Which Comes First: Overeating or Obesity?

Reinterpreting the 1st Law of Thermodynamics

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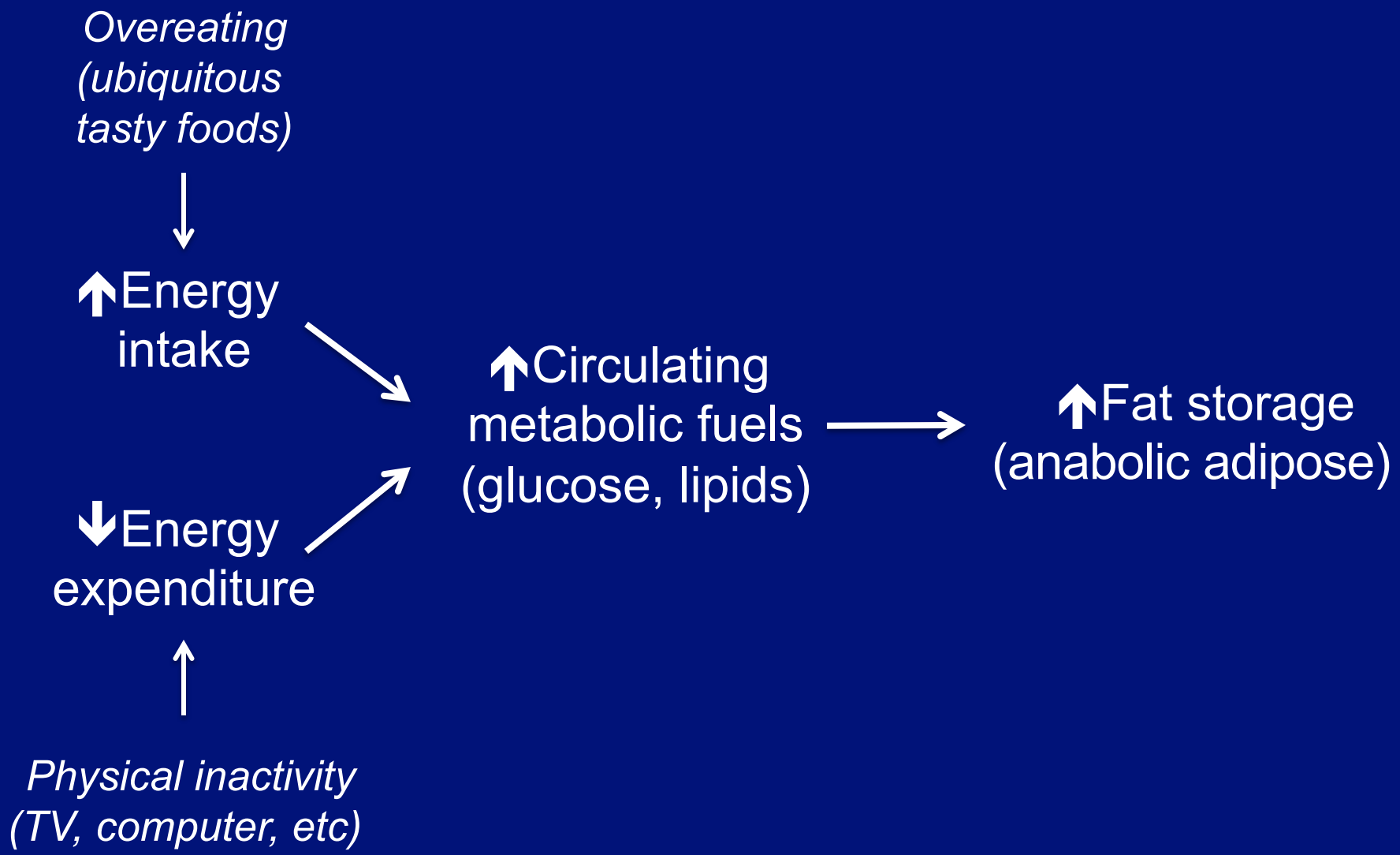
First Law of Thermodynamics

Energy can neither be created or destroyed

Calorie intake - Calorie expenditure = Calories stored (change in adiposity)

Conventional Interpretation of the First Law

Obesity, a failure of voluntary control over energy balance



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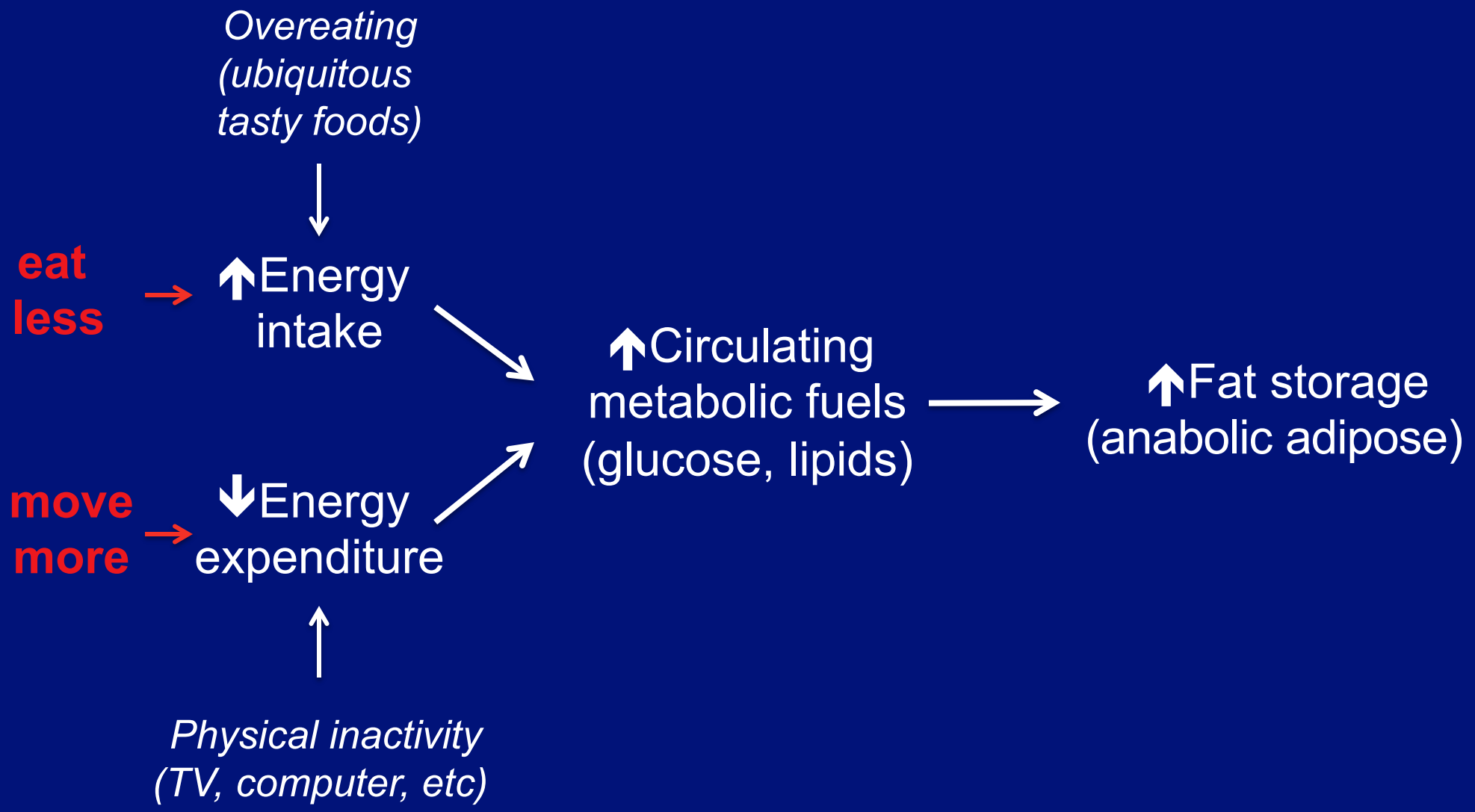


Conventional Obesity Treatment in Adults

National Health & Nutrition Examination Survey 1999-2006

Only 1 in 6 overweight and obese adults in the US report ever having maintained weight loss of at least 10% for 1 year

Kraschnewski et al. Int J Obes. 2010, 34:1644-54

Conventional Obesity Treatment in Children

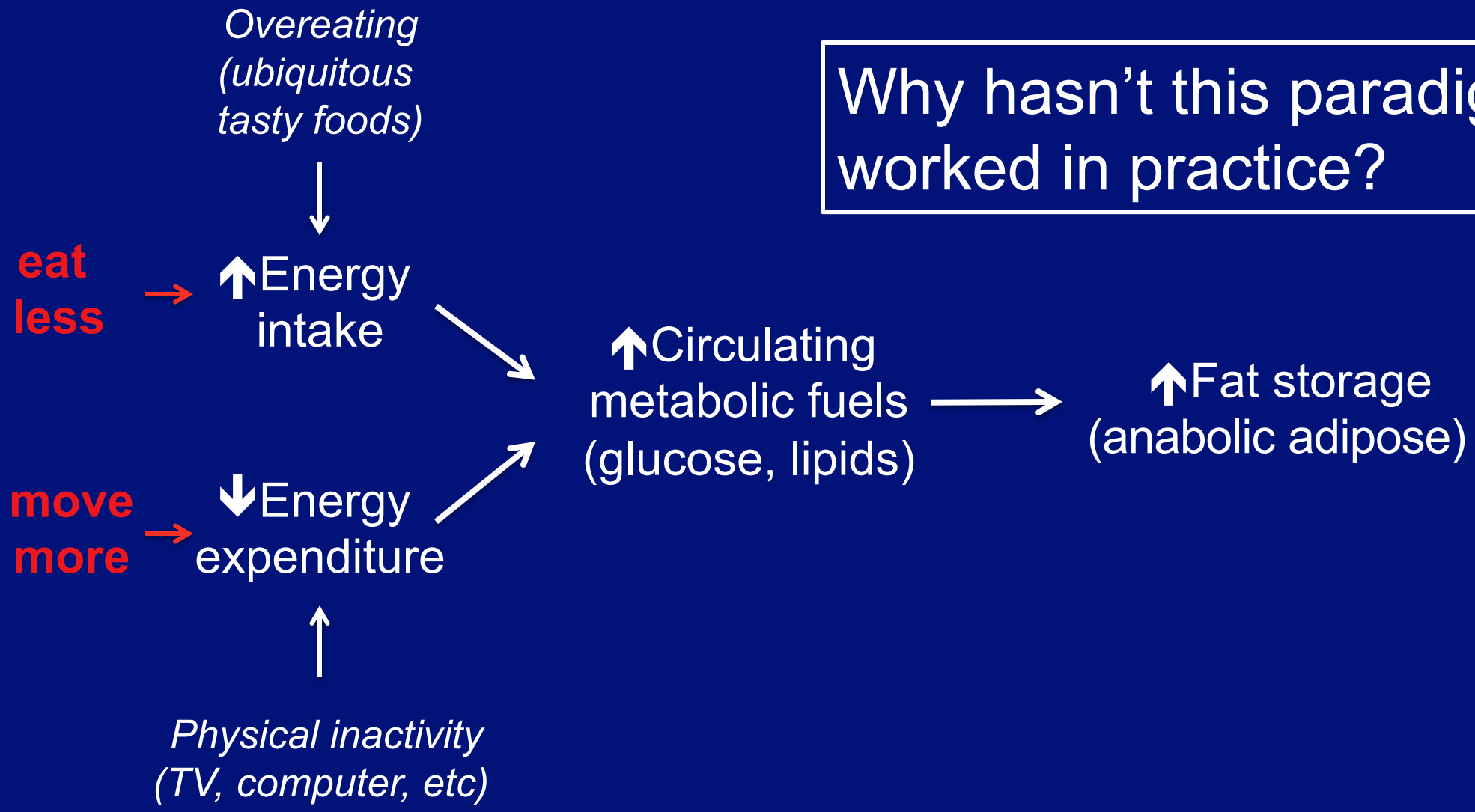
Systematic reviews and meta-analyses

"Most pediatric obesity interventions are marked by small changes in relative weight or adiposity and substantial relapse . . ."

Epstein. Pediatrics 1998, 101:554-70
McGovern. JCEM 2008, 93:4600-5
Kamath. JCEM 2008, 93:4606-15
Waters. Cochrane Rev 2011,12:CD001871

Conventional View of Obesity

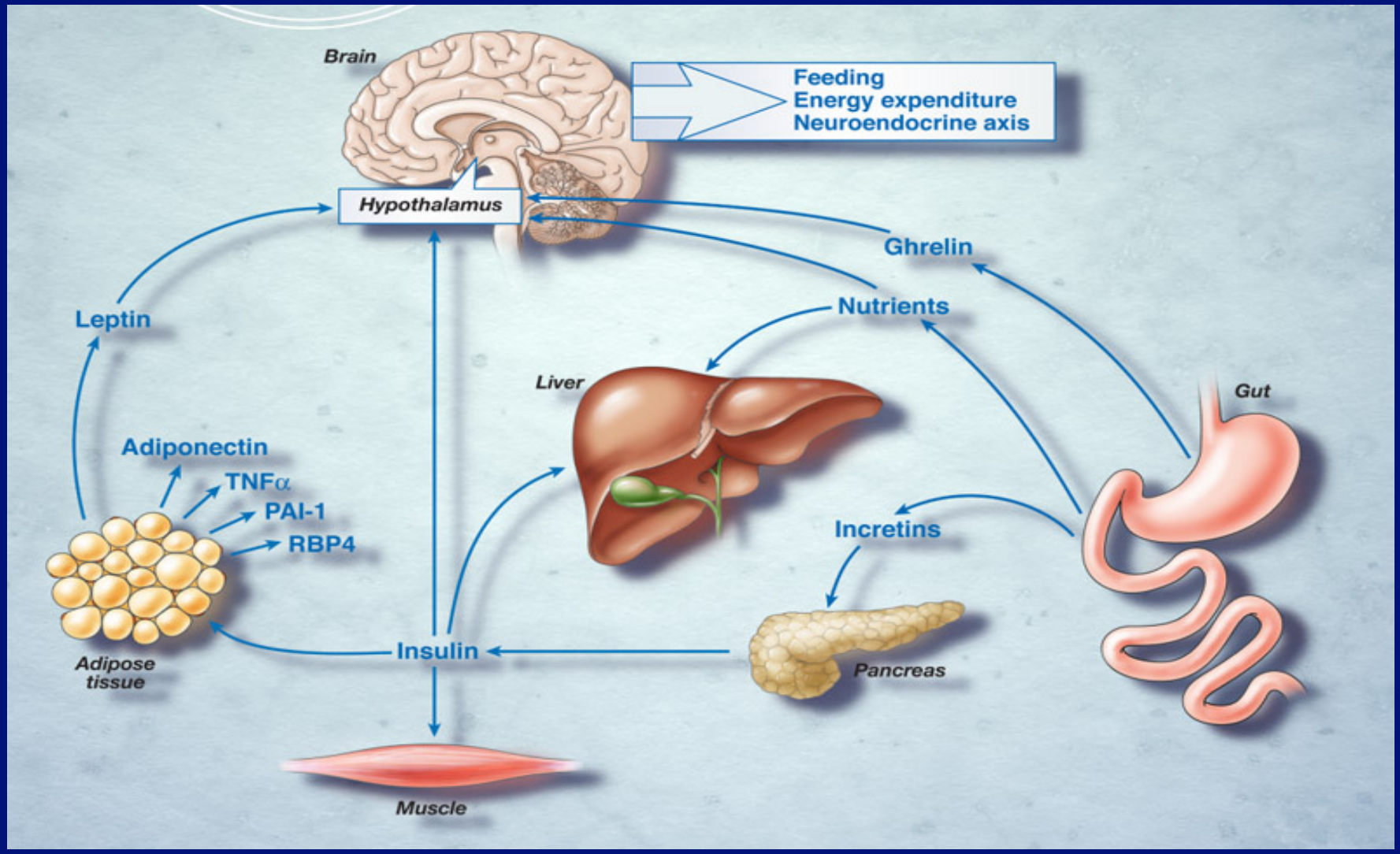
Failure of voluntary control over energy balance



Why hasn't this paradigm worked in practice?

Body Weight is Under Biological Control

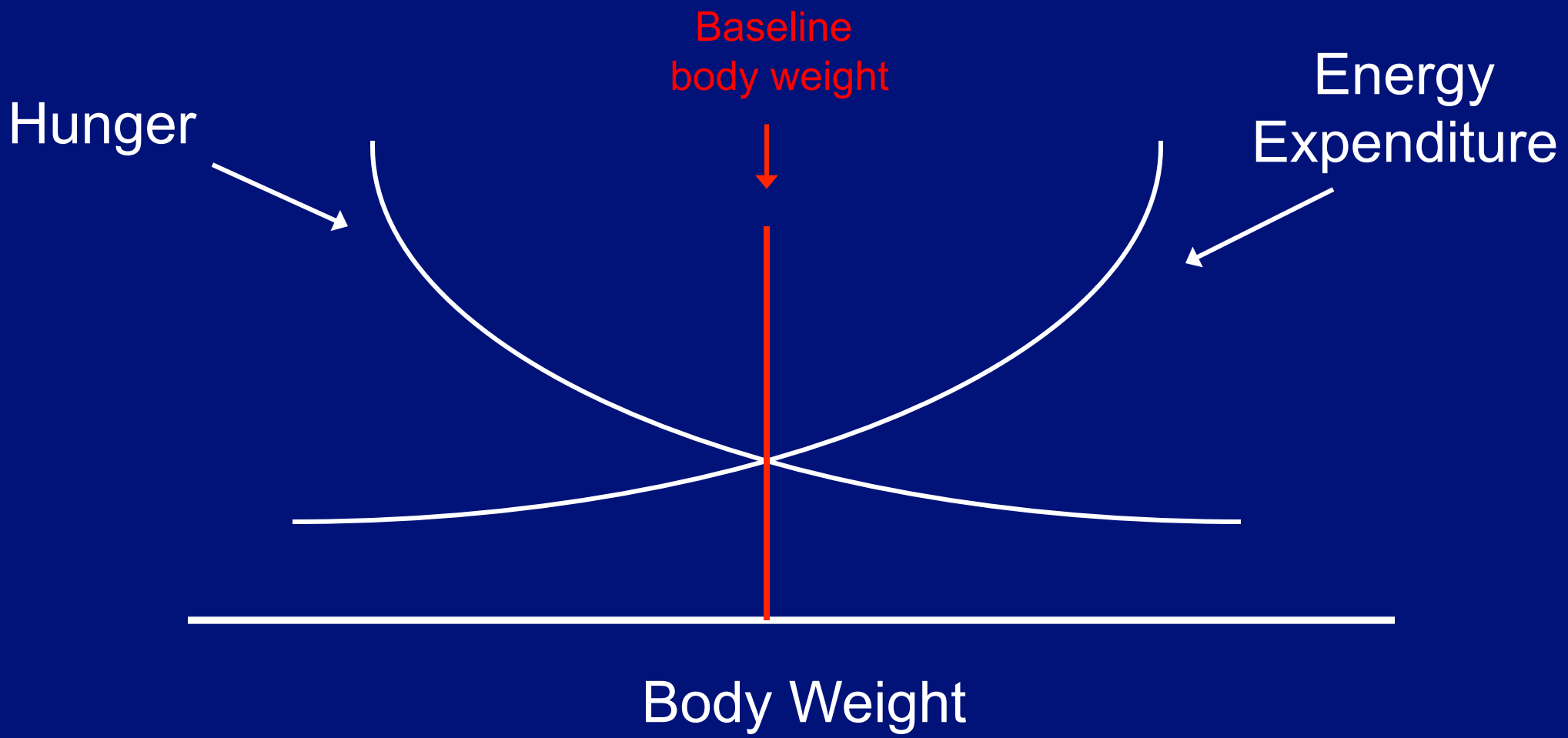
Complex interconnected feedback mechanisms



Ahima, Gastroenterology 2007

Body Weight is Under Biological Control

Physiological adaptations antagonize weight change



Leibel, NEJM 1995, 332:621-8; Kissileff, AJCN 2012, 95:309–17

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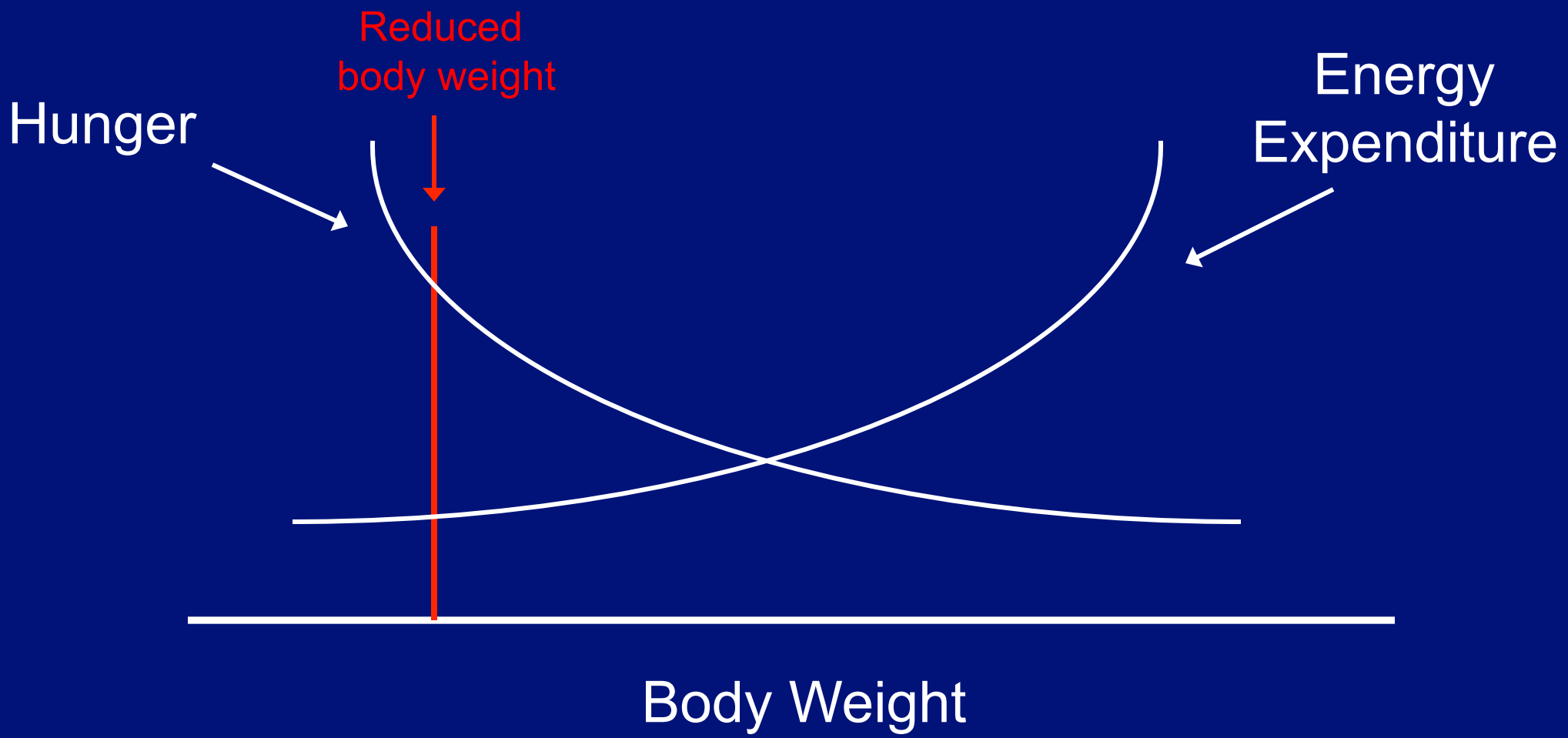

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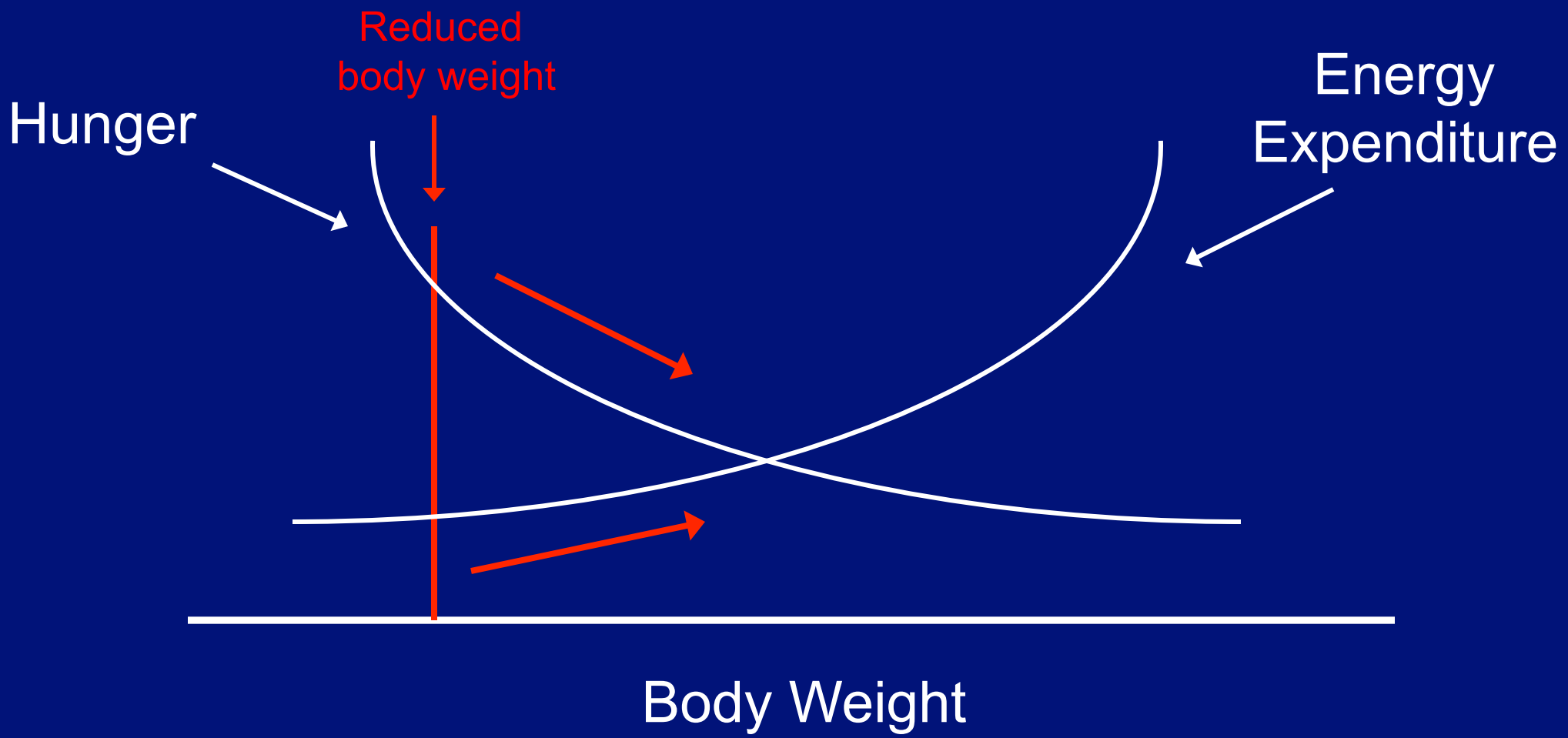

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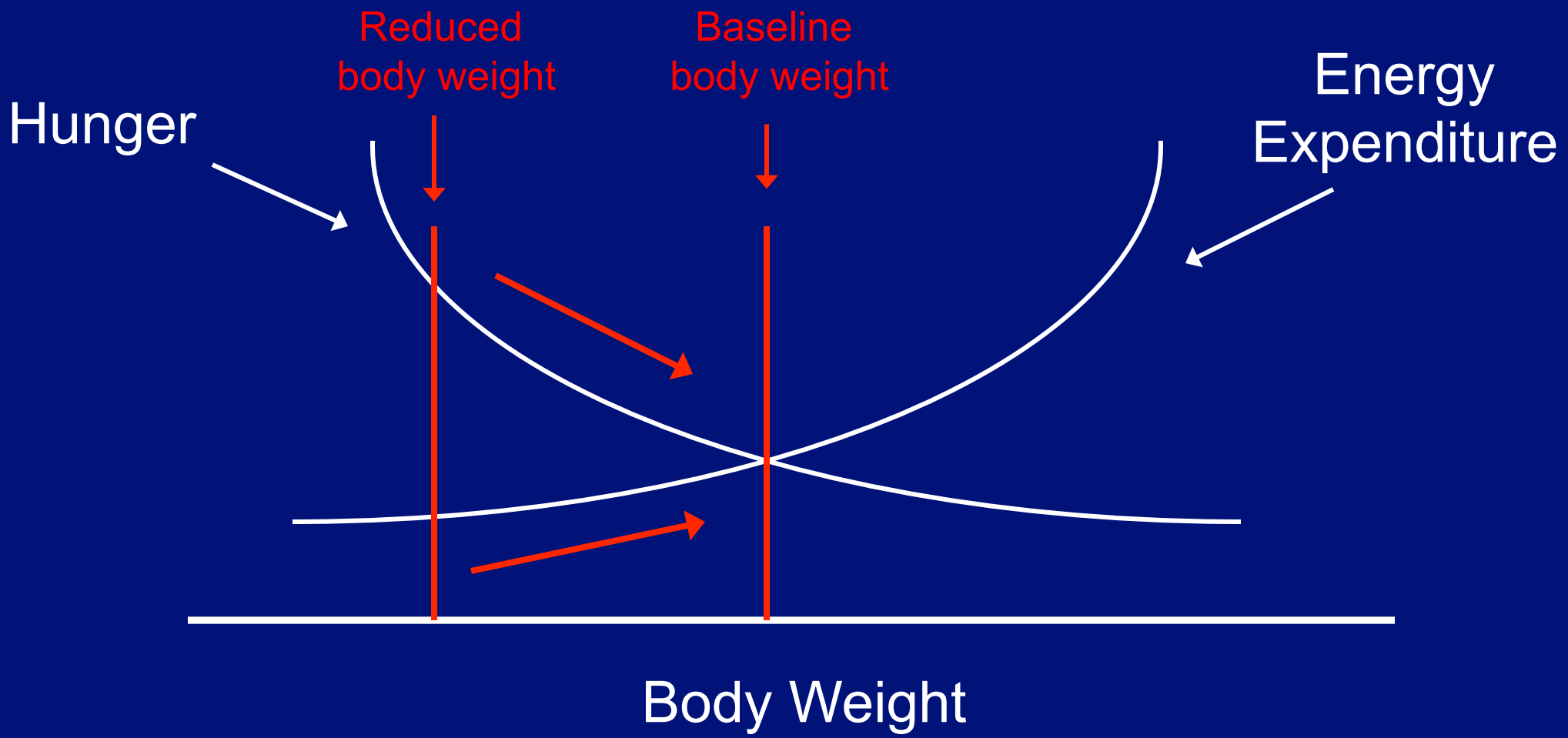

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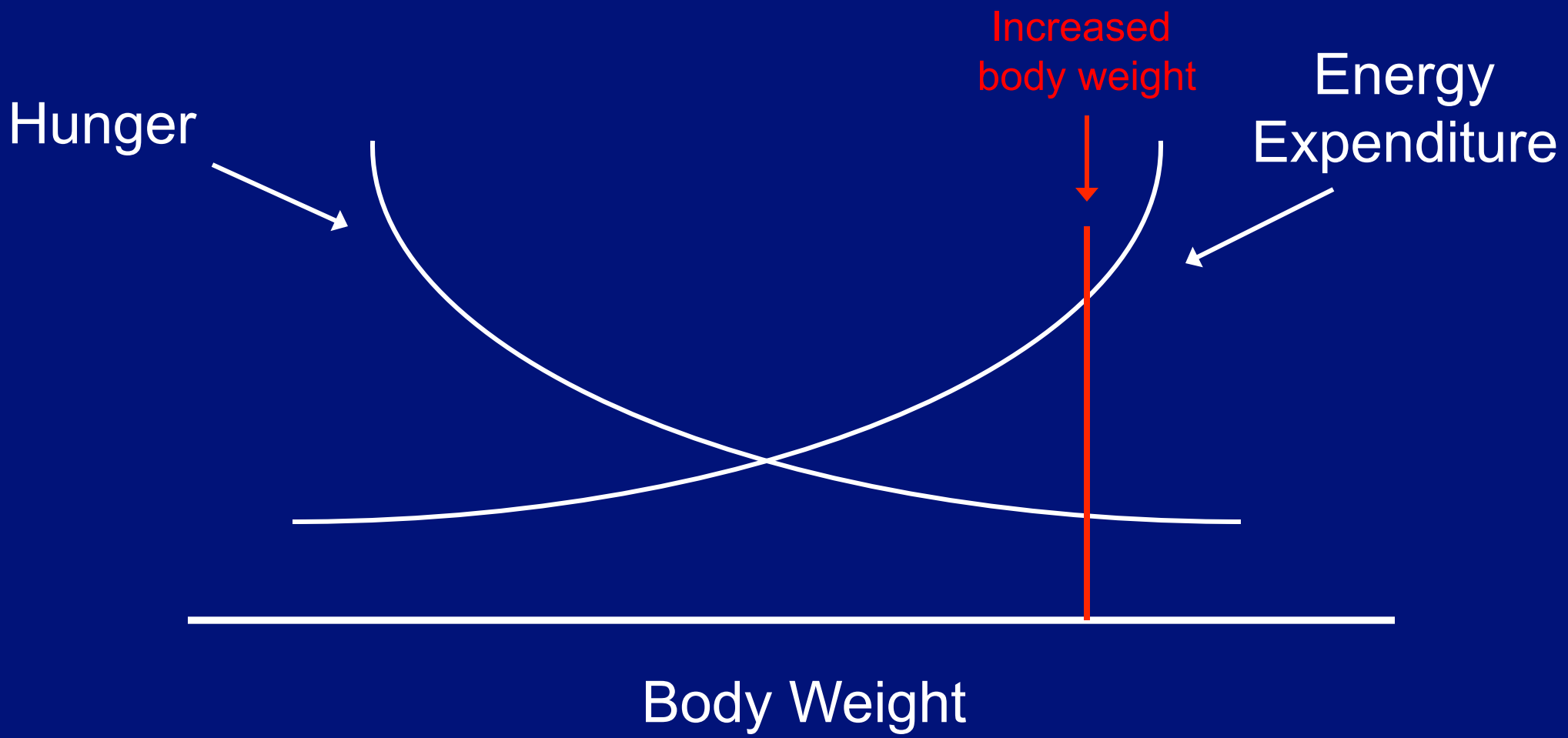

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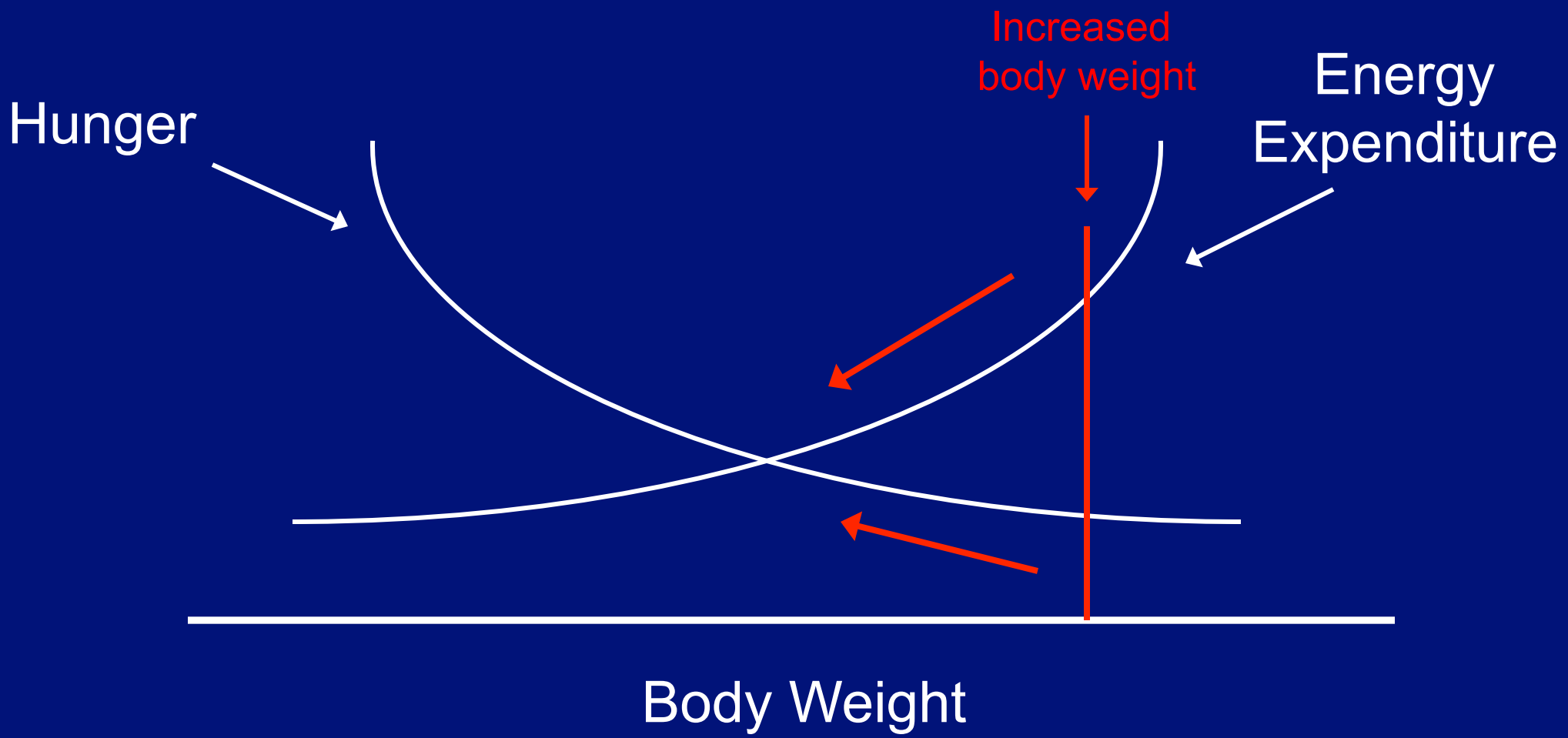

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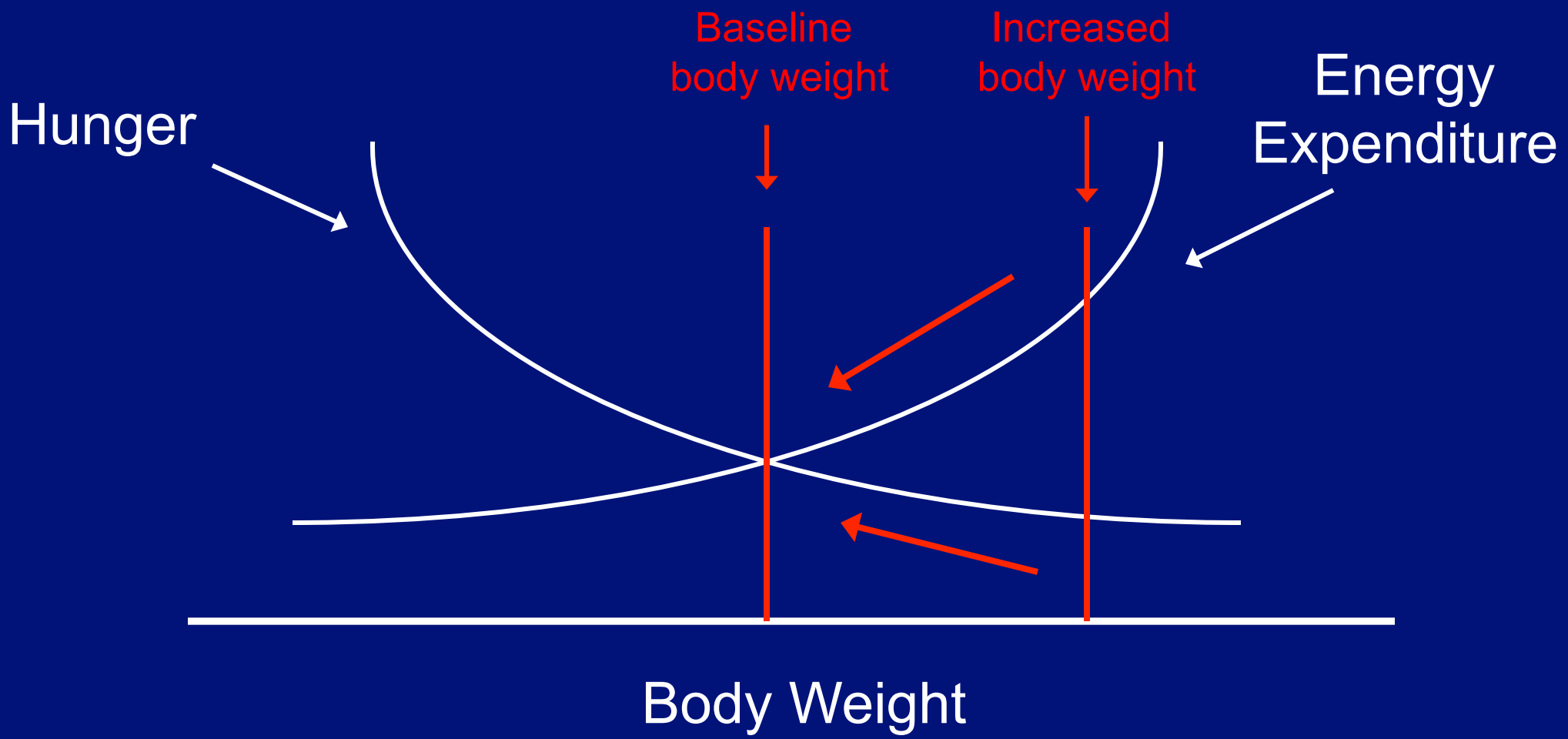

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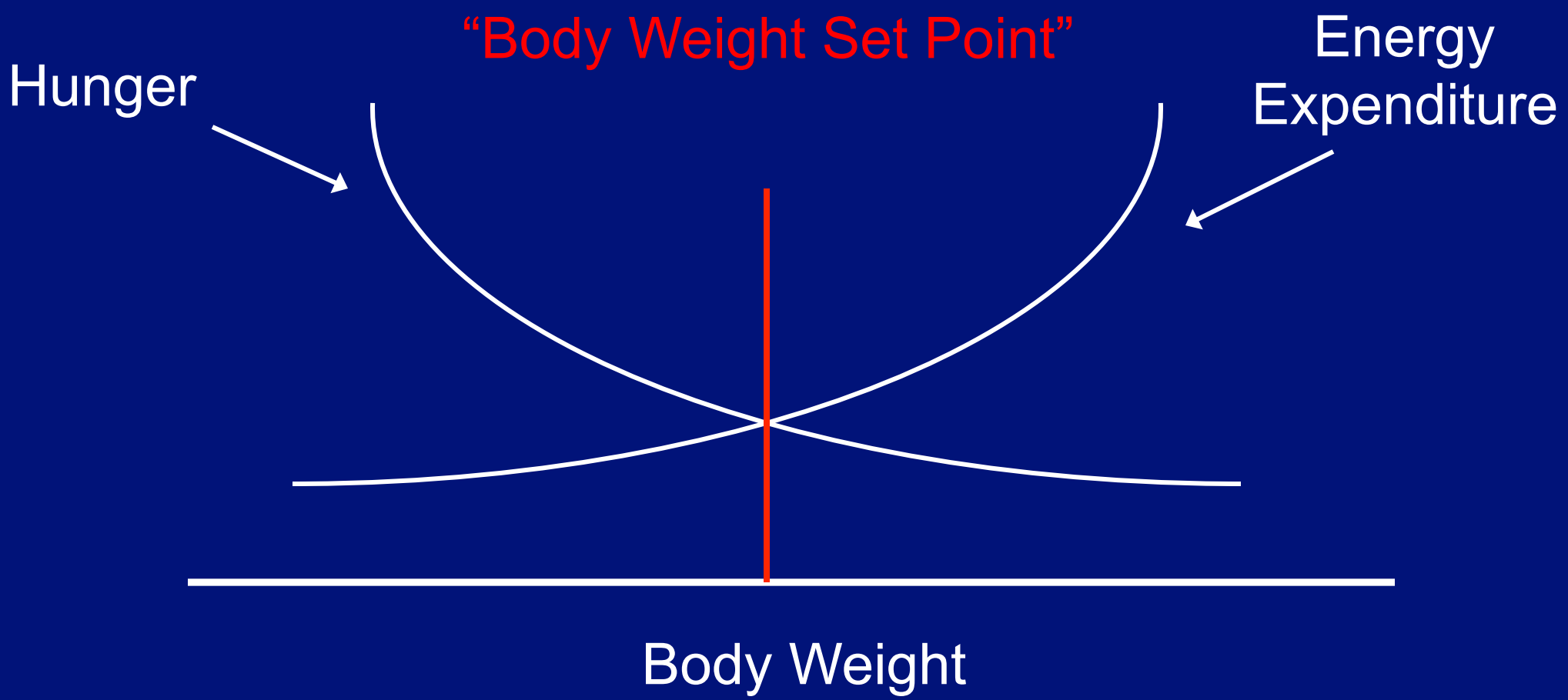
Body Weight is Under Biological Control

Complex interplay of biological & environmental factors



The Obesity Epidemic

Rising BMI among genetically stable populations

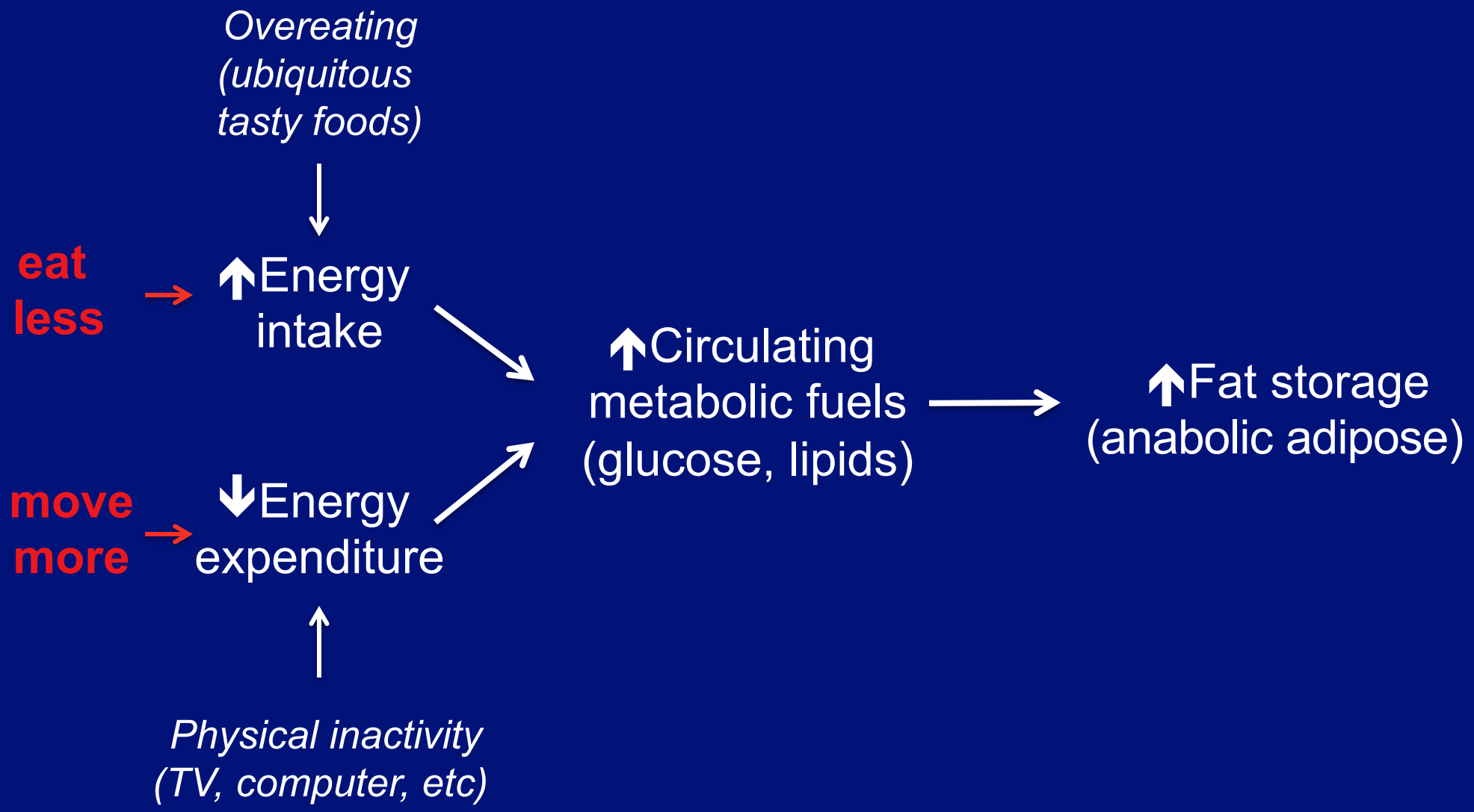
Key Questions:

Why has the level of defended body weight – the observed "Set Point" – increased in recent years?

What can we do about it?

Conventional View of Obesity

Failure of voluntary control over energy balance



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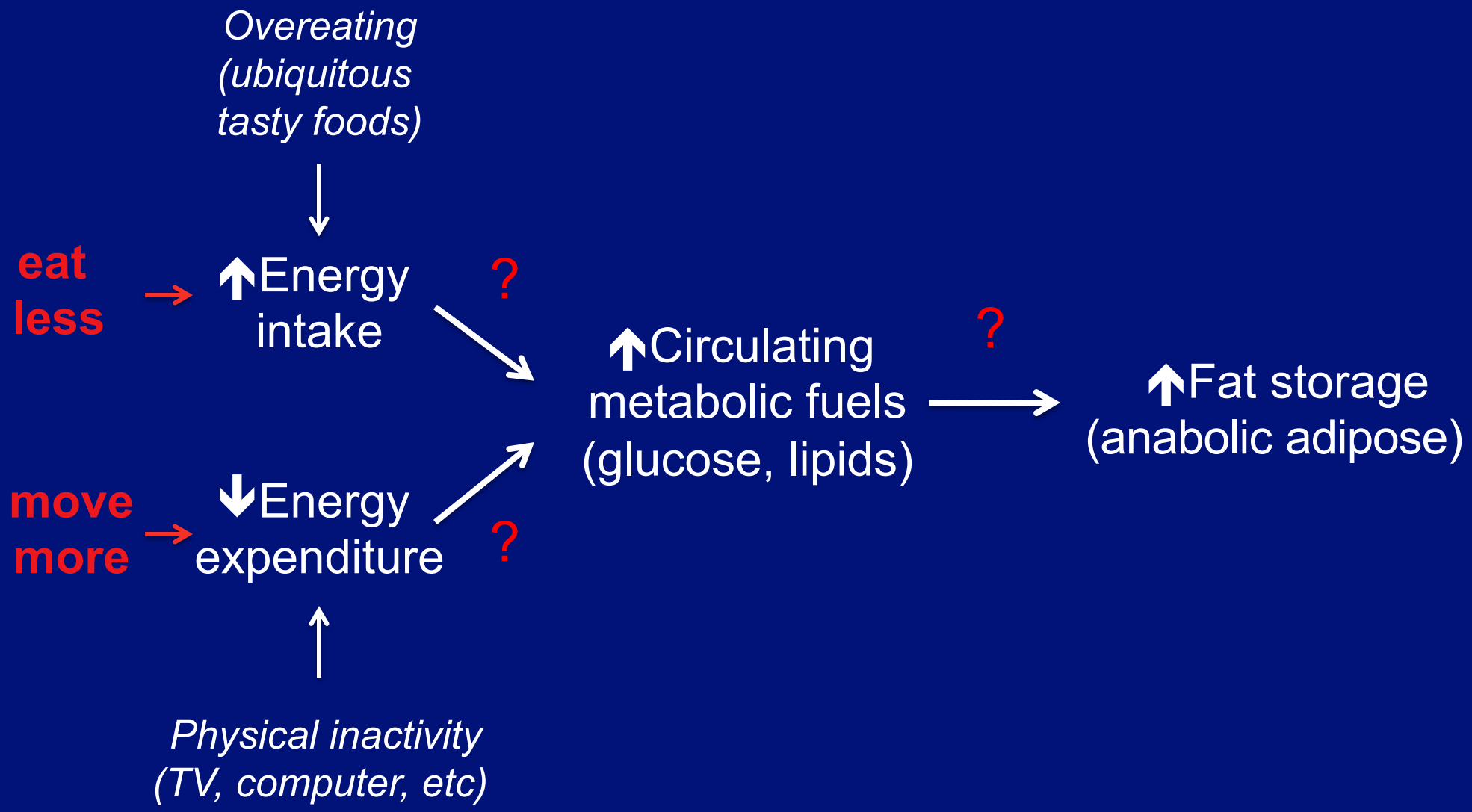
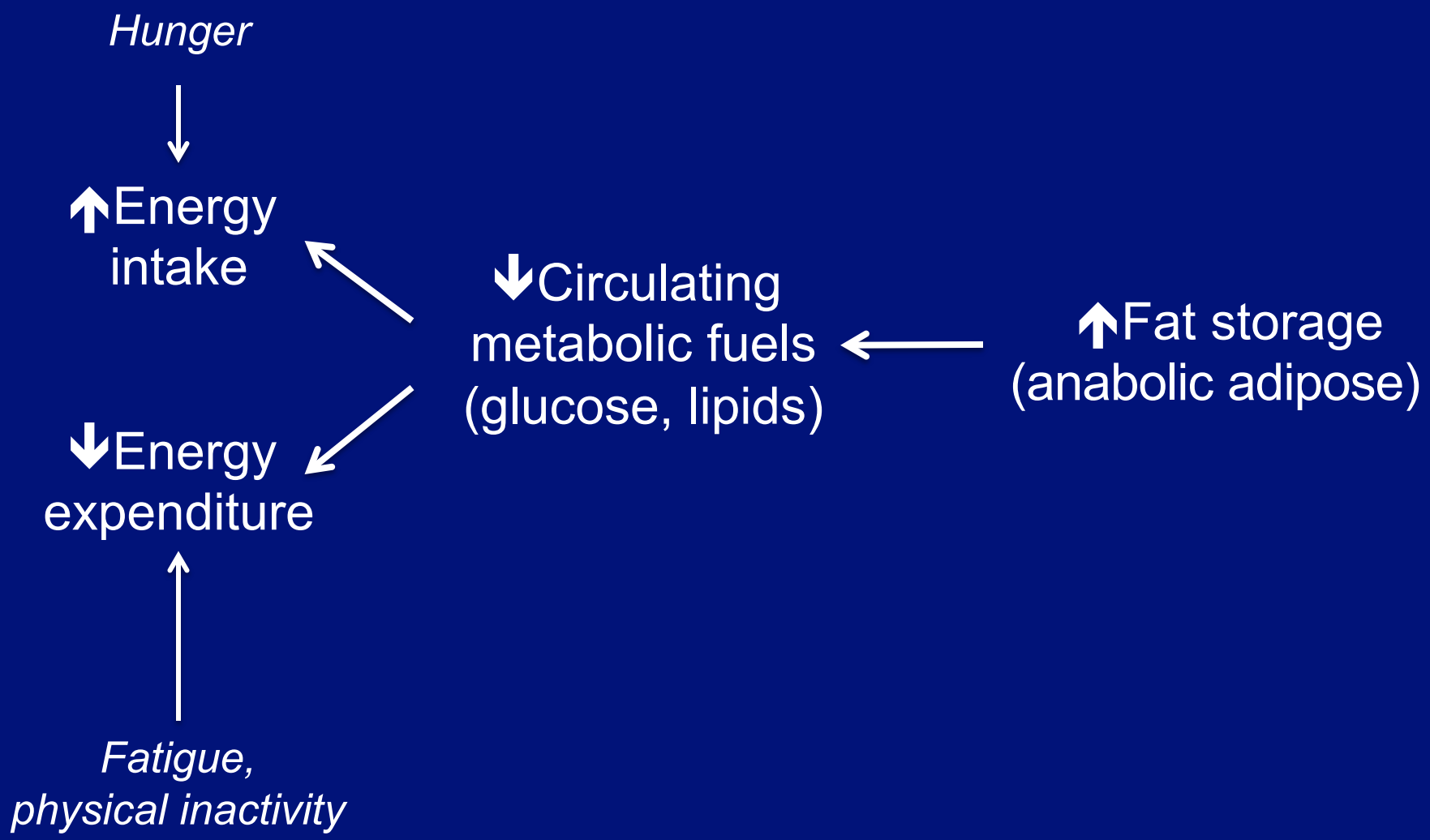


Alternative View of Obesity

Excessive anabolic drive in adipose tissue



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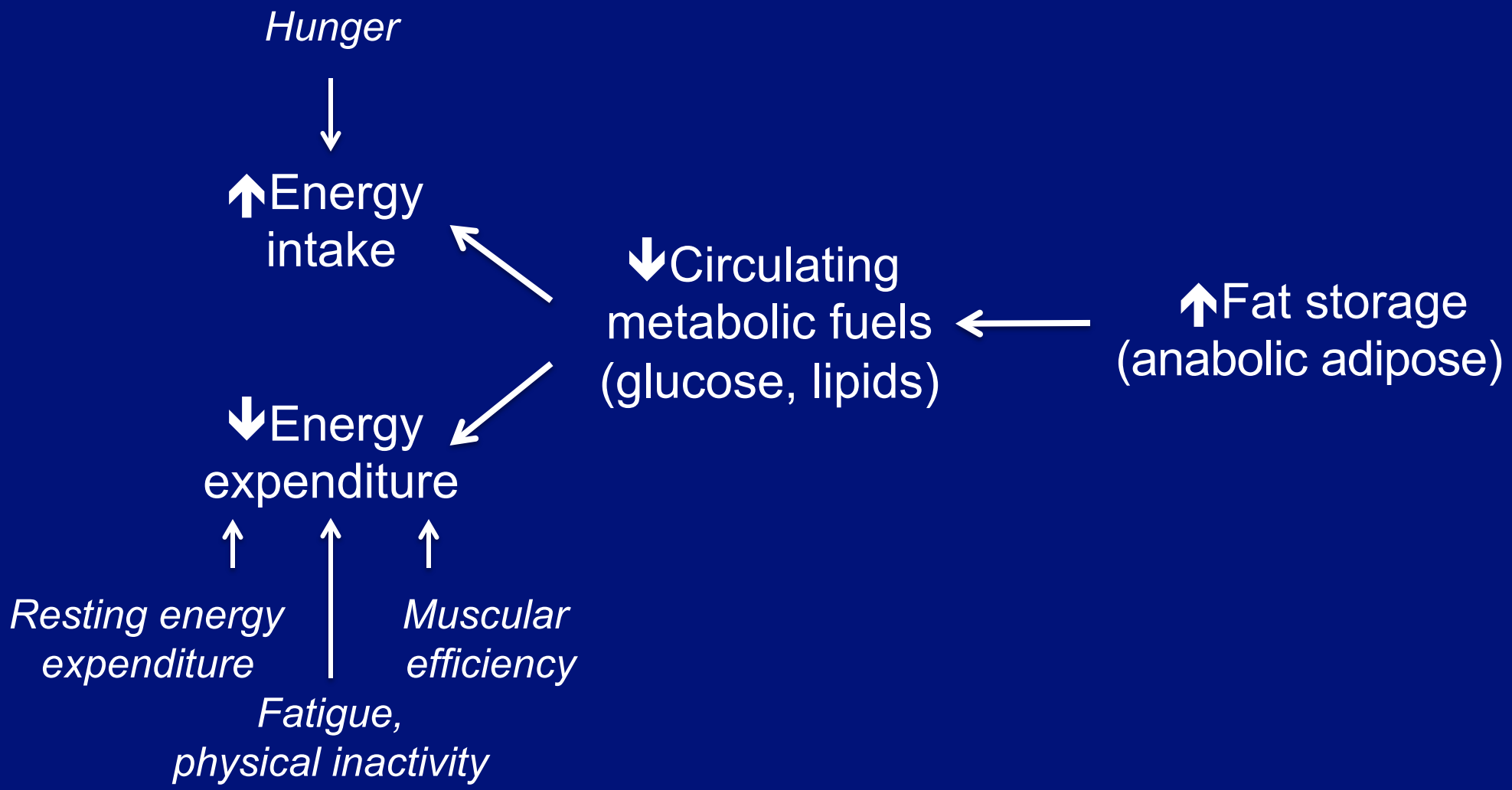

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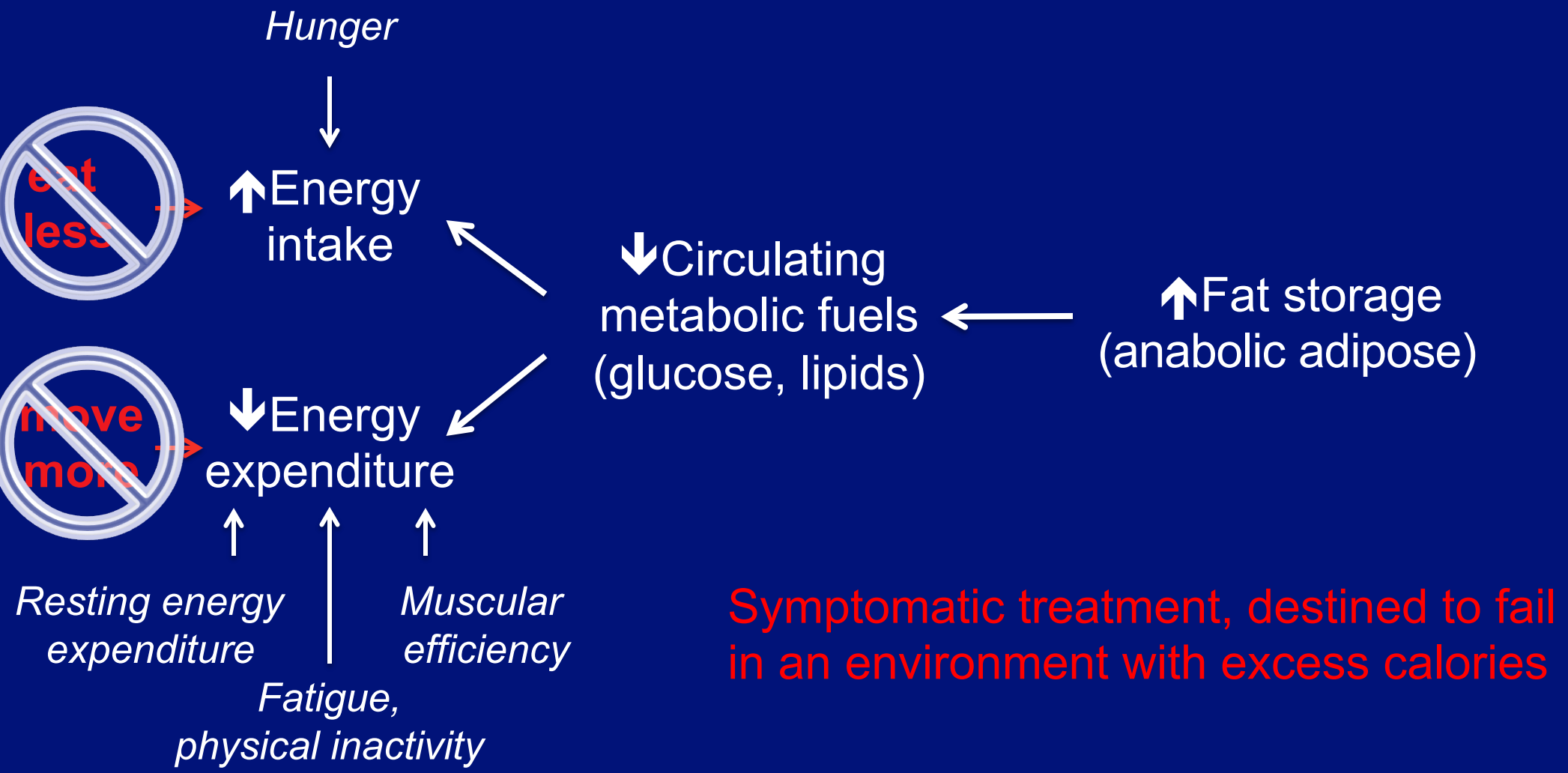

Symptomatic treatment, destined to fail in an environment with excess calories

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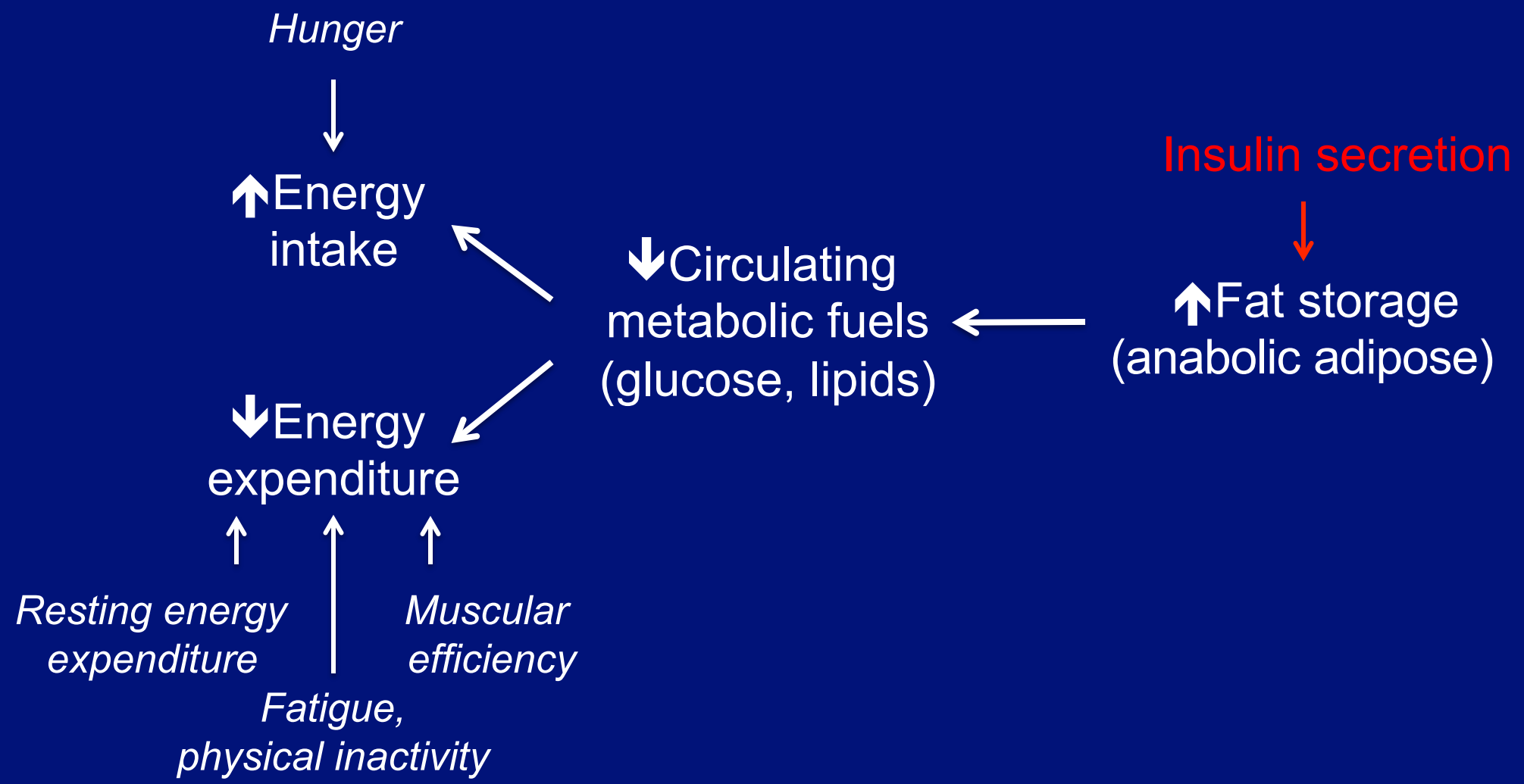

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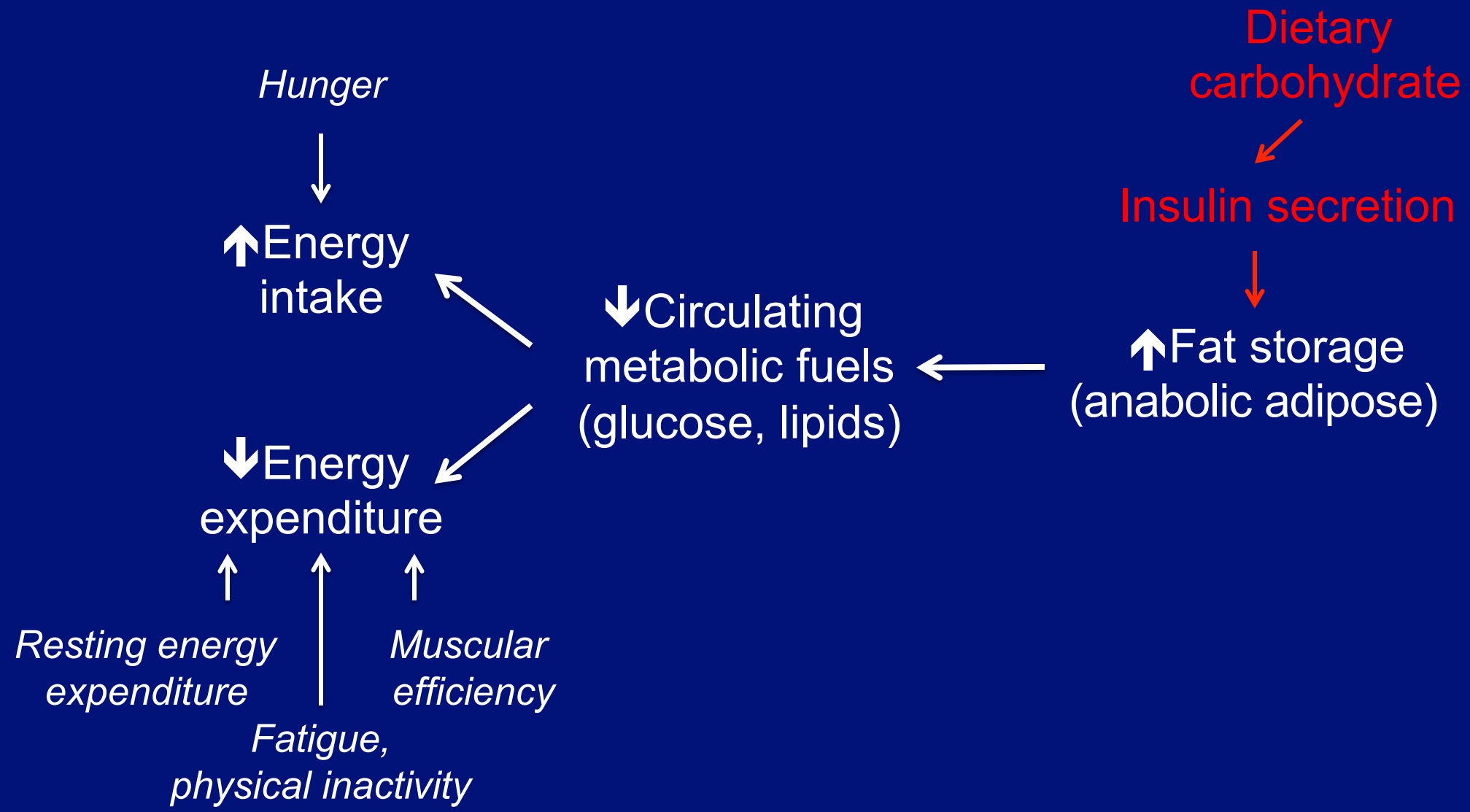


Carbohydrate Amount & Type

Most potent effects of all macronutrients on insulin secretion

- Amount – total carbohydrate (grams)
- Type – glycemic index

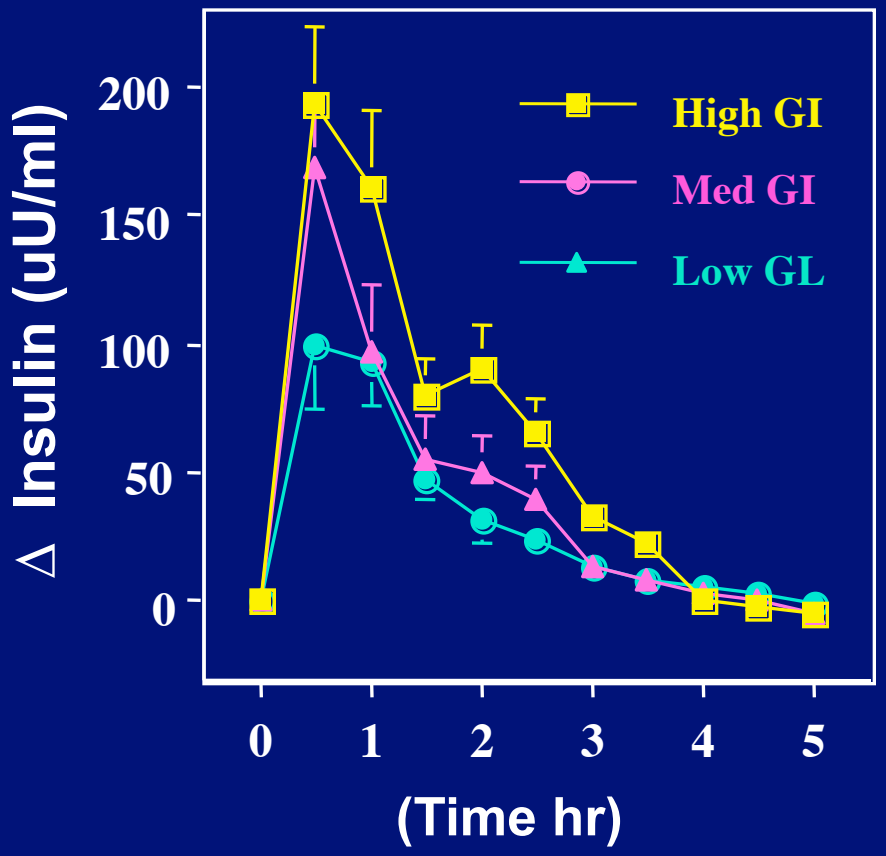
Acute Effects of Processed Carbohydrate

Methods

- Subjects: 12 obese adolescents
- Design: cross-over feeding study on 3 separate days
- Intervention: breakfasts with identical calories:
  - Highly processed carbohydrate (instant oatmeal)
  - Minimally processed carbohydrate (steel-cut oatmeal)
  - No processed carbohydrate (vegetable omelet with fruit)
- Blood tests and hunger followed through the morning

Acute Effects of Glycemic Load

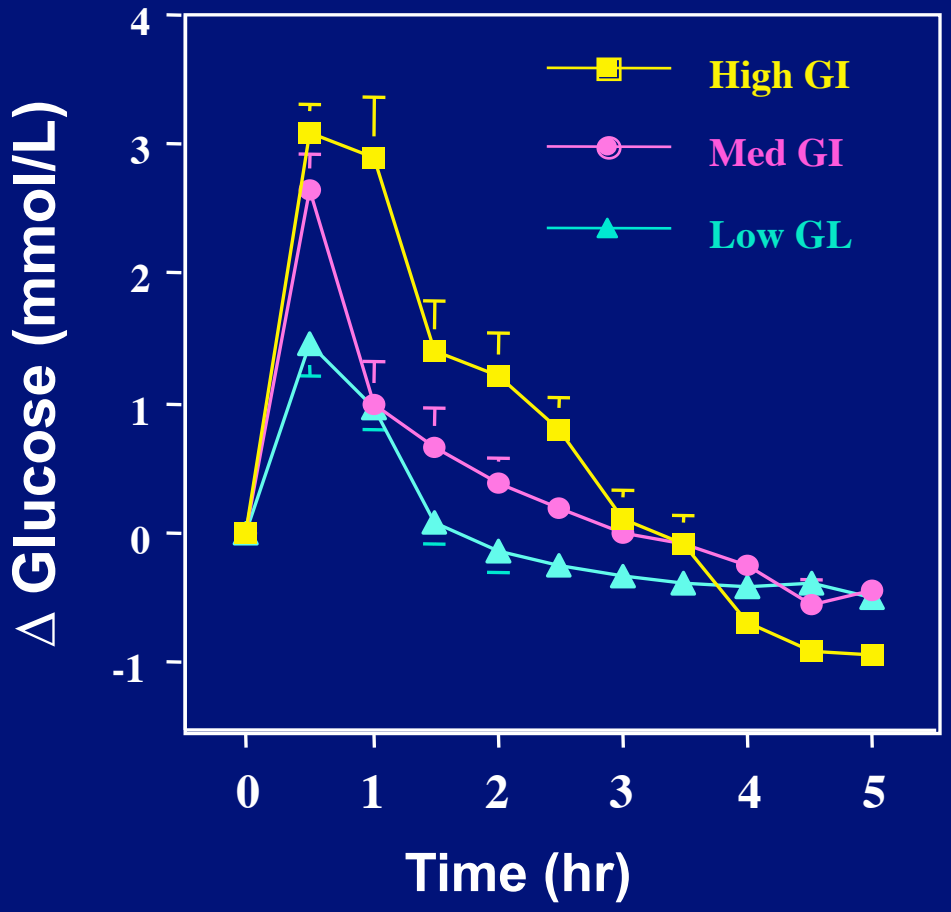
Insulin

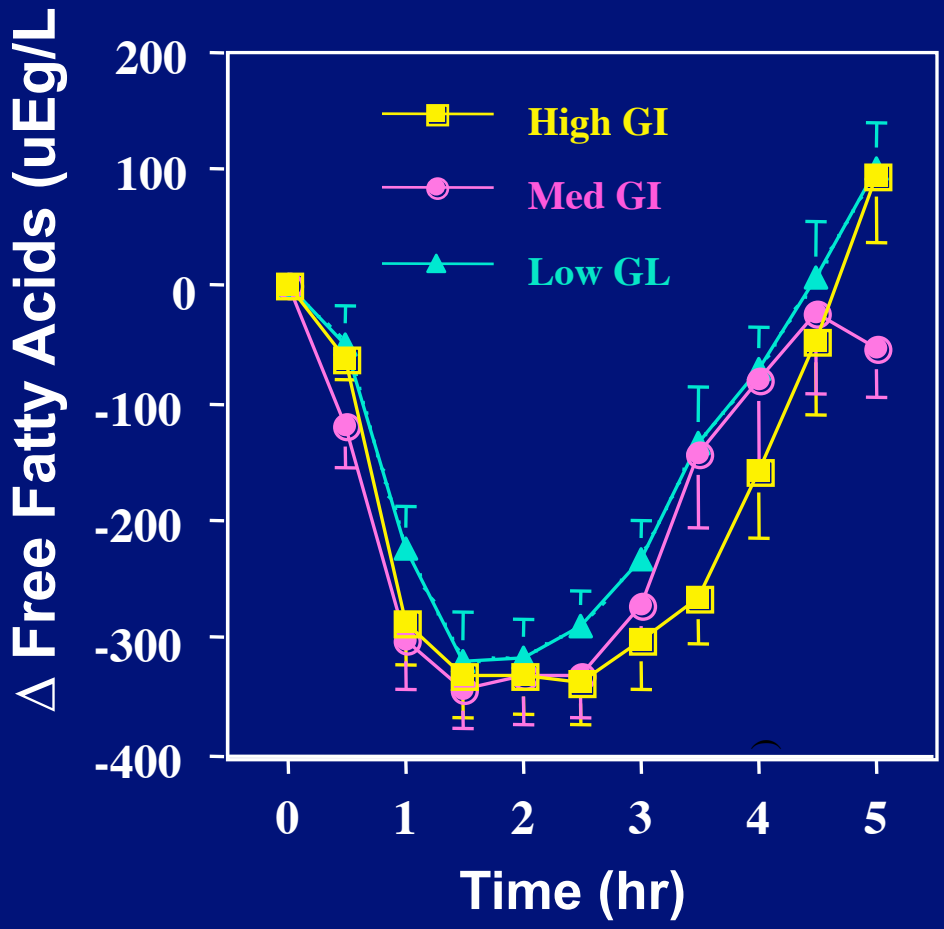


Ludwig. Pediatrics 1999, 103:e26

Acute Effects of Glycemic Load

Metabolic fuels

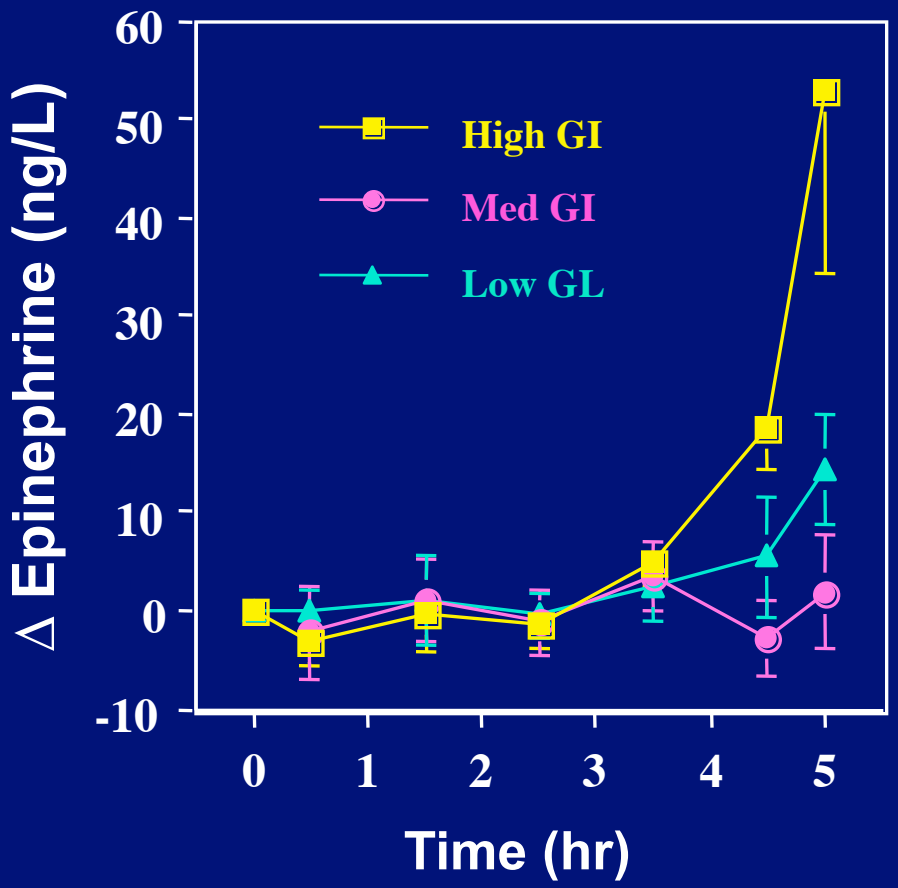




Ludwig. Pediatrics 1999, 103:e26

Acute Effects of Glycemic Load

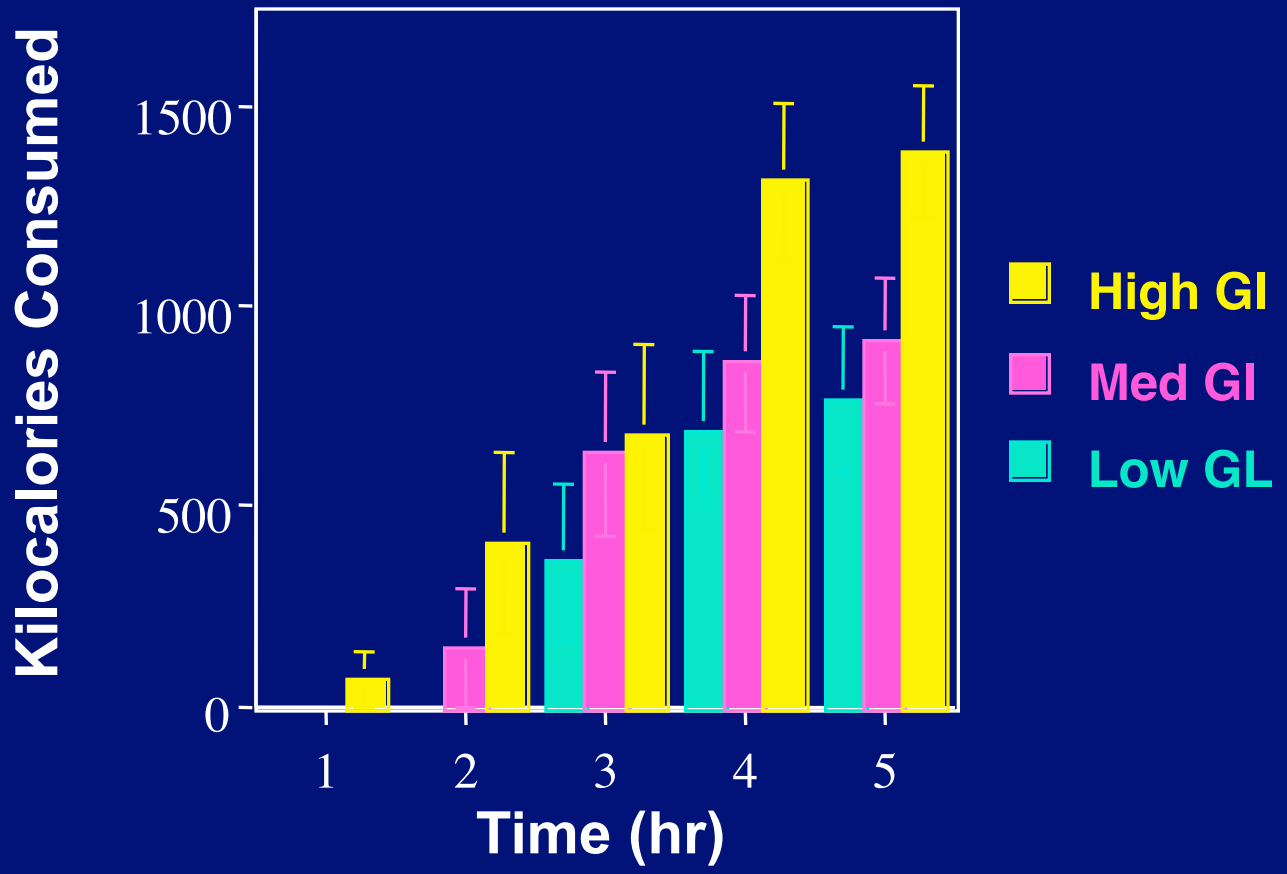
Plasma epinephrine



Ludwig. Pediatrics 1999, 103:e26

Acute Effects of Glycemic Load

Cumulative food intake



Ludwig. Pediatrics 1999, 103:e26

Glycemic Index & Brain Function

Methods

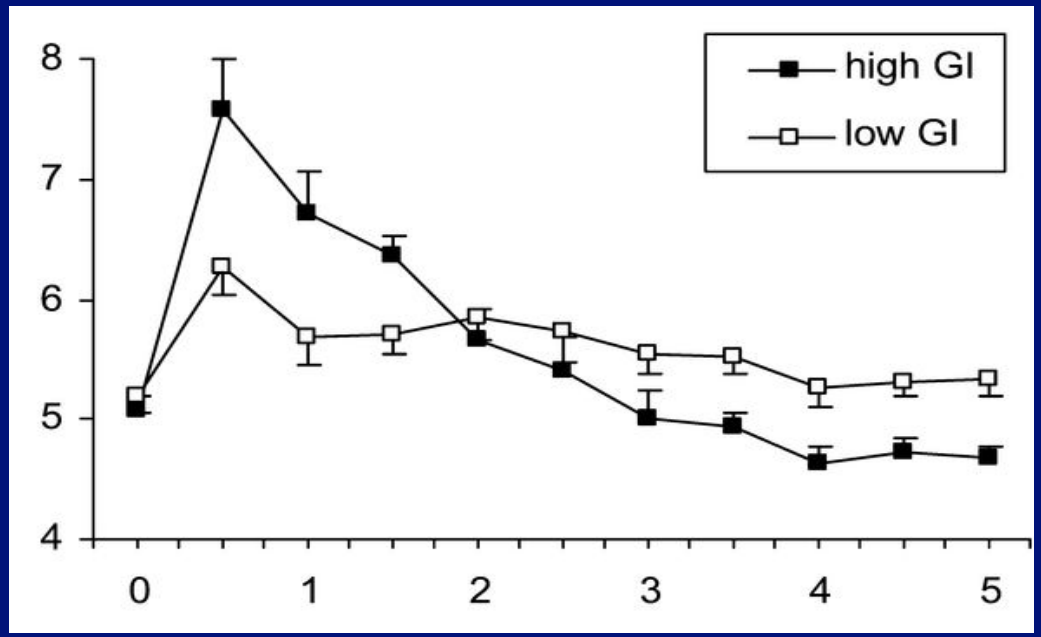
- Subjects: 12 overweight/obese young men
- Design: Double-blind, cross-over feeding study
- Intervention: high vs. low GI liquid meals, controlled for:
  - macronutrients
  - calorie content
  - sweetness
- Neuroimaging: Arterial spin labeling 4 hr after the meal

Lennerz. AJCN 2013, 98:641-7

Glycemic Index & Brain Function

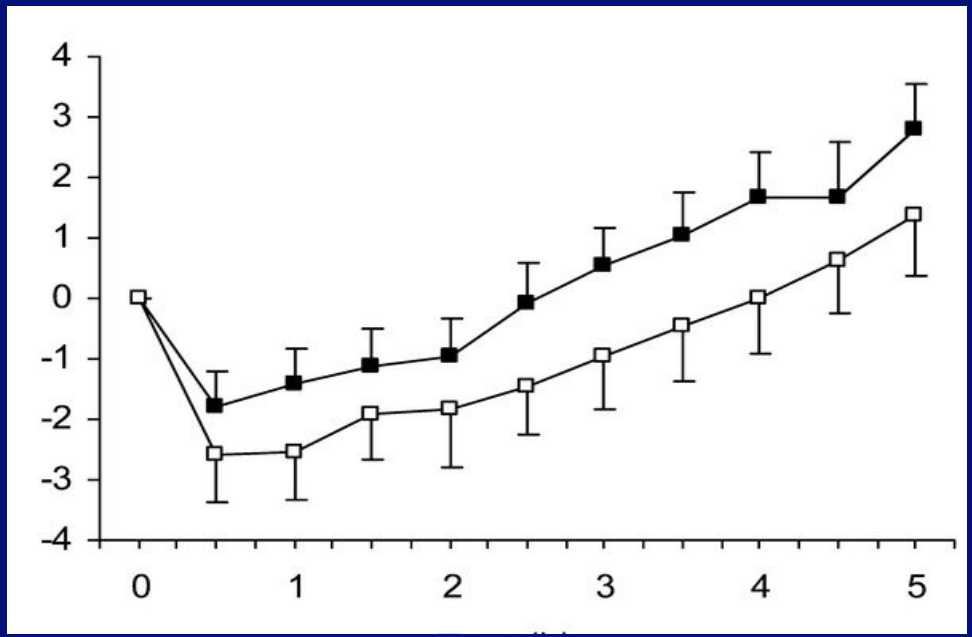
Effects of test meals on plasma glucose and hunger

Plasma Glucose (mmol/L)



Time (hr)

Hunger rating (10-pt scale)

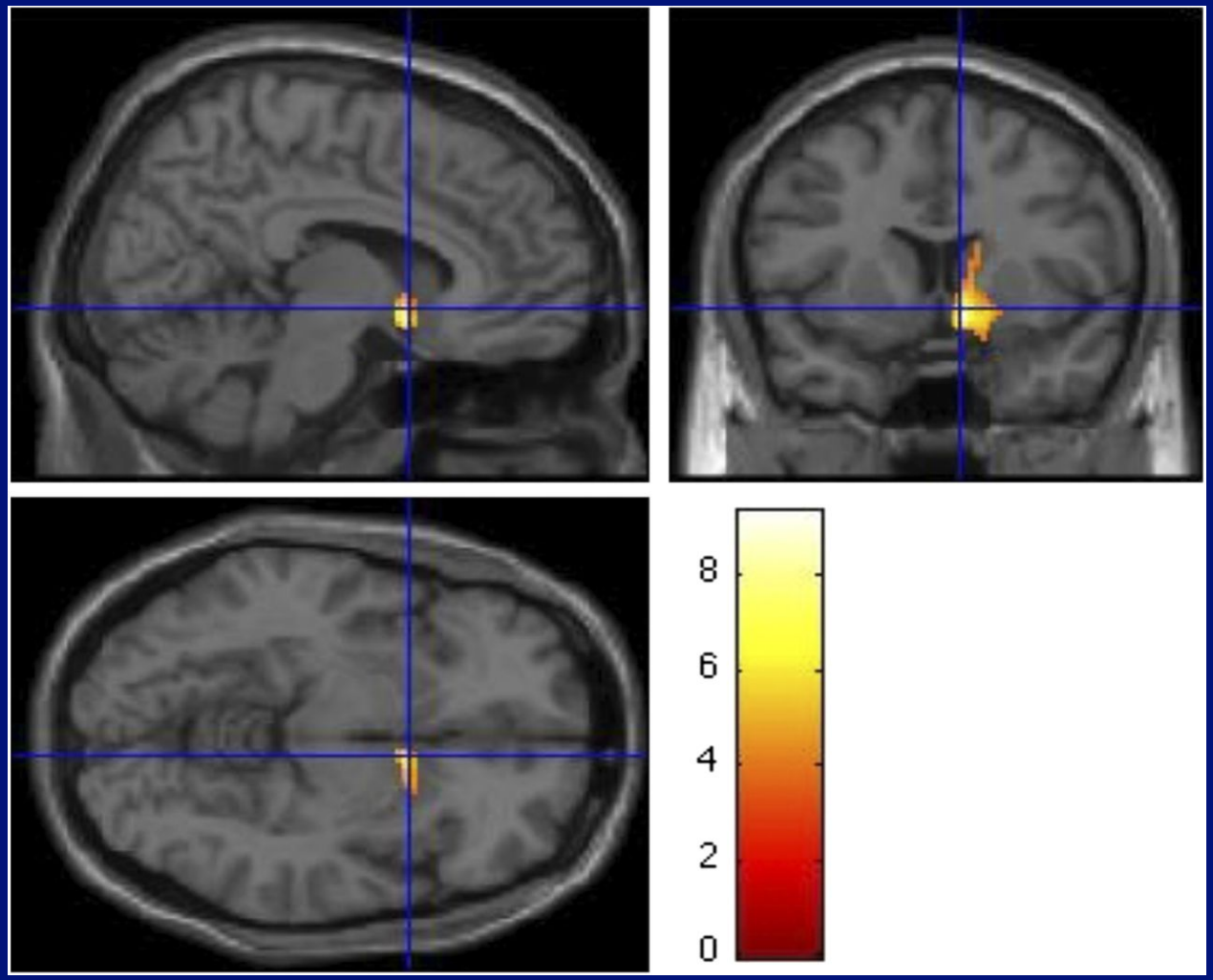


Time (hr)

Lennerz. AJCN 2013, 98:641-7

Glycemic Index & Brain Function

Activation of nucleus accumbens after high GI meal



p<0.001, adjusted for multiple comparisons

Lennerz. AJCN 2013, 98:641-7

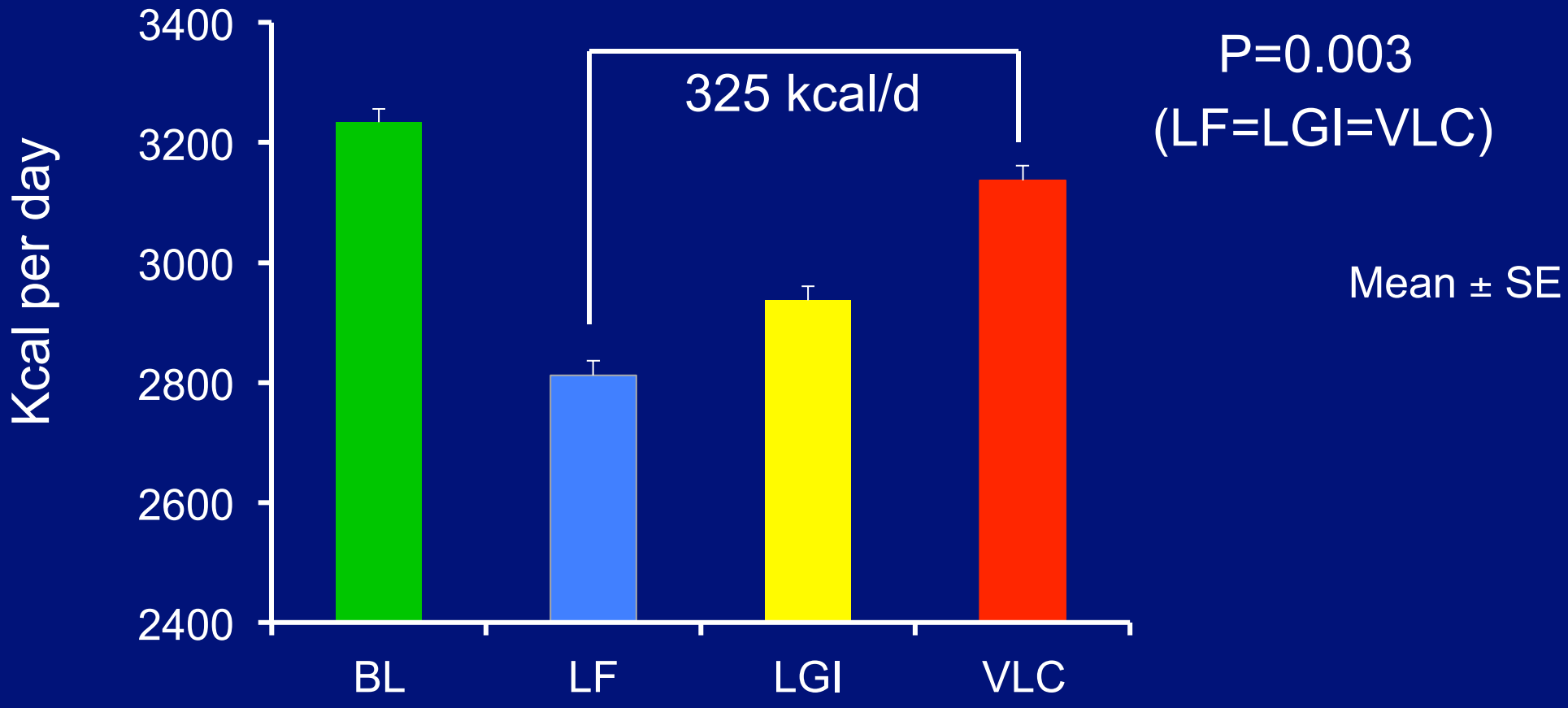
Energy Expenditure & Weight Loss Maintenance

Methods

- 21 obese young adults, studied for 7 months
- 10 to 15% weight loss on a standard low calorie diet
- Then studied during weight maintenance on each of three test diets with the same calories:
  - Low fat (60% carbohydrate, 20% fat, 20% protein)
  - Low glycemic index (40% carbohydrate, 40% fat, 20% protein)
  - Atkins very low carb (10% carbohydrate, 60% fat, 30% protein)
- 1° Endpoint: Resting and total energy expenditure

Energy Expenditure & Weight Loss Maintenance

Effects on total energy expenditure (doubly labeled water)



Ebbeling, JAMA 2012;307:2627-34

Long-term effects of macronutrients on body weight

Behavioral Diet Studies

Characteristically little weight difference between diets

POUNDS LOST Study

Methods

- 811 overweight/obese adults, studied for 2 years
- Assigned to 4 diets designed to differ in macronutrients
  - Carbohydrate: 35 – 65%
  - Fat: 20 – 40%
  - Protein: 15 – 25%
- Intervention: individual and group behavioral counseling

Results

- No difference in body weight according to diet group

Sacks. NEJM 2009, 360:859-73

Behavioral Diet Studies

Characteristically little weight difference between diets

POUNDS LOST Study

Major Limitation: Did not achieve targeted dietary goals

- Reported maximum differences in intakes less than half intended:
  - Fat intake range: 9% absolute difference
  - Protein intake range: 5% absolute difference
- Even these relatively small differences may be overestimated, due to social-desirability bias inherent to self reporting
- Biomarkers demonstrated poor compliance at 2 years:
  - No difference in triglycerides (marker of carbohydrate intake)
  - Nonsignificant difference in N2 excretion (protein intake)
  - RQ differed only slightly throughout study among diets (.81-.84)

Sacks. NEJM 2009, 360:859-73

Feeding Studies

Characteristically substantial effect of dietary composition

DIRECT Study

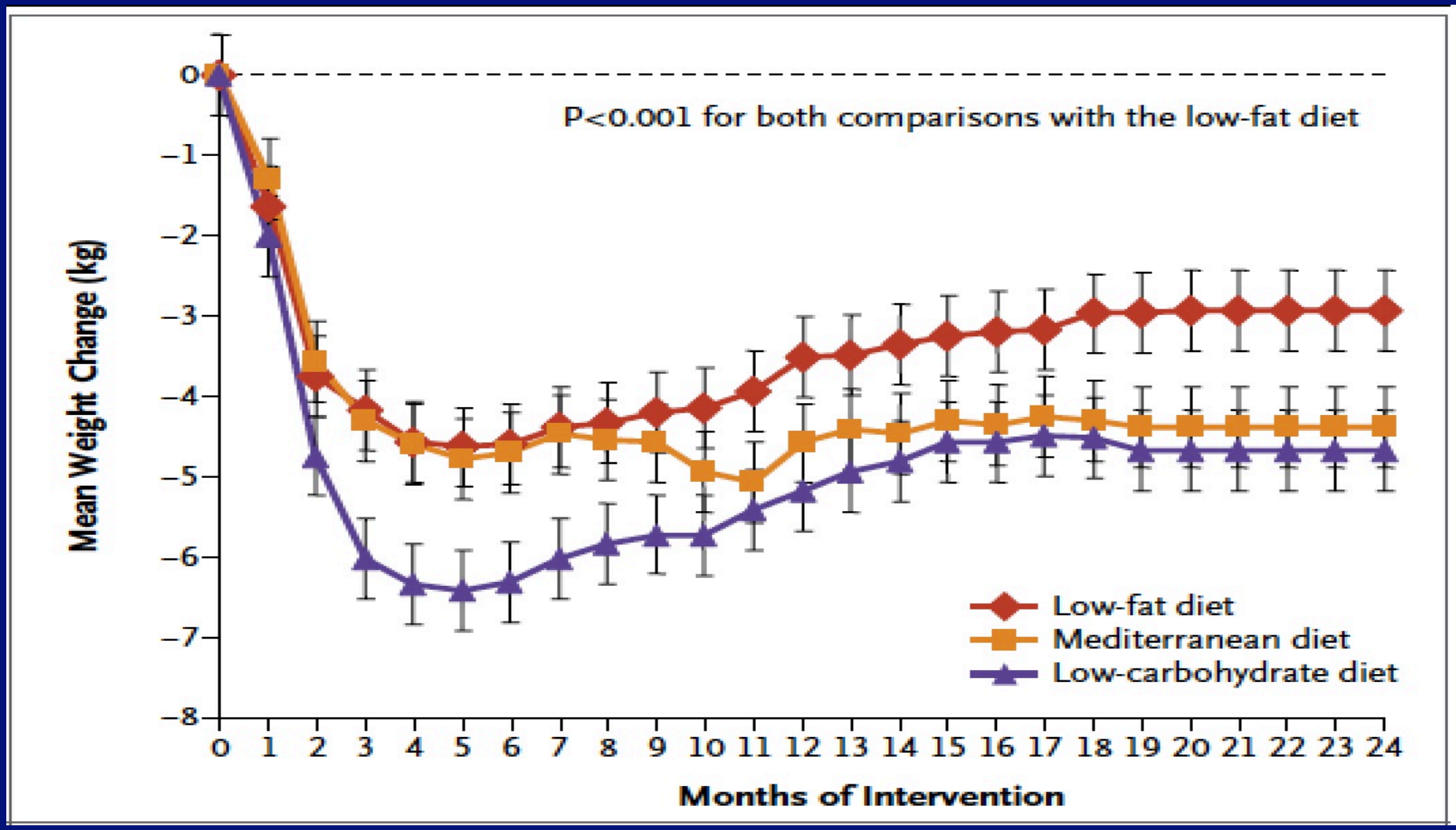
Methods

- 322 obese adults, studied for 2 years
- Assigned to 3 diets designed to differ in macronutrients
  - Low fat, calorie-restricted
  - Mediterranean, calorie-restricted
  - Low carbohydrate, not calorie-restricted
- Intervention based at a work site, with partial food provision
- Completion rates approaching 90%

Shai. NEJM 2008, 359:229-41

Feeding Studies

Characteristically substantial effect of dietary composition



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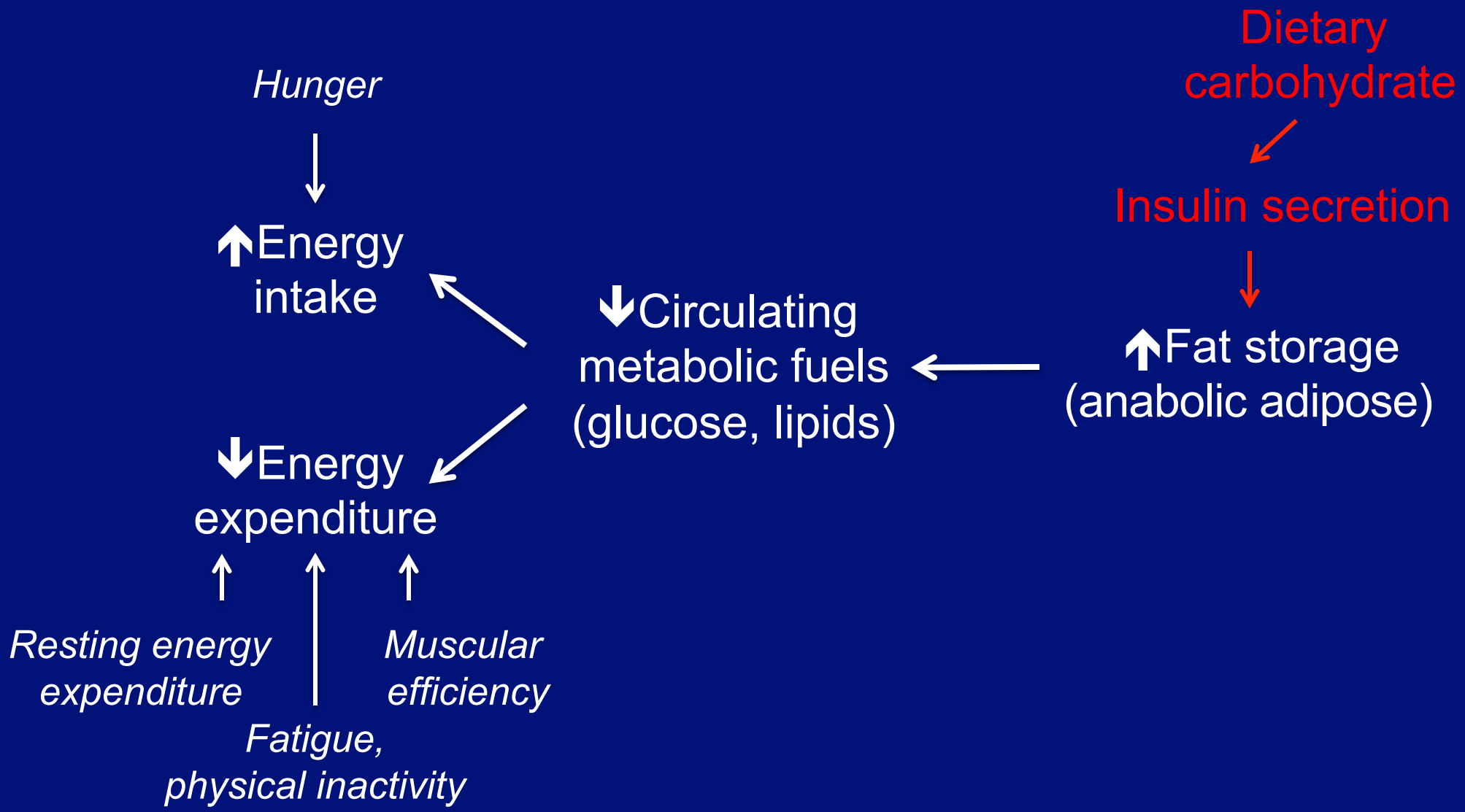

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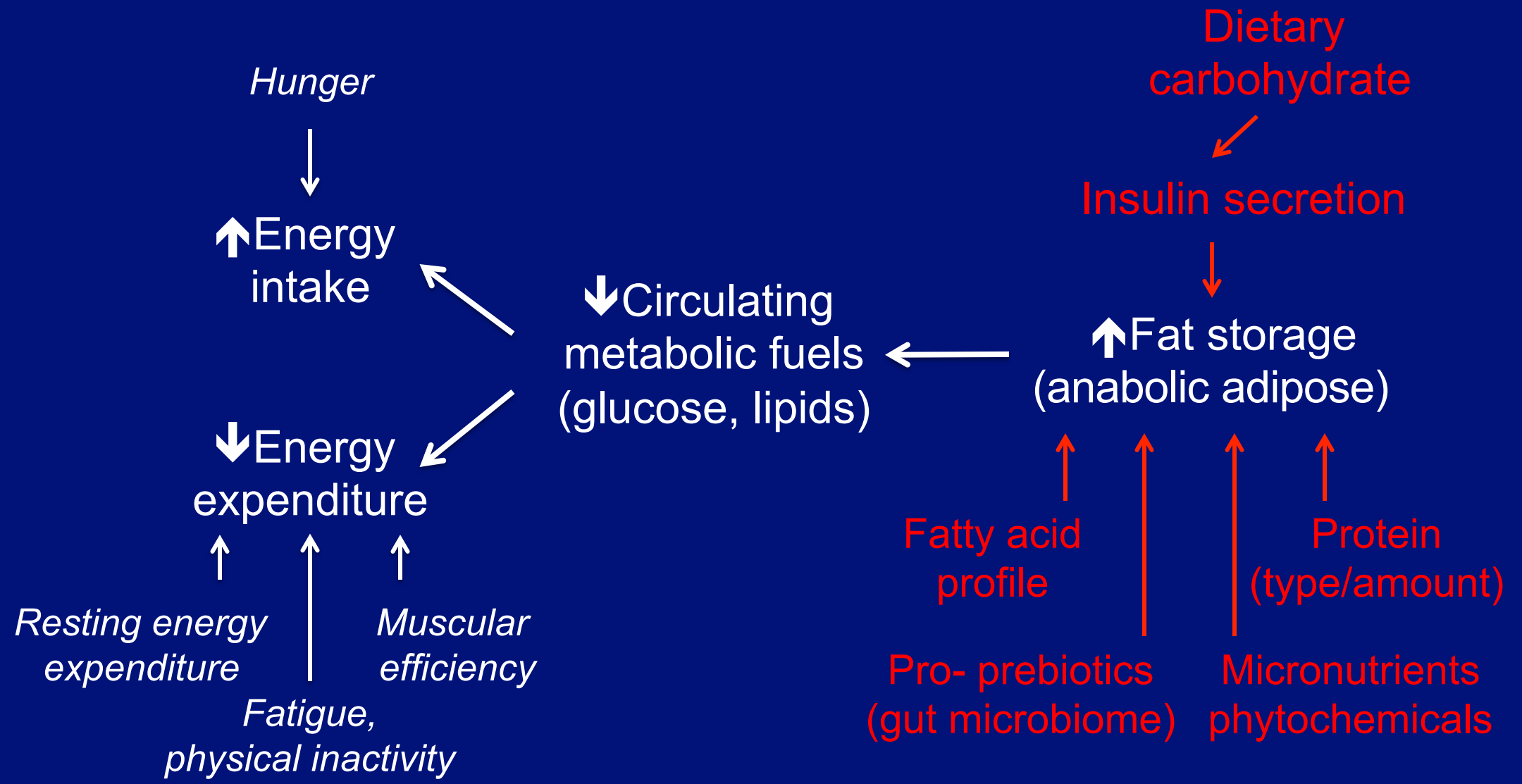

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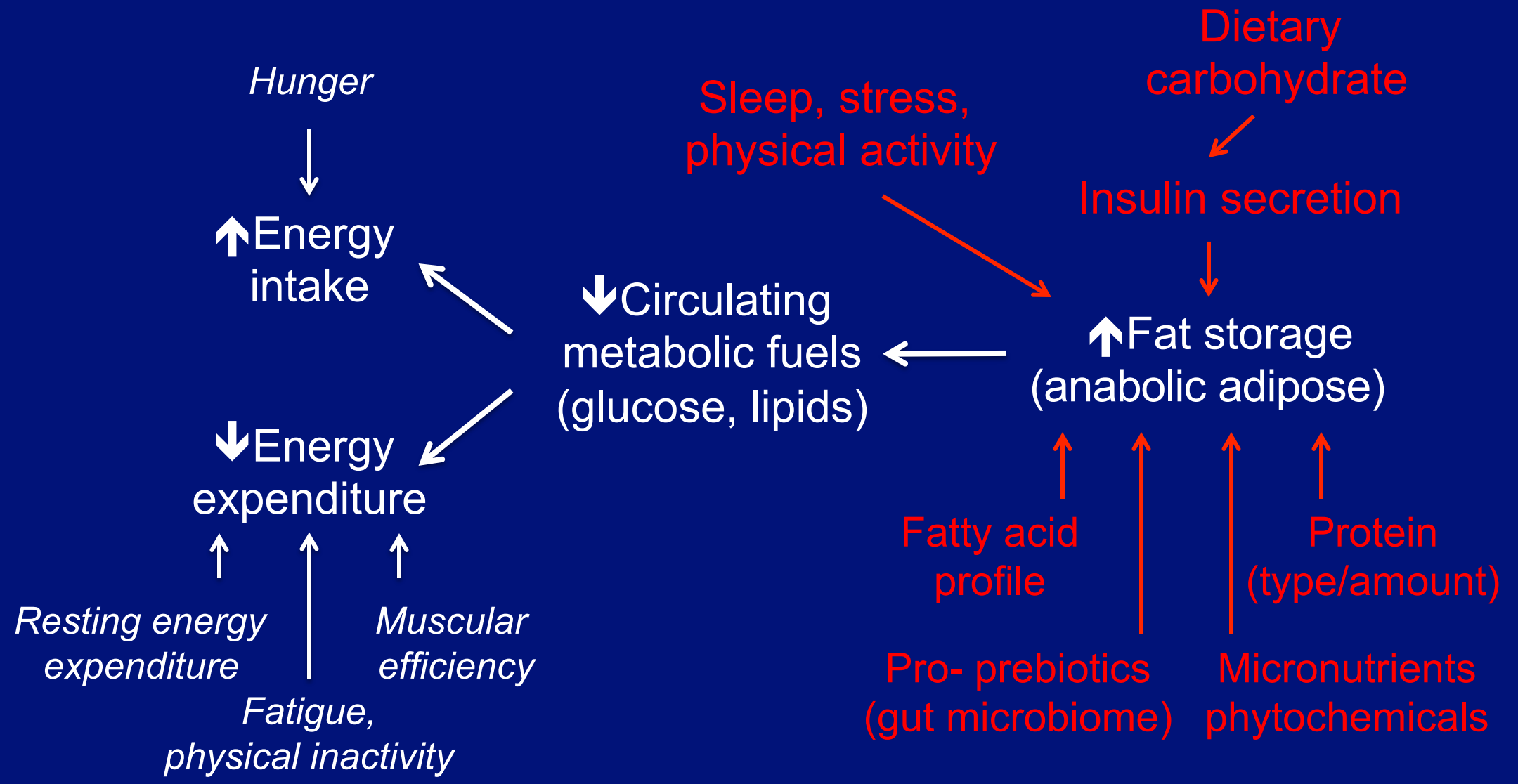
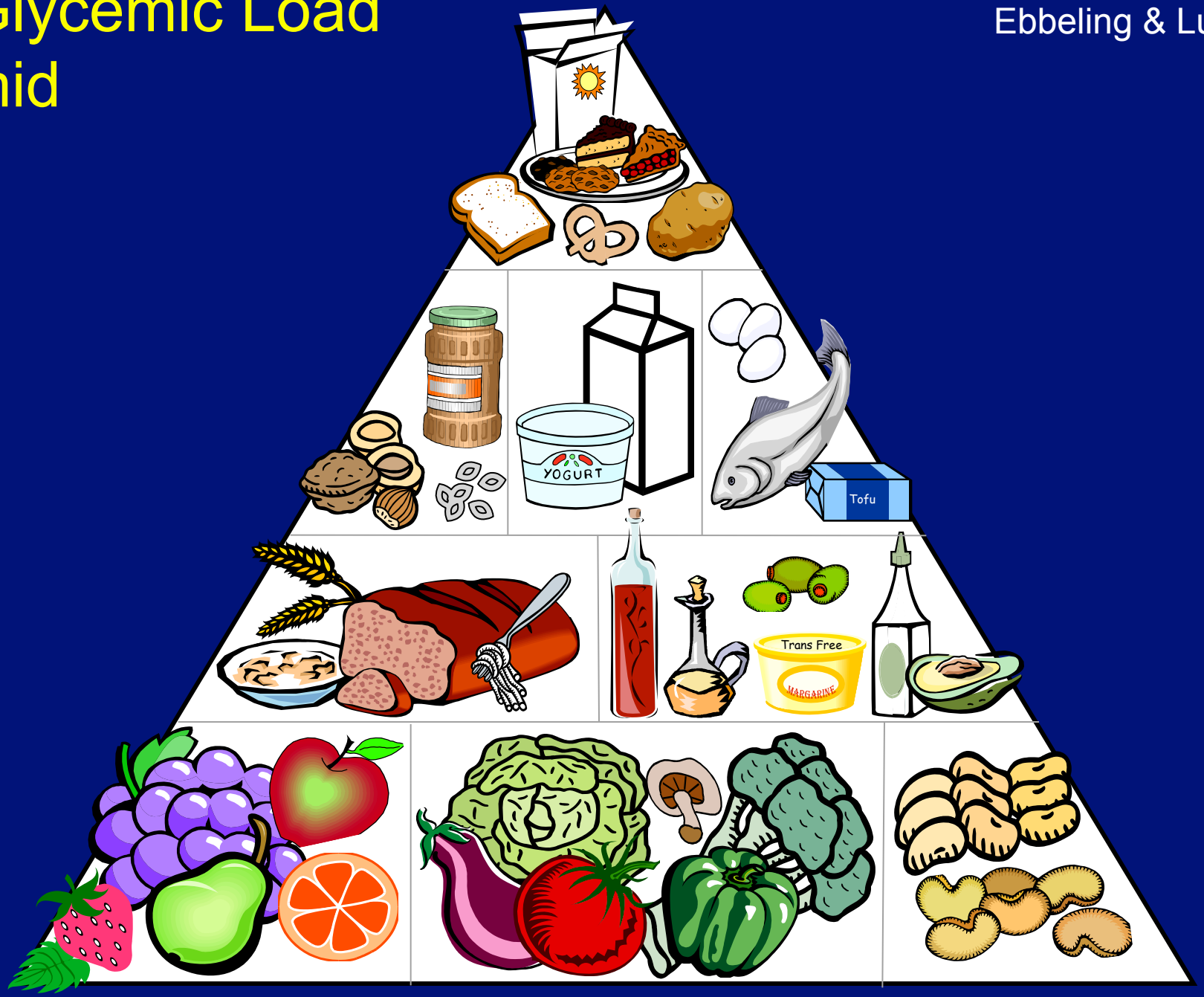


Low Glycemic Load Pyramid



Summary & Conclusions

1. The conventional approach to weight loss, the calorie-restricted diet, has poor efficacy in an environment with unlimited calorie availability
2. An alternative approach aims to reduce anabolic drive, leading to reduced adiposity with *ad libitum conditions*
3. Reduced anabolic drive may be achieved by lowering carbohydrate amount and/or glycemic index, and other qualitative changes in diet
4. Findings from behavioral RCTs must be interpreted cautiously, as they often fail to achieve significant changes in dietary intakes
5. Future research is needed to compare strategies to improve dietary composition vs. reduce calorie intake in the treatment of obesity

Closing Thought

These ideas may be provocative, but they aren't new

The editors of a leading medical journal wrote:

"When we read that 'the fat woman has the remedy in her own hands – or rather between her own teeth' . . . there is an implication that obesity is usually merely the result of unsatisfactory dietary bookkeeping. . . [Although logic suggests that body fat] may be decreased by altering the balance sheet through diminished intake, or increased output, or both . . . [t]he problem is not really so simple and uncomplicated as it is pictured."

JAMA 1924, 83(13):1003

Always Hungry? Conquer Cravings, Retrain Your Fat Cells, and Lose Weight Permanently.

– Grand Central Publishing: January 5, 2016