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# The Biology of Body Weight

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H.K. Ransom Professor of Surgery

University of Michigan

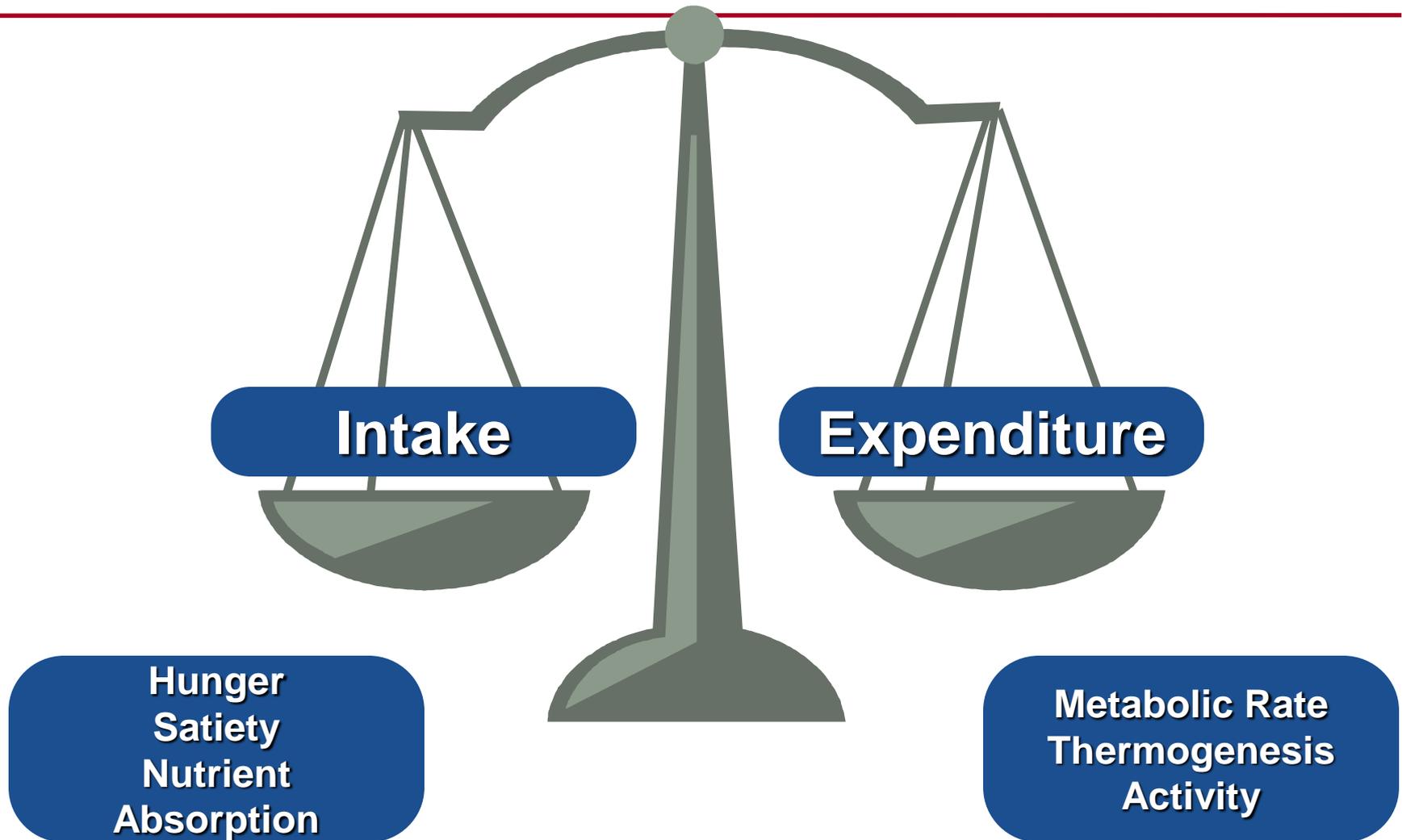
# Disclosures

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- Paid Speaker: Novo Nordisk, Ethicon Endo-Surgery
- SAB/Consultant: Ethicon Endo-Surgery, Novartis, Zealand, Boehringer-Ingelheim, Angiochem, Eisai, Forest Laboratories
- Research Support: Ethicon Endo-Surgery, Novo Nordisk, Boehringer-Ingelheim

# Energy Balance Equation

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# Accuracy!

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**Energy Intake in a Year**

**912,500 calories**

**Gaining 1 pound  
(0.45 kg) in a year**

**4,050 calories**

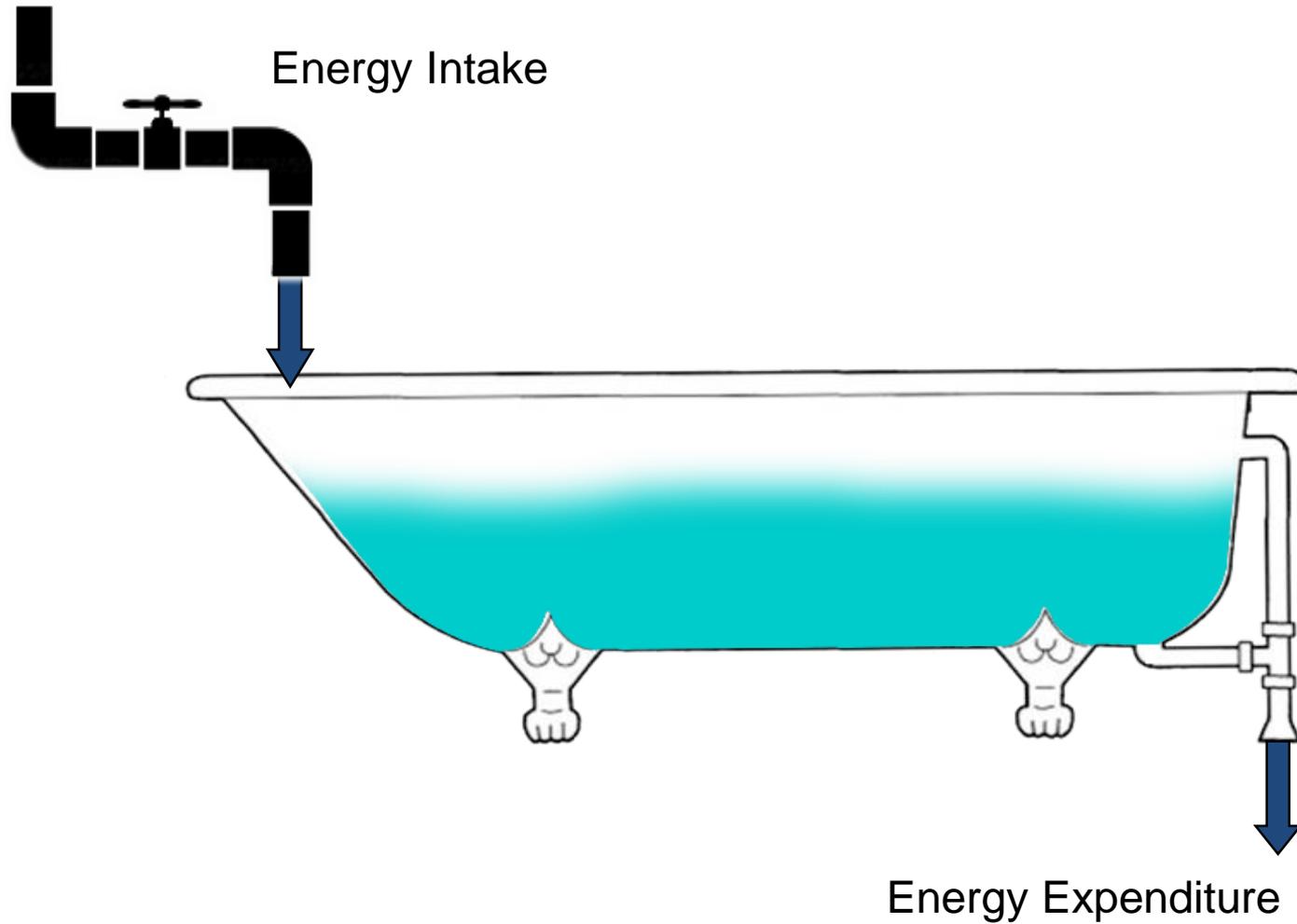
**Error of 0.4%**

*or*

**11 calories/day**

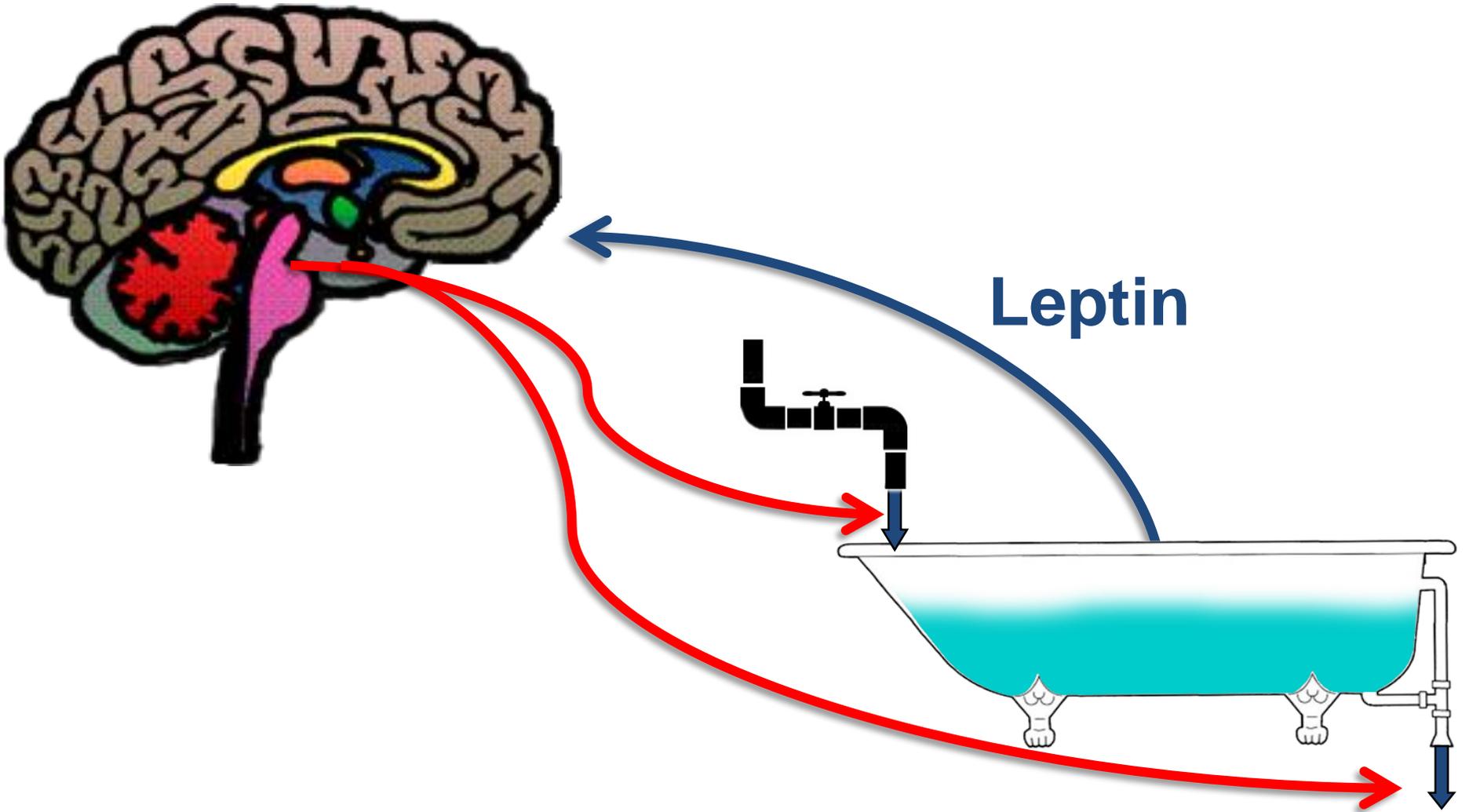
# The Adipose “Bathtub”

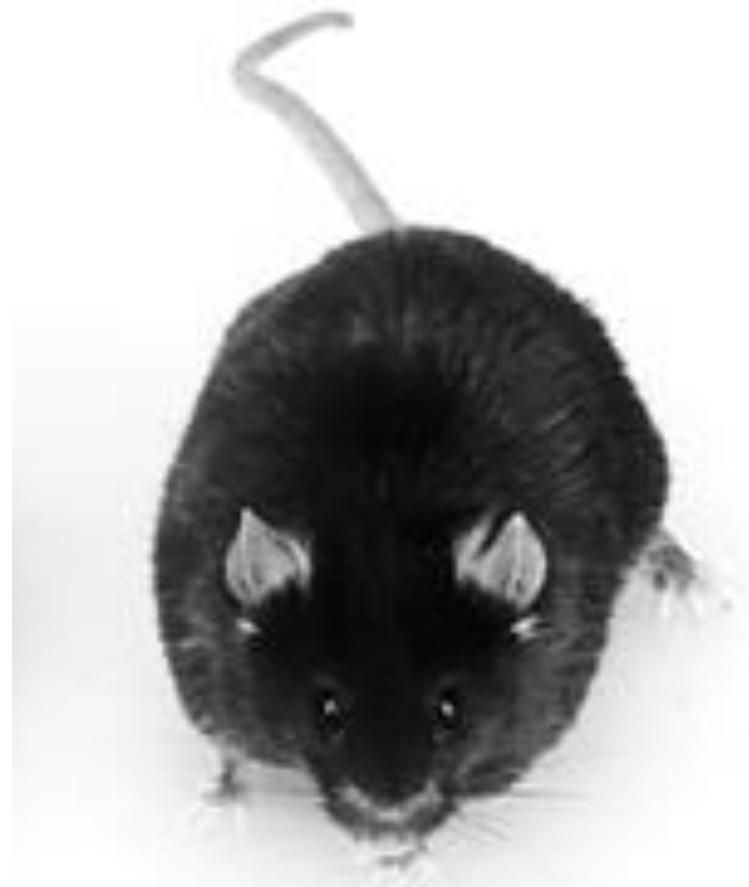
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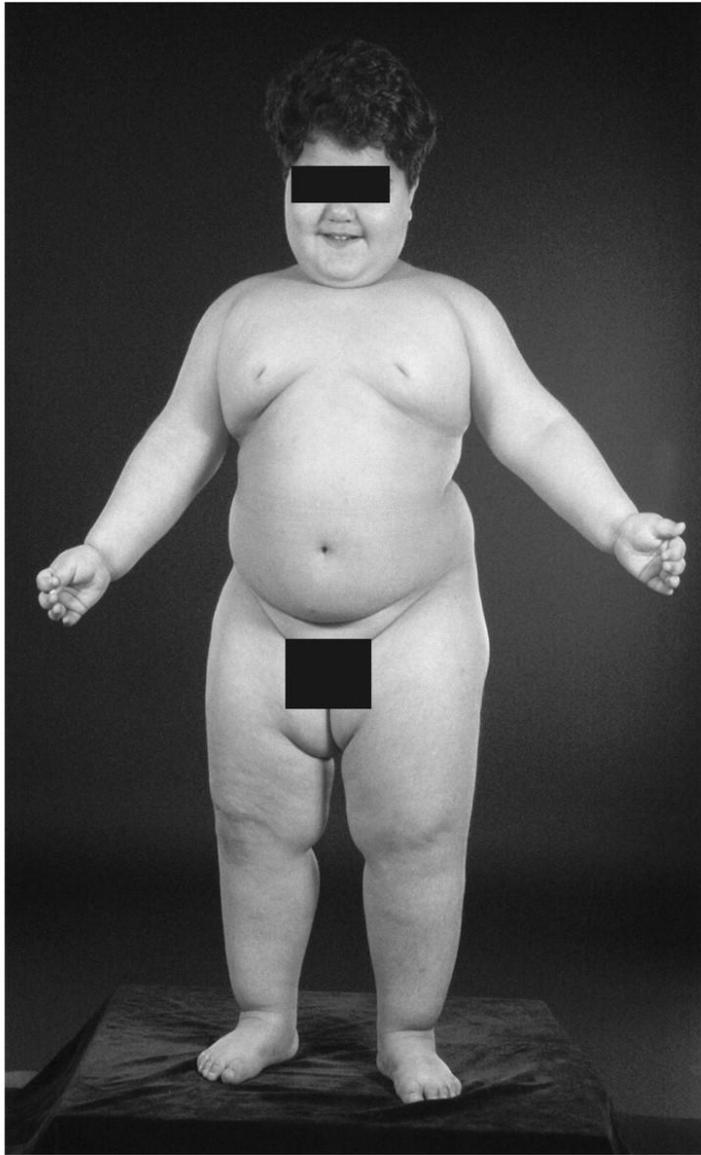


# The Adipose “Bathtub”

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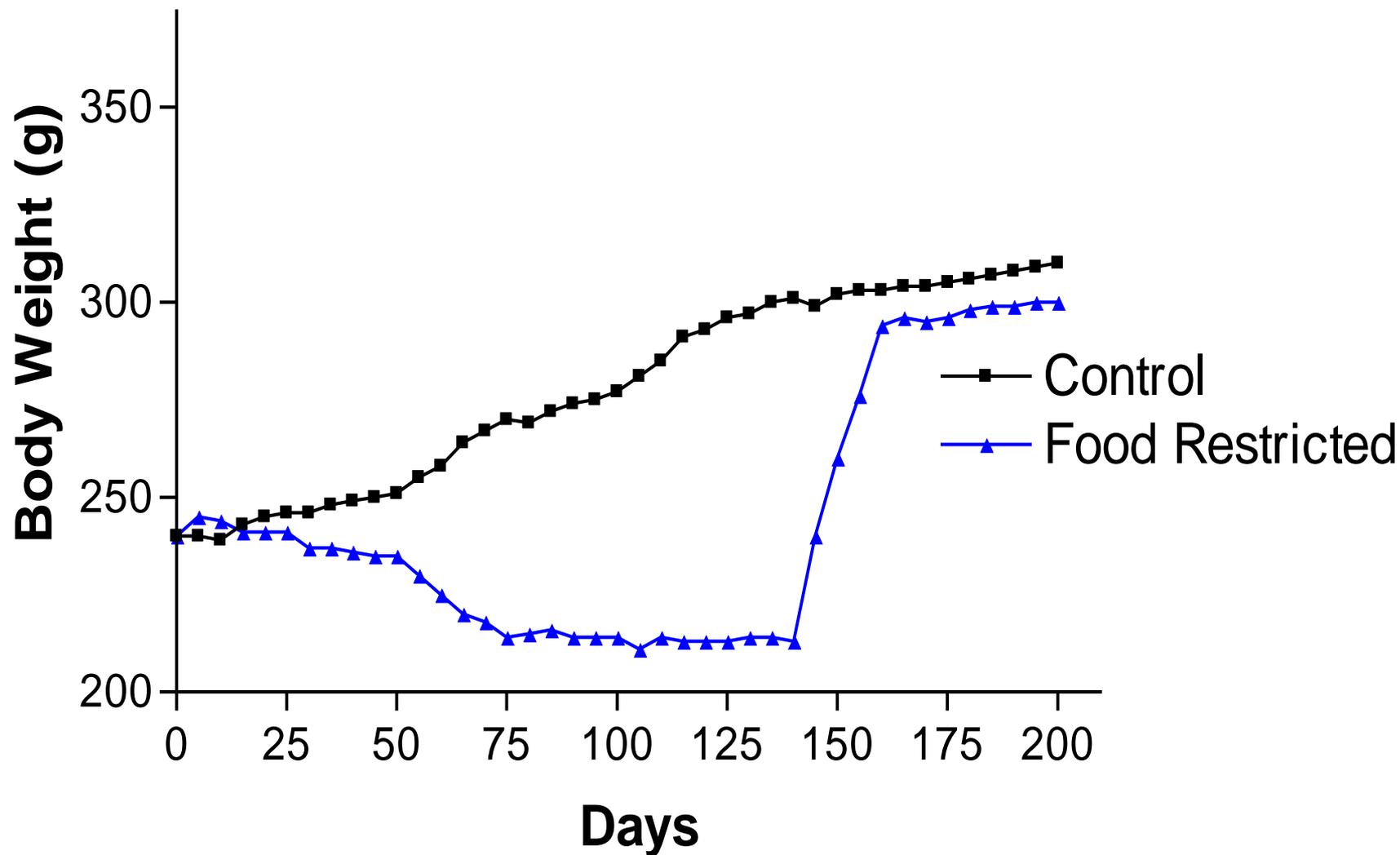




3yr old weighing 42kg

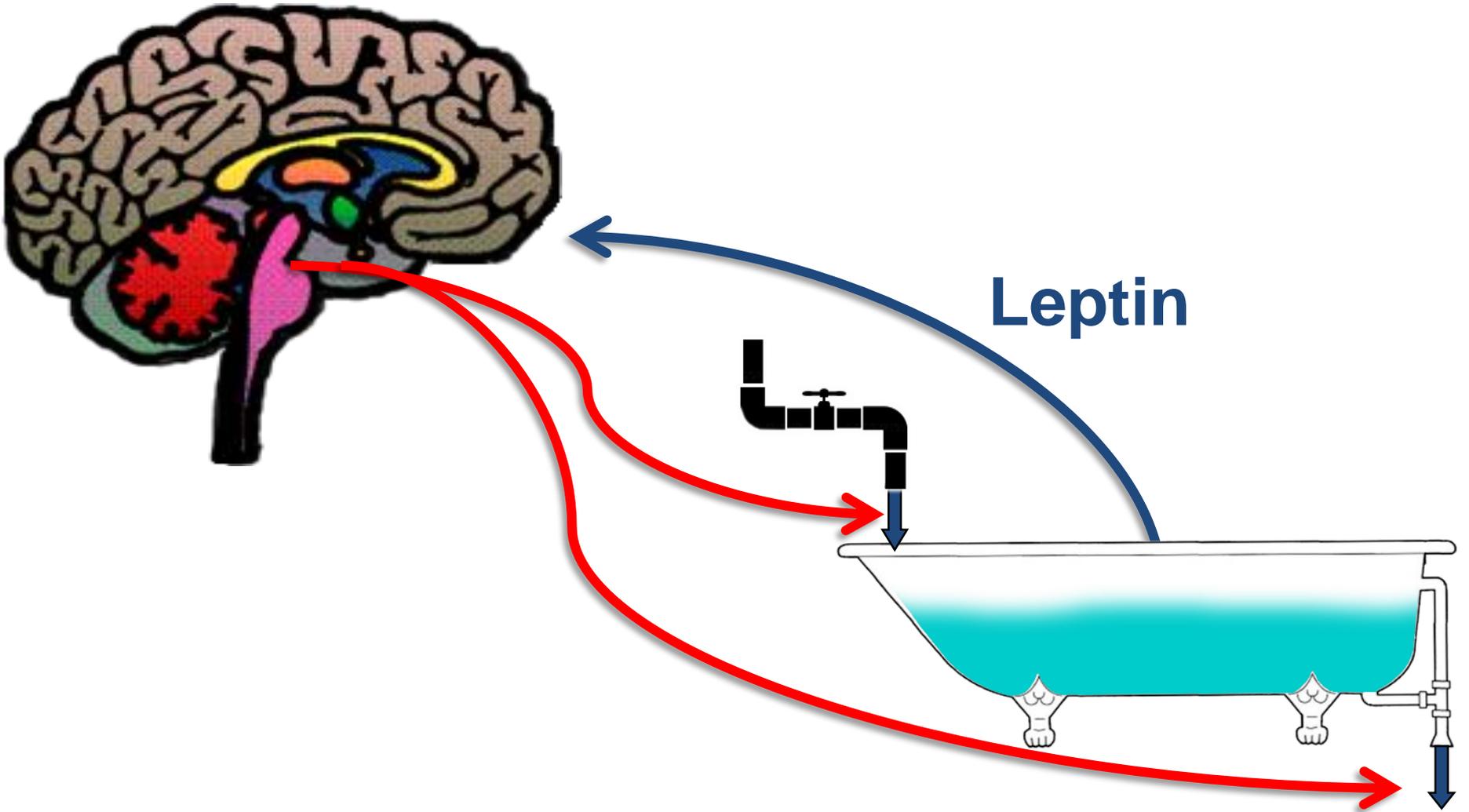
# Negative Energy Balance in Rats

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# The Adipose “Bathtub”

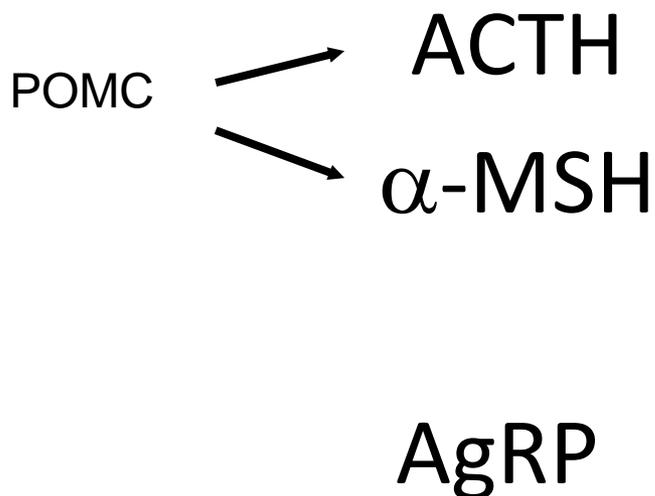
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# Melanocortin System

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## Ligands



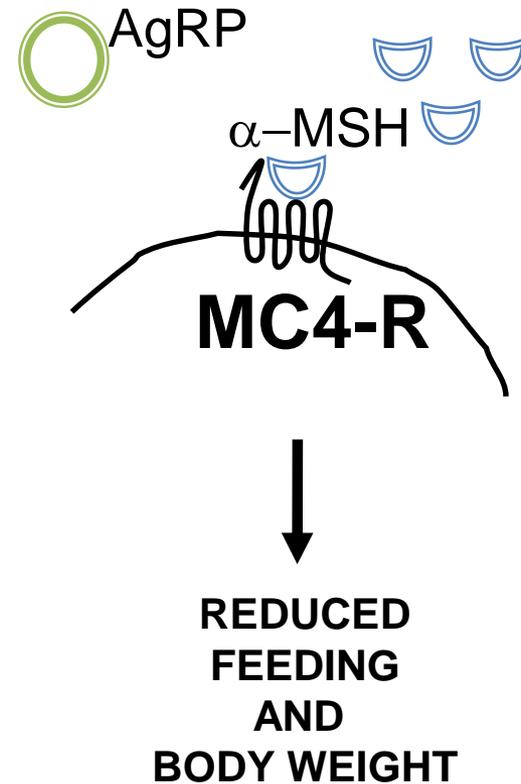
## Receptors

- MC1 (skin and hair)
- MC2 (adrenal)
- MC3 (hypothalamus)
- MC4 (CNS)

# Melanocortin Regulation of Feeding Behavior

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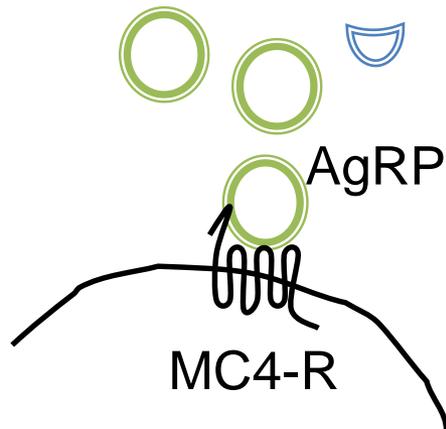
AGONIST



# Melanocortin Regulation of Feeding Behavior

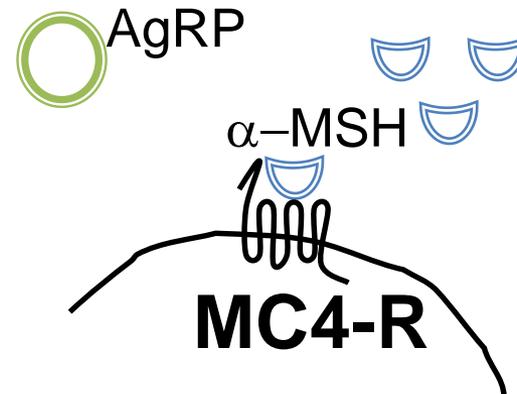
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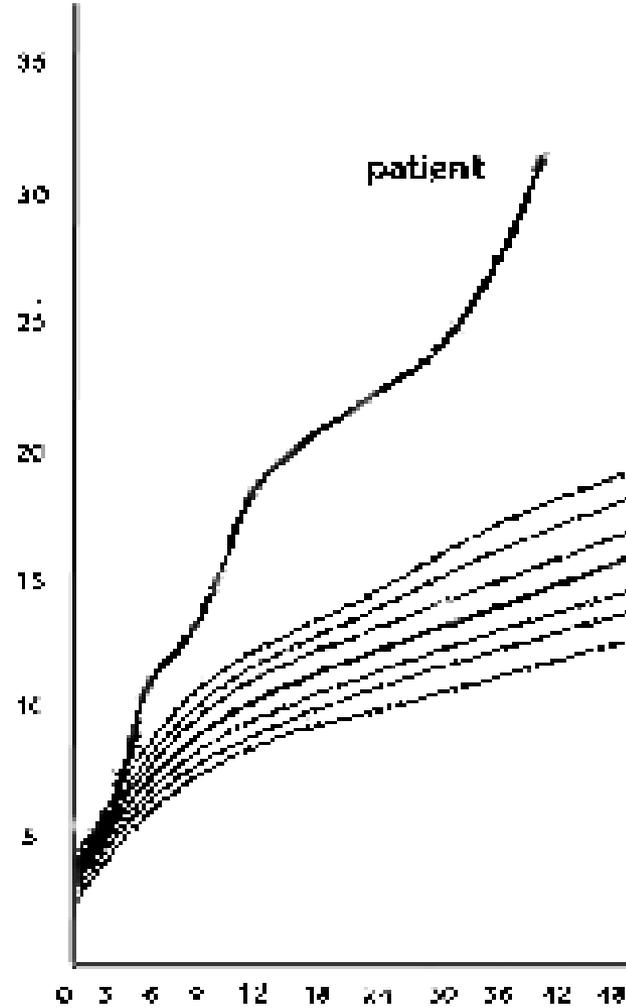
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**INCREASED  
FEEDING  
AND  
BODY WEIGHT**

AGONIST



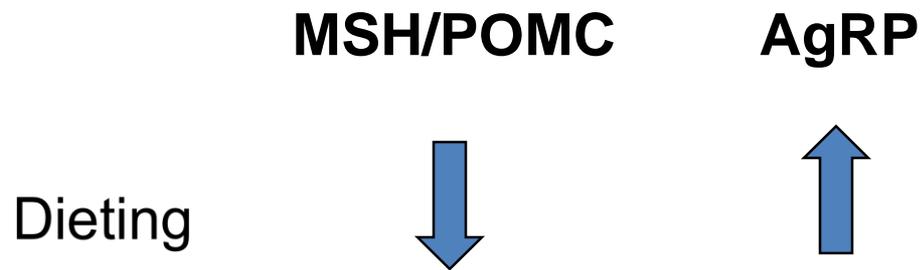
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**REDUCED  
FEEDING  
AND  
BODY WEIGHT**

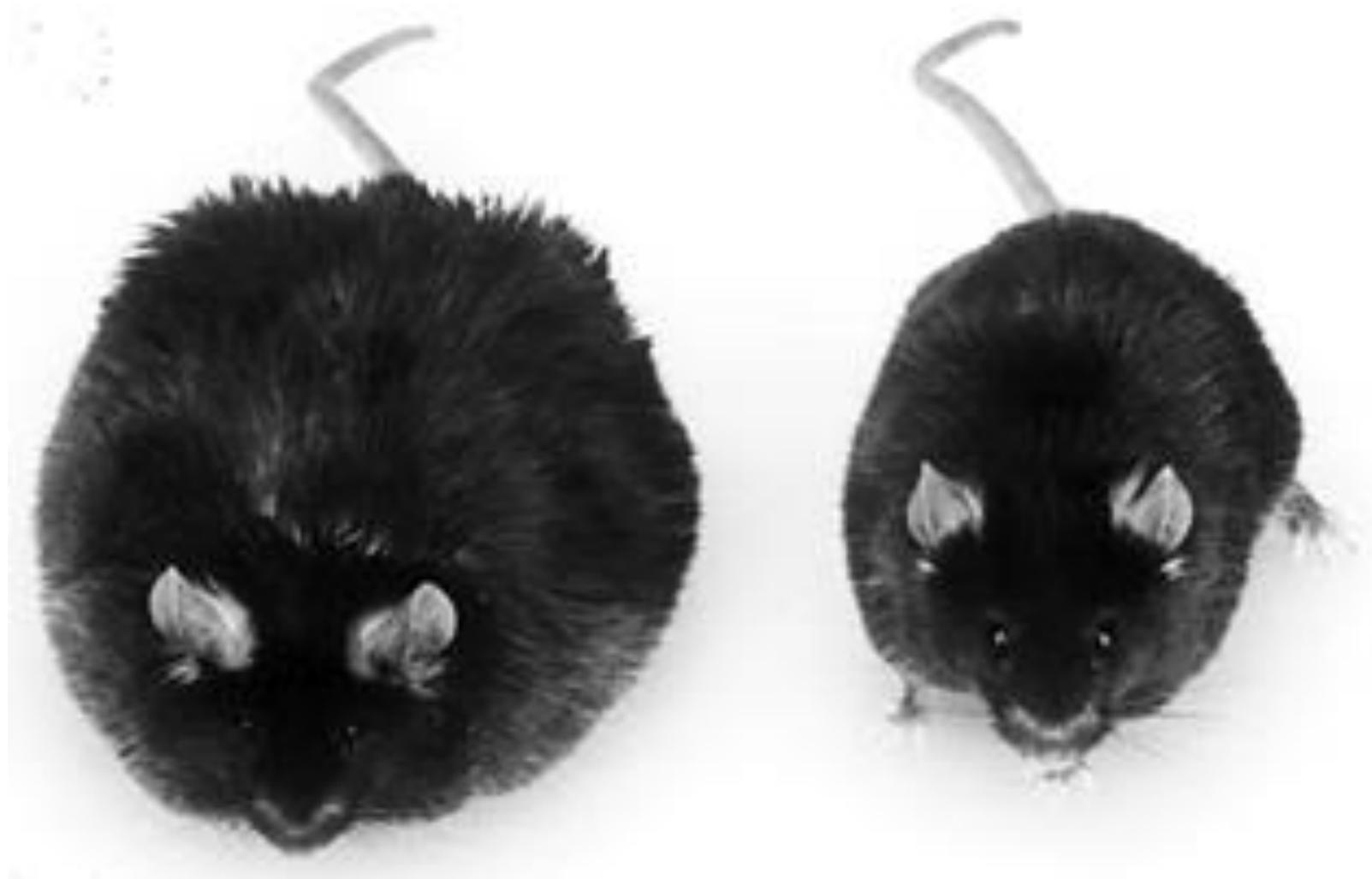
# POMC Mutation



# Adiposity Signals and Melanocortins

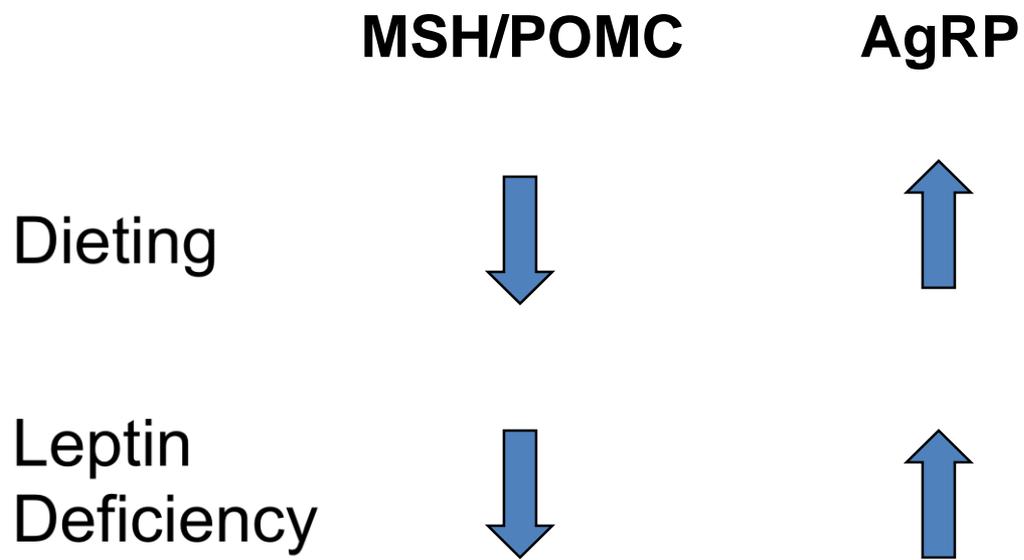
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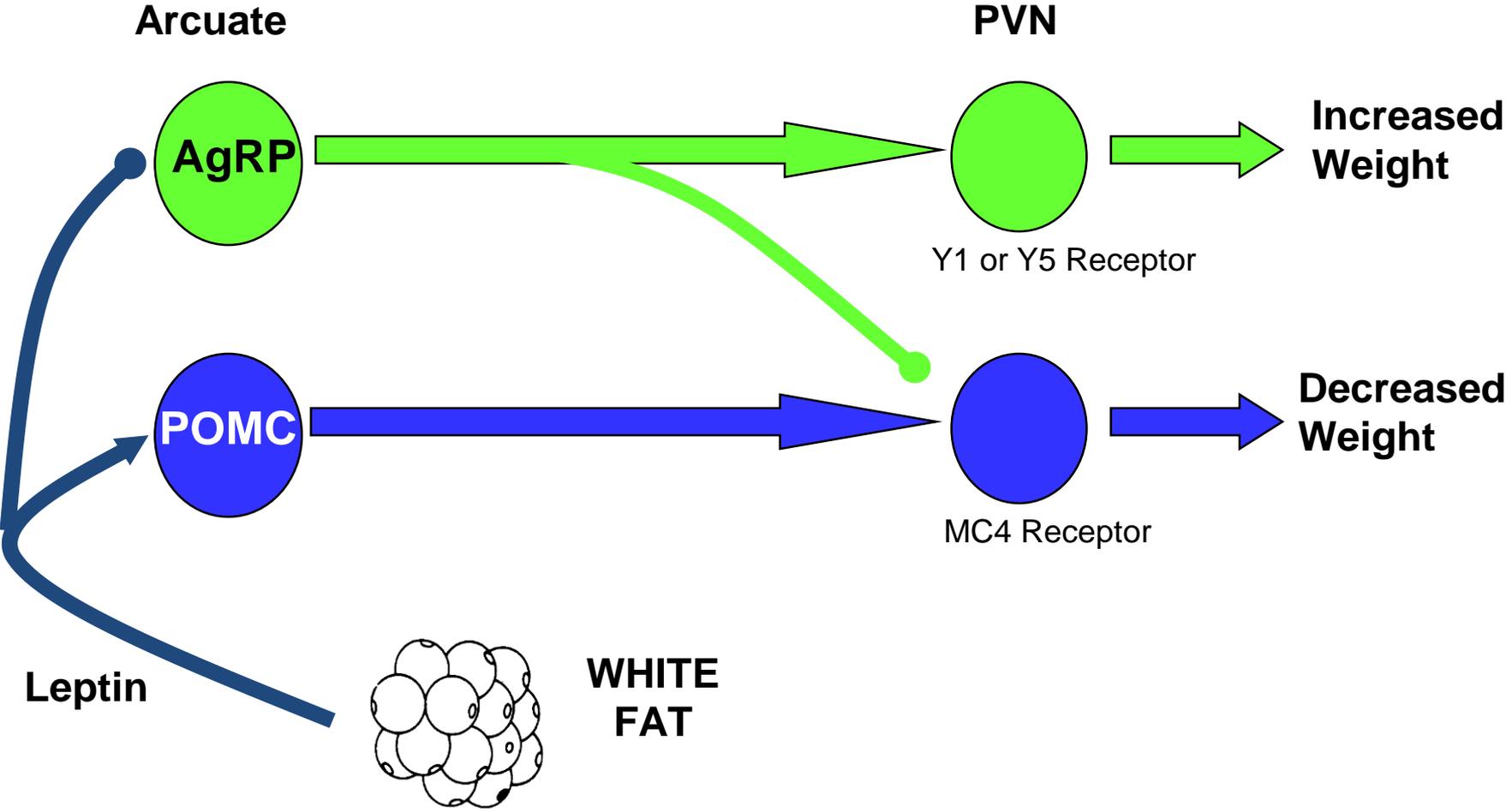
# Leptin and Neuropeptides

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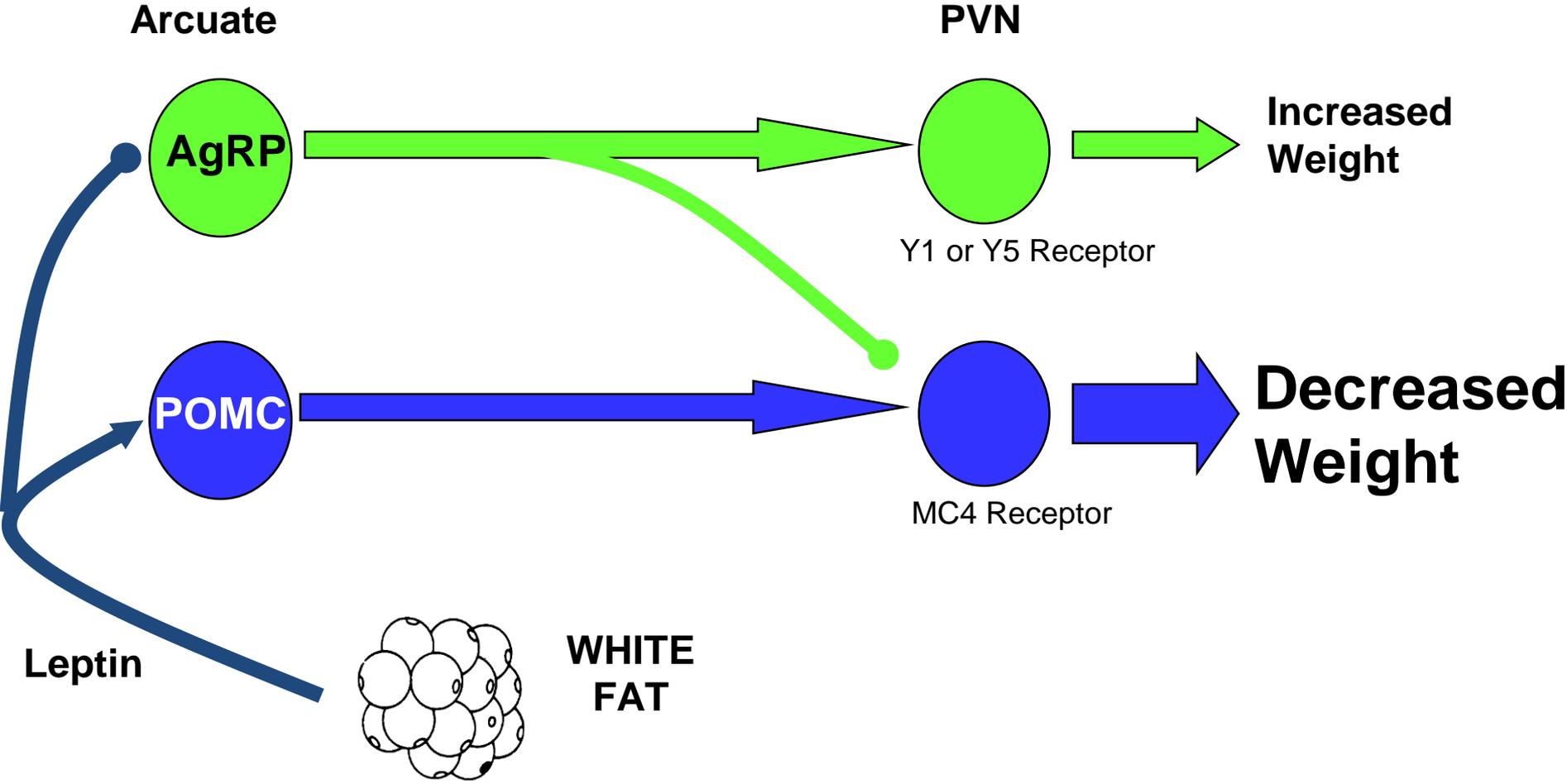
# Model

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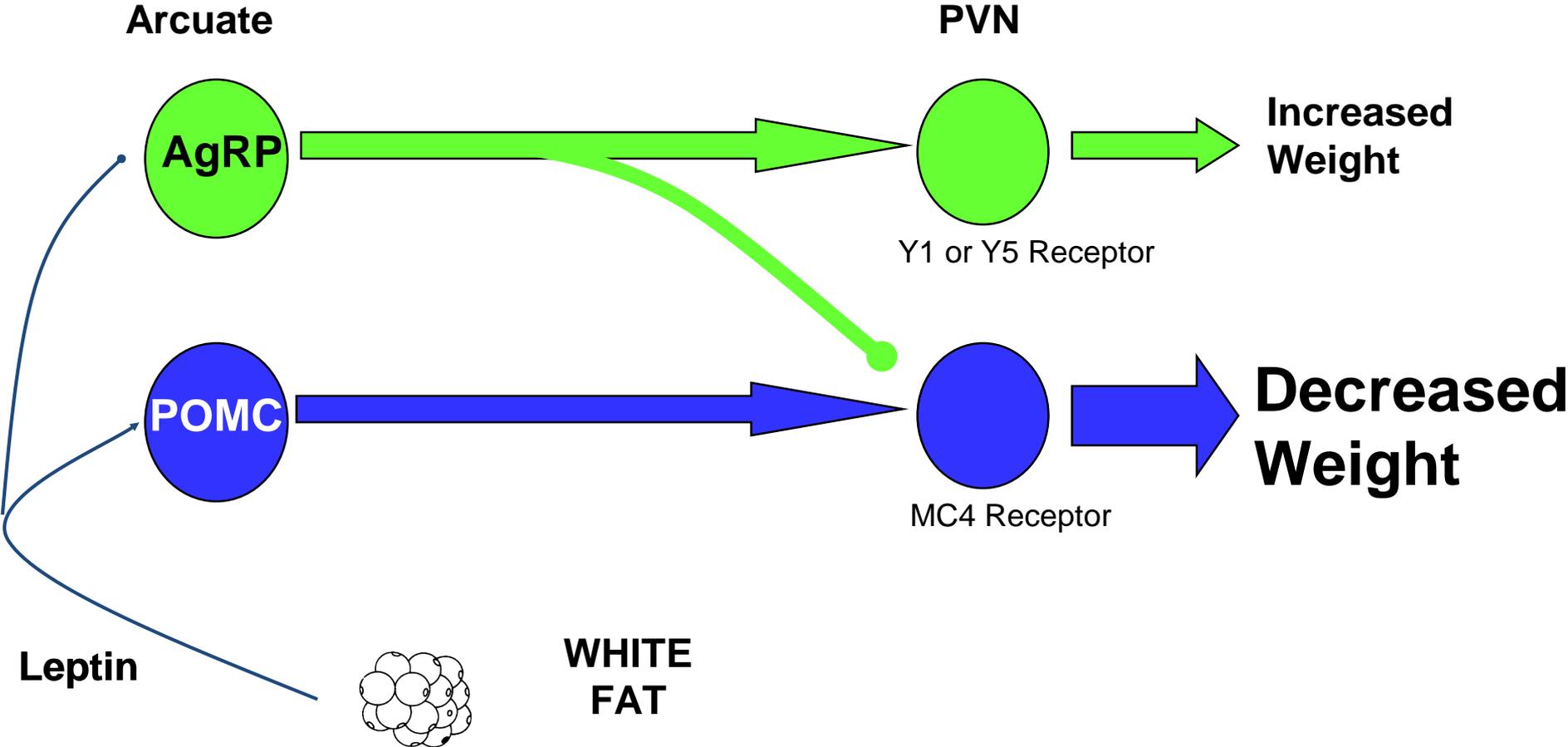
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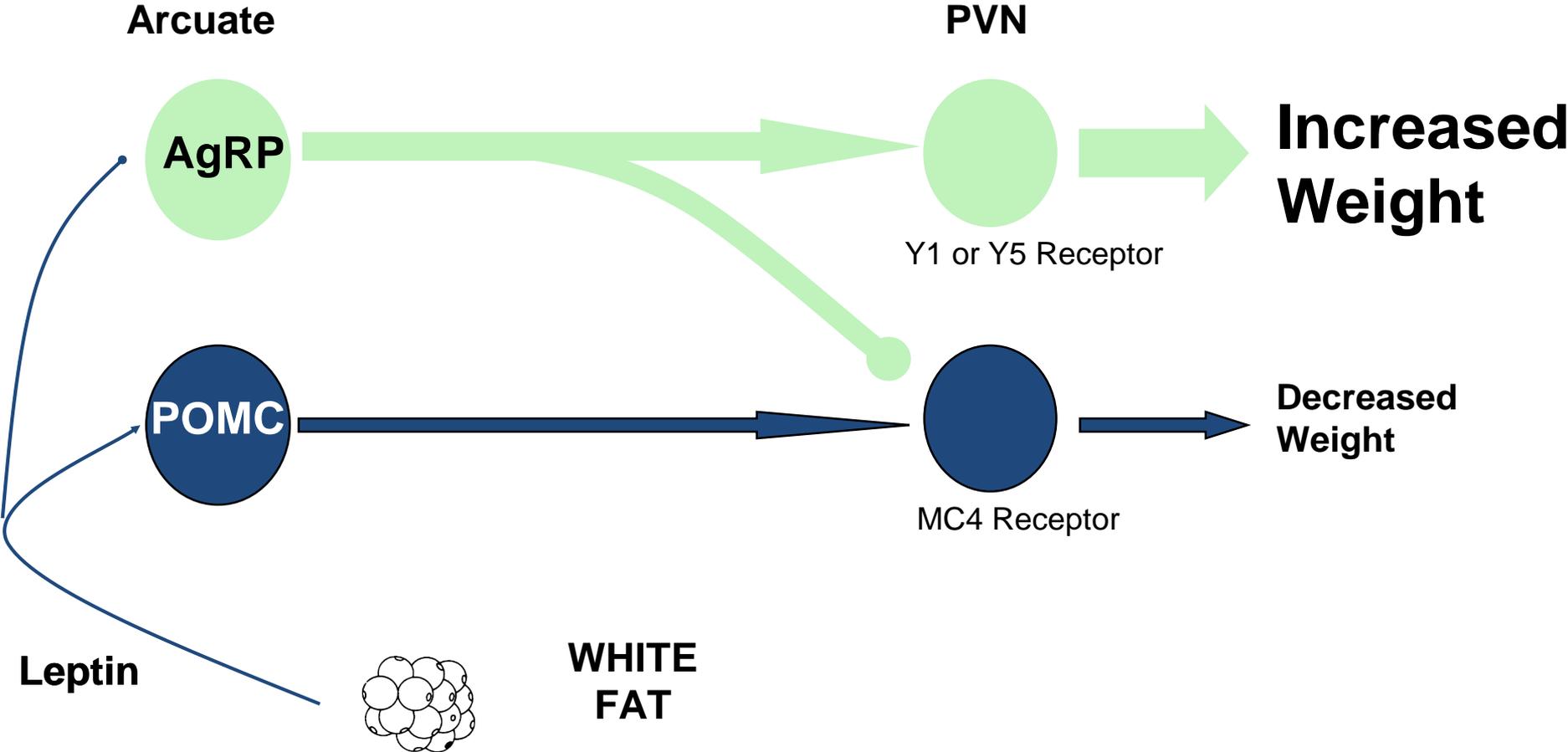
# Model

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# Model

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# Two Questions

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- If the biology of body weight is so accurate, why are we becoming obese?
- Why do some people become obese while others remain lean?

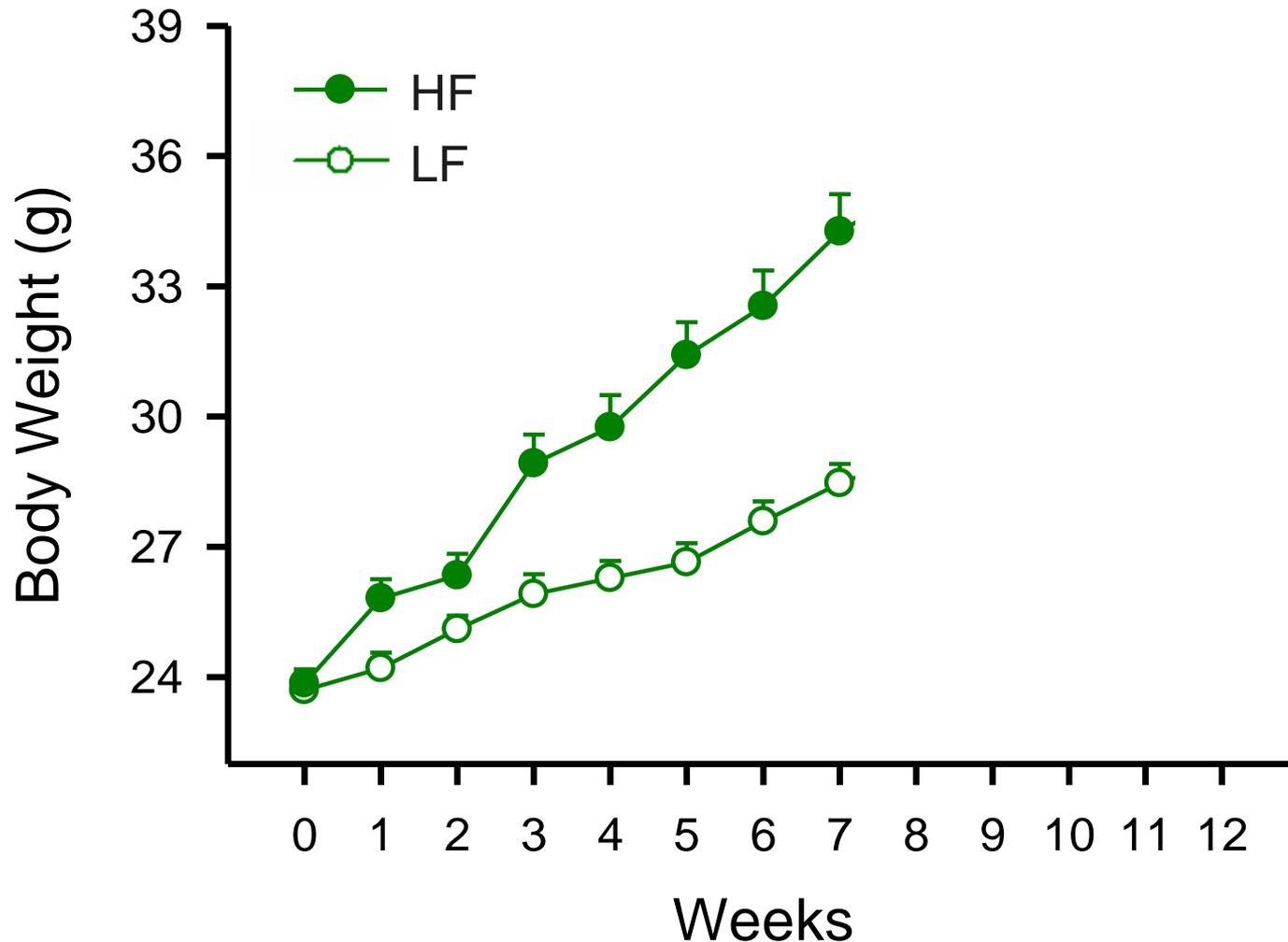
# Two Questions

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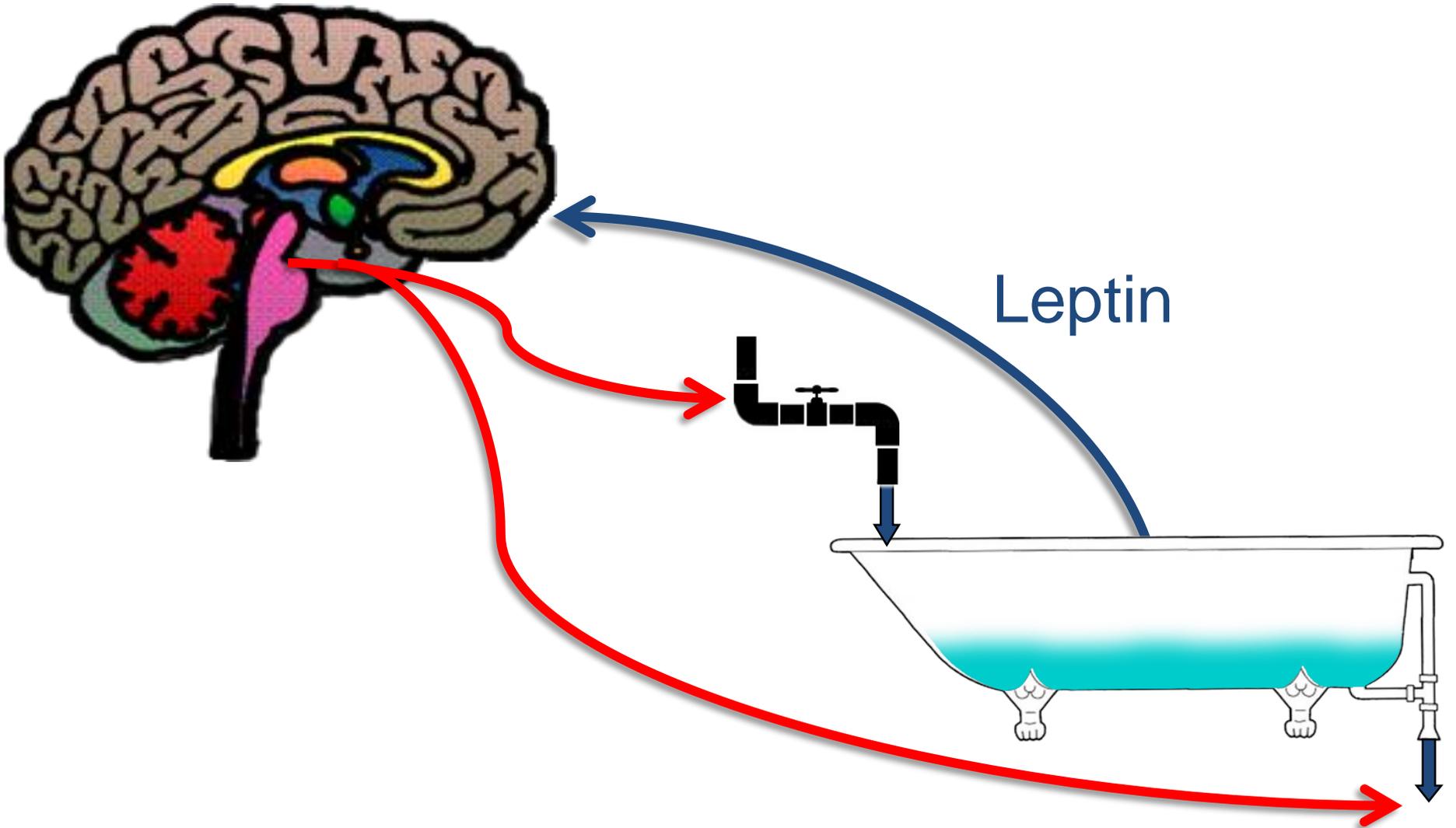
# HF Diets Increase Body Weight in Mice

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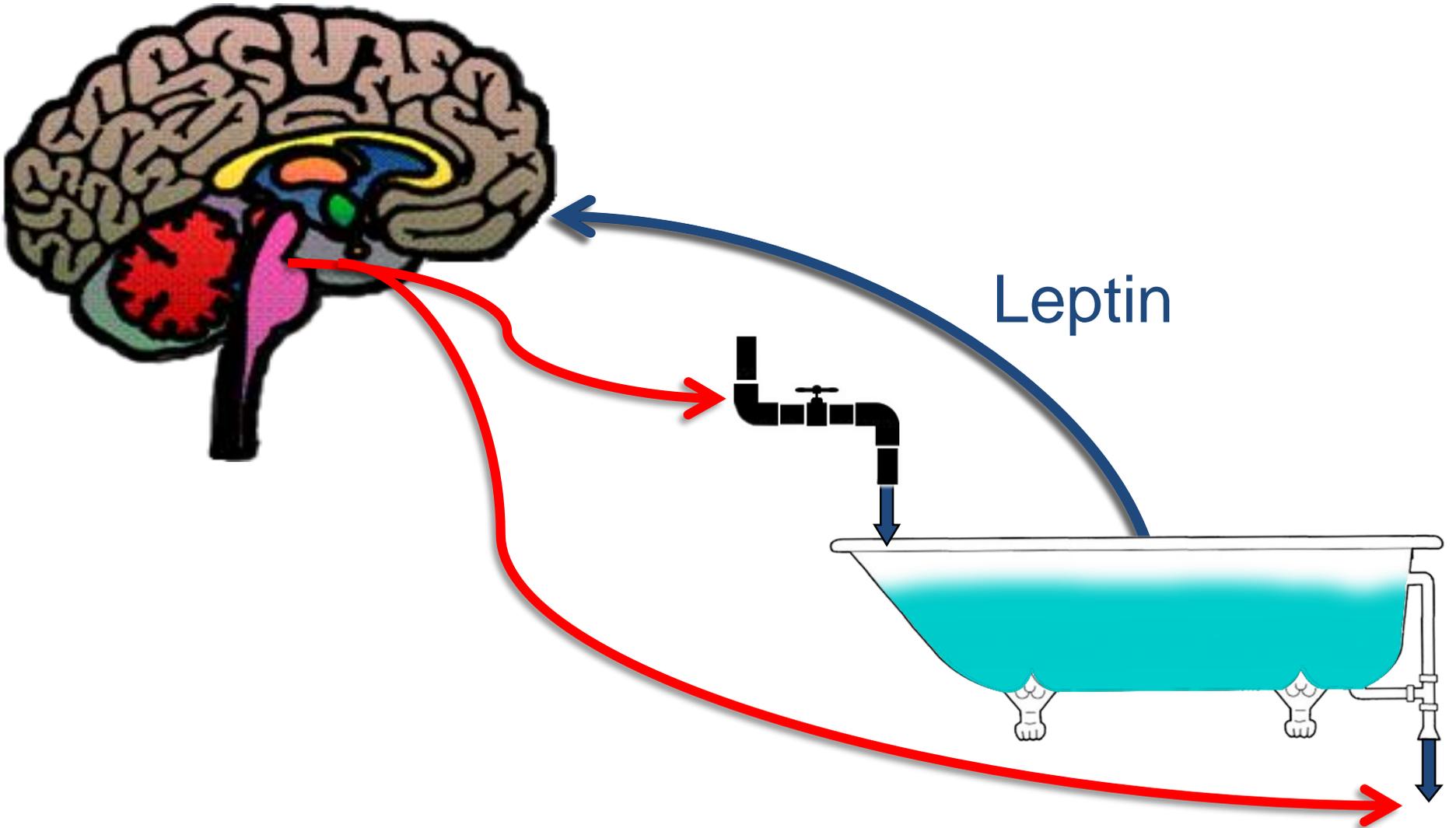
# The Adipose “Bathtub”

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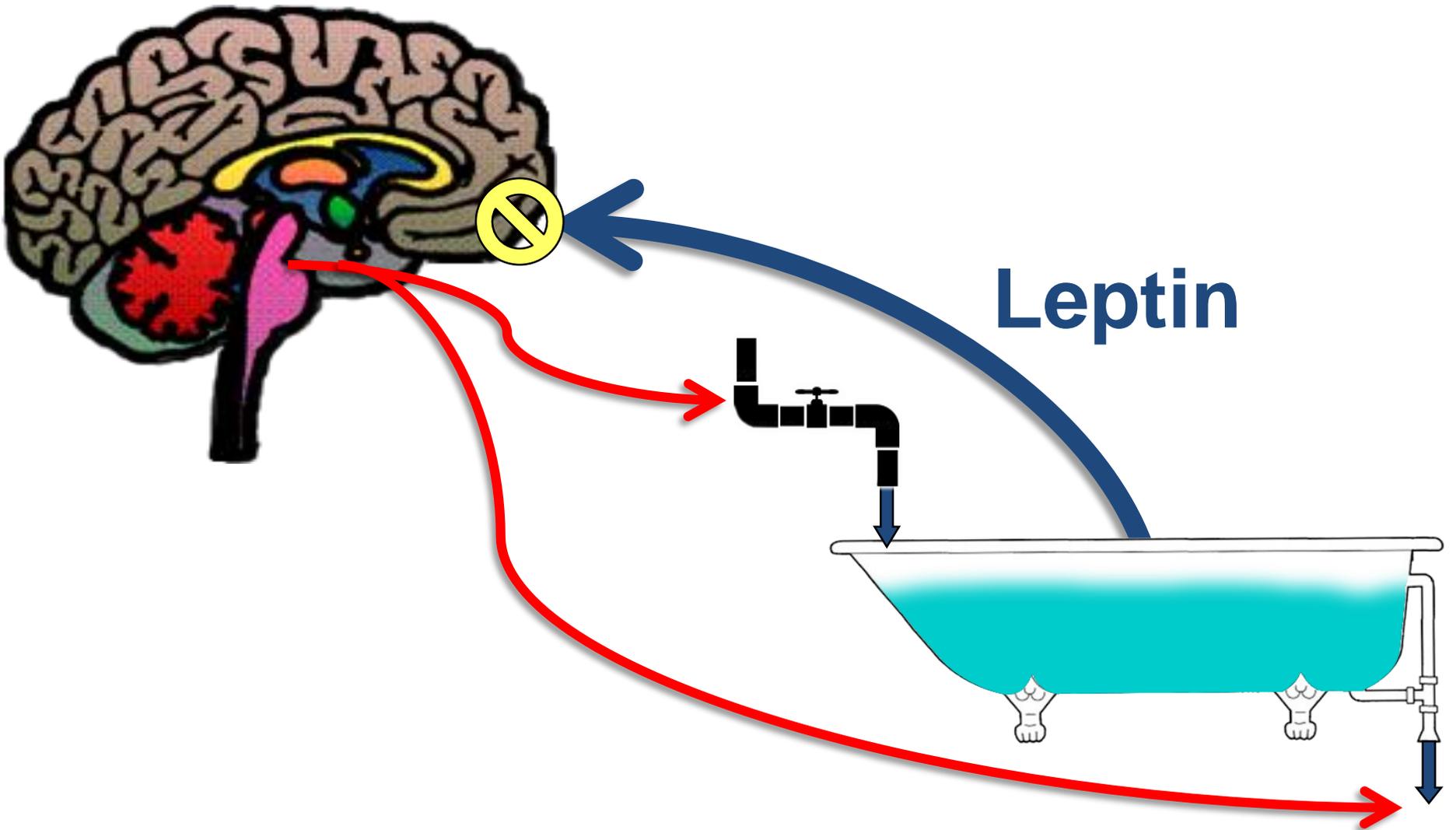
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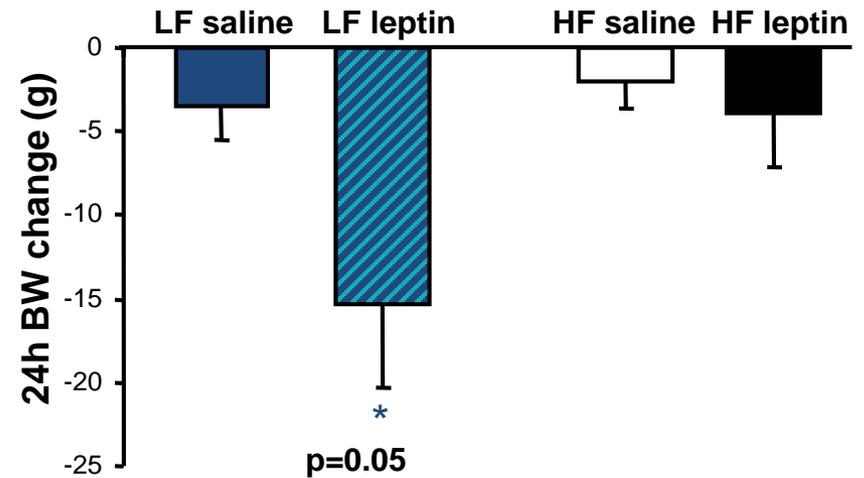
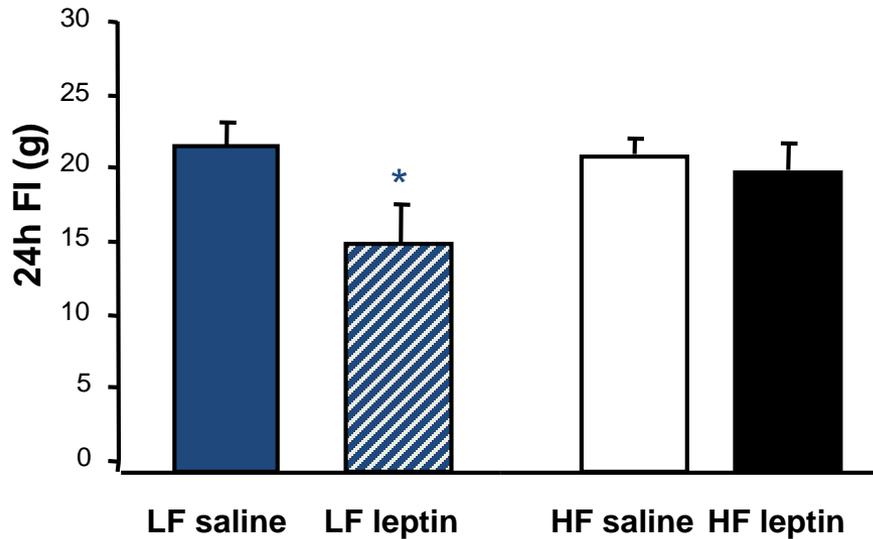


# The Adipose “Bathtub”

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# HF Diet and Leptin Resistance in Rats



# Two Questions

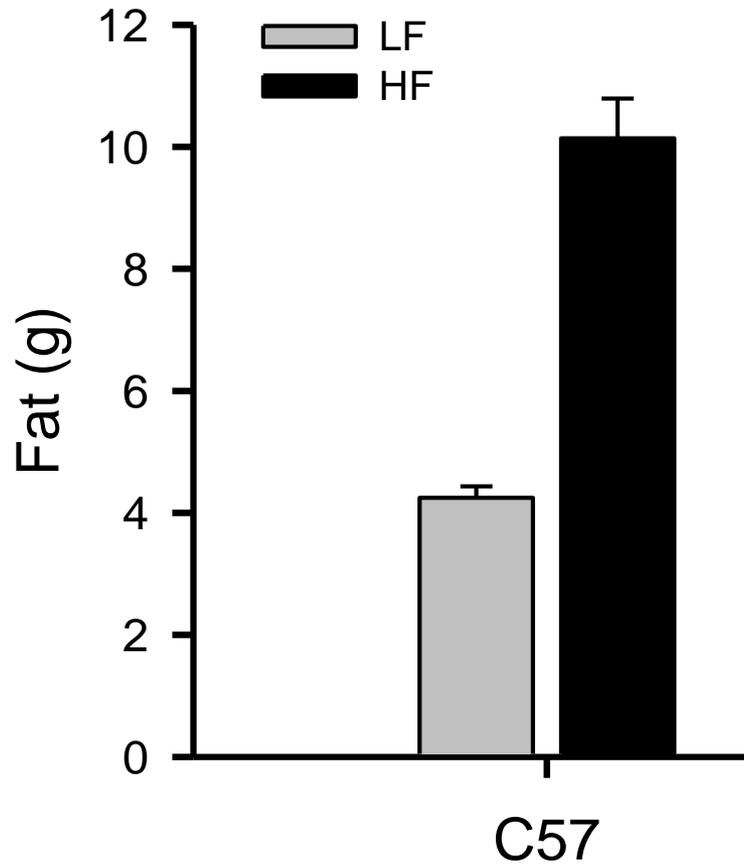
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# Differences in Response to High-Fat Diets in Mice

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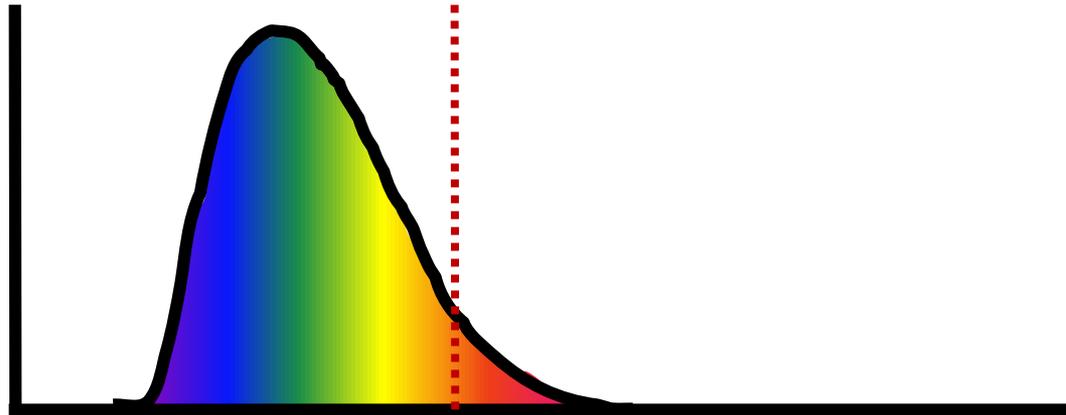
12 weeks on HFD



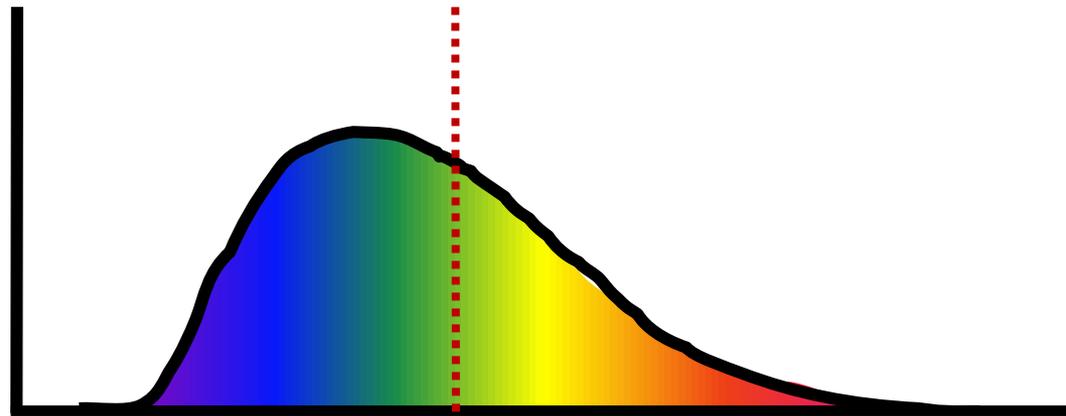
# Gene-Environment Interactions

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Then:



Now:

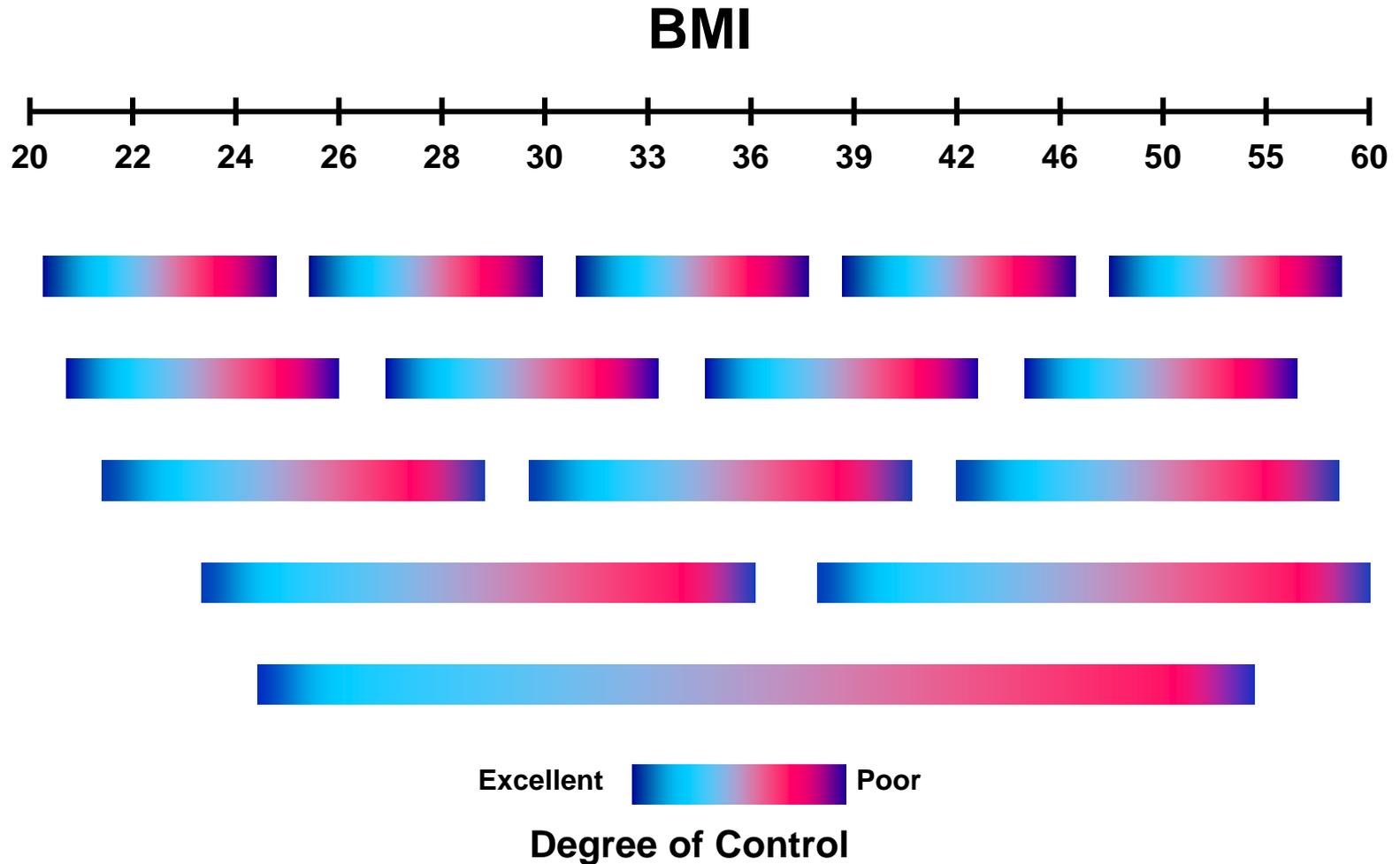


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Body Mass Index

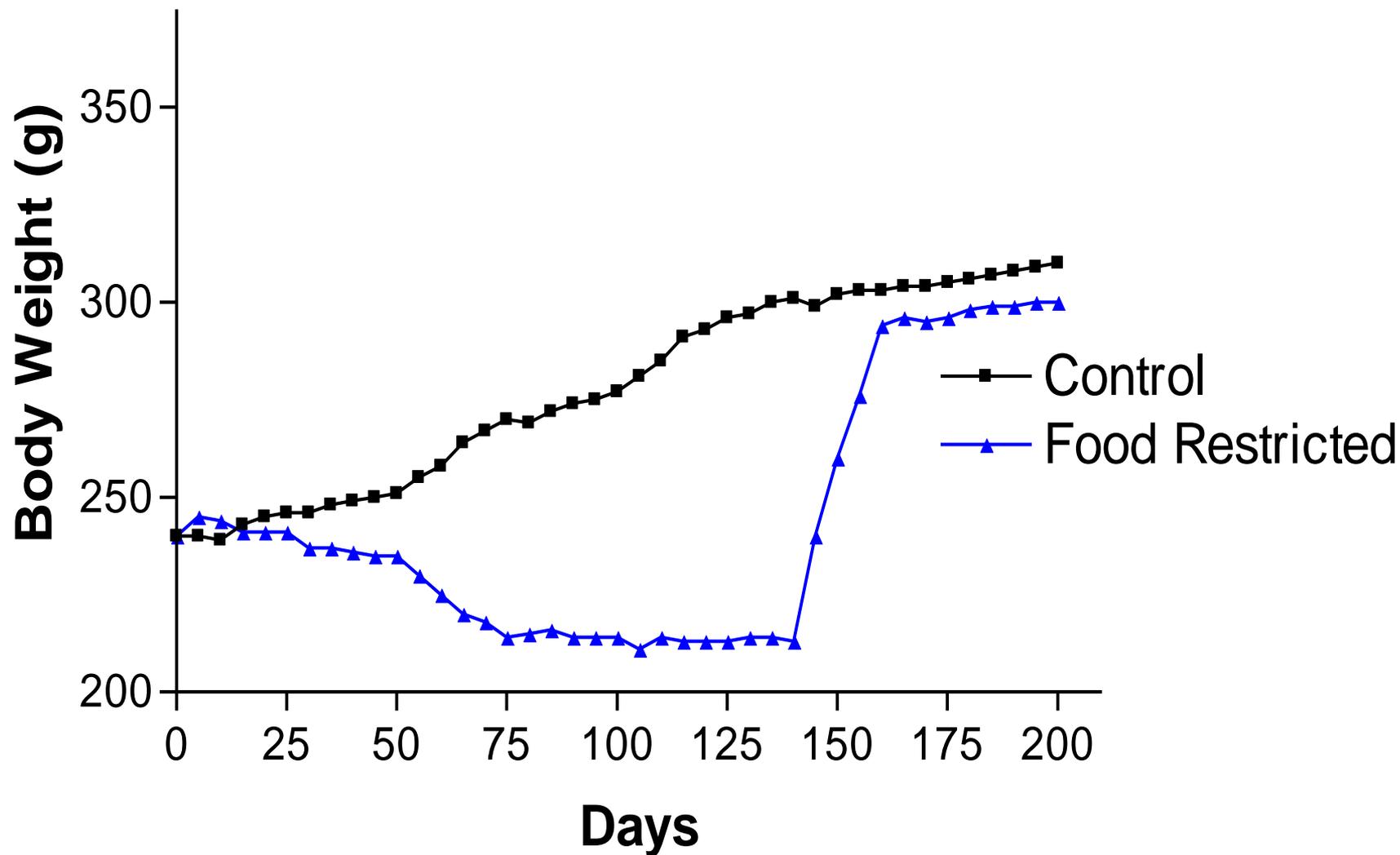
# Natural Variation and Zones of Opportunity

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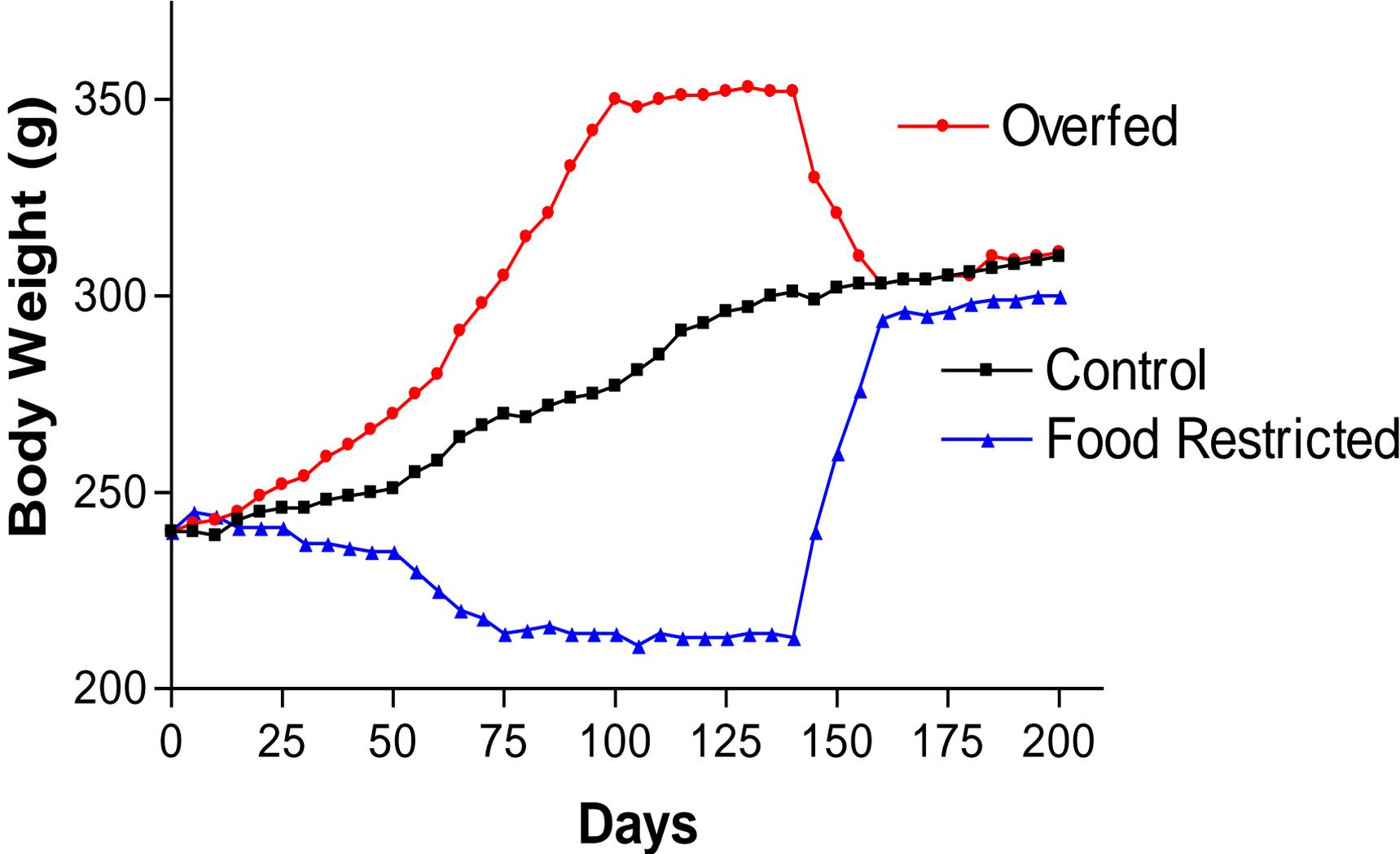
# Negative Energy Balance in Rats

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# Positive Energy Balance in Rats

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# Exercise and Weight Regulation

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Hadza Tribesman

Hunter-Gatherer

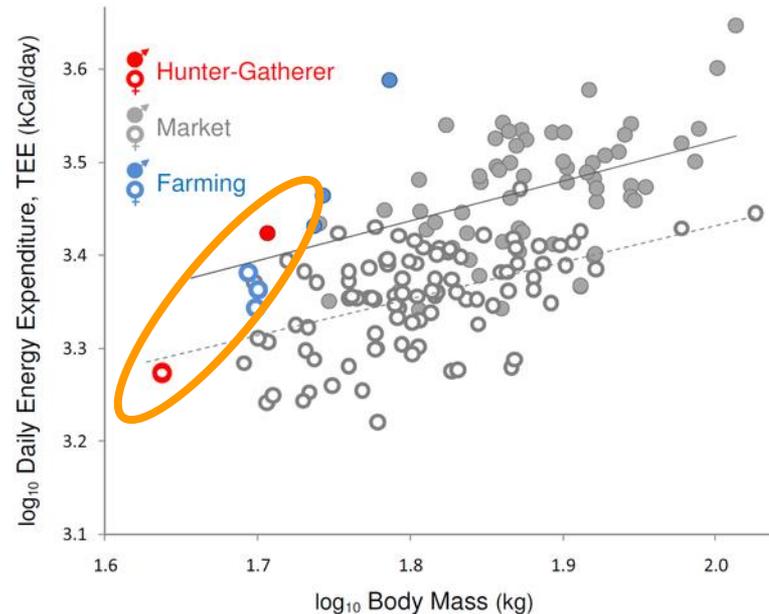
Exercises 300-500 kcal/day

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How much more energy is expended daily by the hunter-gatherer Hadza?

# The Normal Physiology of Energy Balance

## Hunter-Gatherer Hadza and Westerners Have *Equal* Daily Energy Expenditure



“... human daily **energy expenditure** may be an evolved physiological trait largely independent of cultural differences.”

# Energy Output

- Basal metabolic rate
- Thermogenesis
- Exercise and physical activity
- NEAT

