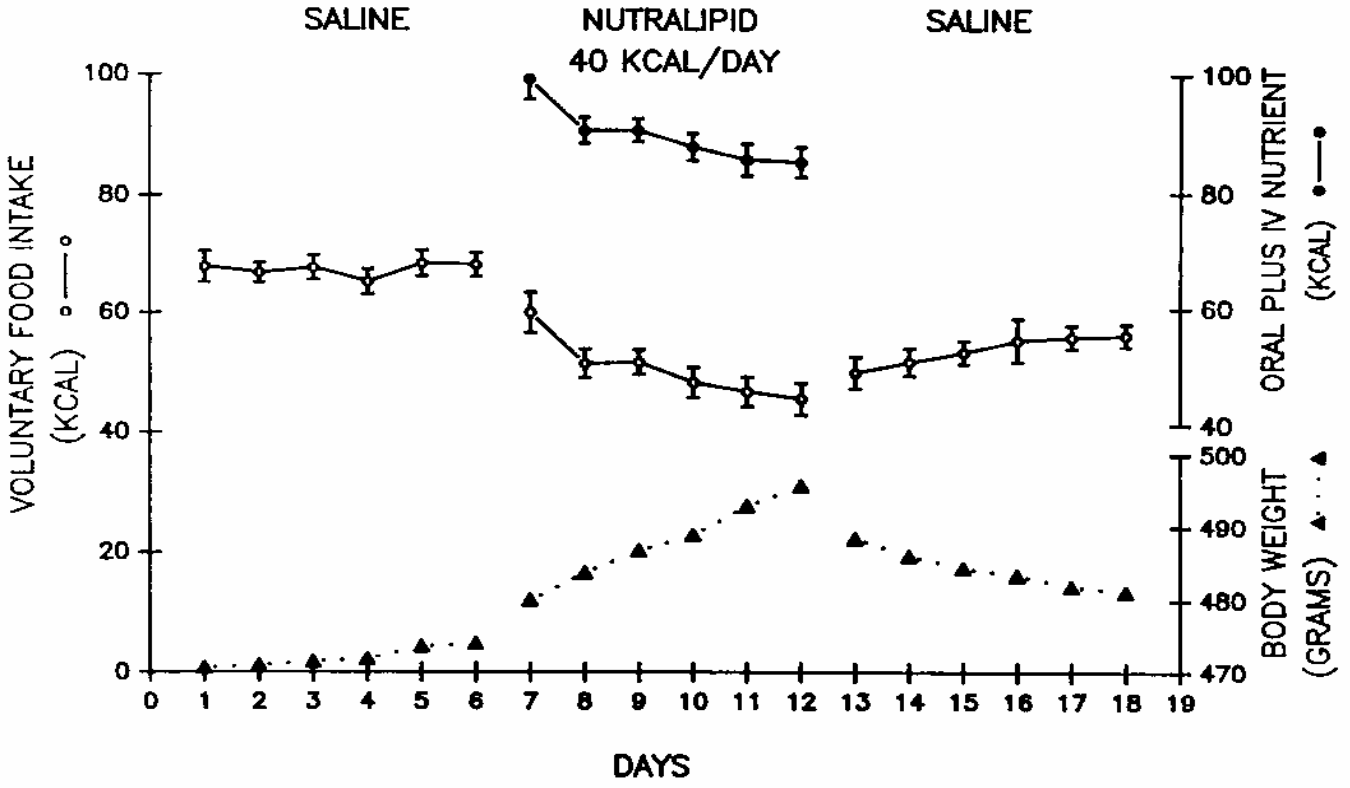



Fig. 5. Mean daily food intake (±SE) and body weight for 8 rats receiving infusions of lipid (Nutralipid, 40 kcal/day iv) on *days 7–12*.

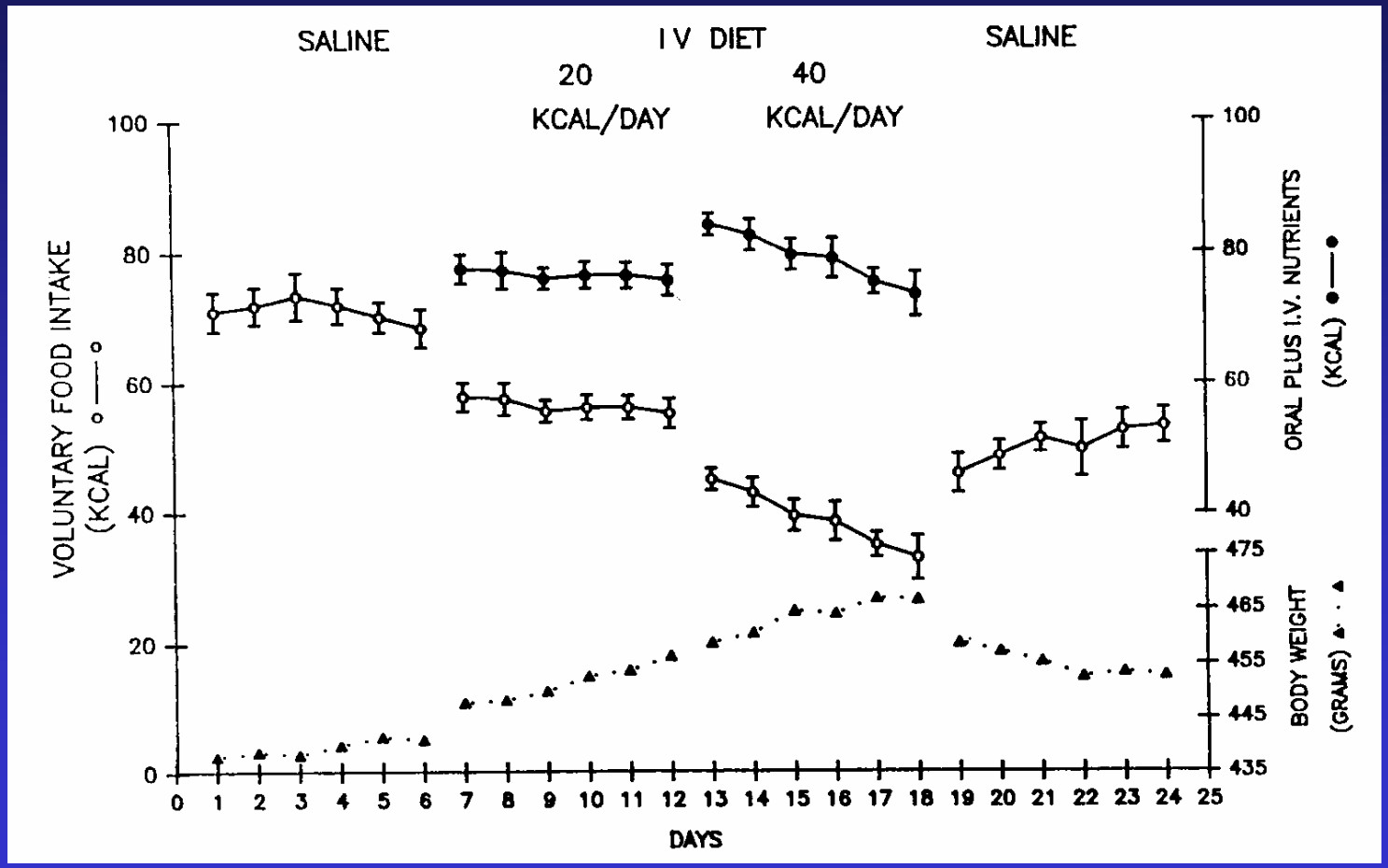
# Strengths of these Studies

- **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.**

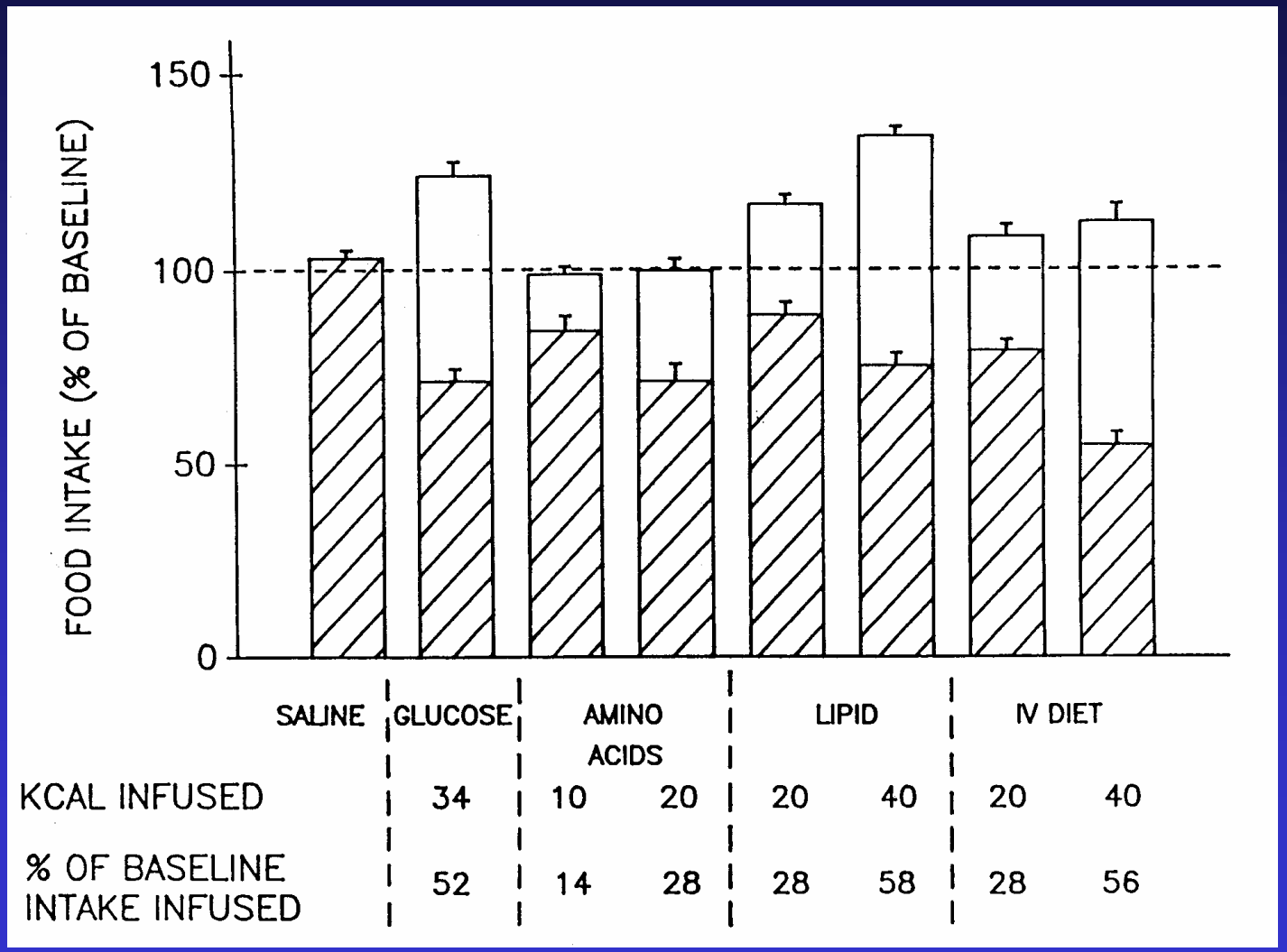
# Major weakness

- 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


FOOD INTAKE (% OF BASELINE)
150
100
50
0
SALINE
GLUCOSE
AMINO ACIDS
LIPID
IV DIET
KCAL INFUSED
34
10
20
20
40
20
40
% OF BASELINE INTAKE INFUSED
52
14
28
28
58
28
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 glucoreceptors, but they must serve other purposes.**

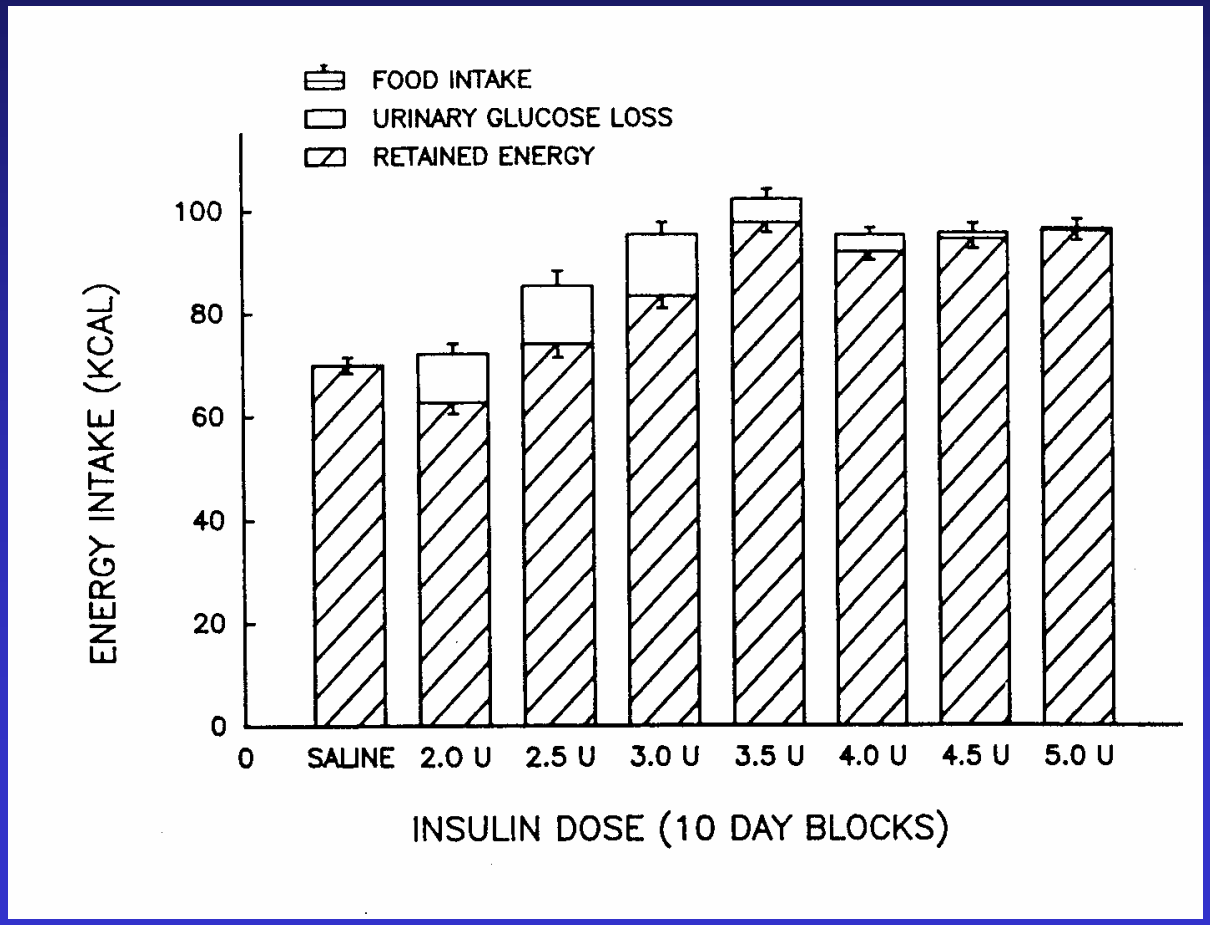
# Future Directions

- 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.

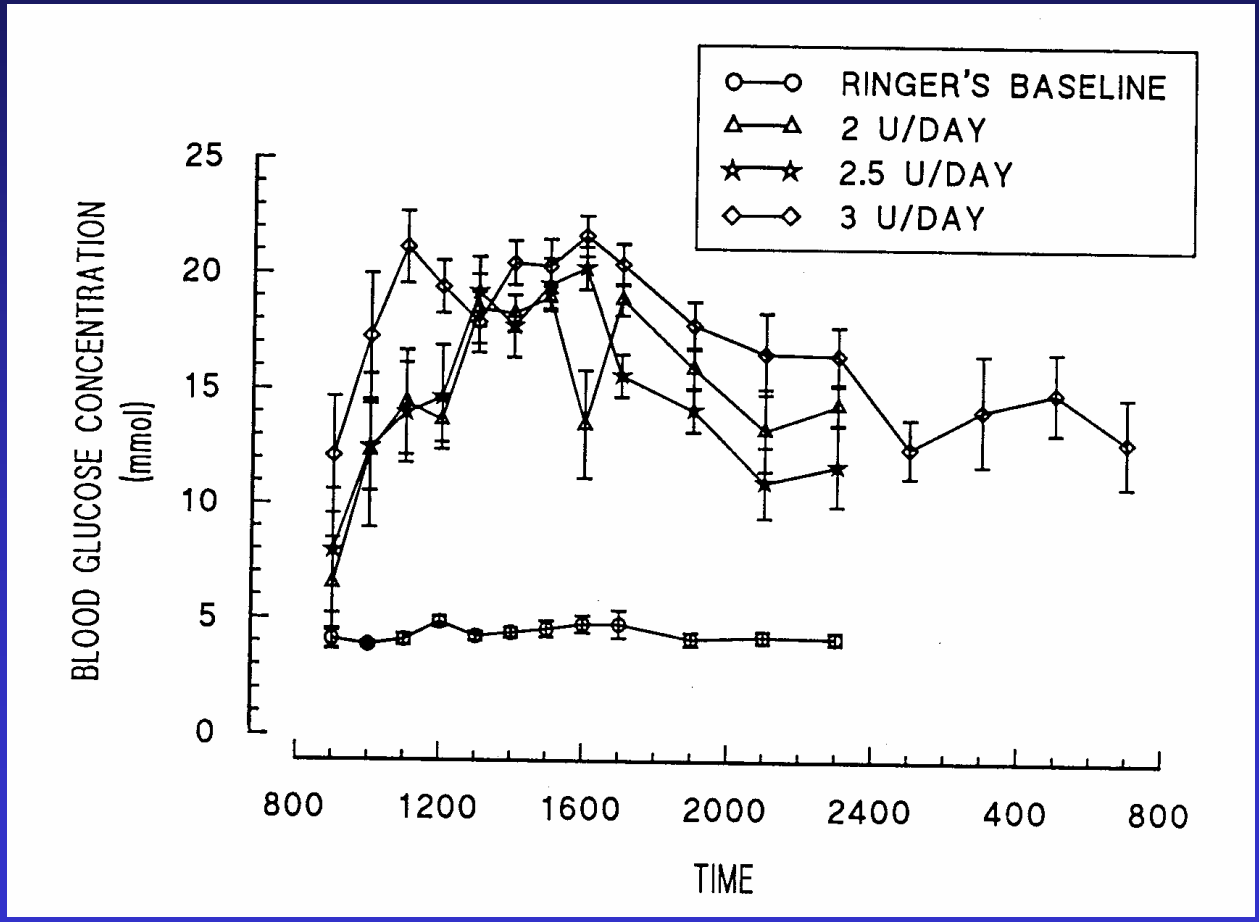
# Role of Insulin in Energy Balance

- The main hormone that causes nutrients to shift into tissues is insulin.
- Does the shift of nutrients into tissues alter food intake?

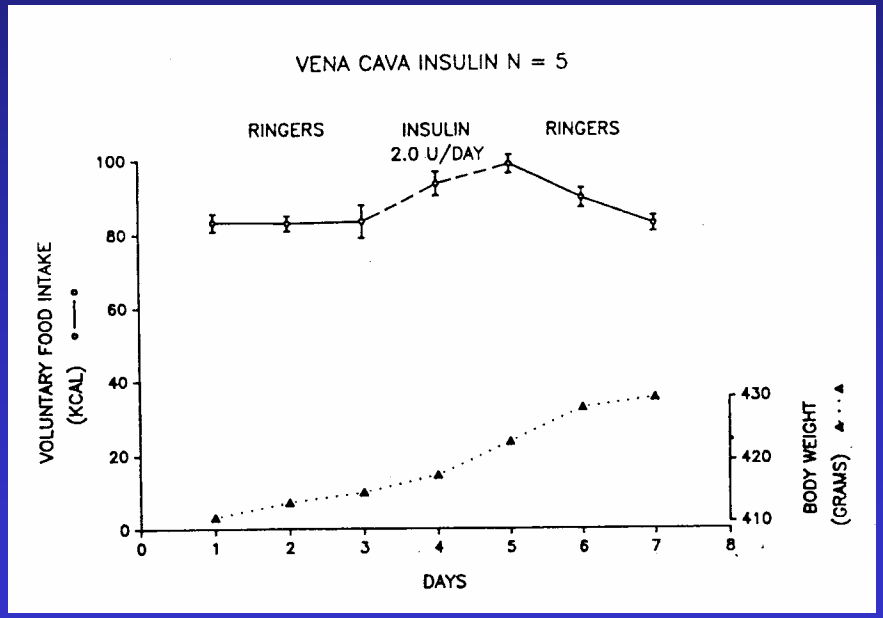
# Food Intake in Diabetic Rats Infused with Insulin

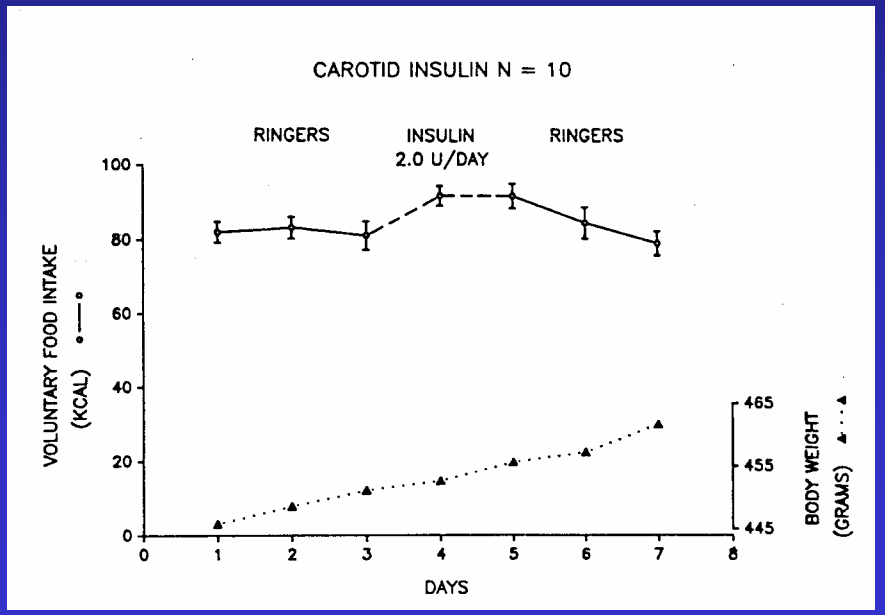


# 24 Hour Blood Glucose Levels



# 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 blood-stream are the major causes of reduced food intake.**
- **Insulin which moves nutrients out of the blood causes increases in daily food intake**