



Unraveling the Mechanisms of Ultra-processed Foods

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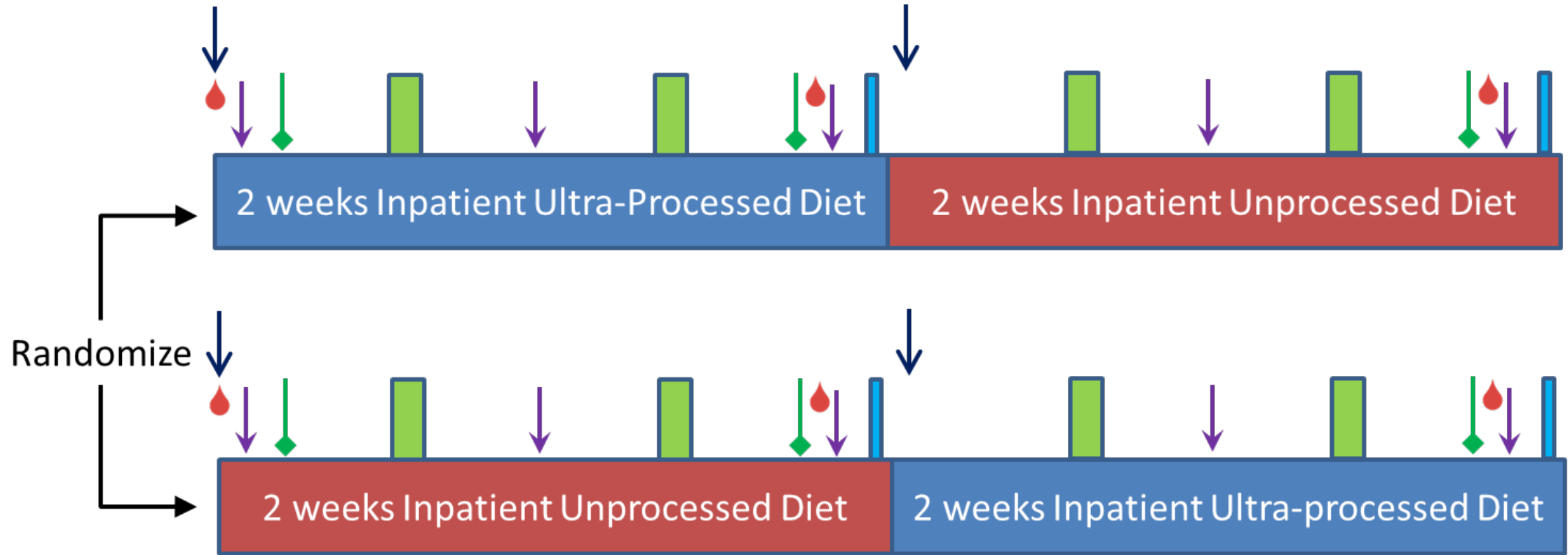


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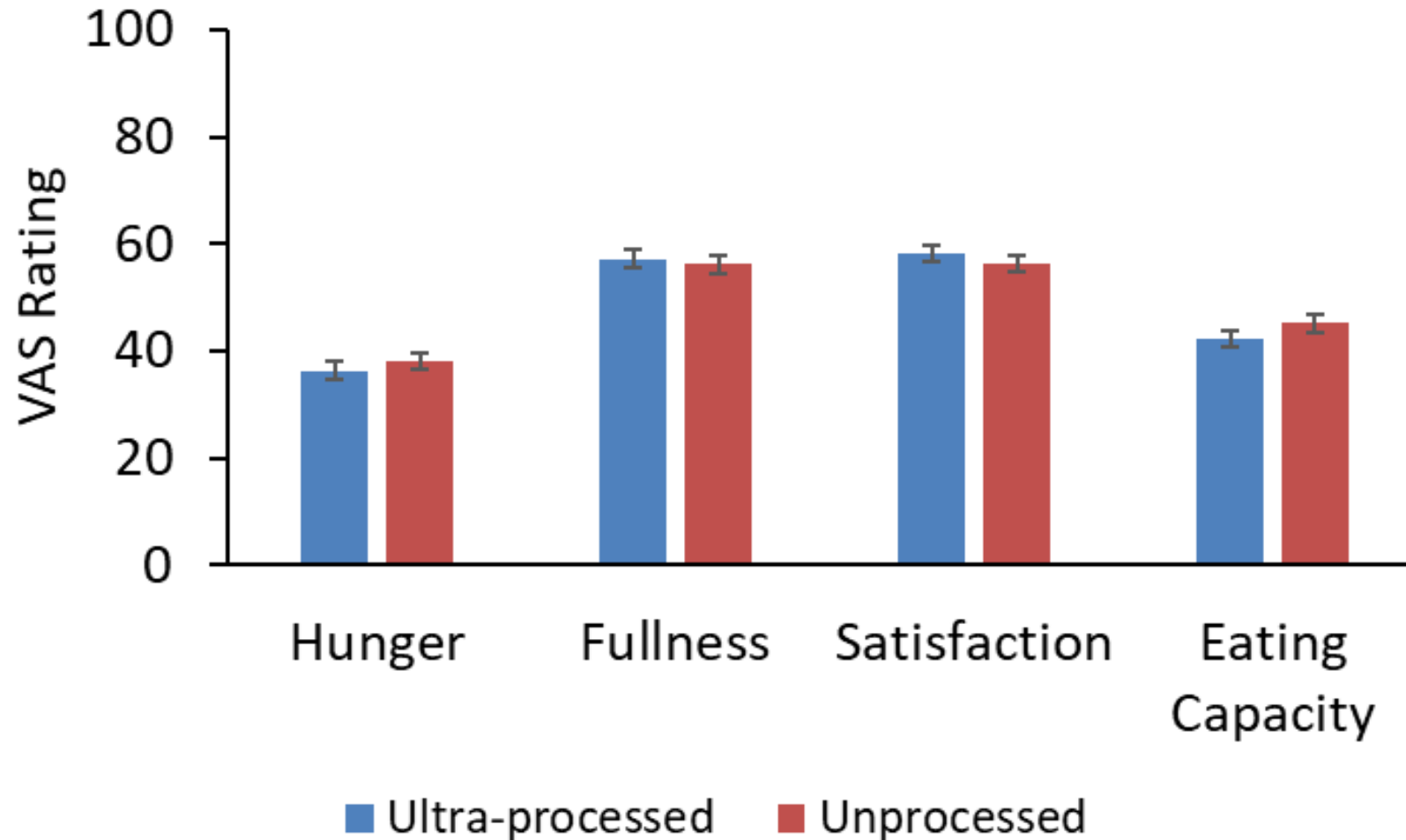
Ultra-processed vs Unprocessed Ad Libitum Diet Study



Diets matched for Presented Calories, Fat, Carbs, Sugar, Sodium, Fiber, Glycemic Load

↓ DLW ● Fasted Blood ↓ DXA ↓ MRI MRS ■ 24hr Chamber ■ OGTT

No Differences in Self-Reported Appetite Measures

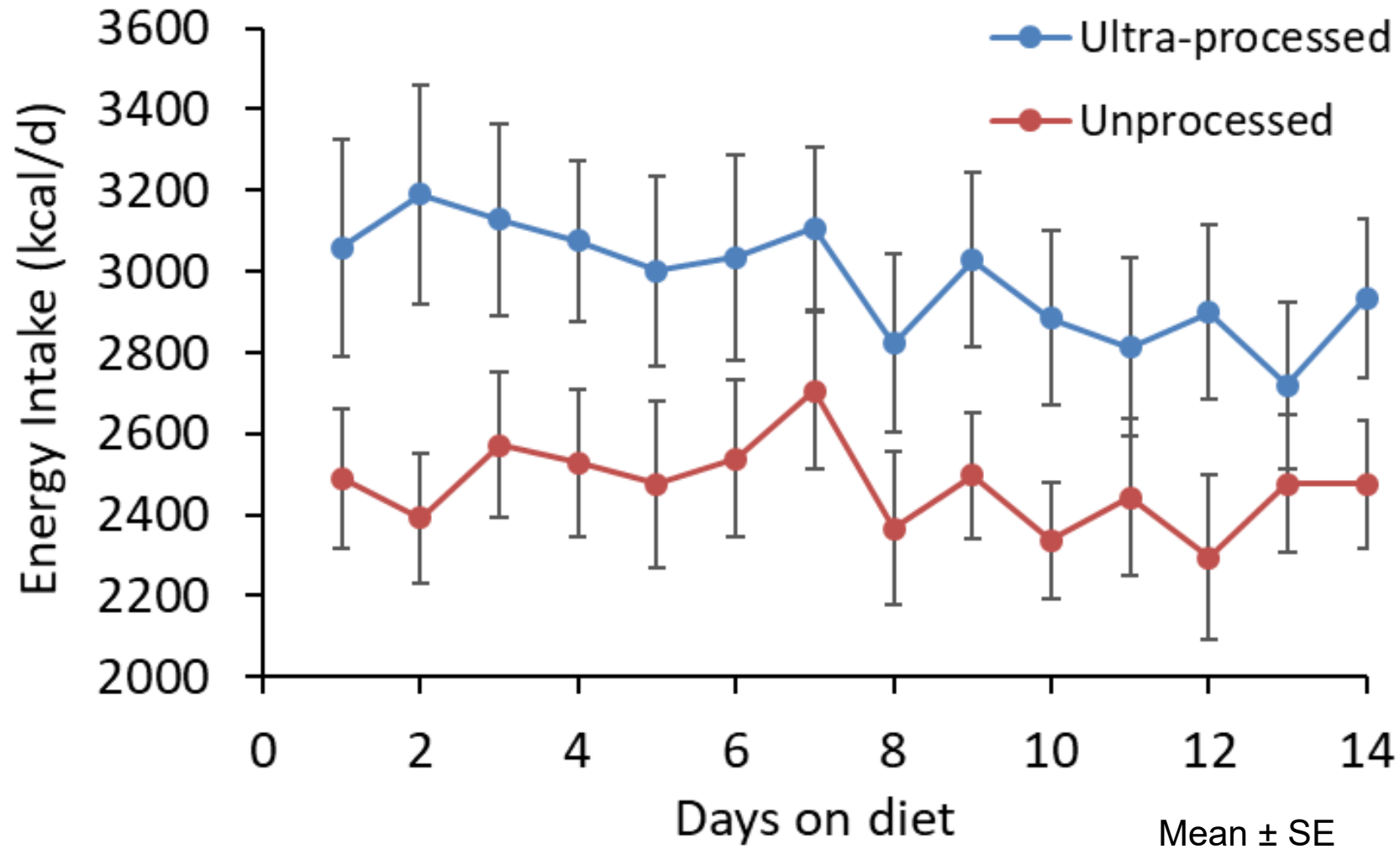


Mean ± SE

KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

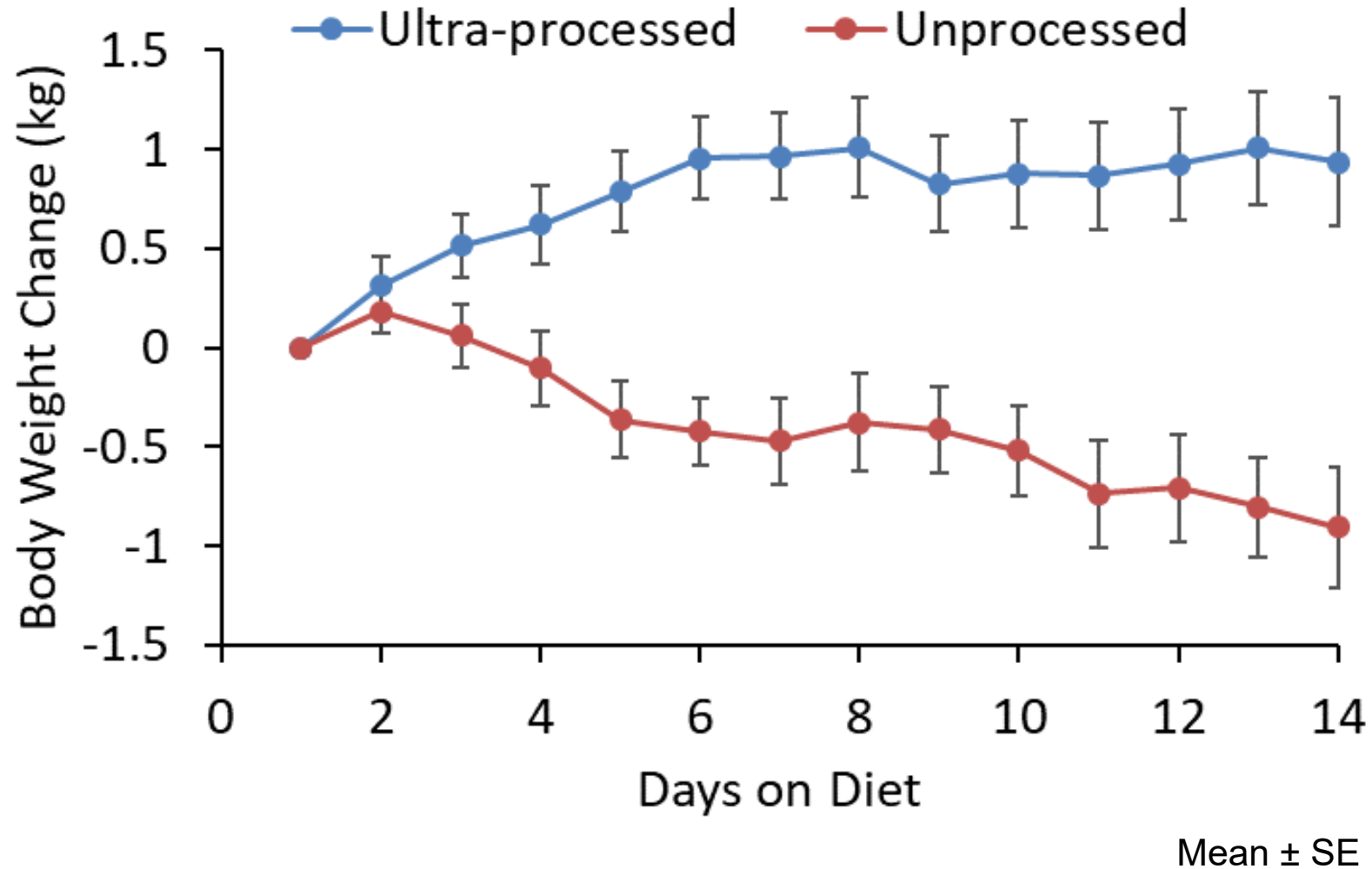
Ultra-processed Diet Caused Increased Intake

$\Delta EI = 508 \pm 106 \text{ kcal/d}; P=0.0001$



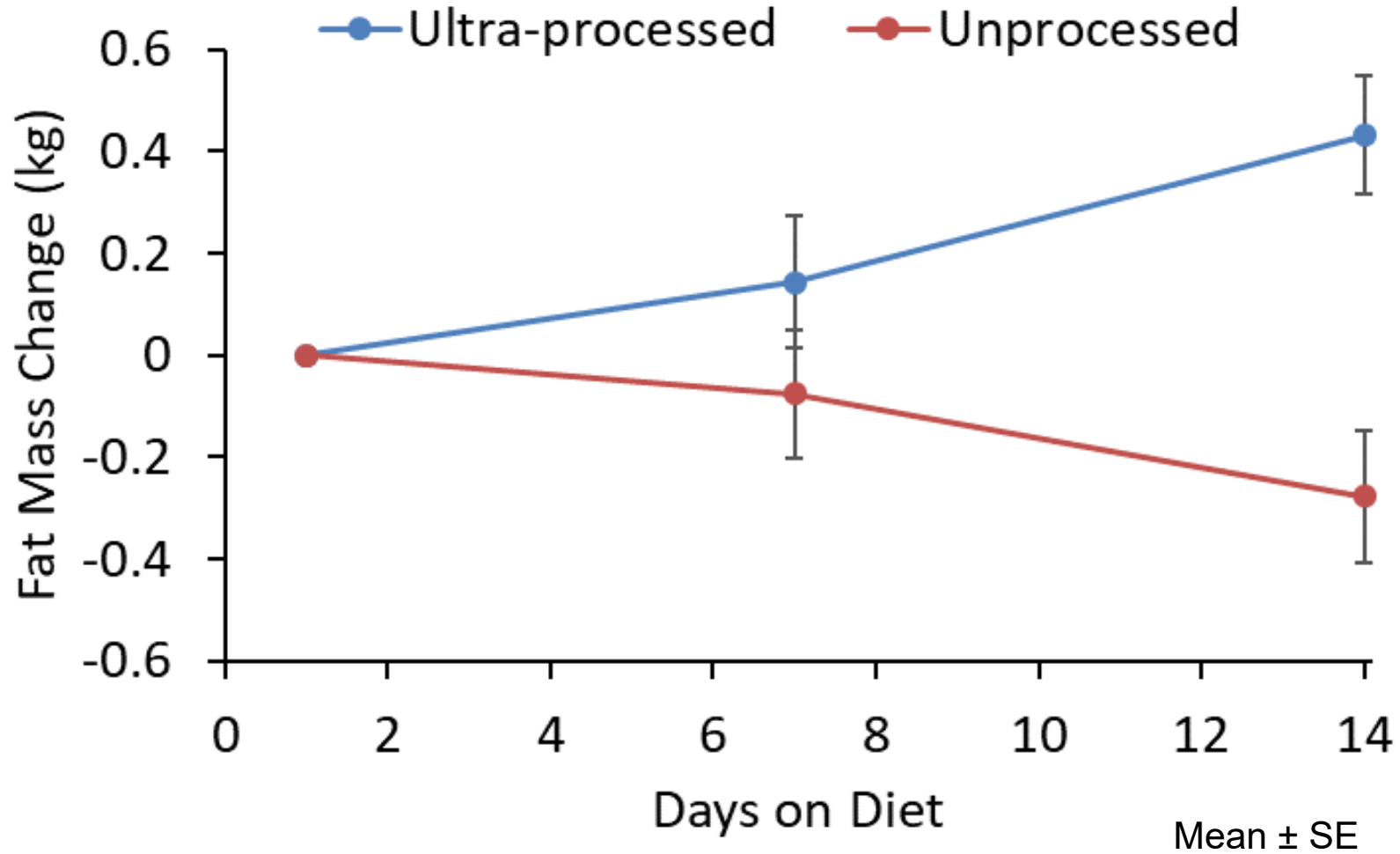
KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Ultra-processed Diet Caused Weight Gain



KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Ultra-processed Diet Caused Body Fat Gain



KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

What Mediated the Ultra-processed vs Unprocessed Effect?

Table 2 | Mediation analyses (N=20; 1635 Meals)

Ultraprocessed versus unprocessed diet study				
Mediator	Estimate	Standard error	P value	
Hyper-palatable Food	%HPF			
	NDE	69.8	13.6	<0.0001
	NIE	50.3	6.3	<0.0001
	% Mediated	41.9	6.5	<0.0001
Energy Density	ED			
	NDE	65.9	19.8	0.001
	NIE	54.1	15.3	0.0004
	% Mediated	45.1	13.6	0.001

New Study Ongoing: [ClinicalTrials.gov NCT05290064](https://ClinicalTrials.gov/ct2/show/study/NCT05290064)

Compare *ad libitum* energy intake between 4 test diets provided for one week each in a randomized, counterbalanced sequence. All test diets are matched for macronutrients, fiber, sugar, and sodium:

1. Minimally processed diet **low** in non-beverage energy density & **low** in hyper-palatable foods (MPF II)
2. Ultra-processed diet **high** in non-beverage energy density & **high** in hyper-palatable foods (UPF hh)
3. Ultra-processed diet **high** in non-beverage energy density & **low** in hyper-palatable foods (UPF hl)
4. Ultra-processed diet **low** in non-beverage energy density & **low** in hyper-palatable foods (UPF ll)

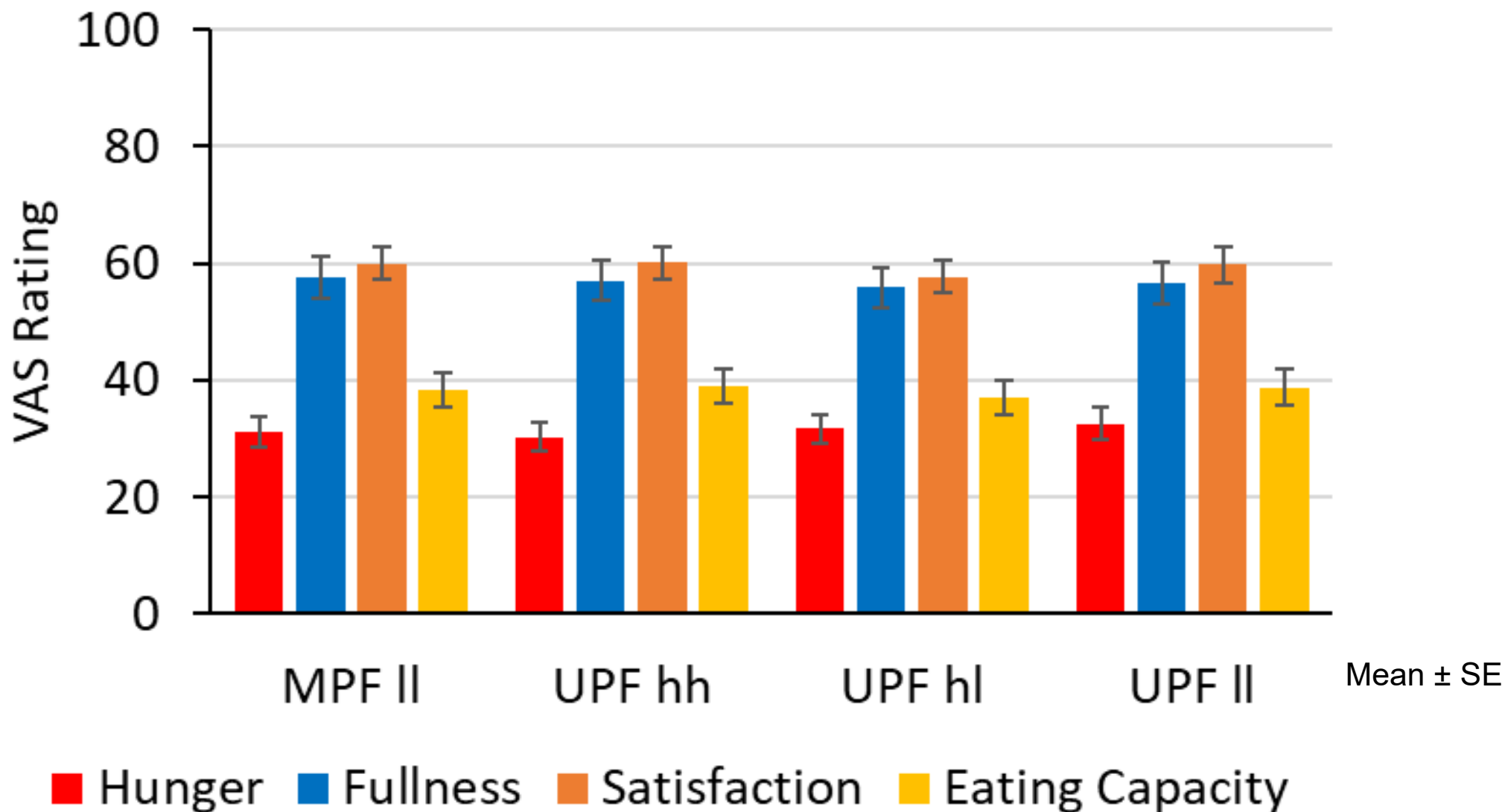
Average Composition of the 7-day Menus

	MPF II	UPF hh	UPF hl	UPF II
Three Daily Meals				
Ultra-Processed Foods (% of energy)	0	88	80	81
Hyperpalatable foods (% of energy)	53	74	56	55
Non-beverage Energy Density (kcal/g)	0.99	1.95	1.90	1.01
Energy Density (kcal/g)	0.98	0.97	1.15	0.99
Carbohydrate (% of energy)	46	47	46	45
Fat (% of energy)	35	35	35	35
Protein (% of energy)	19	18	19	20
Sodium (mg/1000 kcal)	2247	1945	1891	2373
Fiber (g/1000 kcal)	21	21	21	18
Sugars (g/1000 kcal)	34	32	34	32

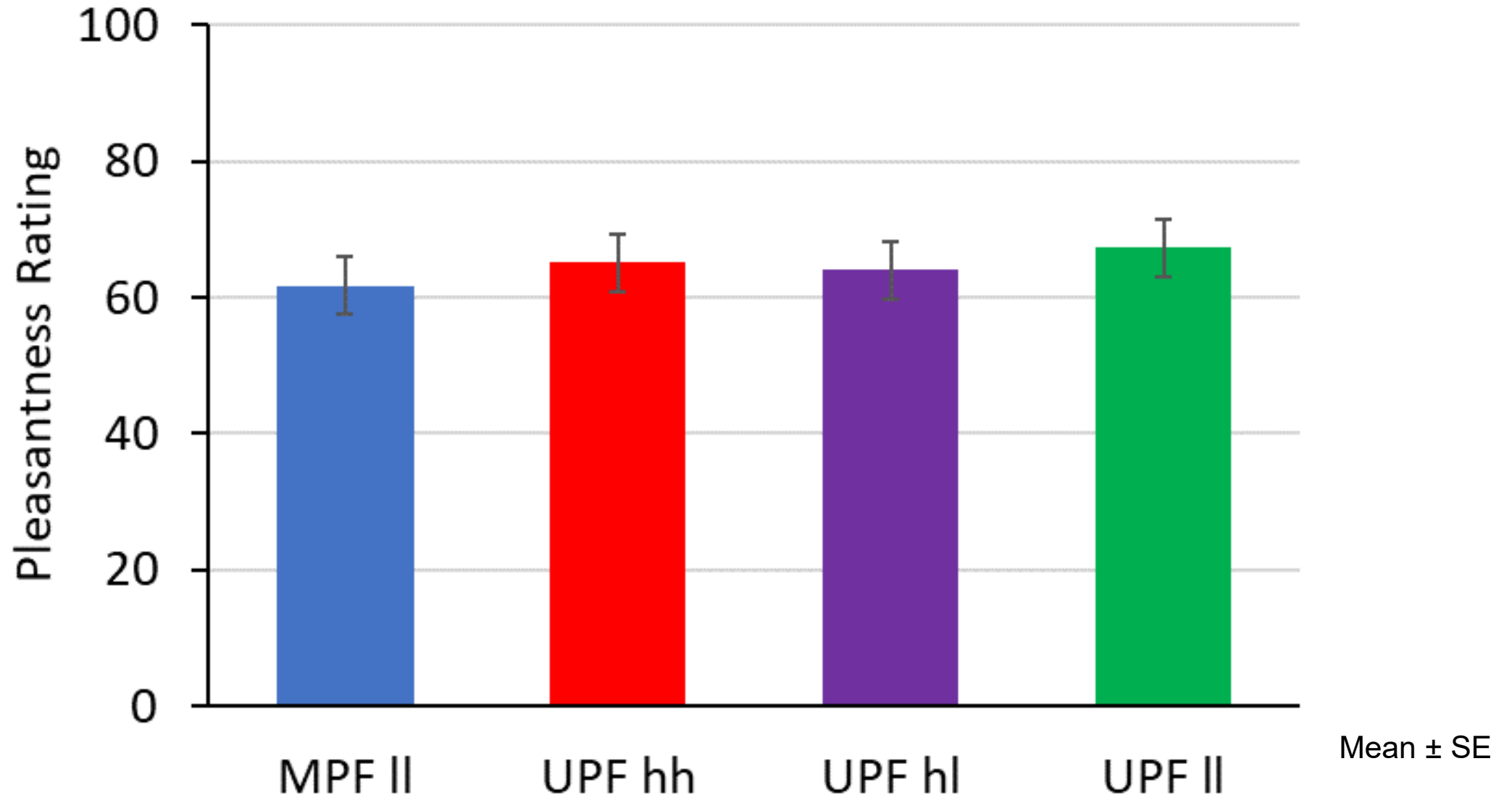
Baseline Participant Characteristics

	Mean \pm SD (min, max)
Males/ Females	11/7
Age (y)	33.6 \pm 10.4 (19, 52)
Height (cm)	172.8 \pm 8.0 (158, 185)
Body Weight (kg)	86.9 \pm 18.1 (61.7, 119.1)
BMI (kg/m ²)	29.0 \pm 5.4 (20.8, 41.8)
Fat Mass (kg)	29.2 \pm 15.6 (6.8, 66.1)
% Body Fat	32.4 \pm 12.8 (10.2, 55.5)

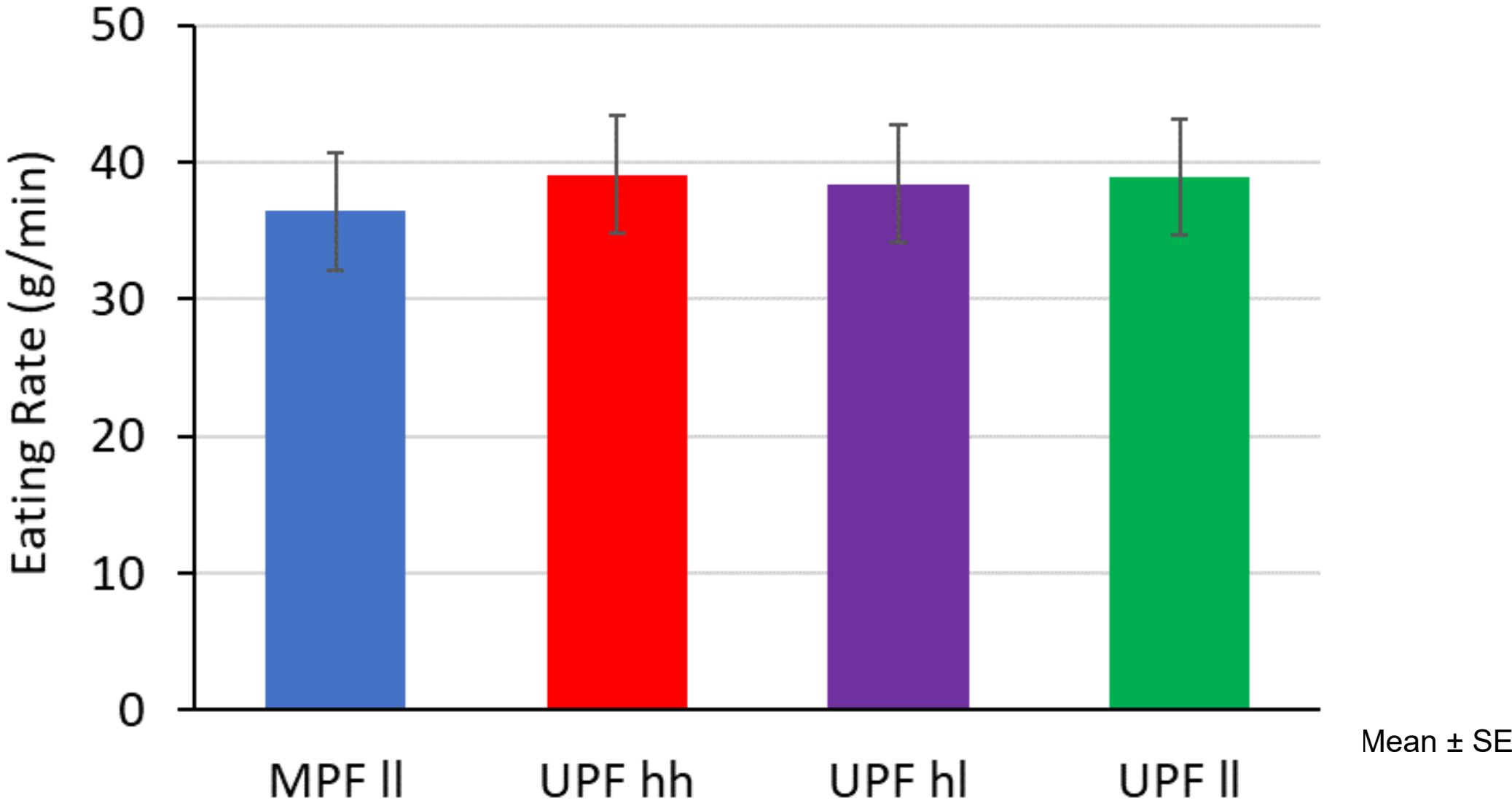
No Significant Differences in Appetite Ratings



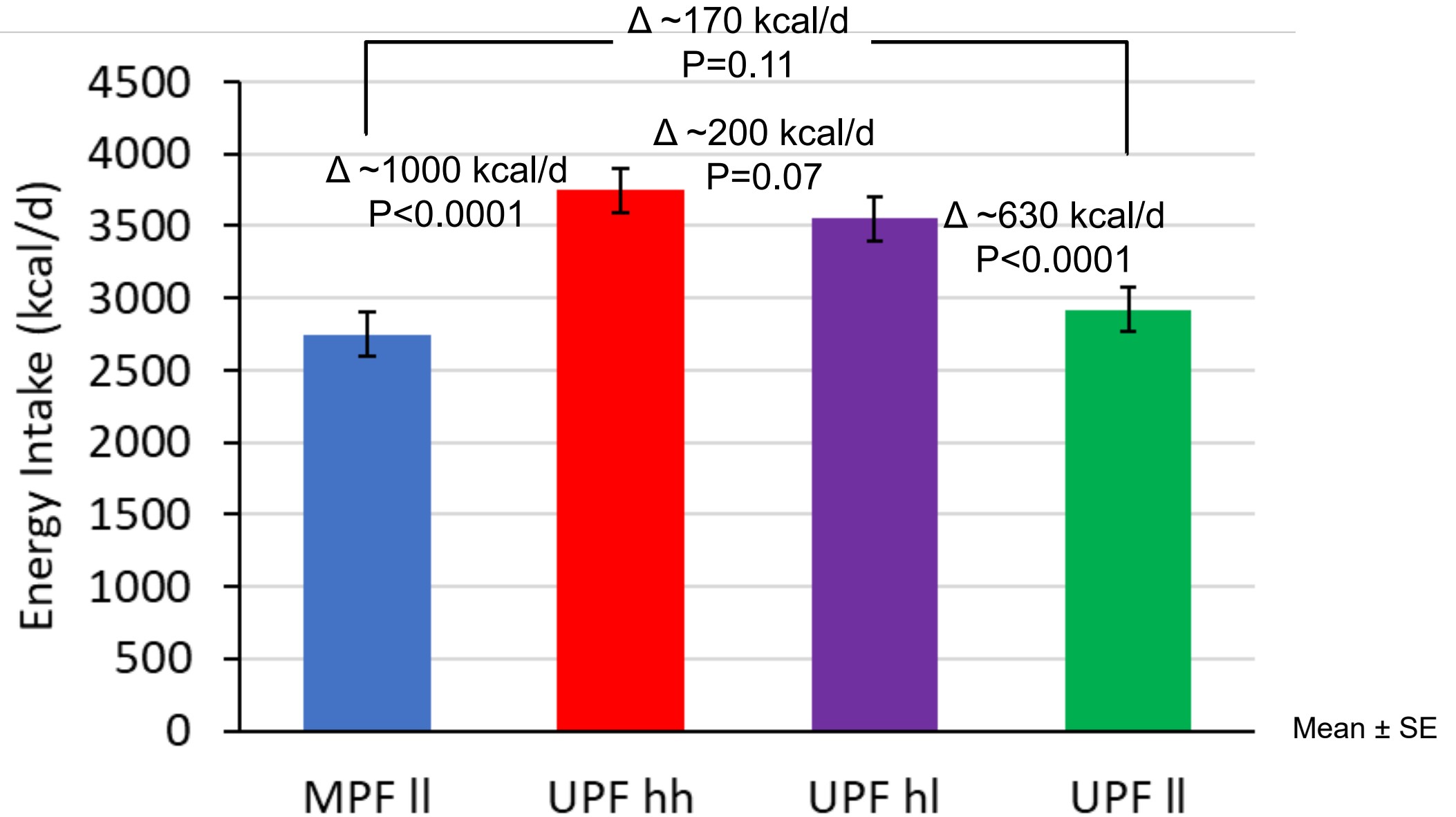
No Significant Differences in Meal Pleasantness Ratings



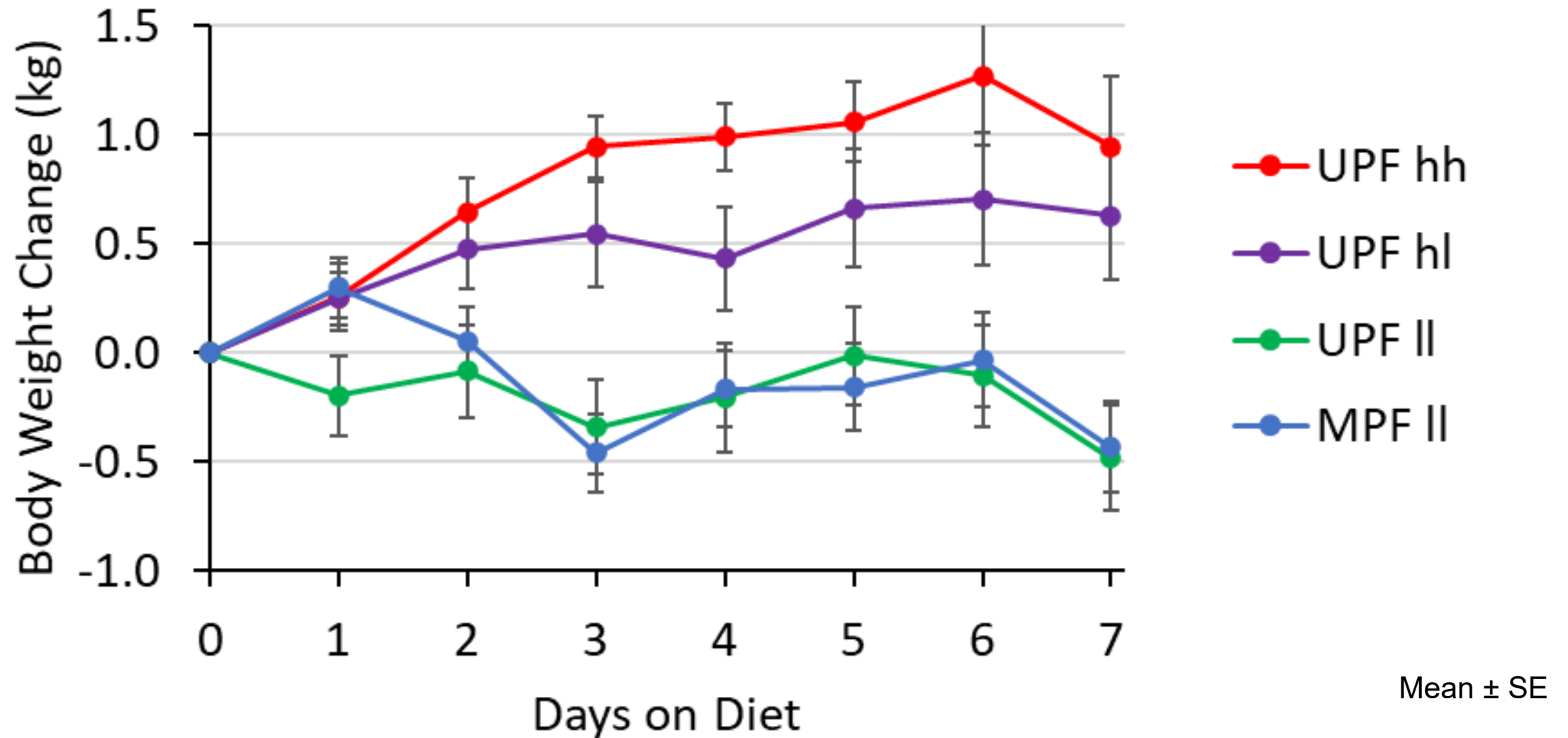
No Significant Differences in Meal Eating Rate



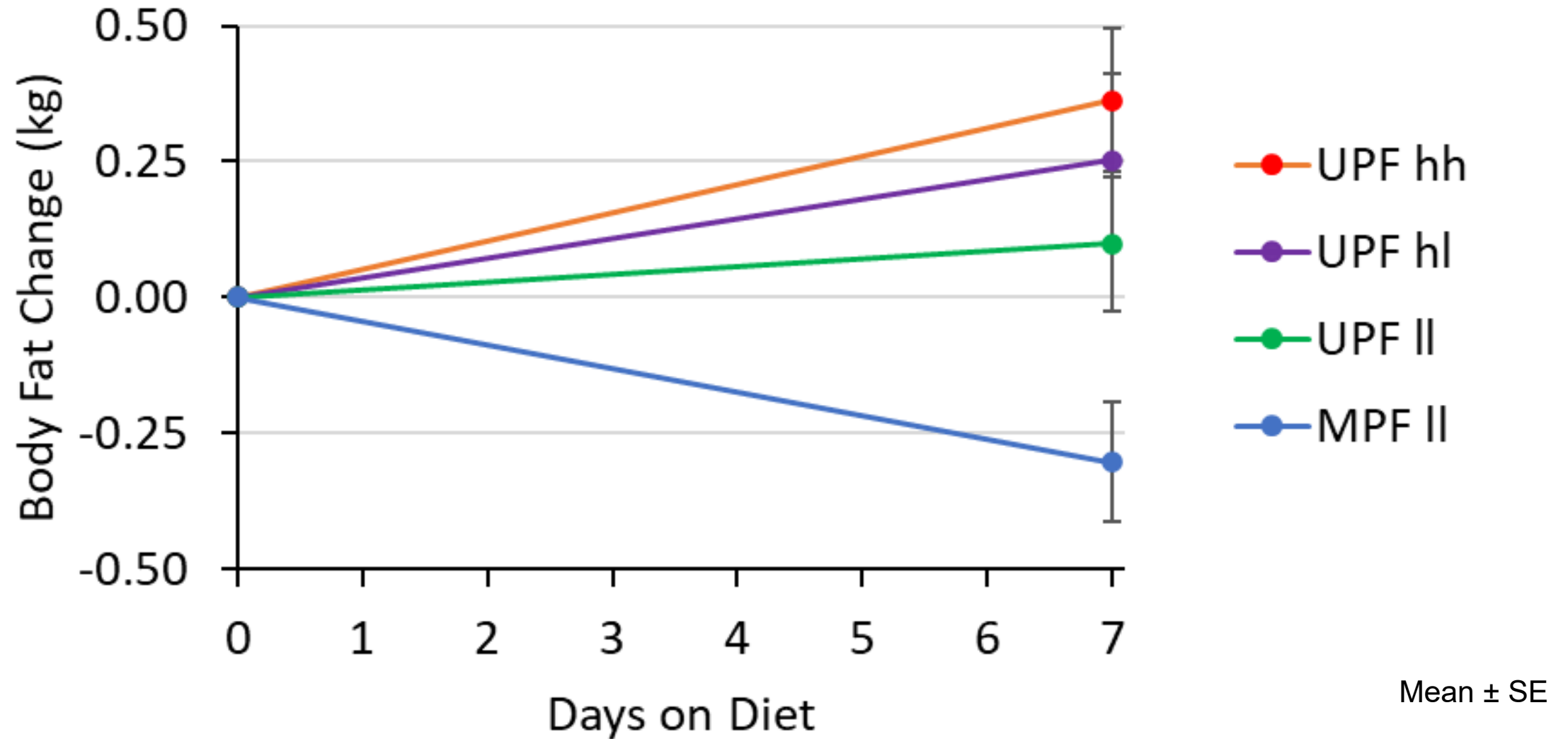
Primary Outcome: Ad Libitum Energy Intake Differences



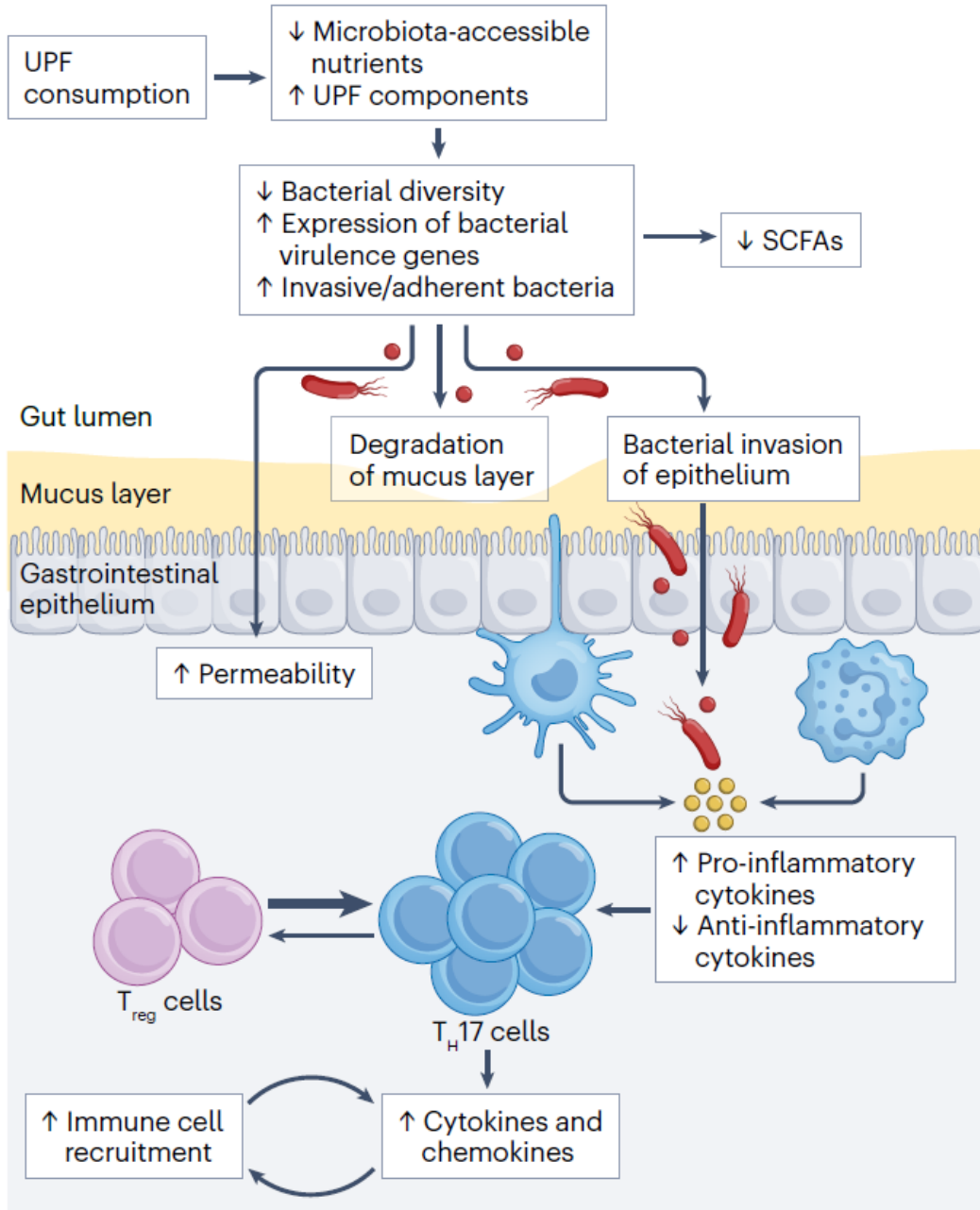
Weight Changes Correspond to Energy Intake Differences



Only the Minimally Processed Diet Led to Body Fat Loss



Ultra-processed Food Mechanisms: Beyond Obesity



Ultra-processed foods: increasing the risk of inflammation and immune dysregulation?

Katherine A. Maki, Michael N. Sack & Kevin D. Hall

Ultra-processed foods (UPFs) are industrially formulated products that contain synthetic ingredients but minimal whole-food components. Diets high in UPFs are associated with increased risk of immune dysregulation-linked diseases such as inflammatory bowel disease and potentially autoimmune disease. Several putative mechanisms have been proposed to explain this association, and these need urgent research attention.

KA Maki et al. *Nat Rev Immunol* 24:453-4 (2024).

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Volunteer Study Participants

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