Regulation & Dynamics of Human Body Weight

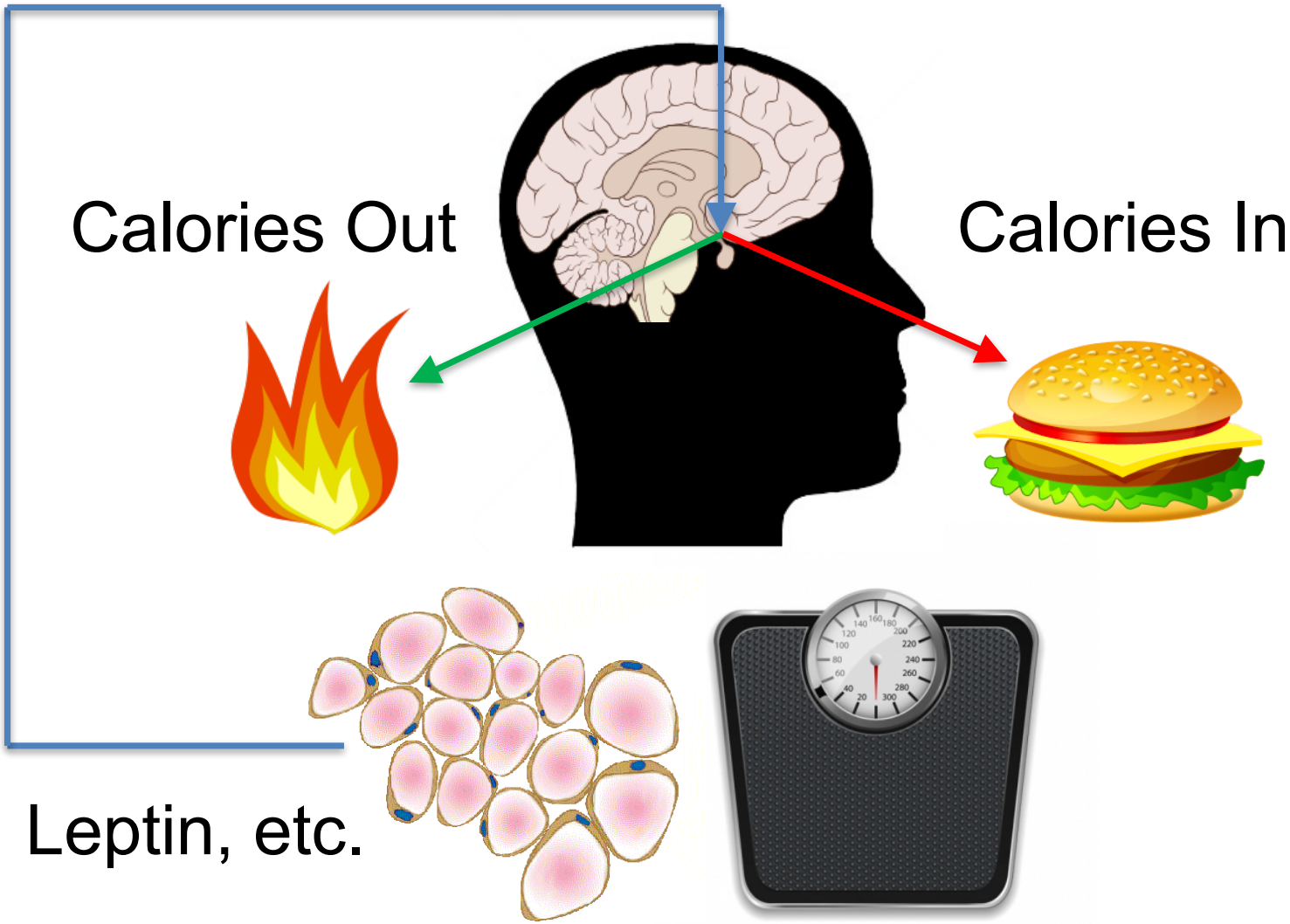
Kevin D. Hall, Ph.D.
National Institute of Diabetes & Digestive & Kidney Diseases
National Institutes of Health

January 17, 2017

Intramural Research Program
Our Research Changes Lives

one program
many people
infinite possibilities

Regulation of Body Weight



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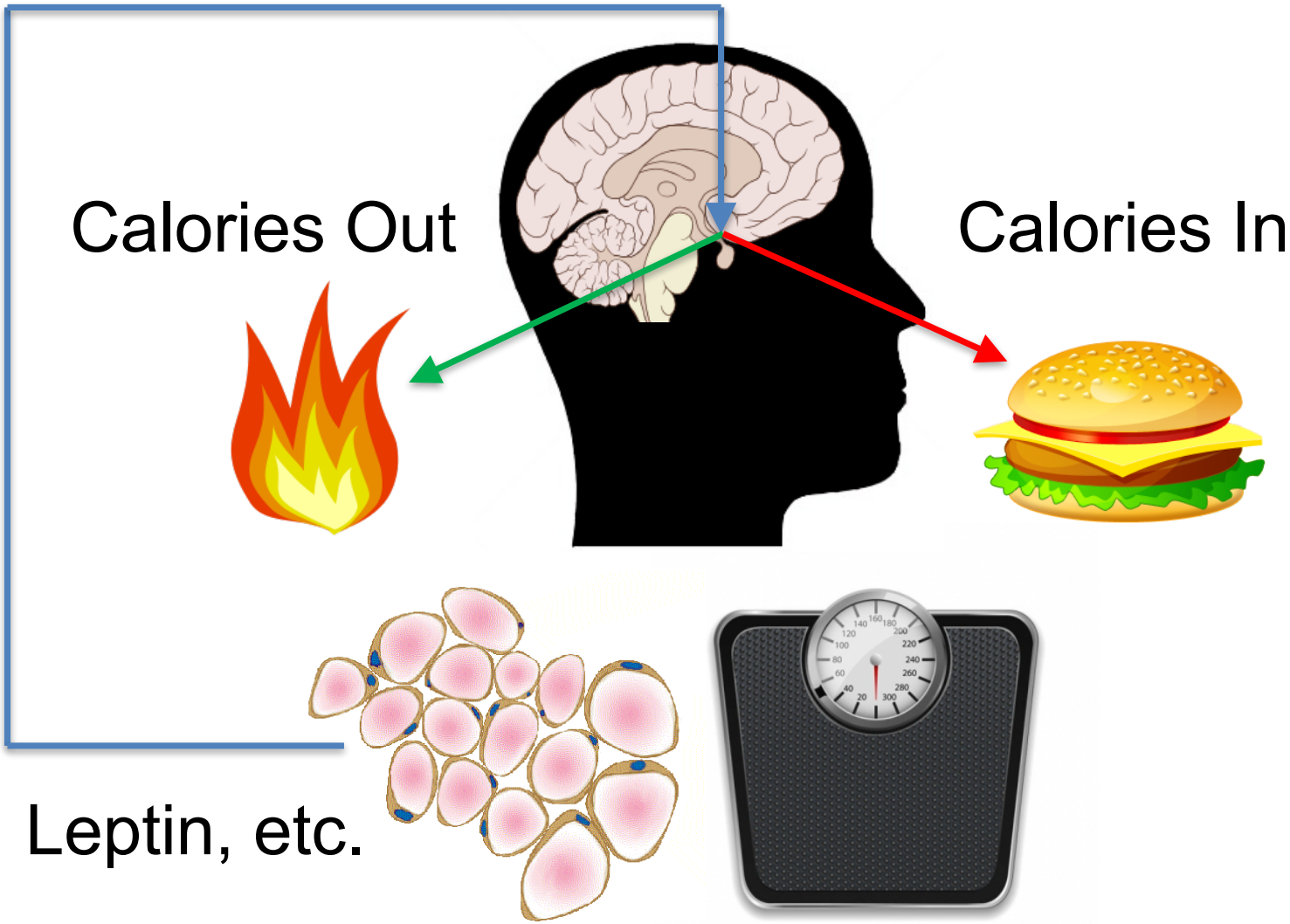
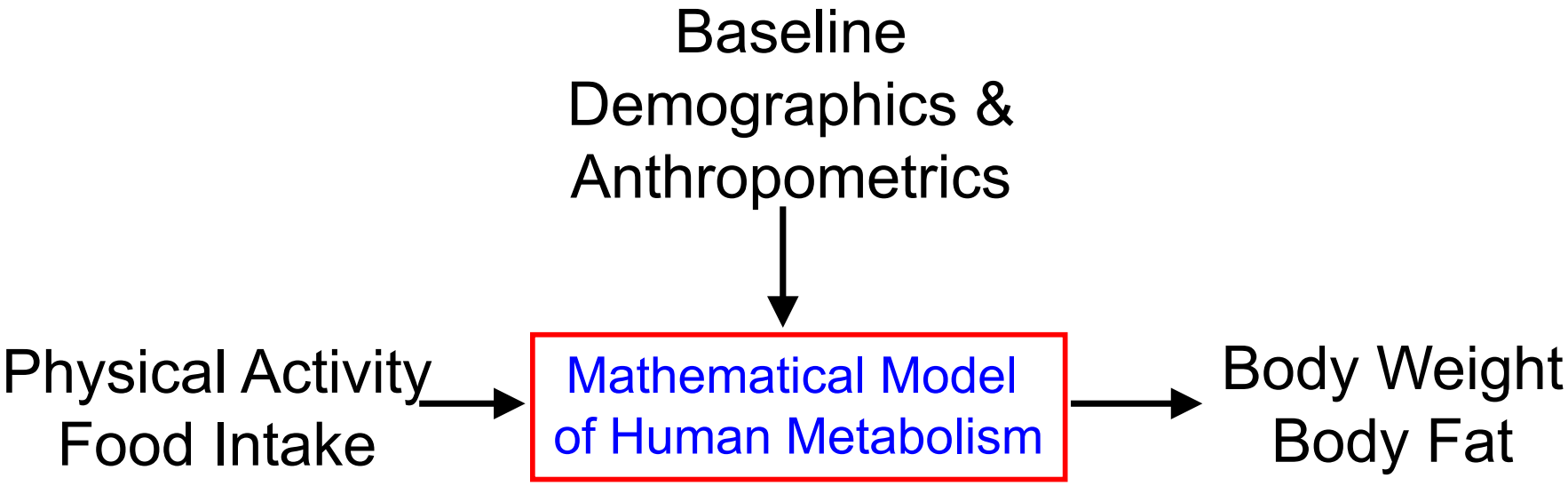


Mathematical Modeling of Metabolism



KD Hall. *The Lancet* **378**:826-37 (2011)

KD Hall. *Am J Physiol.* 298(3): E449-66 (2010)

Body Weight Planner | *Balancing Your Food and Activity*

Step 1 of 4 - Enter your starting information

Switch

Starting Information

U.S. Units | Metric Units

Weight	190			lbs
Sex	Female			
Age	30			yrs
Height	5	ft.	7	in.
Physical Activity Level	1.6			

Estimate Your Level

Next Step

Starting Information

Enter your starting information, including your weight, sex, age, height, anc physical activity level.

Physical Activity Level

Click the "Estimate Your Level" button to find your physical activity level.

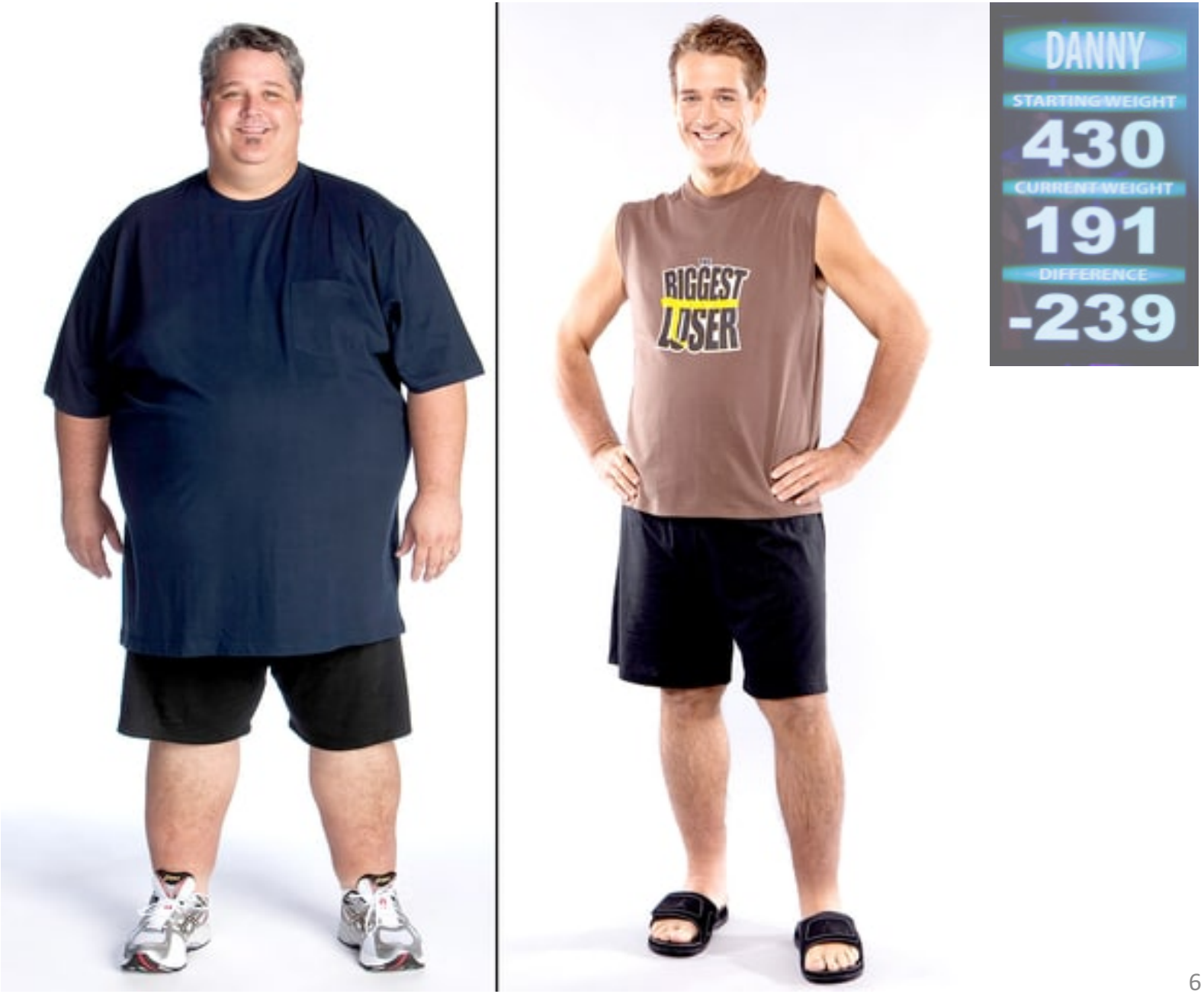
Typical physical activity level numbers range from 1.4 (sedentary) to 2.5 (v active).

The default value of 1.6 describes someone who does very light activity at or work (mostly sitting) and moderate physical activity (such as walking or cycling) at least once a week.

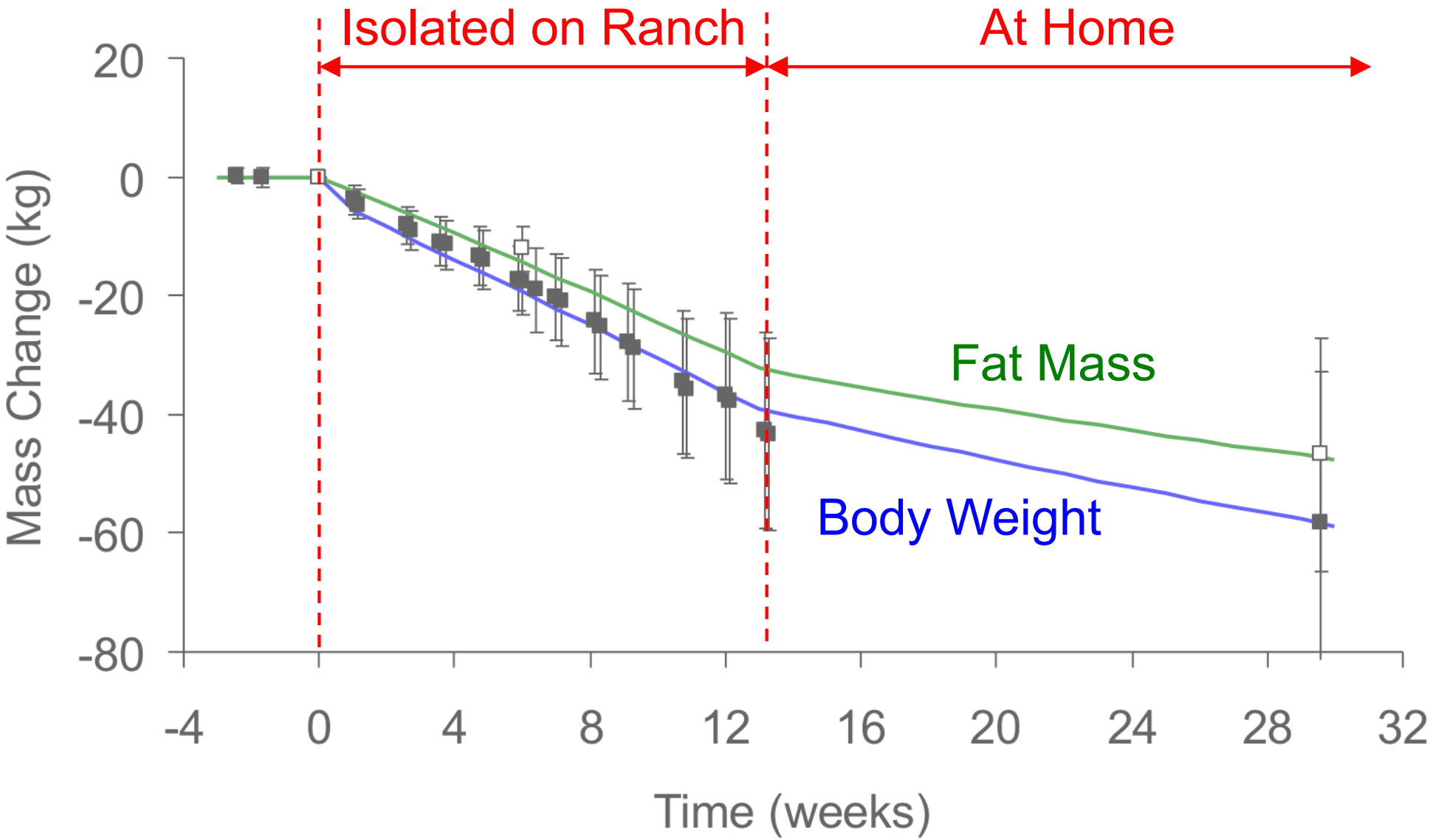
BWplanner.niddk.nih.gov

Disclaimer: This information is for use in adults defined as individuals 18 years of age or older and not by younger people, or pregnant or breast women. This information is not intended to provide medical advice. A health care provider who has examined you and knows your medical histor

The Biggest Loser Competition



Biggest Loser Data & Model Simulations



KD Hall. *Obesity* 21(5):957-9 (2013)

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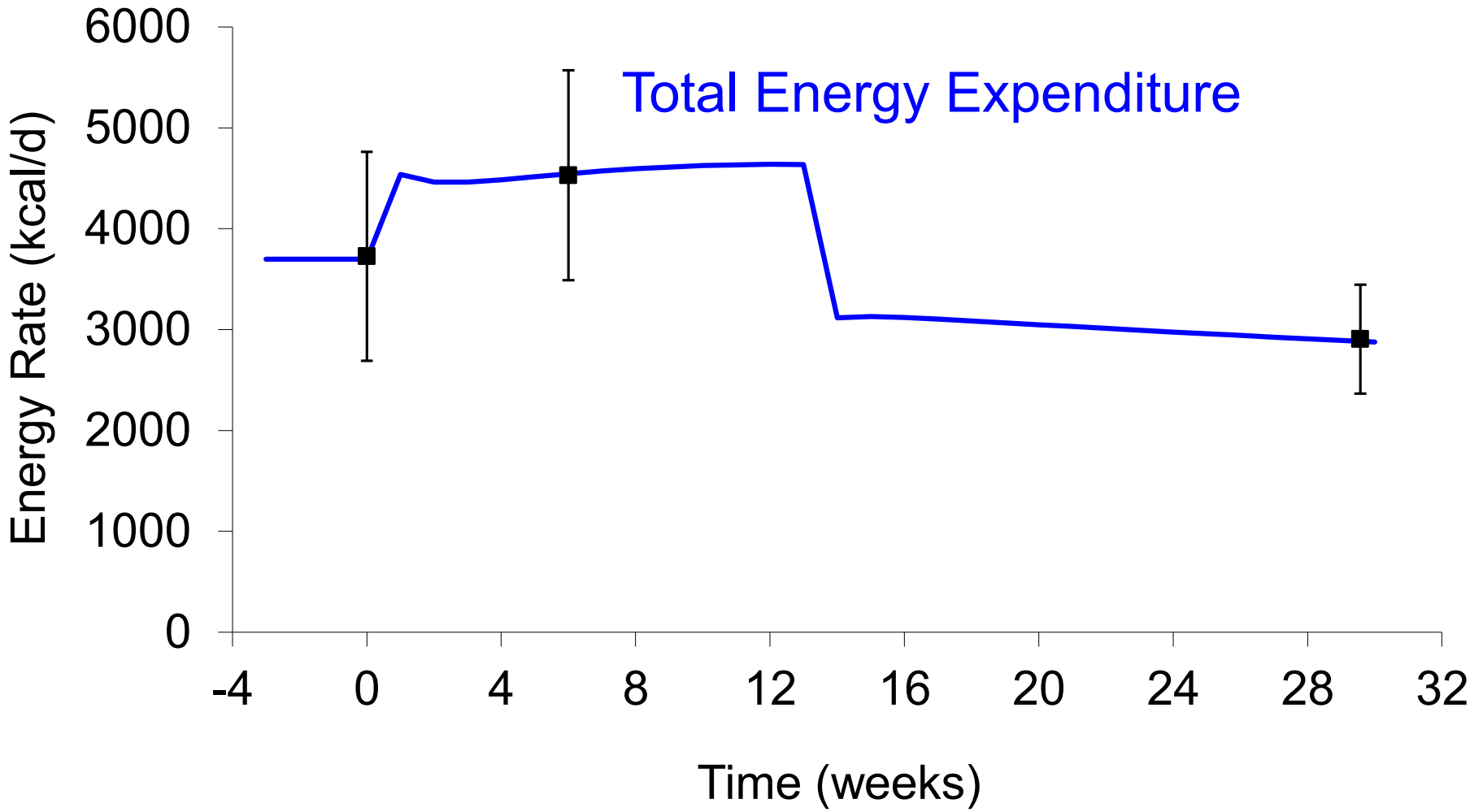

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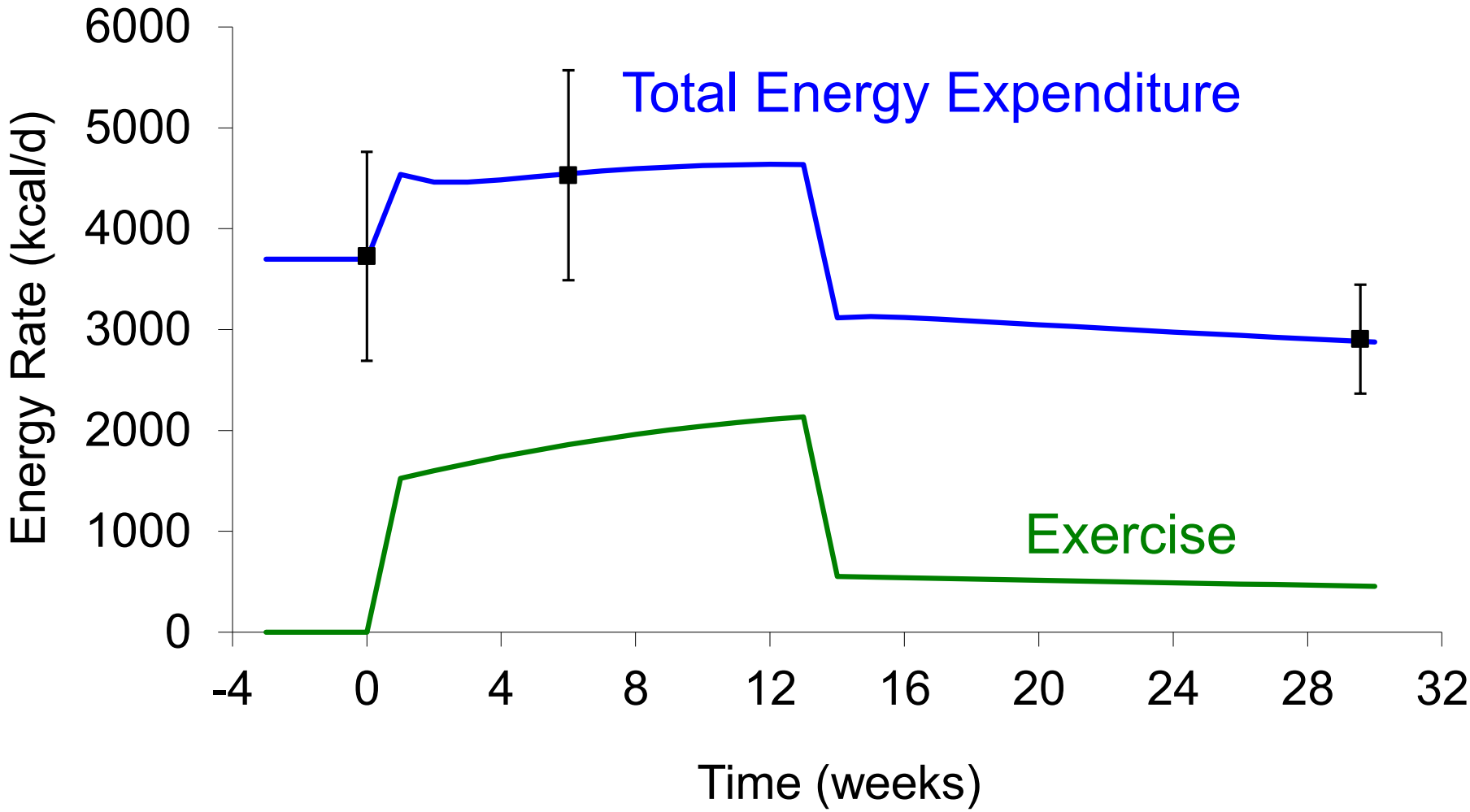

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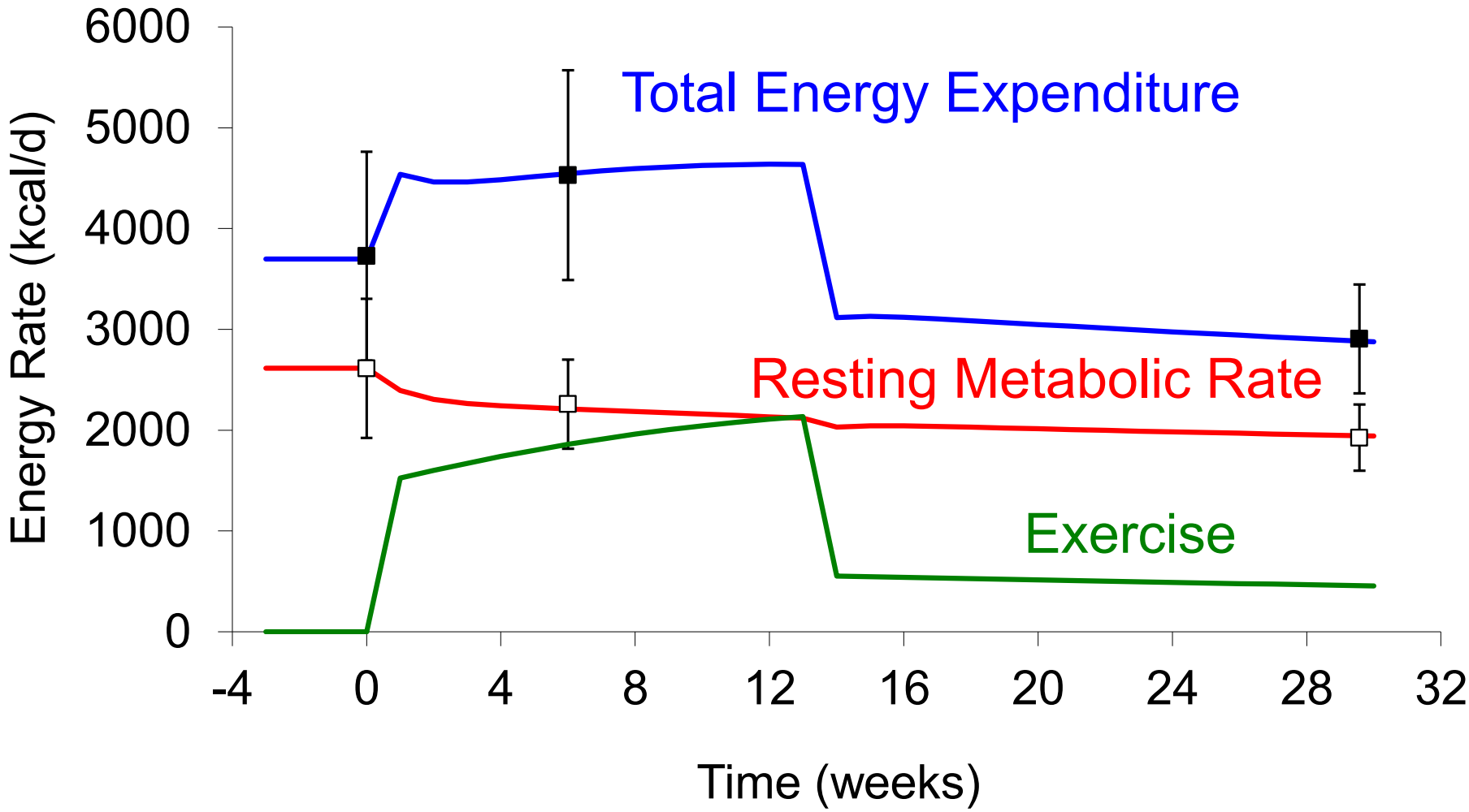

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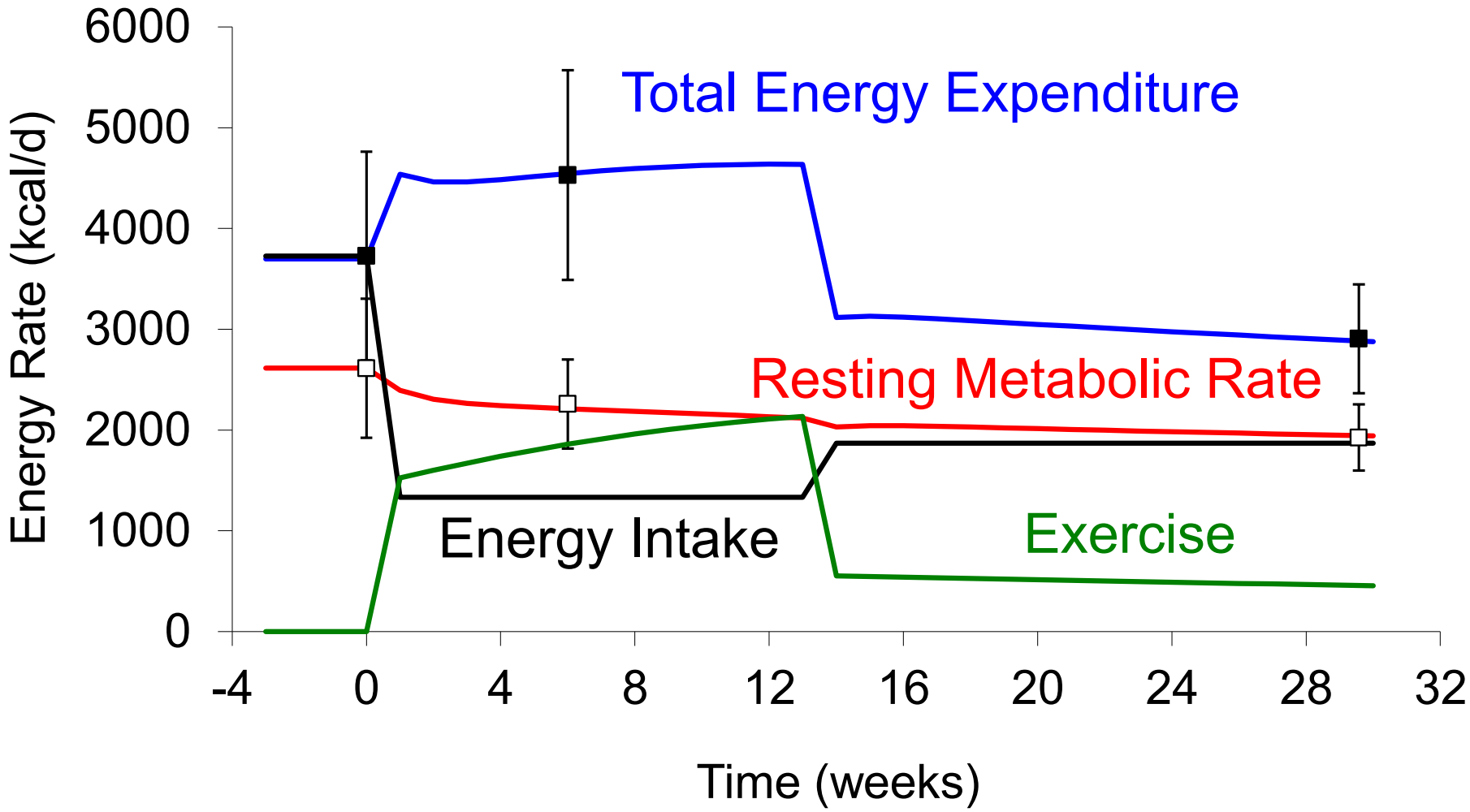
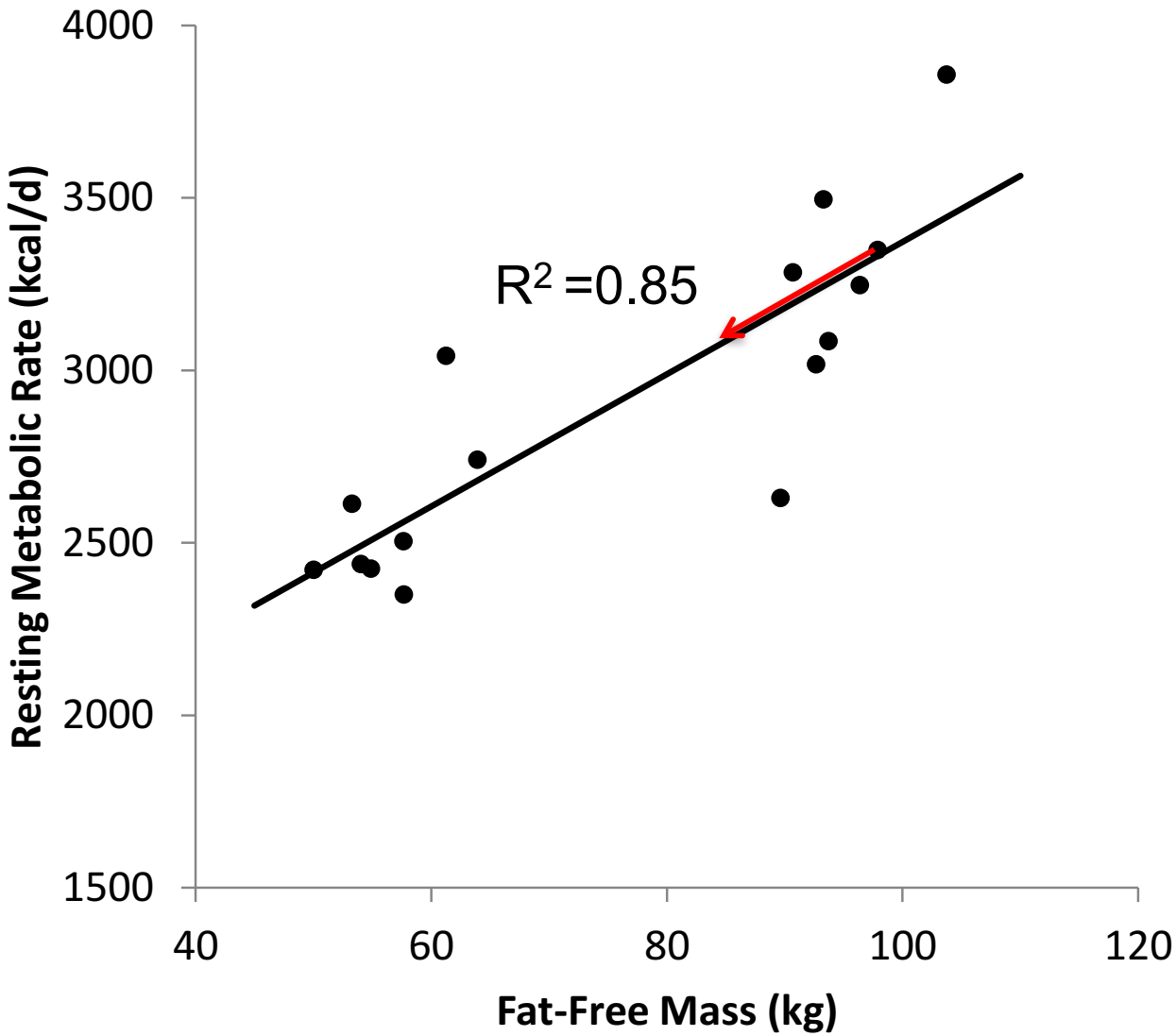
Biggest Loser Data & Model Simulations



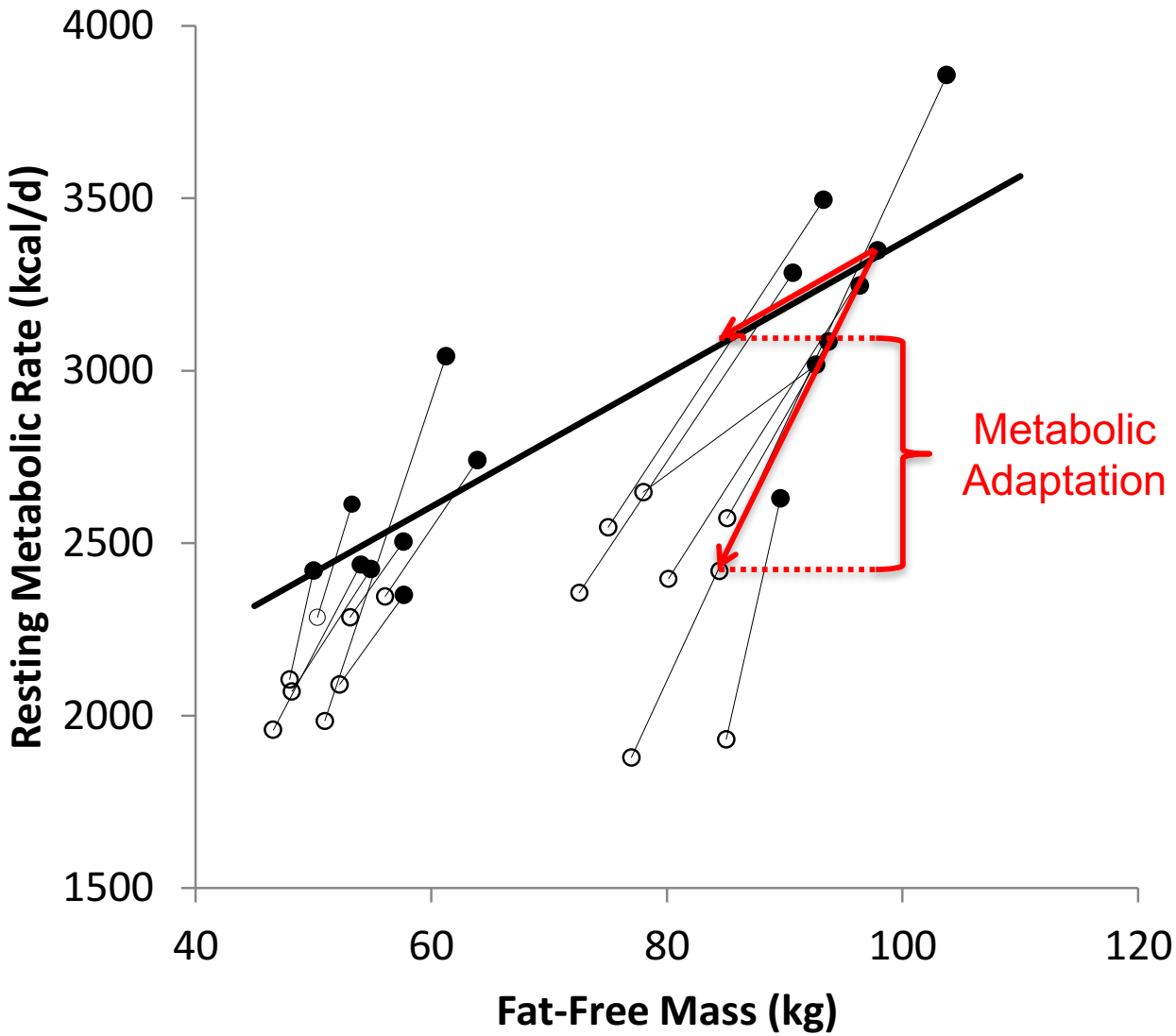
KD Hall. *Obesity* 21(5):957-9 (2013)

Metabolic Rate before the Biggest Loser



DL Johannsen et al. *JCEM* 97(7):2489–2496 (2012)

Metabolic Rate after the Biggest Loser



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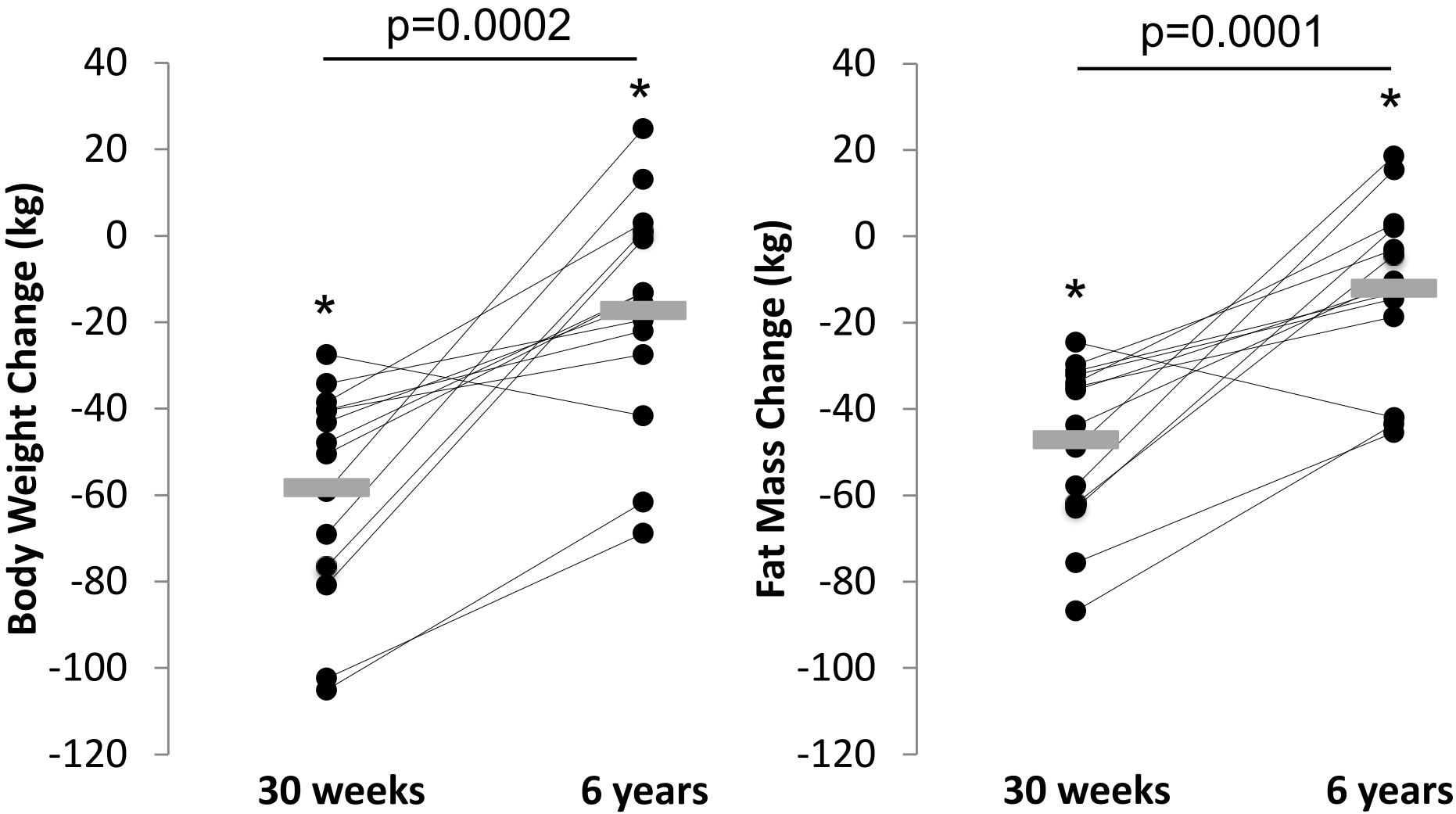
THE SCIENCE OF FAT

After 'The Biggest Loser,' Their Bodies Fought to Regain Weight

Contestants lost hundreds of pounds during Season 8, but gained them back. A study of their struggles helps explain why so many people fail to keep off the weight they lose.

By GINA KOLATA MAY 2, 2016

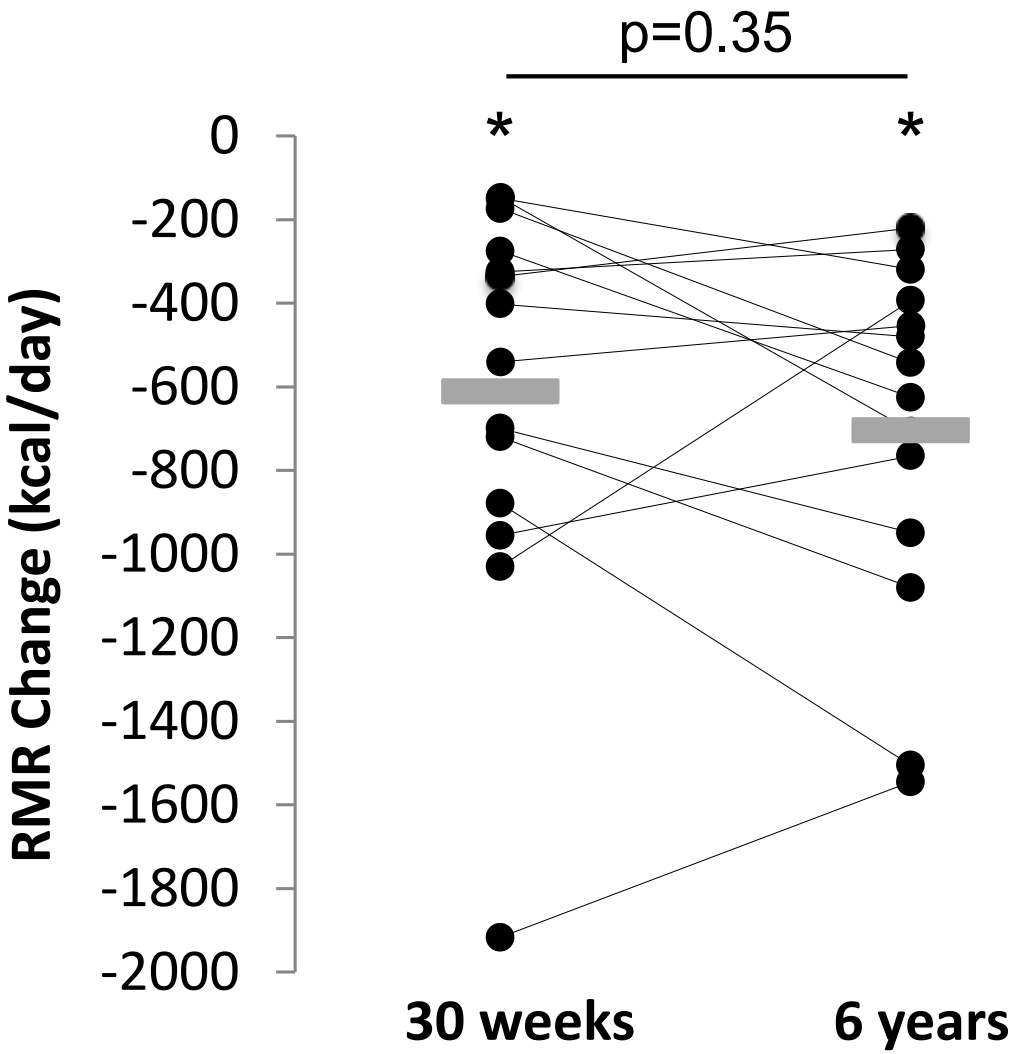
Body Weight & Fat Mass



*p <0.05 vs. baseline

E Fothergill et al. *Obesity* 24:1612-1619 (2016)

Resting Metabolic Rate Remained Low



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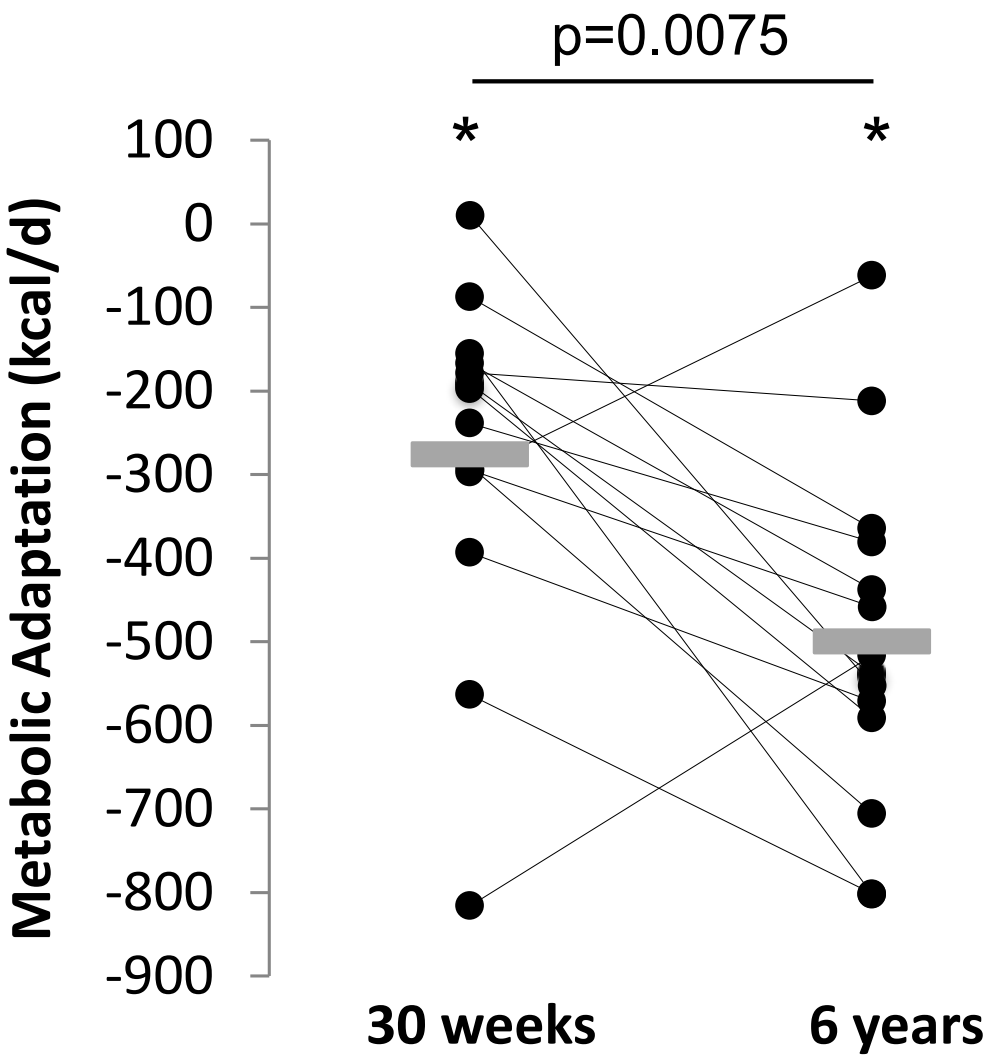
E Fothergill et al. *Obesity* 24:1612-1619 (2016)

Metabolic Adaptation Persisted



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Spring Model of Metabolic Adaptation

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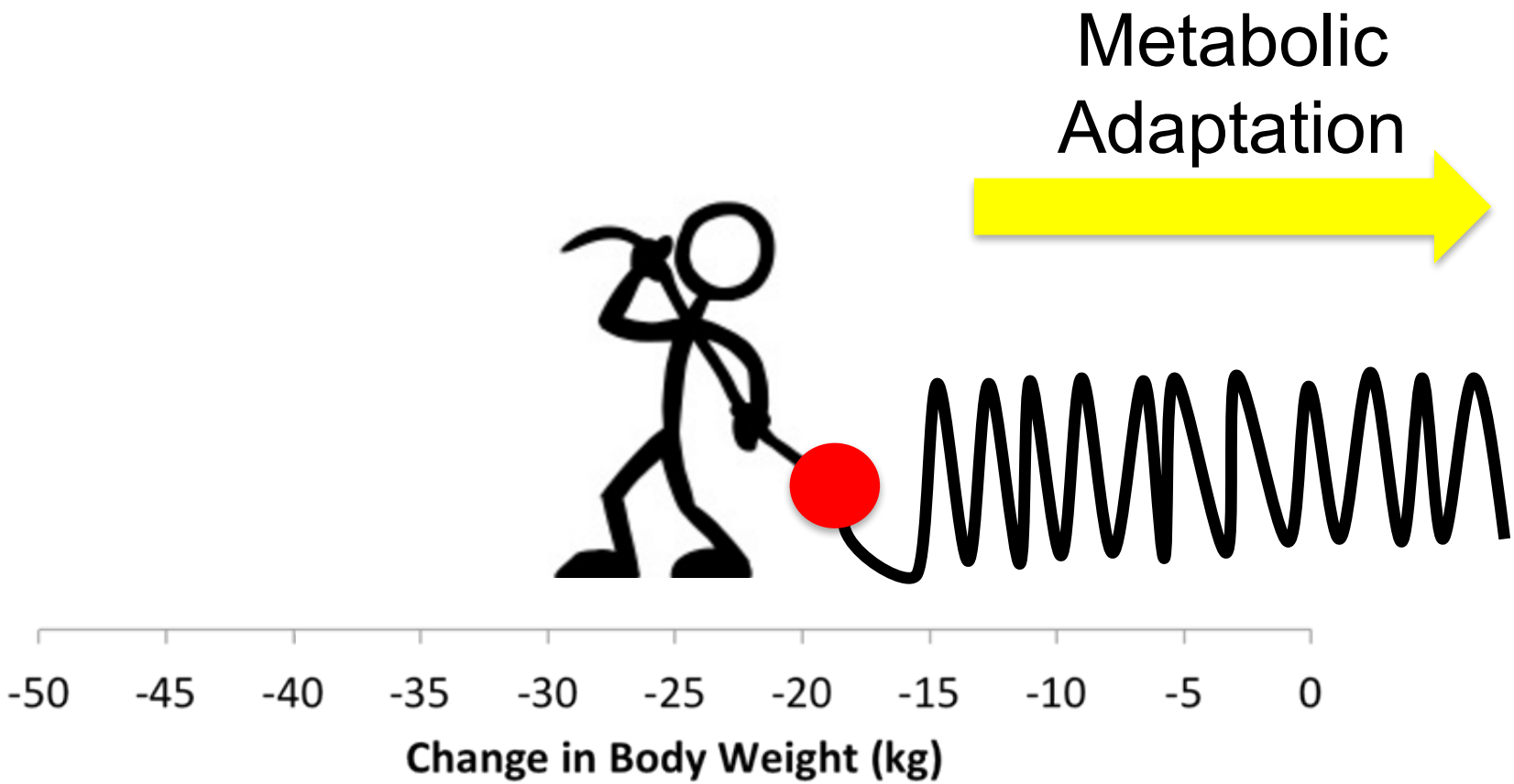
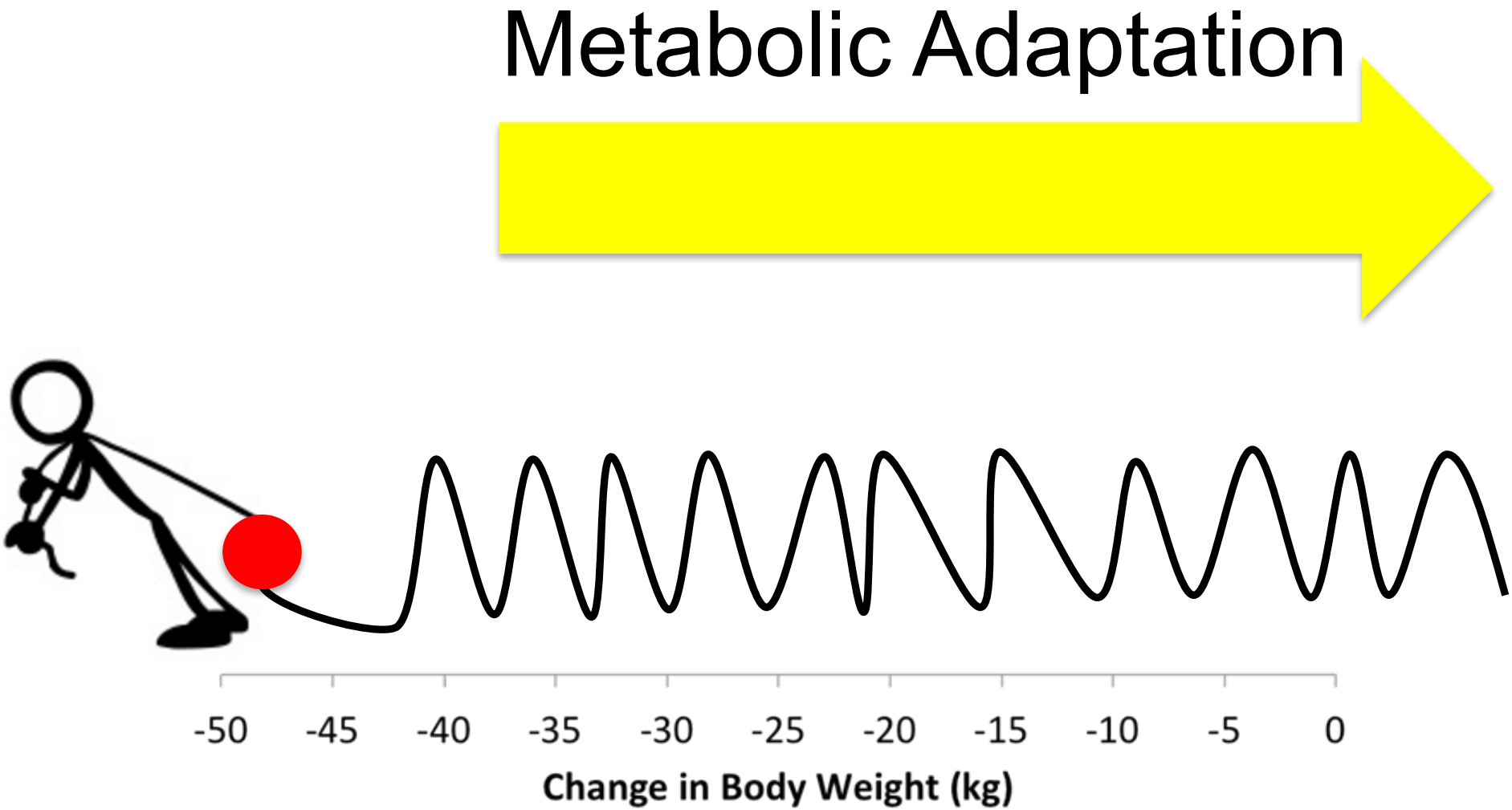
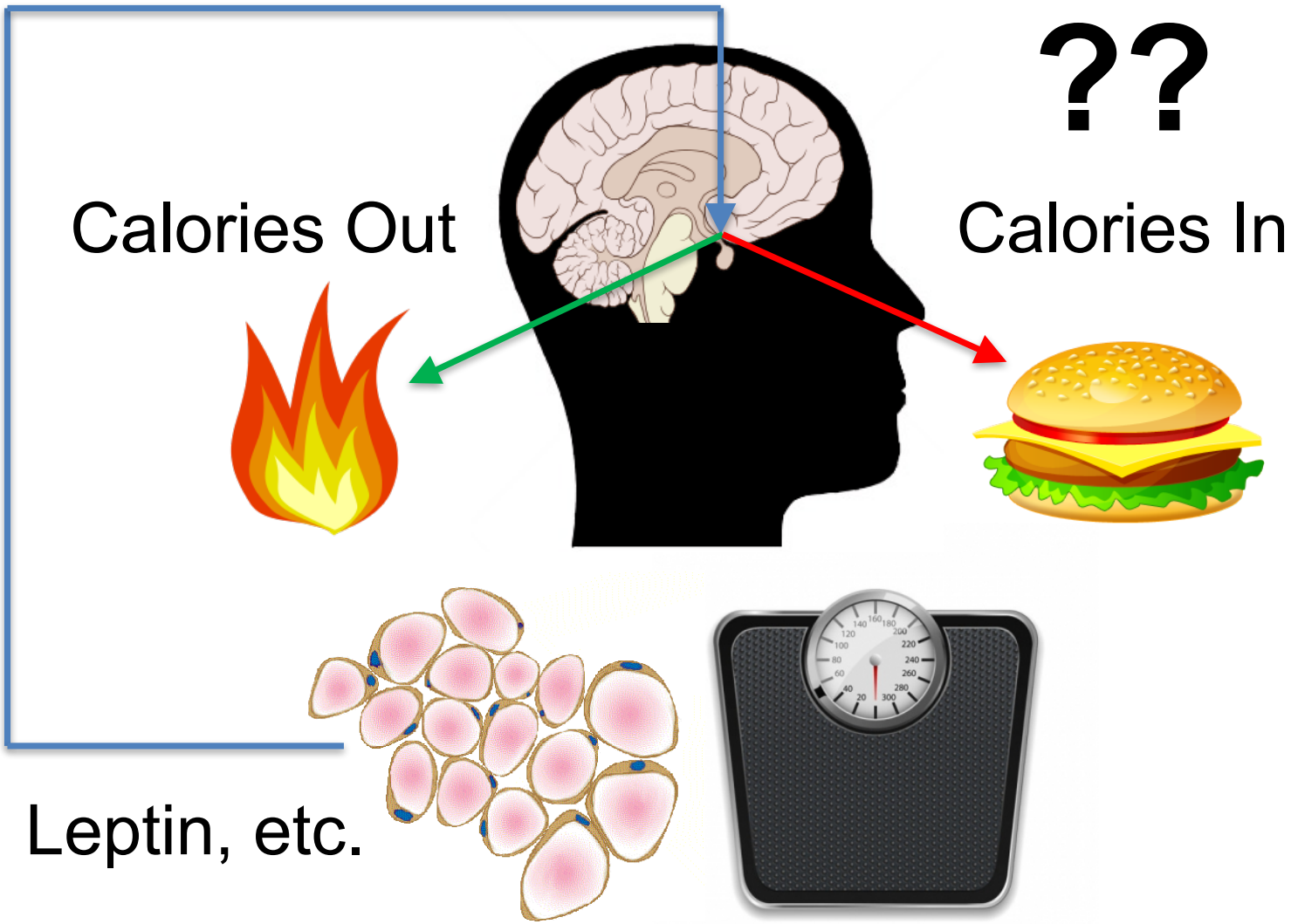


Spring Model of Metabolic Adaptation



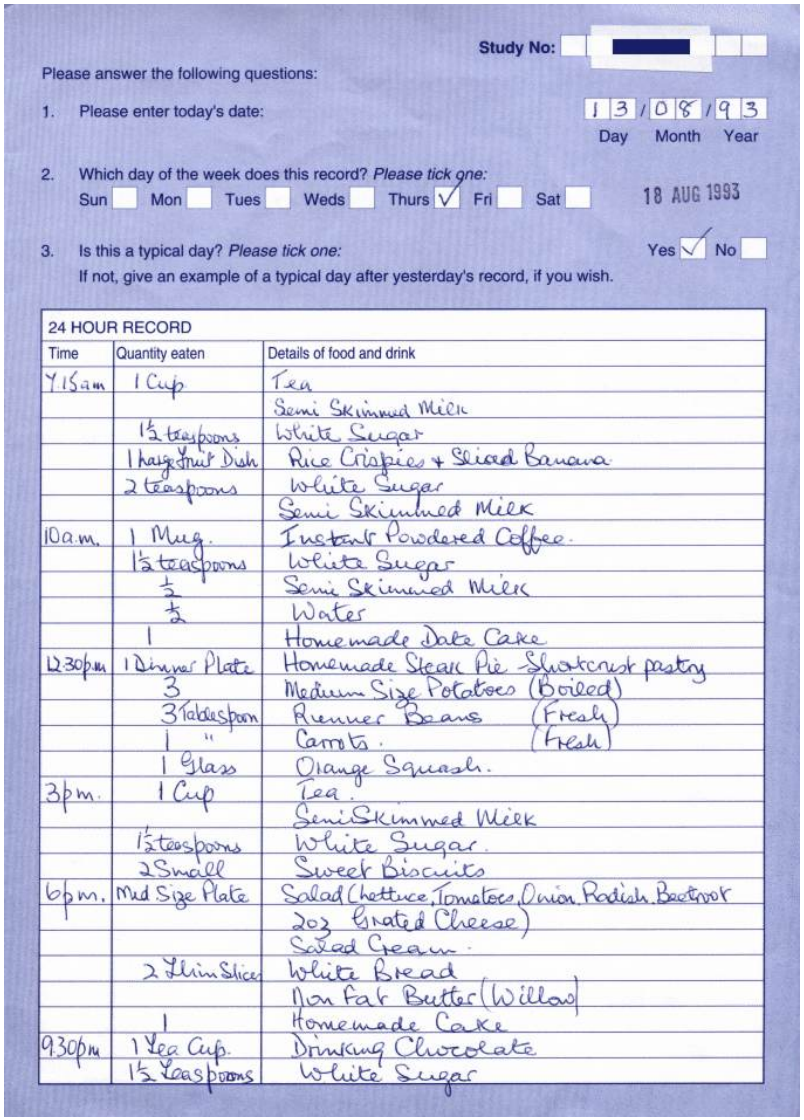
What about Regulation of Food Intake?



The fundamental flaw in obesity research

J. T. Winkler

obesity reviews (2005) **6**, 199–202



Study No: [redacted]

Please answer the following questions:

1. Please enter today's date: 13 / 08 / 93 (Day Month Year)

2. Which day of the week does this record? *Please tick one:*
Sun ☐ Mon ☐ Tues ☐ Weds ☐ Thurs ☑ Fri ☐ Sat ☐ 18 AUG 1993

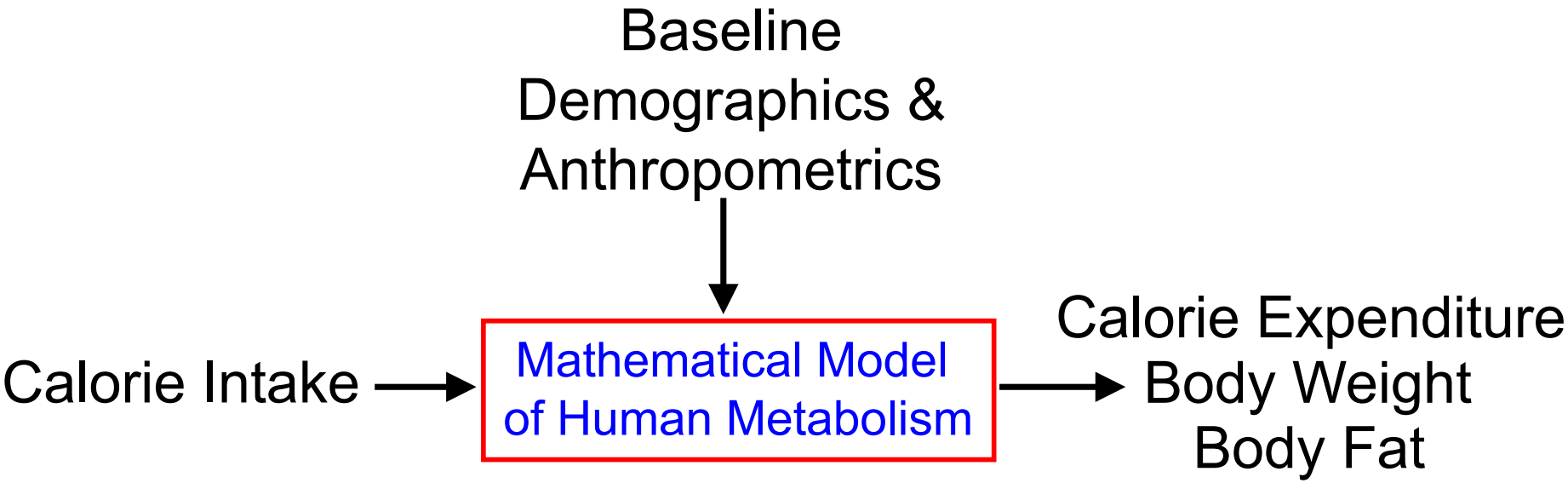
3. Is this a typical day? *Please tick one:* Yes ☑ No ☐
If not, give an example of a typical day after yesterday's record, if you wish.

24 HOUR RECORD

Time	Quantity eaten	Details of food and drink
7.15am	1 Cup	Tea
		Semi Skimmed Milk
	1½ teaspoons	White Sugar
	1 half fruit Dish	Rice Crispies + Sliced Banana
	2 teaspoons	White Sugar
		Semi Skimmed Milk
10a.m.	1 Mug.	Instant Powdered Coffee.
	1½ teaspoons	White Sugar
	½	Semi Skimmed Milk
	½	Water
	1	Homemade Date Cake
12.30pm	1 Dinner Plate	Homemade Steak Pie. Shortcrust pastry
	3	Medium Size Potatoes (Boiled)
	3 Tablespoon	Runner Beans (Fresh)
	1 "	Carrots. (Fresh)
	1 Glass	Orange Squash.
3pm.	1 Cup	Tea.
		Semi Skimmed Milk
	1½ teaspoons	White Sugar.
	2 Small	Sweet Biscuits
6pm.	Med Size Plate	Salad (lettuce, Tomatoes, Onion, Radish, Beetroot
		2oz Grated Cheese)
		Salad Cream.
	2 Thin Slices	White Bread
		Non Fat Butter (Willow)
	1	Homemade Cake
9.30pm	1 Tea Cup.	Drinking Chocolate
	1½ teaspoons	White Sugar

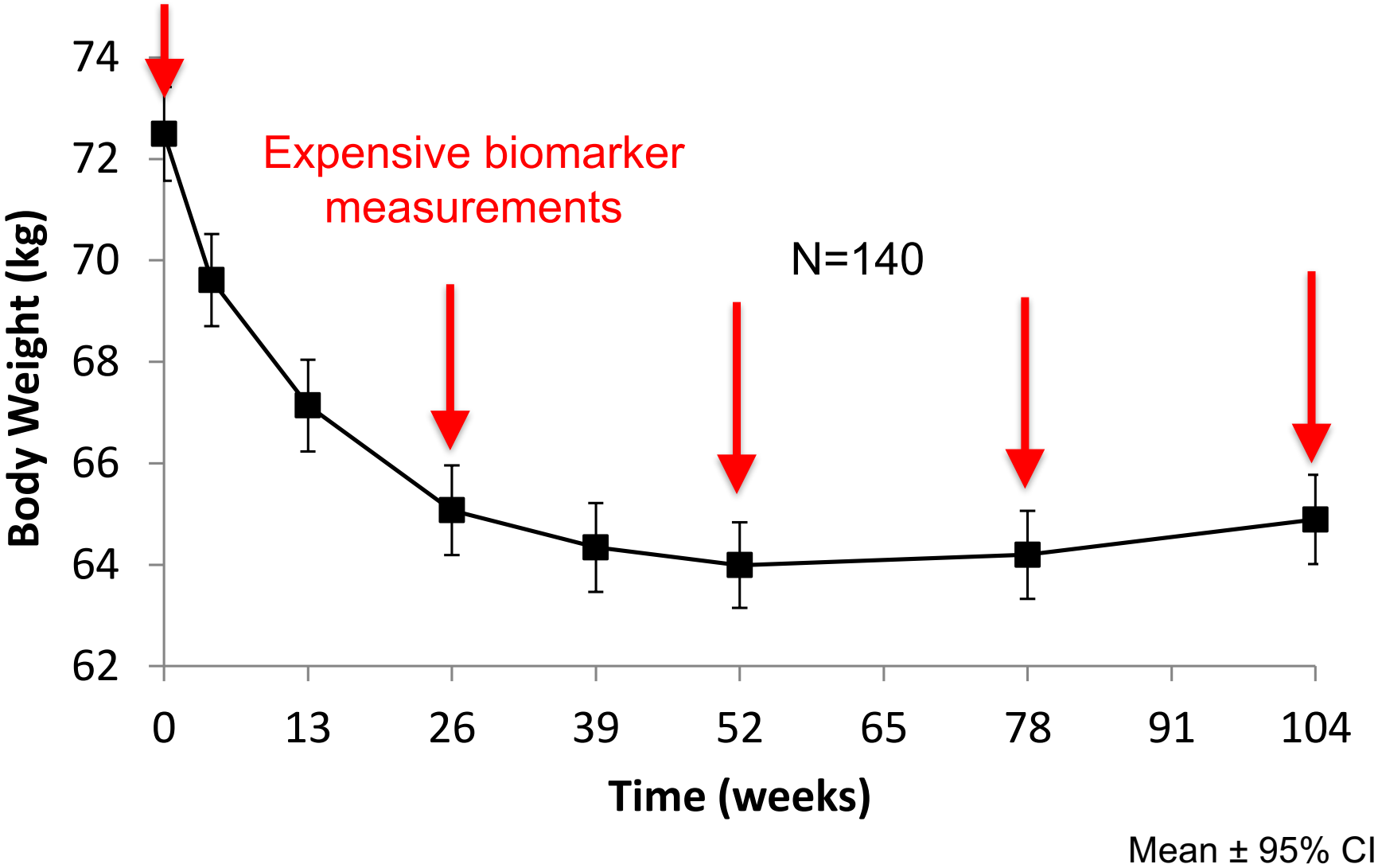
How often, in the past 3 months, did you eat the following?	never	Less than 1 time per week	1-3 times per week	4-6 times per week	1 time per day	2-3 times per day	4 or more times per day	What was your usual serving size, relative to the following?	1	½ or less	1 ½ or more
Fruit (apples, bananas, oranges, etc.)								½ cup raw fruit; ½ medium apple or large orange			
Vegetables (carrots, mushrooms, potatoes, etc.)								½ cup cooked or raw; 1 carrot or stalk celery			
Chicken (fried chicken, in soup, grilled chicken, etc.)								3-4 oz; ½ large or 1 small breast; 2 drumsticks			
Turkey (turkey dinner, turkey sandwich, in soup, etc.)								3-4 oz; 6-8 very thin slices; 1-3 thick slices			
Fish and Seafood (tuna, shrimp, crab, etc.)								3-4 oz; 1 can of tuna; 6 medium shrimp			
Pork (ham, pork chops, ribs, etc.)								3-4 oz; 1 pork chop; 2 ribs; 3-4 slices bacon			
Beef (steak, meatballs, in tacos, etc.)								3-4 oz; ¼ lb burger; 3-6 slices roast beef			
Other Meat (duck, lamb, venison, etc.)								3-4 oz; a piece about the size of your palm			
Nuts (almonds, cashews, walnuts, etc.)								¼ cup or 1 handful; 20 almonds; 2 tbsp nut butter			
Beans (tofu, chickpeas, chili, etc.)								½ cup cooked beans; ¼ cup hummus or tofu			
Dairy (cheese, milk, yogurt, etc.)								3 slices cheese; 1 cup milk; 1 cup yogurt			
Eggs (omelet, in salad, in baked goods, etc.)								1 egg; ¼ cup scrambled eggs or ½ cup egg salad			
Grains (breads, pasta, rice, etc.)								1 slice bread or pizza; ½ cup rice or pasta			
Sweets (candy, cookies, pie, etc.)								2 small cookies; 1 slice cake or pie			
Caffeinated Soft Drinks (cola, diet cola, energy drinks, etc.)								1 can (12 oz) soda; small fountain drink			
Coffee and Tea (hot coffee, iced coffee, black tea, etc.)								6 oz hot coffee or tea; small iced coffee			

Math Models to Calculate Calorie Intake?



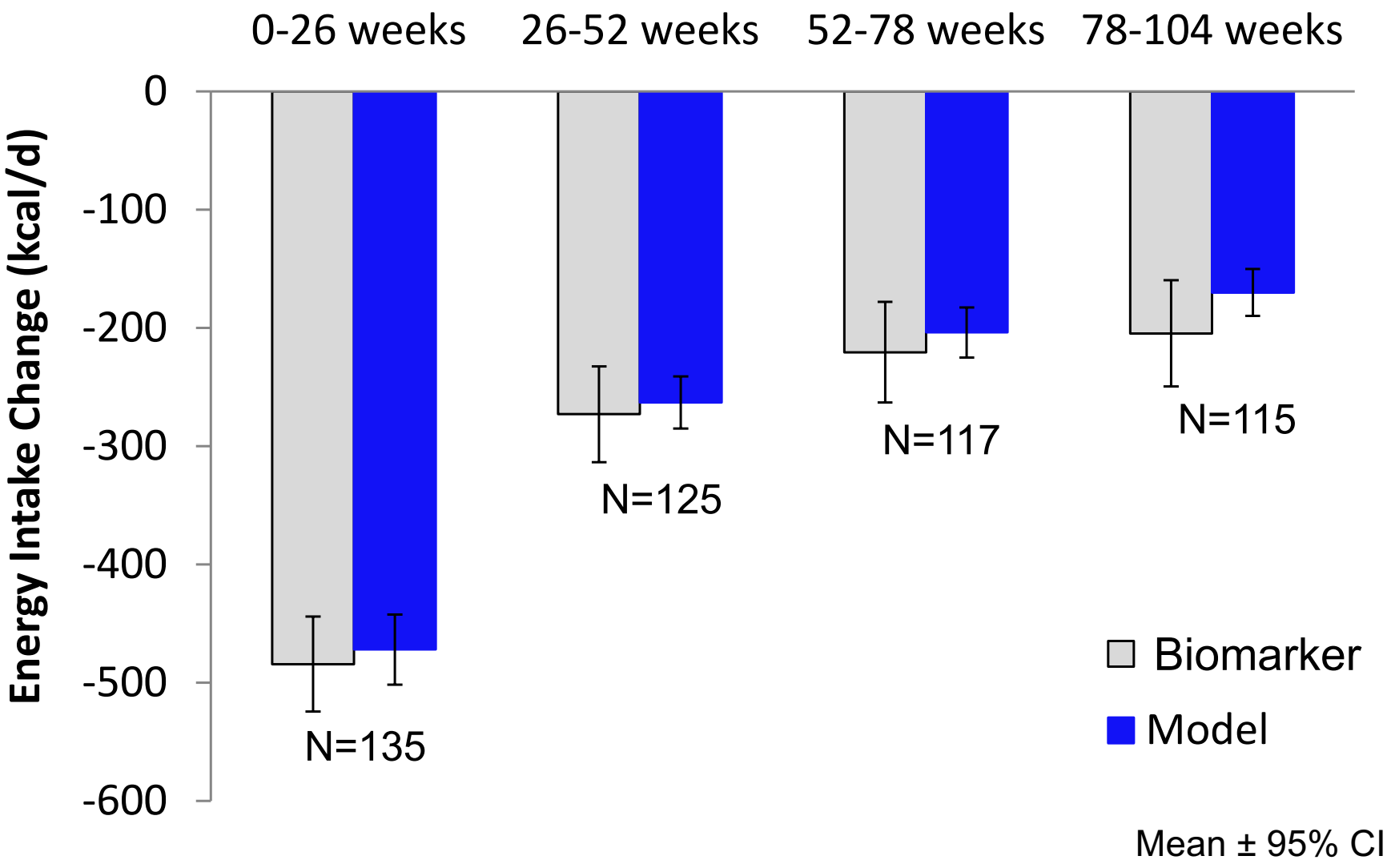
A. Sangvhi et al. *Am J Clin Nutr.* 102:353-358 (2015)

Caloric Restriction for 2 Years



A. Sangvhi et al. *Am J Clin Nutr.* 102:353-358 (2015)

Calorie Intake Changes over 2 Years



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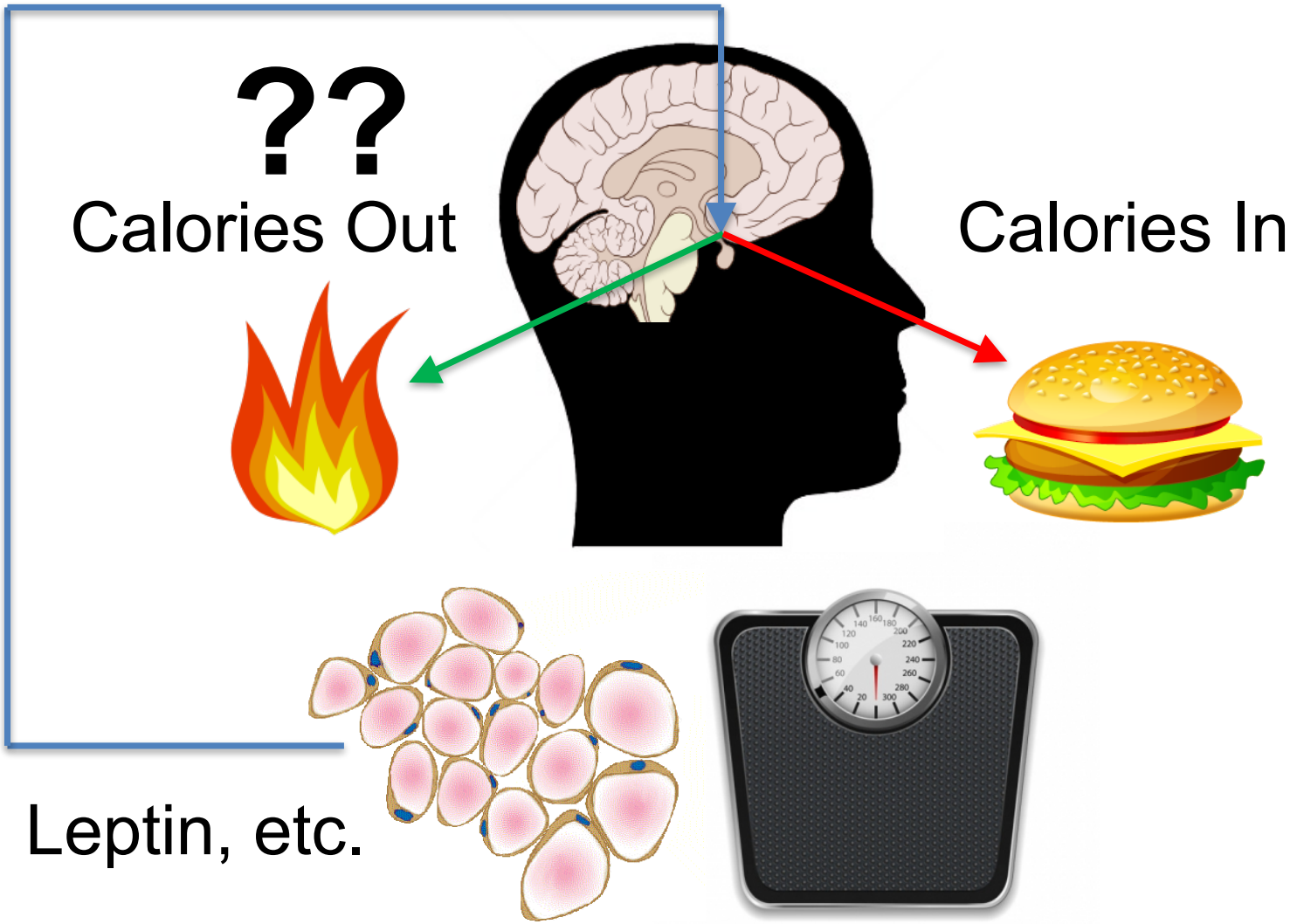
How can we Perturb Energy Expenditure?



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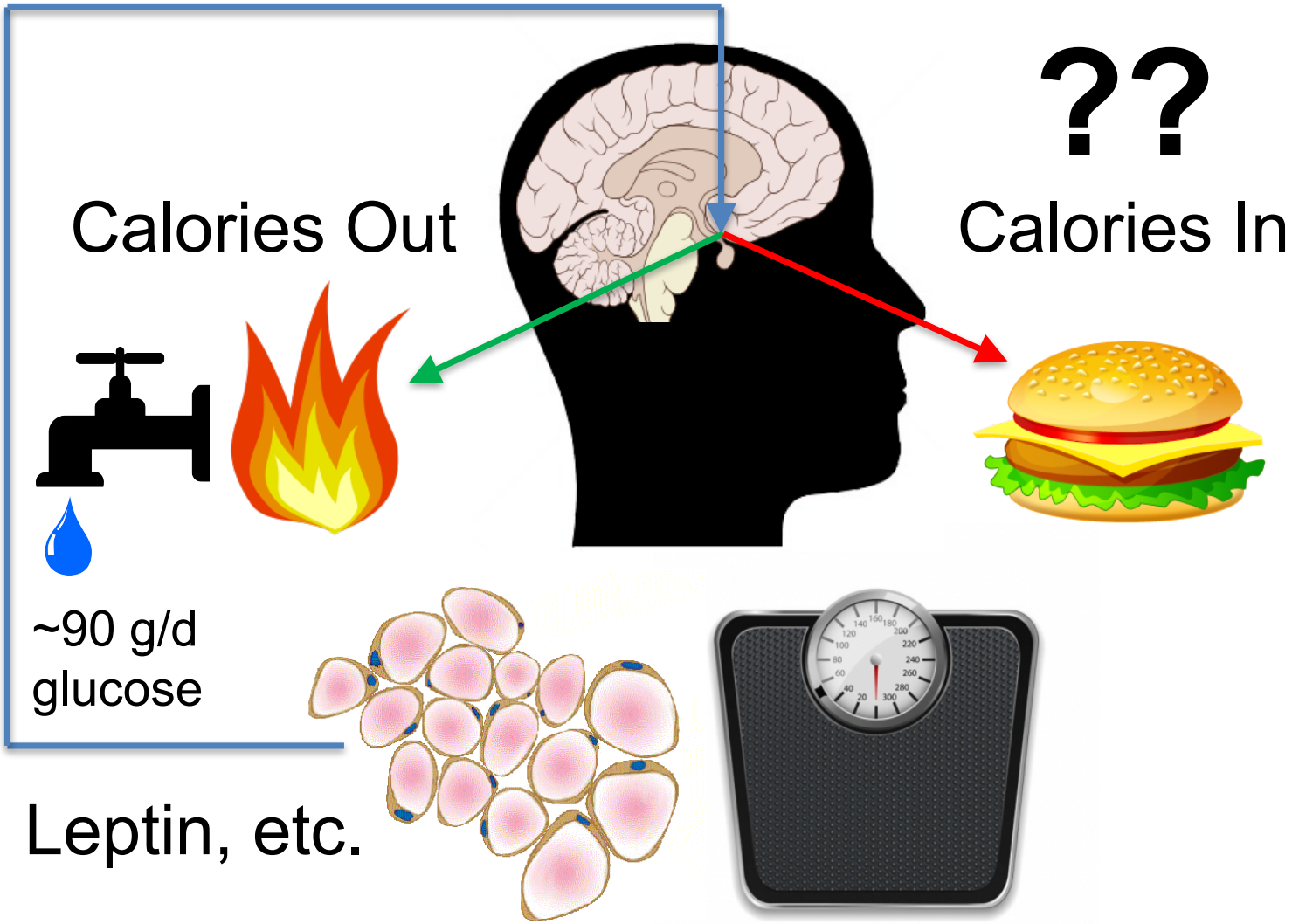
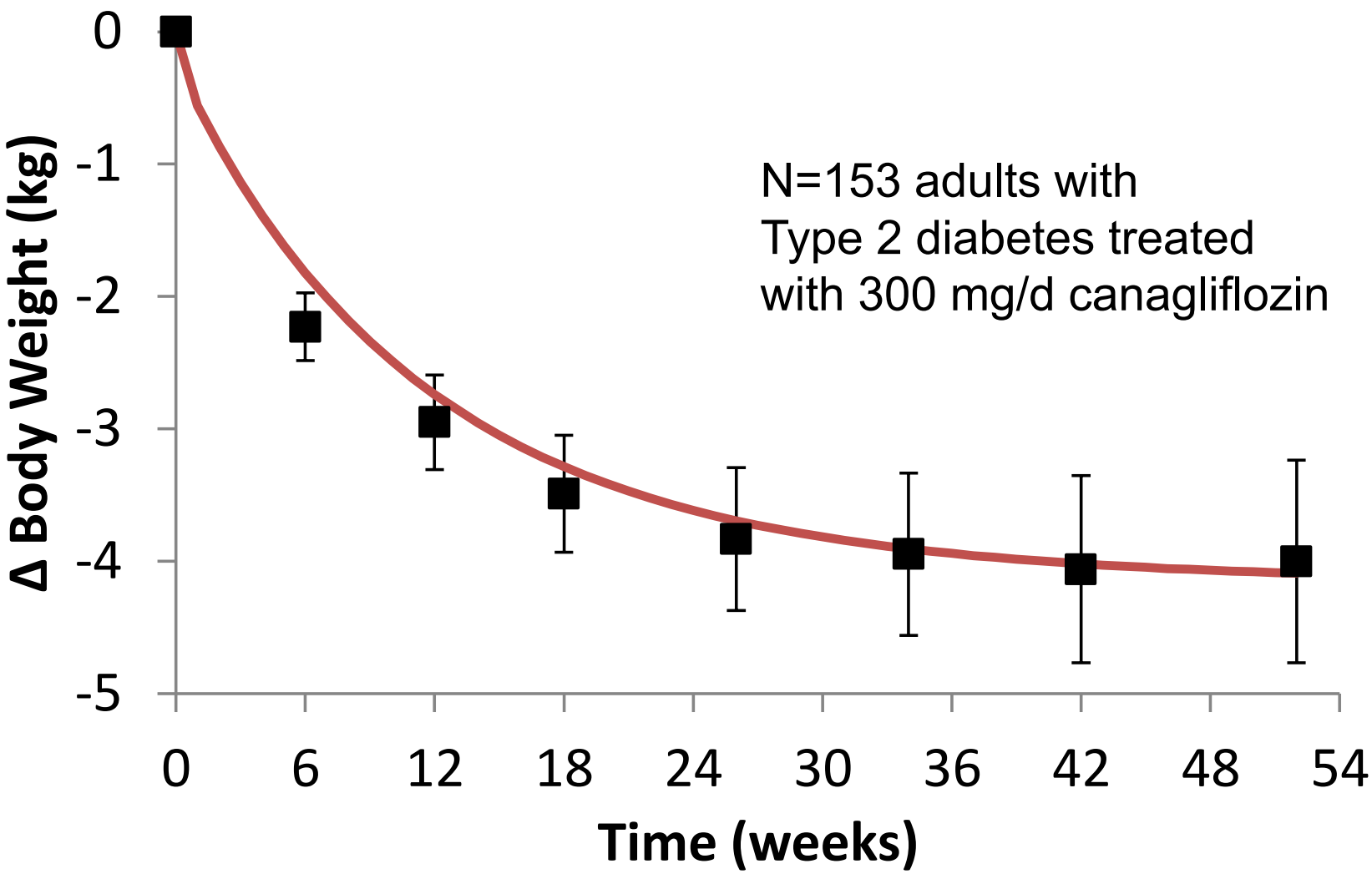
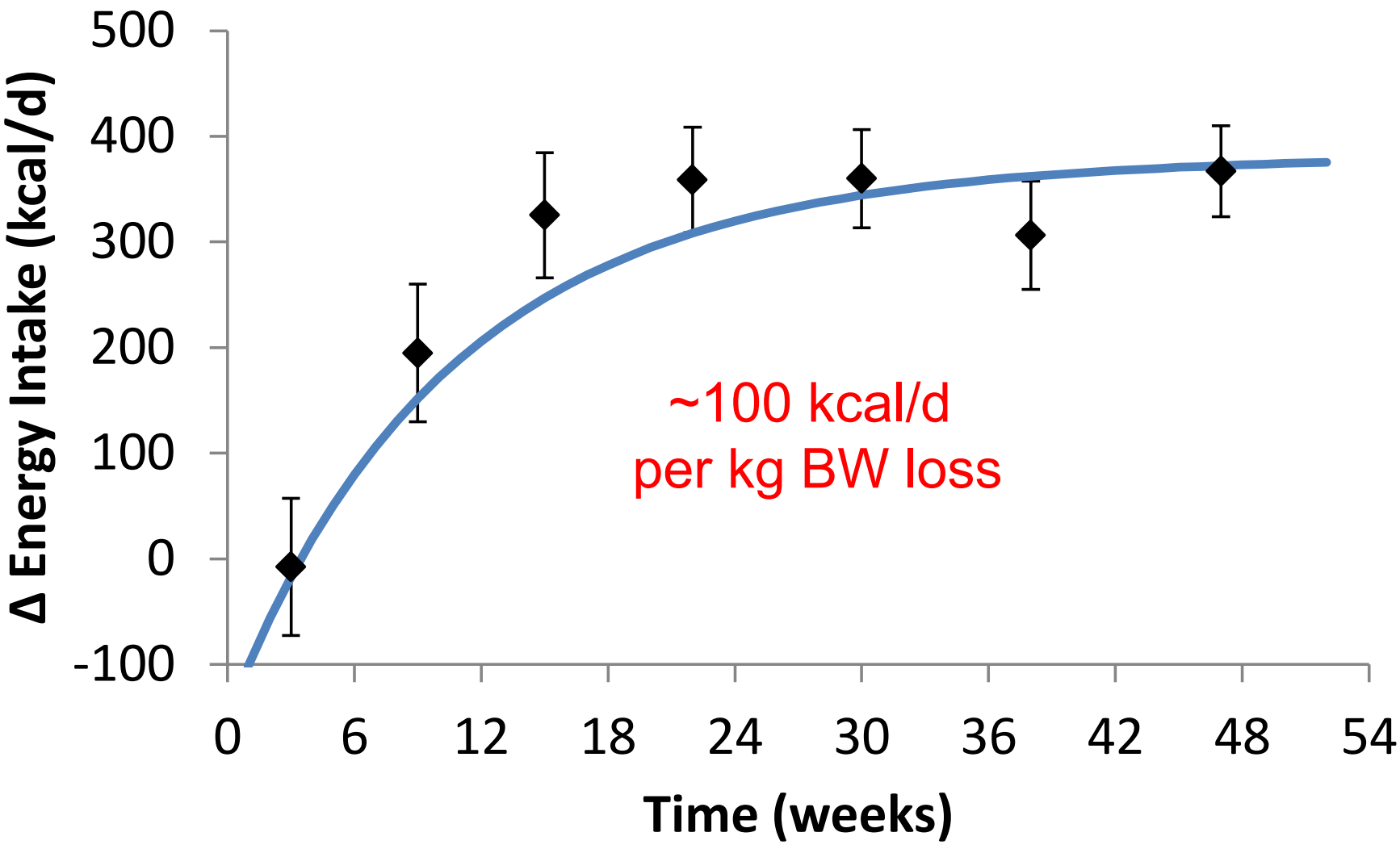


Weight Changes during SGLT2 Inhibition



D. Polidori, A. Sanghvi, R. Seeley, K.D. Hall. *Obesity,* 24:2289 (2016)

Intake Changes during SGLT2 Inhibition



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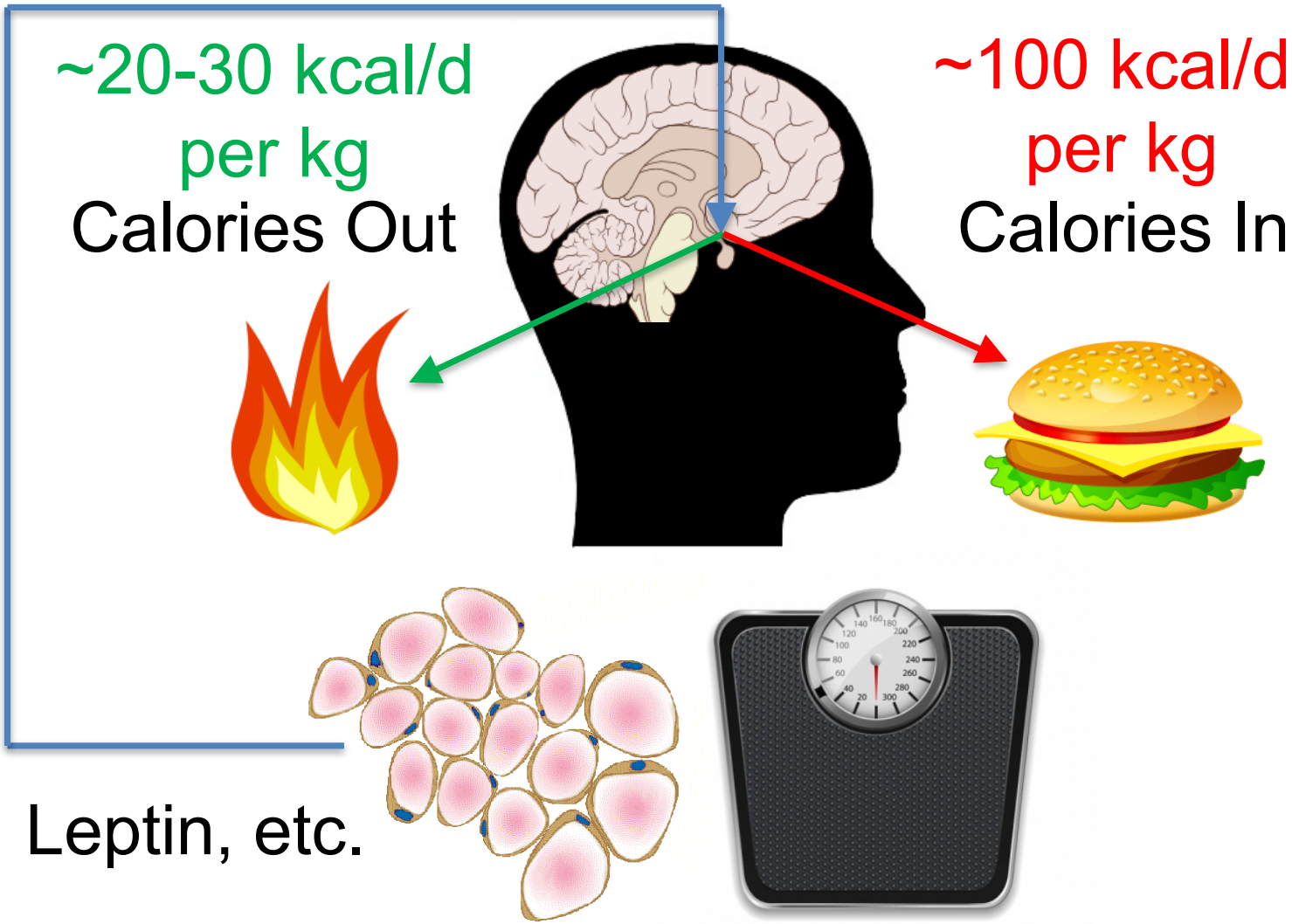
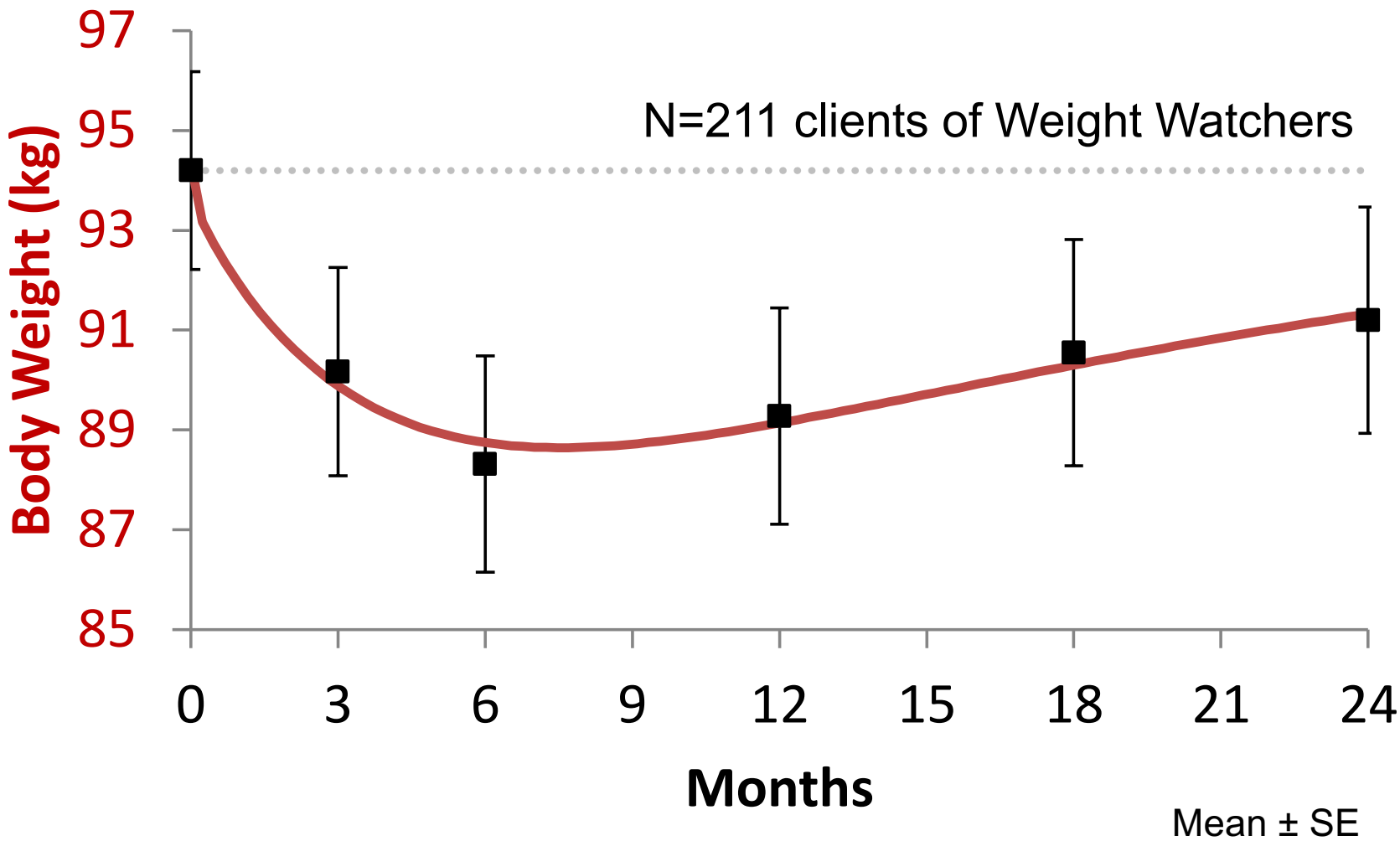
Regulation of Body Weight

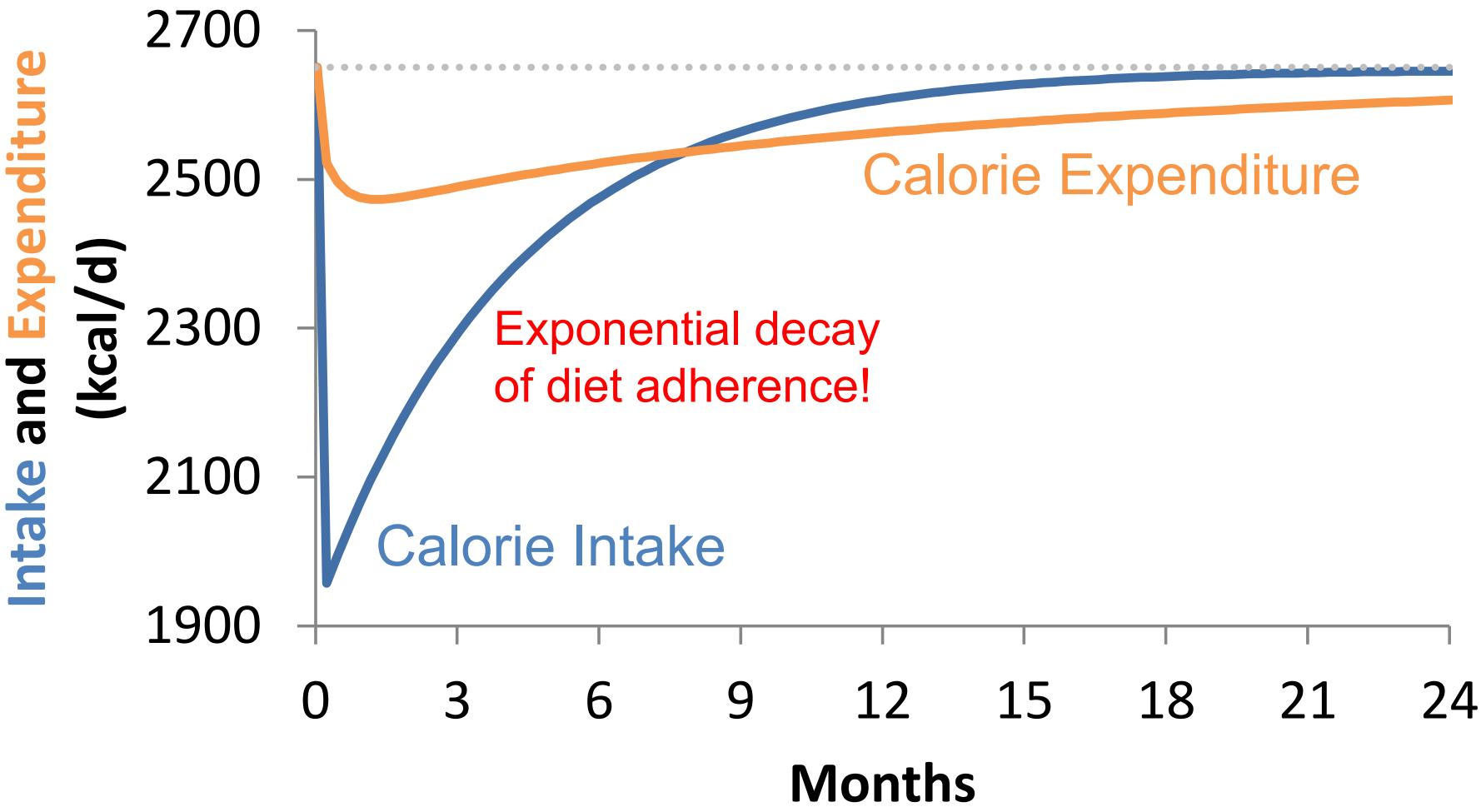


Typical Weight Loss with Lifestyle Change



Data from S. Heshka et al. *JAMA* 289:1792-1798 (2003)

Corresponding Calorie Balance Dynamics



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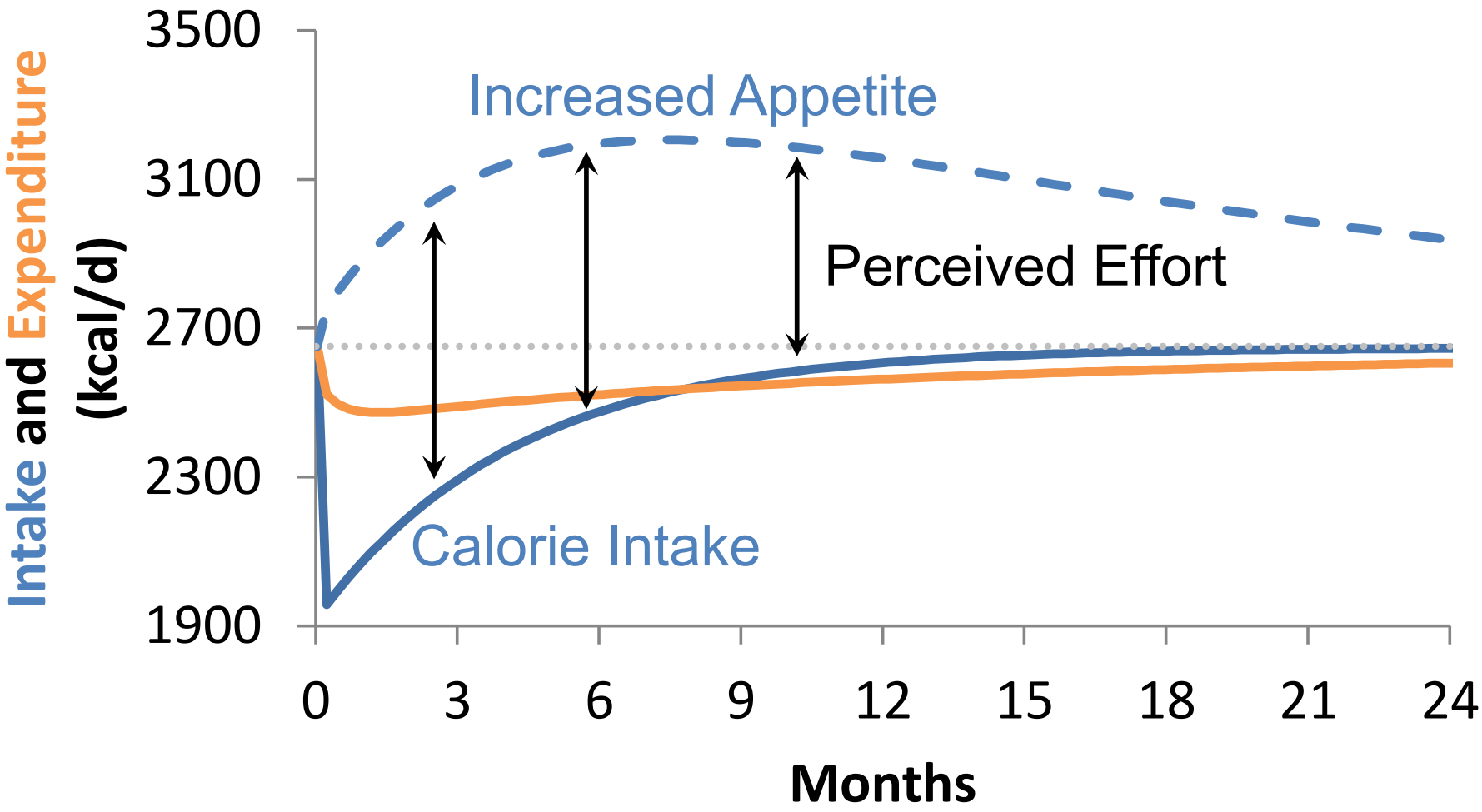
Interpreting Lifestyle Weight Loss



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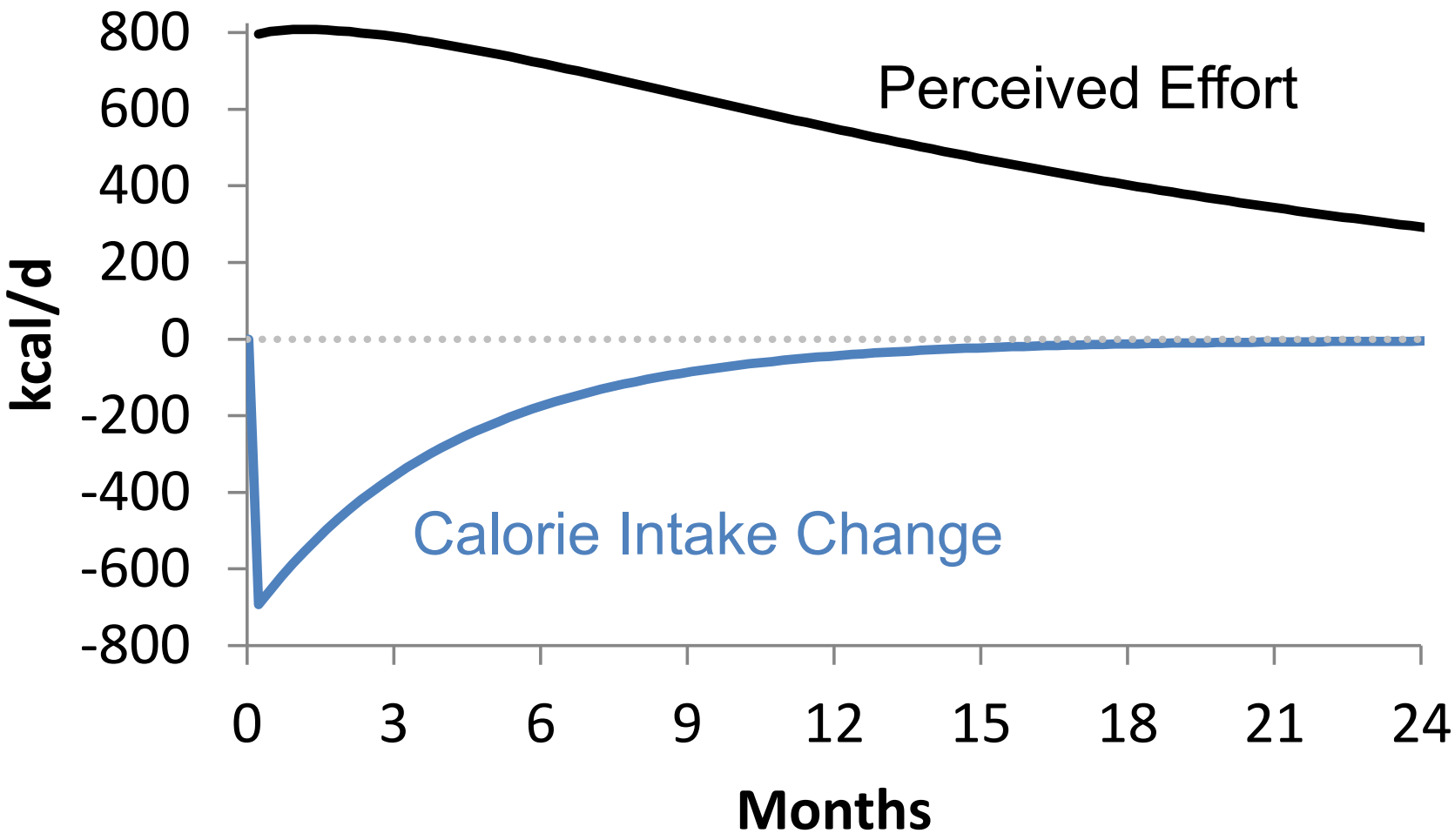

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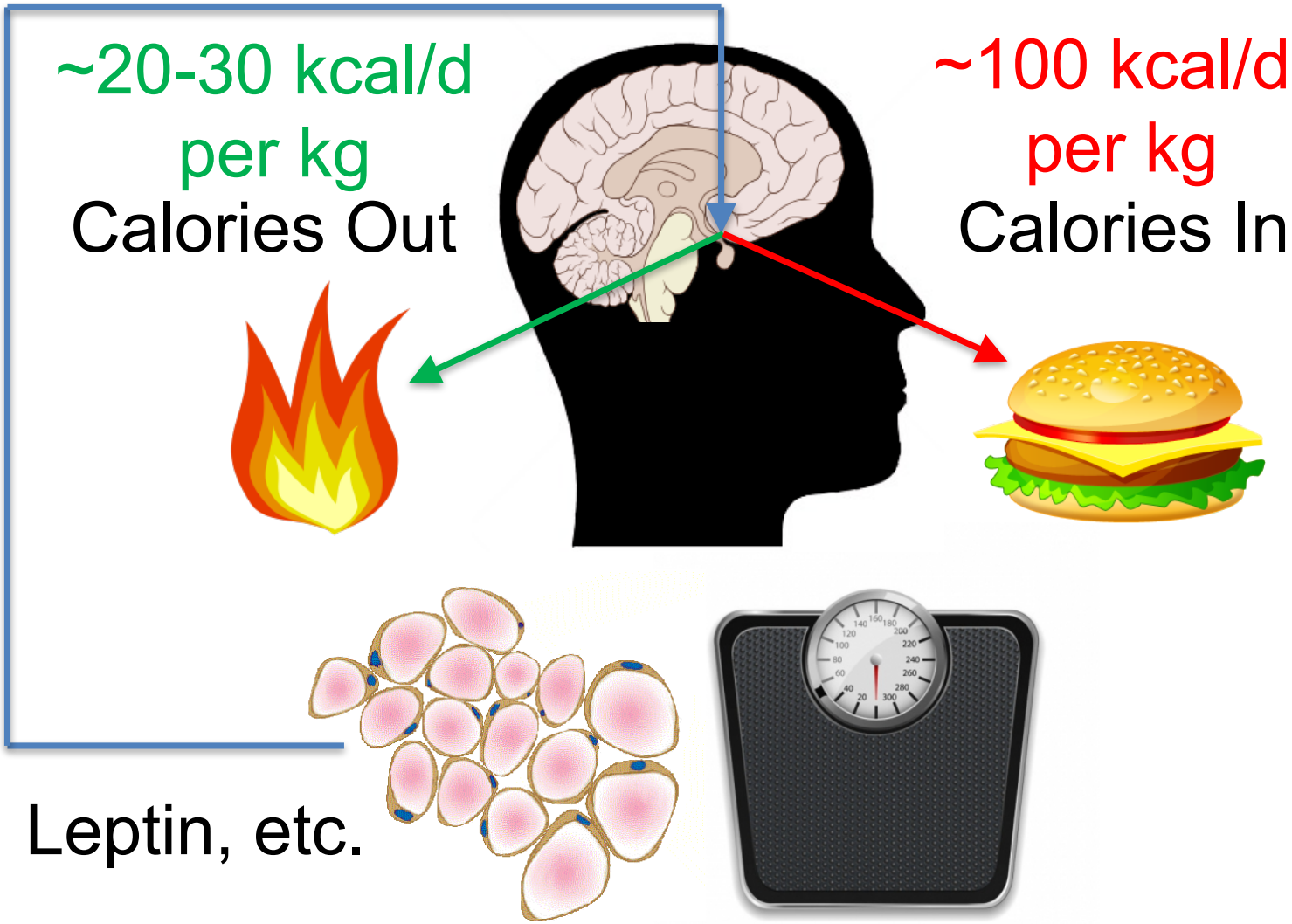
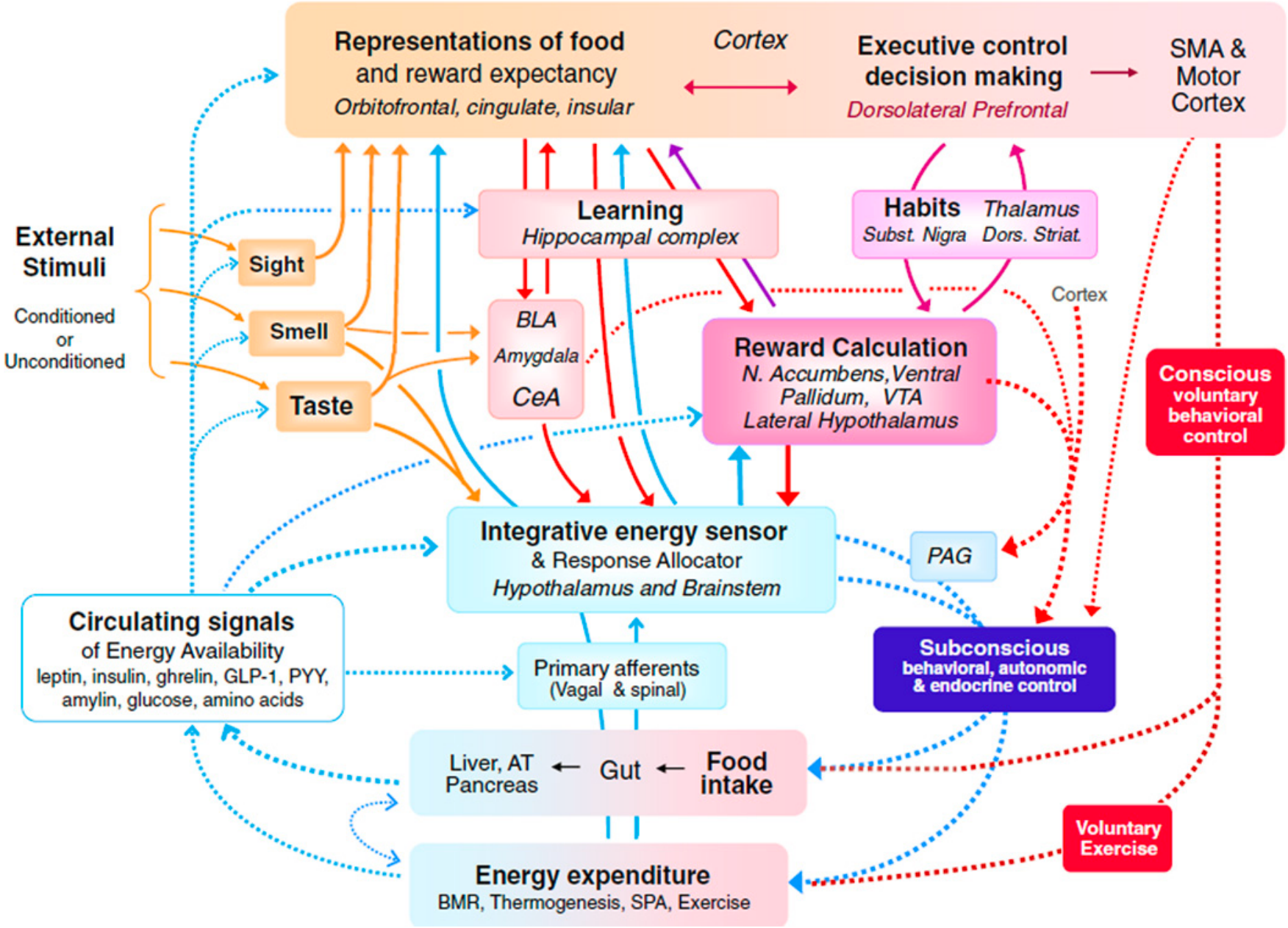
Homeostatic Regulation of Body Weight



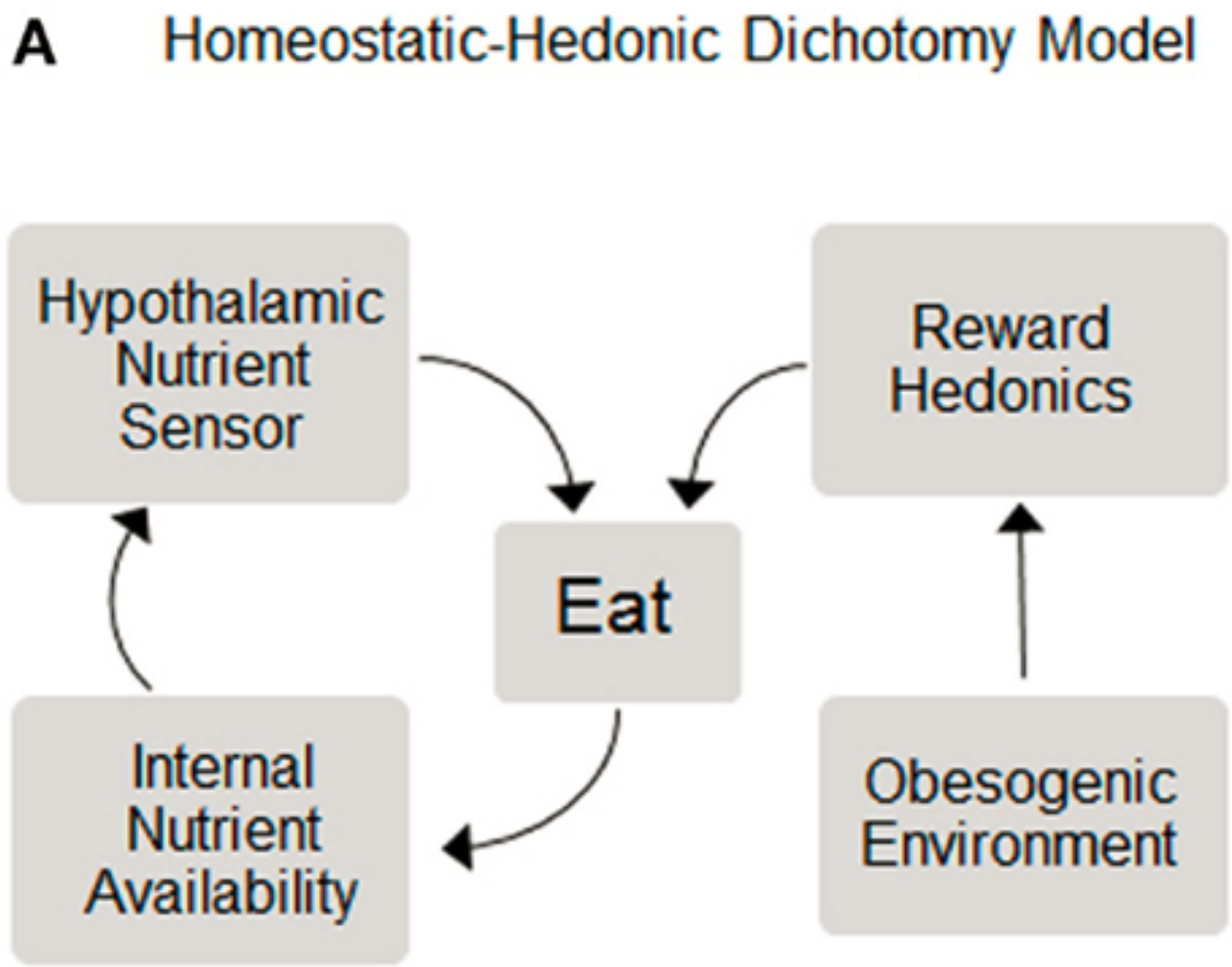
Homeostatic & Hedonic Food Intake

Homeostatic & Hedonic Food Intake



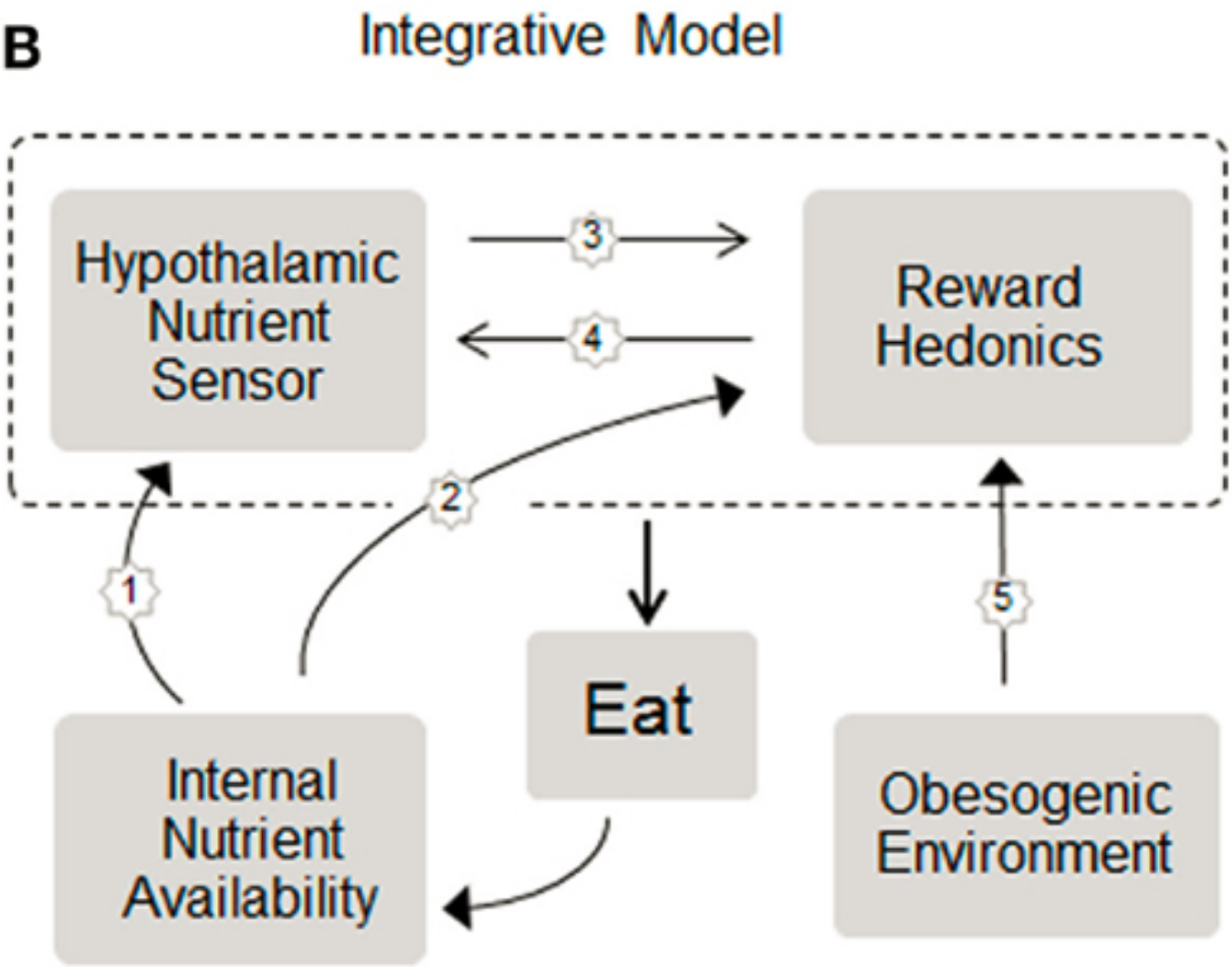
H.R. Berthoud. *Proc. Nutr. Soc.* 71:478-87 (2012)

Homeostatic & Hedonic Food Intake



H. Münzberg, et al. *Front Nutr.* (2016)

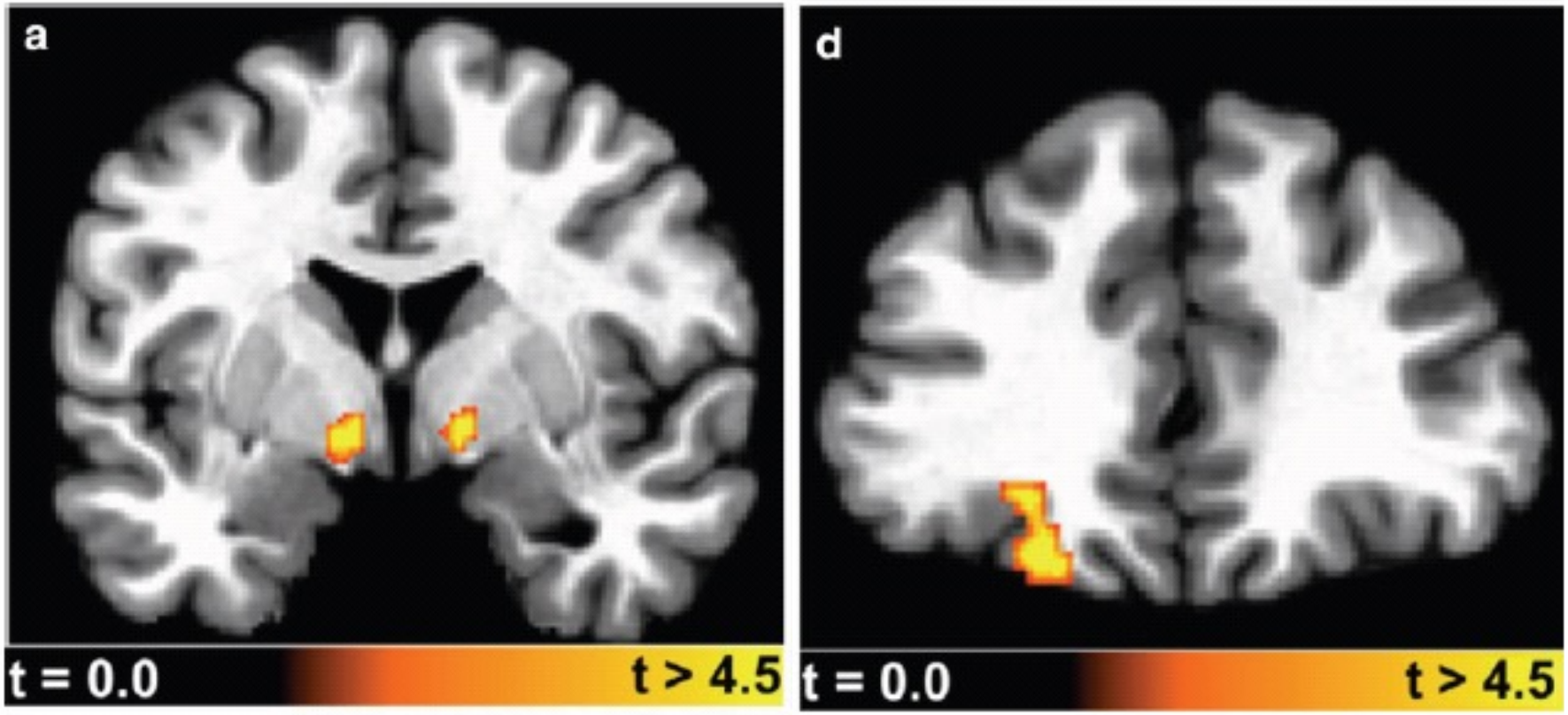
Homeostatic & Hedonic Food Intake



H. Münzberg, et al. *Front Nutr.* (2016)

Non-homeostatic Food Intake

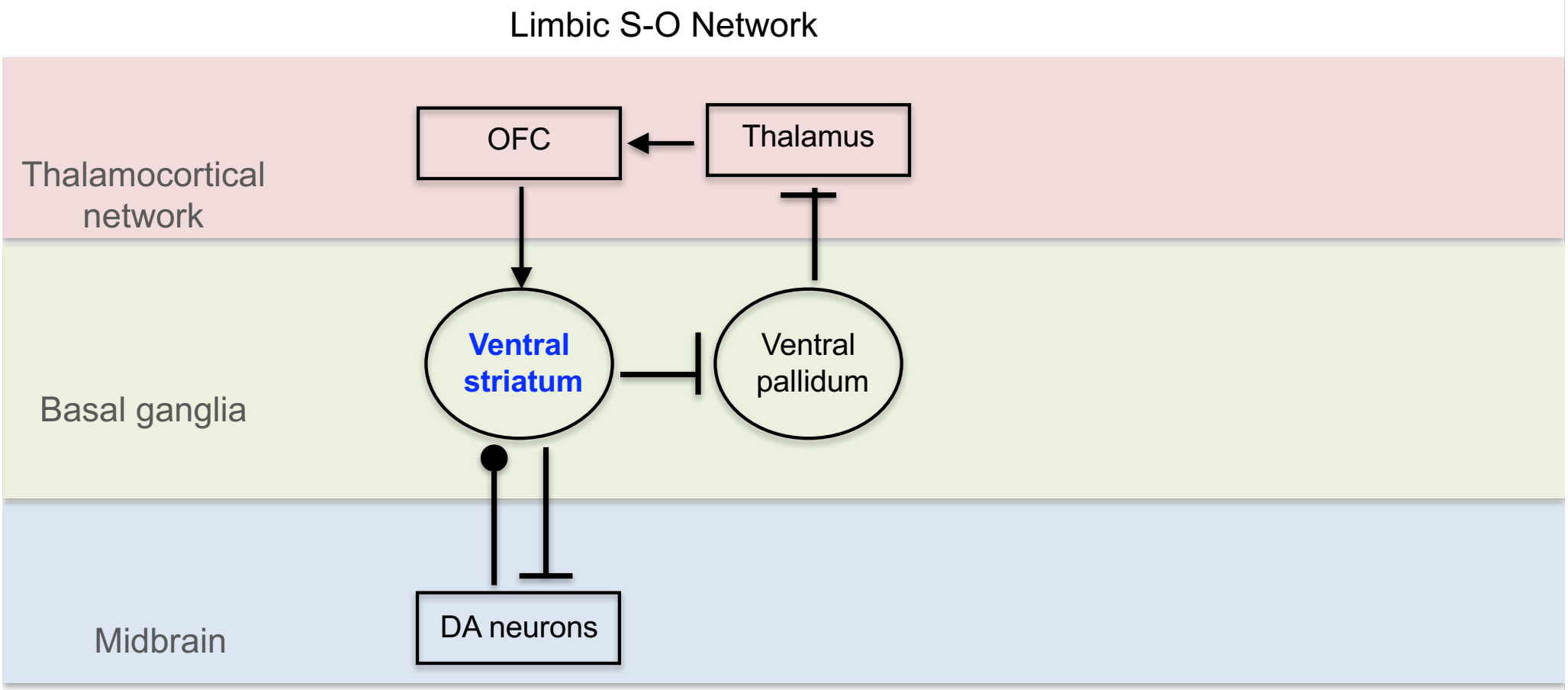
Neural Correlates of Hedonic Food Inference



Ventral Pallidum **Orbital Frontal Cortex**

WK Simmons et al. *Brain Structure & Function* (2013)

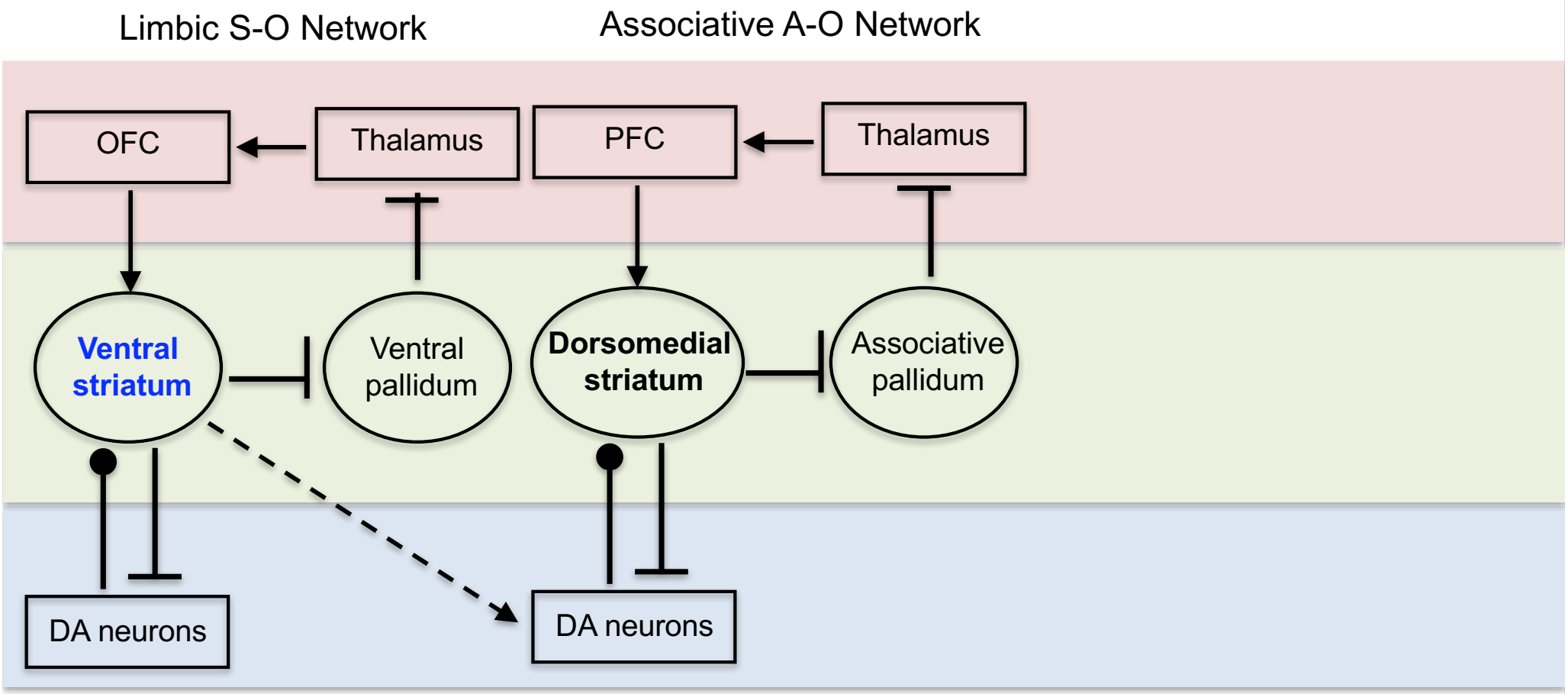
Cortico-Basal Ganglia Networks



Reward & Motivation

Adapted from HH Yin & BJ Knoweton. *Nat. Rev. Neurosci*. 7:464-76 (2006).

Cortico-Basal Ganglia Networks



Reward & Motivation

Goal-directed Behavior

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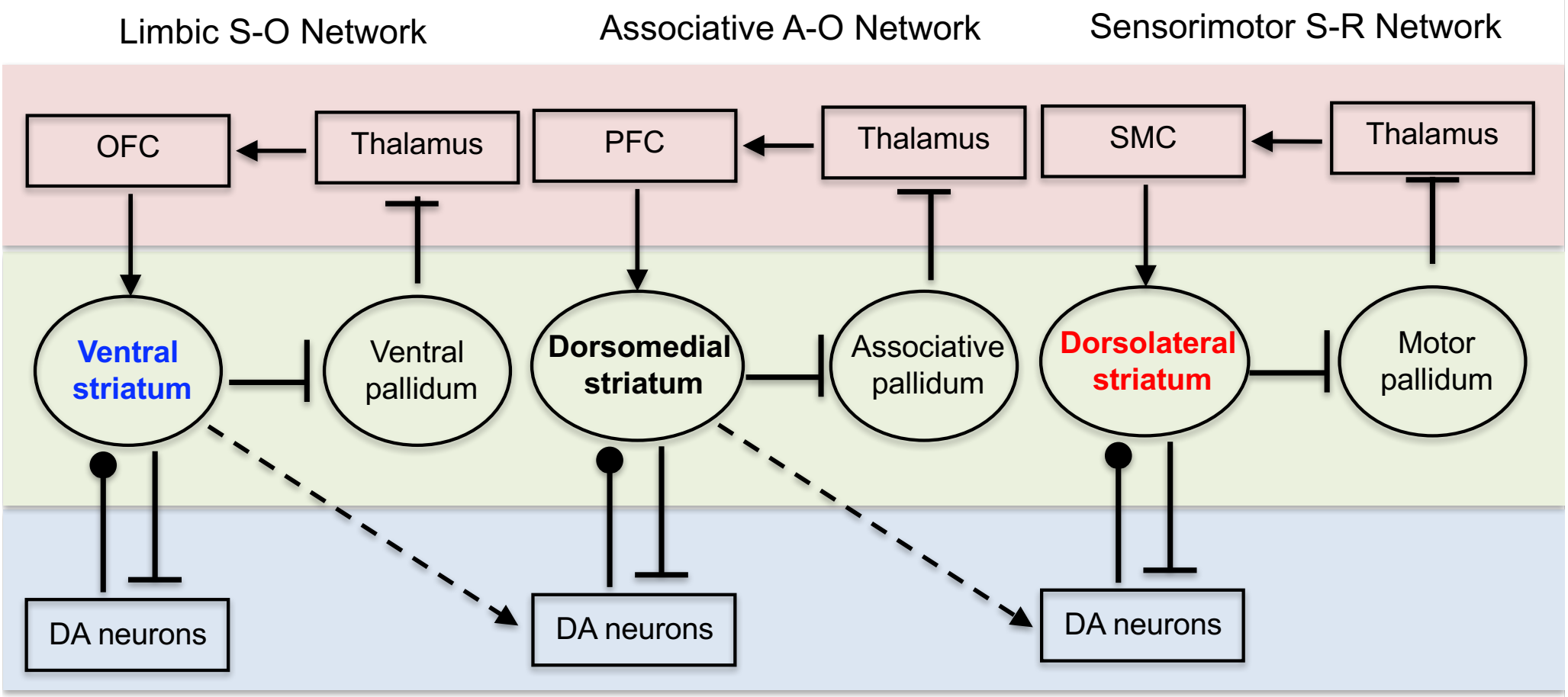
Cortico-Basal Ganglia Networks



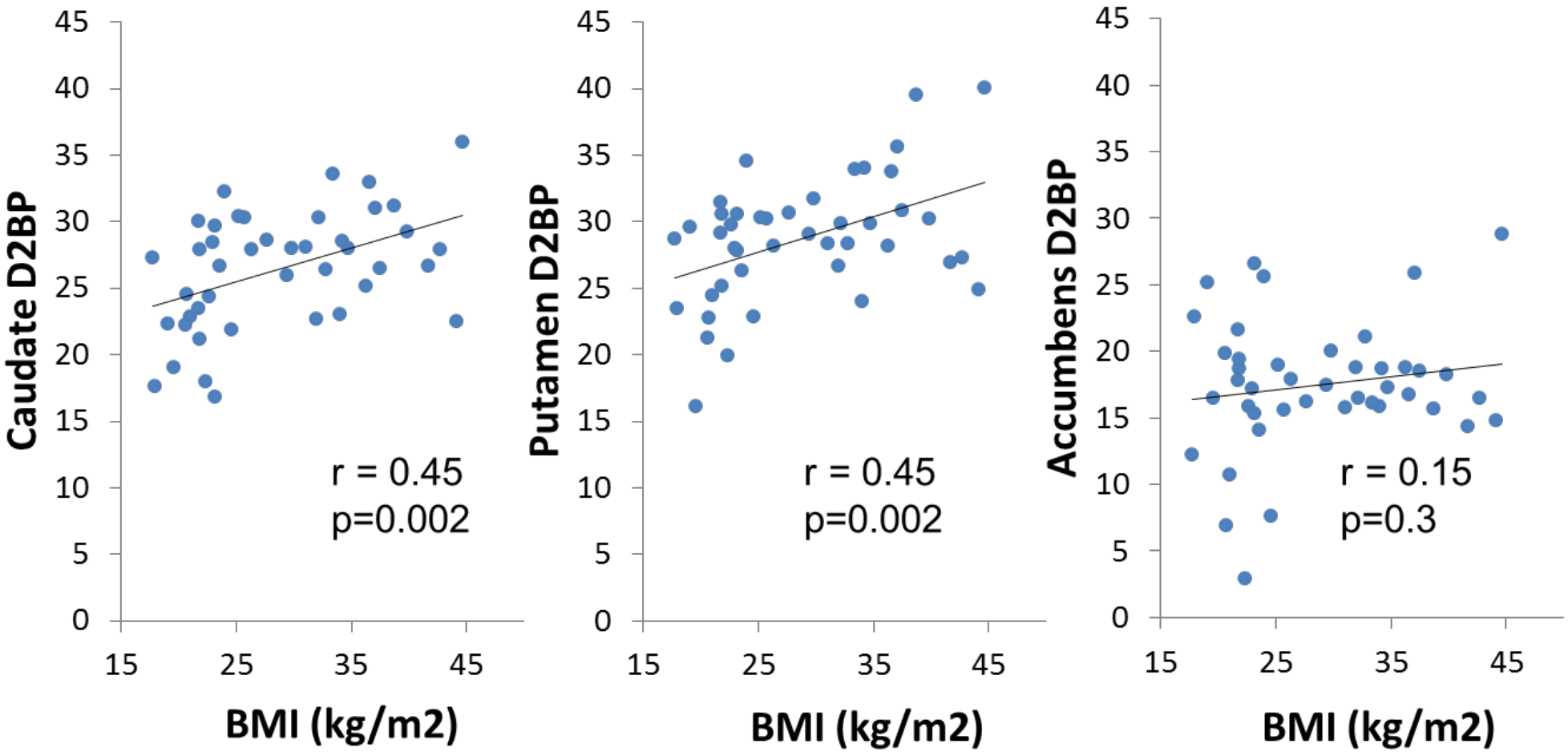
Reward & Motivation

Goal-directed Behavior

Habitual Behavior

Adapted from HH Yin & BJ Knoweton. *Nat. Rev. Neurosci*. 7:464-76 (2006).

Striatal ROI Dopamine D2/D3 Receptor Binding Potential



J. Guo et al. *Mol. Psychiatry* (2014)

Dopamine D2BP Correlation Patterns with Obesity & Opportunistic Eating

43 Subjects
BMI: 18-45 kg/m^2

J. Guo et al. *Mol. Psychiatry* (2014)

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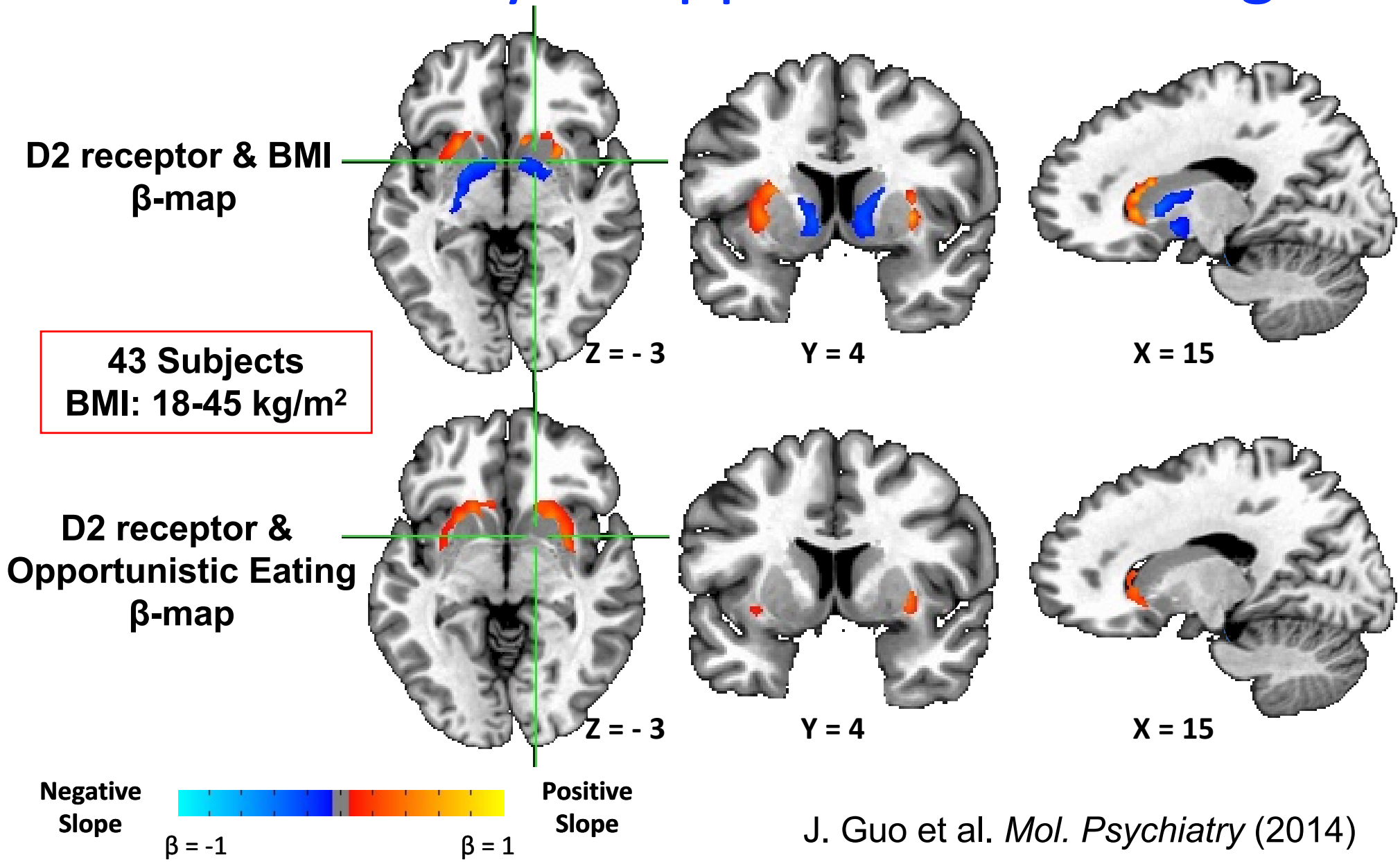


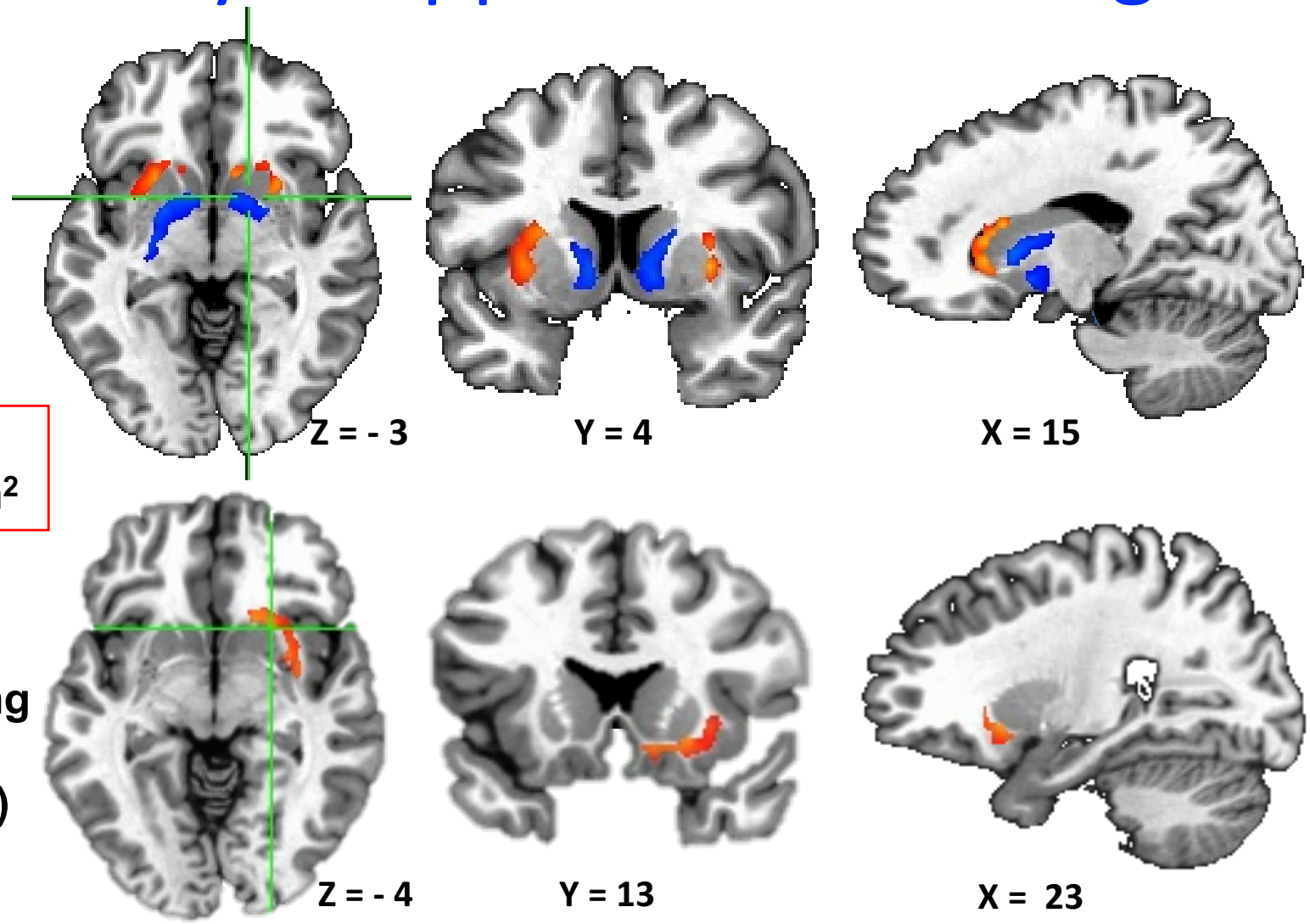
J. Guo et al. *Mol. Psychiatry* (2014)

Dopamine D2BP Correlation Patterns with Obesity & Opportunistic Eating

D2 receptor & BMI β-map

43 Subjects
BMI: 18-45 kg/m²

D2 receptor & Opportunistic Eating β-map (corrected for BMI)



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Intramural NIH

Amber Courville (CC)
Peter Herscovitch (CC)
John Ingeholm (NIMH)
Seth Kallman (NIMH)
Alex Martin (NIMH)
Lydia Milbury (NIMH)
Kristina Rapuano (NIMH)
Nancy Sebring (CC)
W. Kyle Simmons (NIMH)
Nora Volkow (NIDA)

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Alison Baskin
Robert Brychta
Thomas Bemis
Dhruva Chandramohan
Kong Chen
I-Ling Chen
Helen Cheung
Kavya Devaraconda
Courtney Duckworth
Erin Fothergill
Stephanie Goodwin
Juen Guo
Gail Hall
Lilian Howard
Peter Jordan
Nick Knuth
Brooks Leitner
Bernard Miller
Laura Musse
Carla Prado
Emma Preuschl
Marc Reitman
Arjun Sanghvi
Mario Siervo
Monica Skarulis
Wayne Staton
Terri Wakefield
Mary Walter
Peter Walter
Laura Yannai

Extramural Collaborators

Naji Abumrad (Vanderbilt)
CALERIE Study Group
Britta Göbel (Sanofi)
Brian Gilmore (PBRC)
Robert Huizenga (UCLA)
Darcy Johannsen (PBRC)
Jennifer Kerns (DC VA Med Center)
Rudy Leibel (Columbia)
Pamela Marks-Shulman (Vanderbilt)
Corby Martin (PBRC)
Laurel Mayer (Columbia)
Eric Ravussin (PBRC)
David Polidori (J&J)
Leanne Redman (PBRC)
Jennifer Rood (PBRC)
Michael Rosenbaum (Columbia)
Robyn Tamboli (Vanderbilt)
Randy Seeley (U Michigan)
Steven R. Smith (TRI)
Jon Moon (MEI)
B. Tim Walsh (Columbia)

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