



## **Gary Frost**

Imperial College London,  
England

# Maintenance of weight loss and diabetes remission: barriers and solutions

Gary Frost – Section for Nutrition Research, Imperial College London

---

# Disclosure

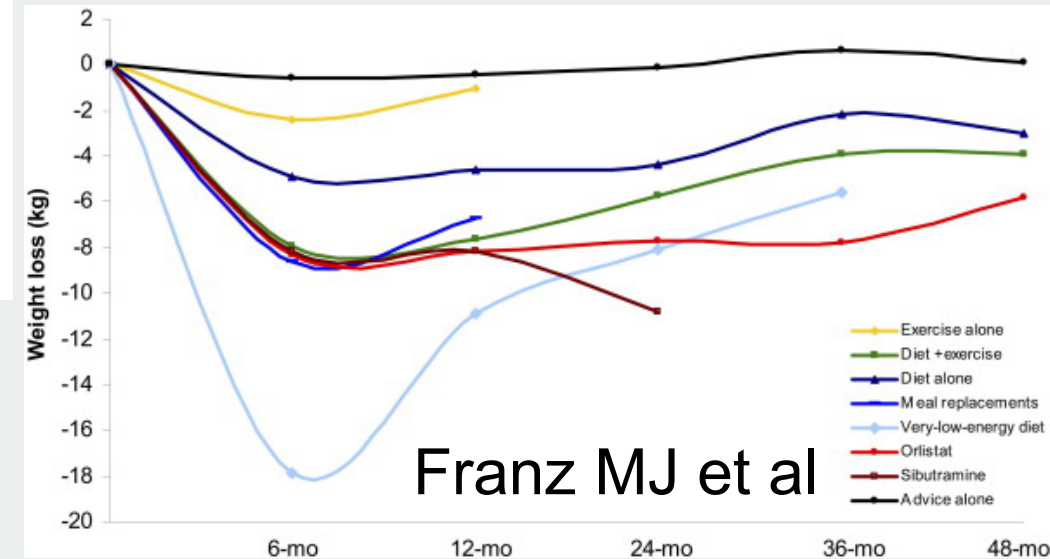
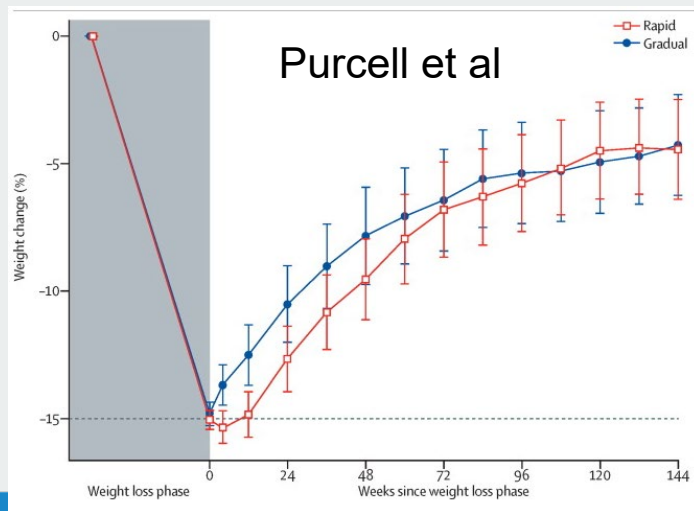
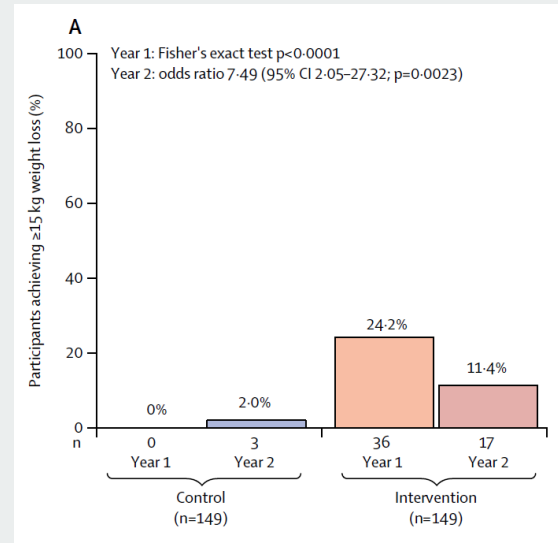
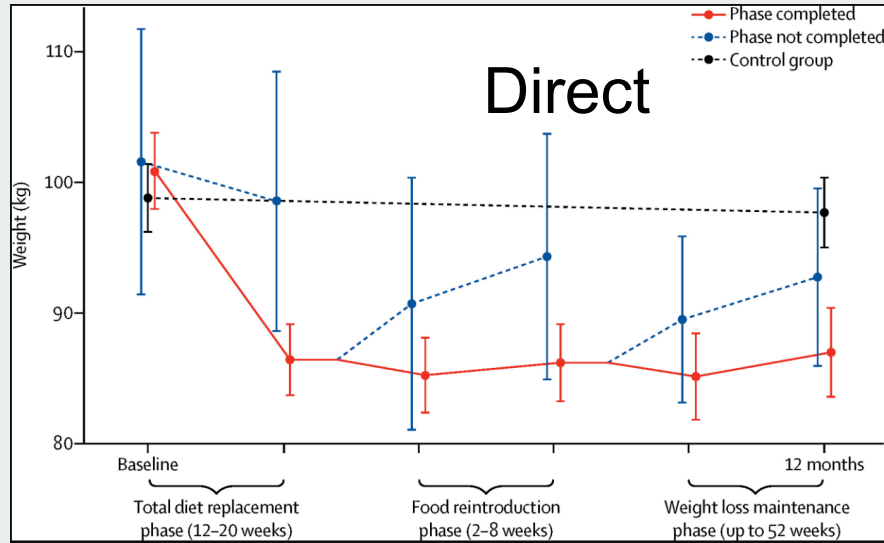
- Received funding from Cambridge Weight Plan Limited
  - Director of a new spin out company Satisfied which markets inulin propionate ester
  - Received educational funding from Nestle
  - Currently funded by BBSRC, MRC and NIHR
-

# What is weight loss maintenance?

- Wing and Hill: individuals who have intentionally lost at least 10% of their body weight and kept it off at least one year
  - Real life McGuire et al 20.6% met the criteria for successful weight loss maintenance: they had intentionally lost at least 10% of their body weight and maintained it for at least 1 year
-

## Is it a rail crash?

- Stunkard and McLaren-Hume's 1959 study of 100 obese individuals, which indicated that, 2 y after treatment, only 2% maintained a weight loss of 9.1 kg (20 lb) or more
  - Kassirer and Angell 1998 opinion "many people cannot lose much weight no matter how hard they try, and promptly regain whatever they do lose, the vast amounts of money spent on diet clubs, special foods, and over-the-counter remedies, estimated to be on the order of \$30 billion to \$50 billion yearly, is wasted"
-



This is not the same as weight gain in population 0.5kg /year

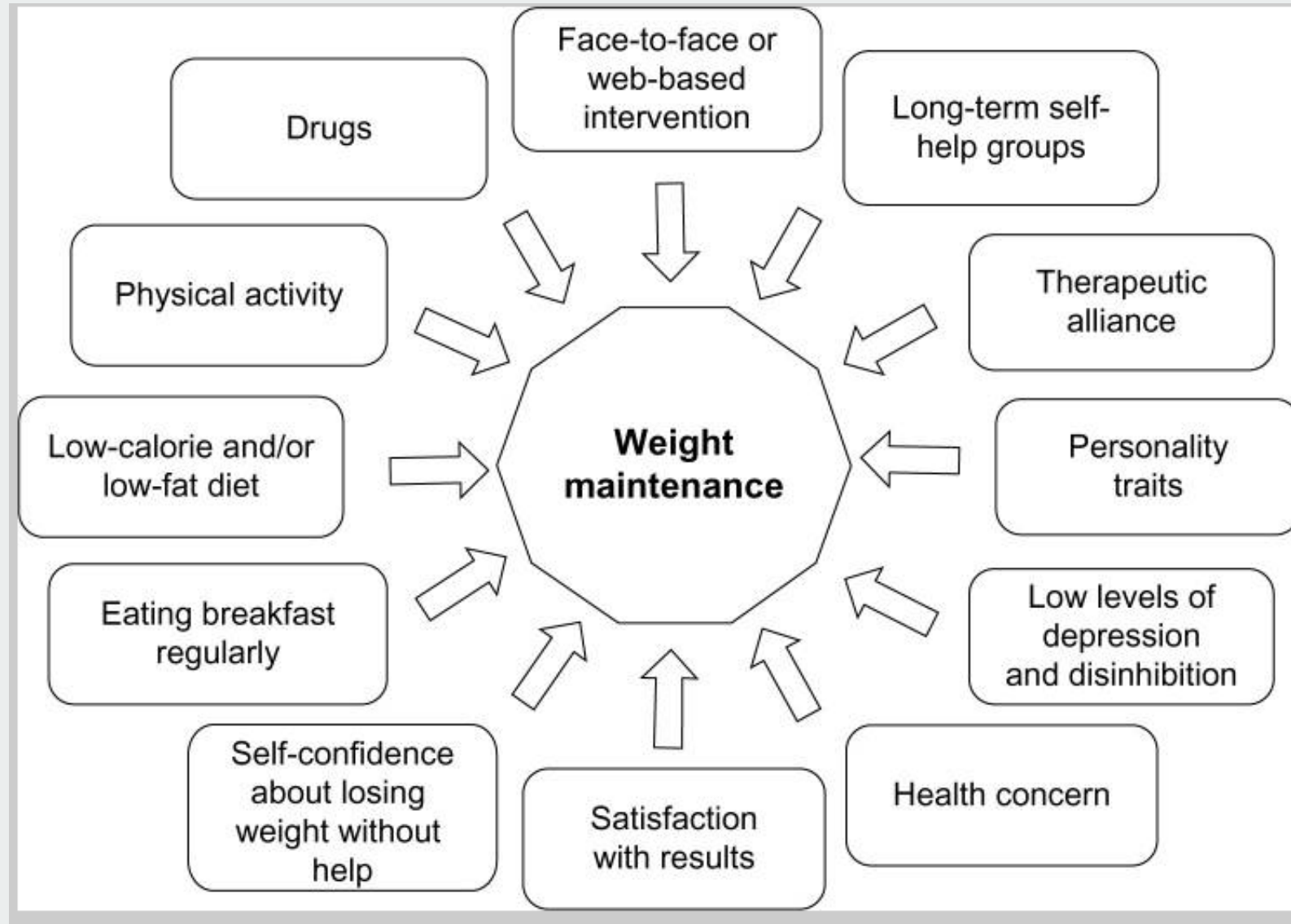
**Why???**

---

## National Weight Control Registry – what relates to success?

- Maintenance of weight loss of 2 years
- Emotional regulation
  - Low levels of dietary disinhibition
  - Low levels of depression
- Dietary consistency
- Weight gain management
- Contact with a counsellor



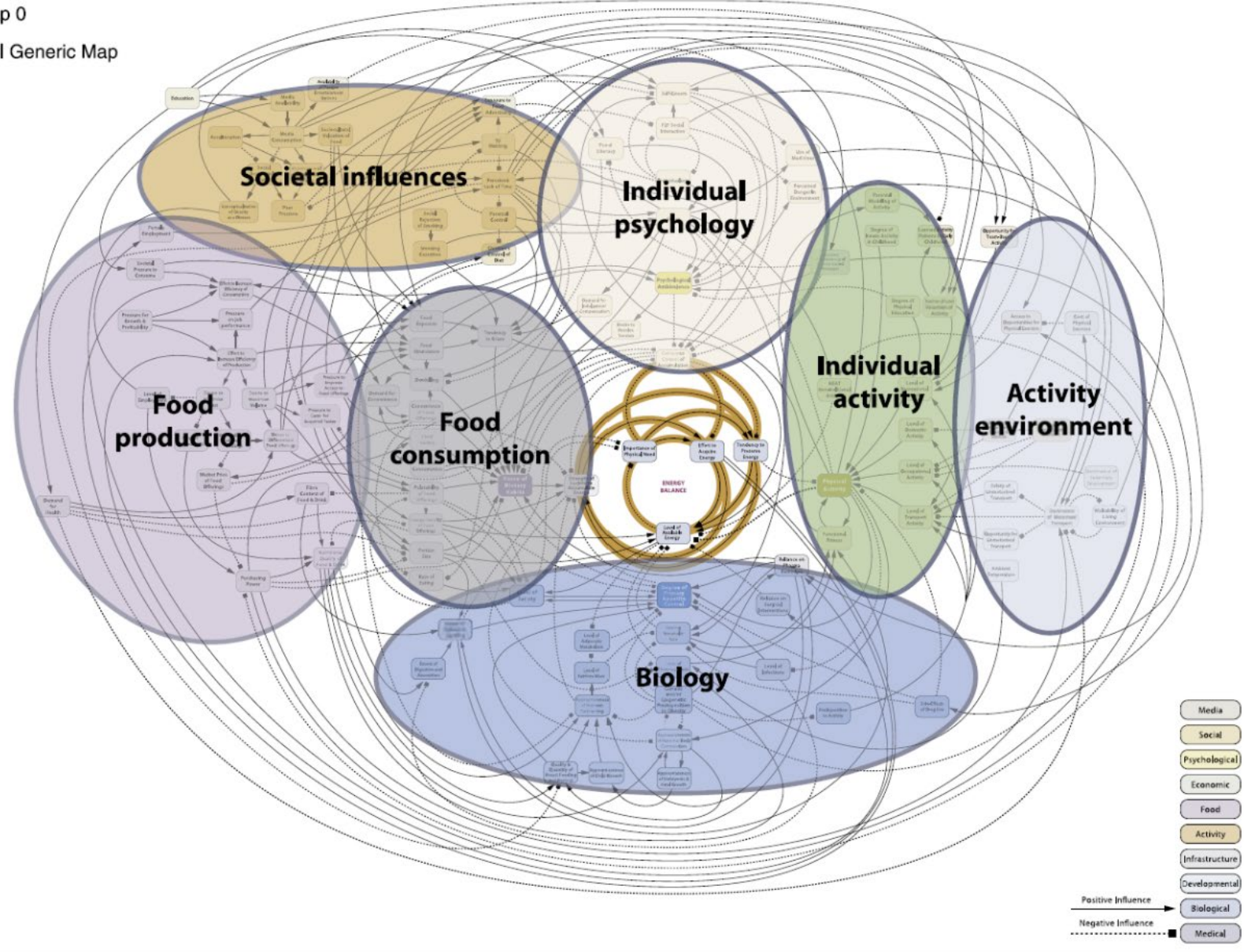


Imperial College  
London

# Food environment

Energy dense highly  
palatable food.

Map 0  
Full Generic Map



## Why does it go wrong

- For every kg lost energy expenditure falls by 20-30 kcal but appetite drive increases by 100kcal
  - Unravelling biological, psychosocial, educational, and environmental determinants of such individual variability will be an active area of obesity research for the foreseeable future
-

**Is it all wrapped up  
with Survival?**

---

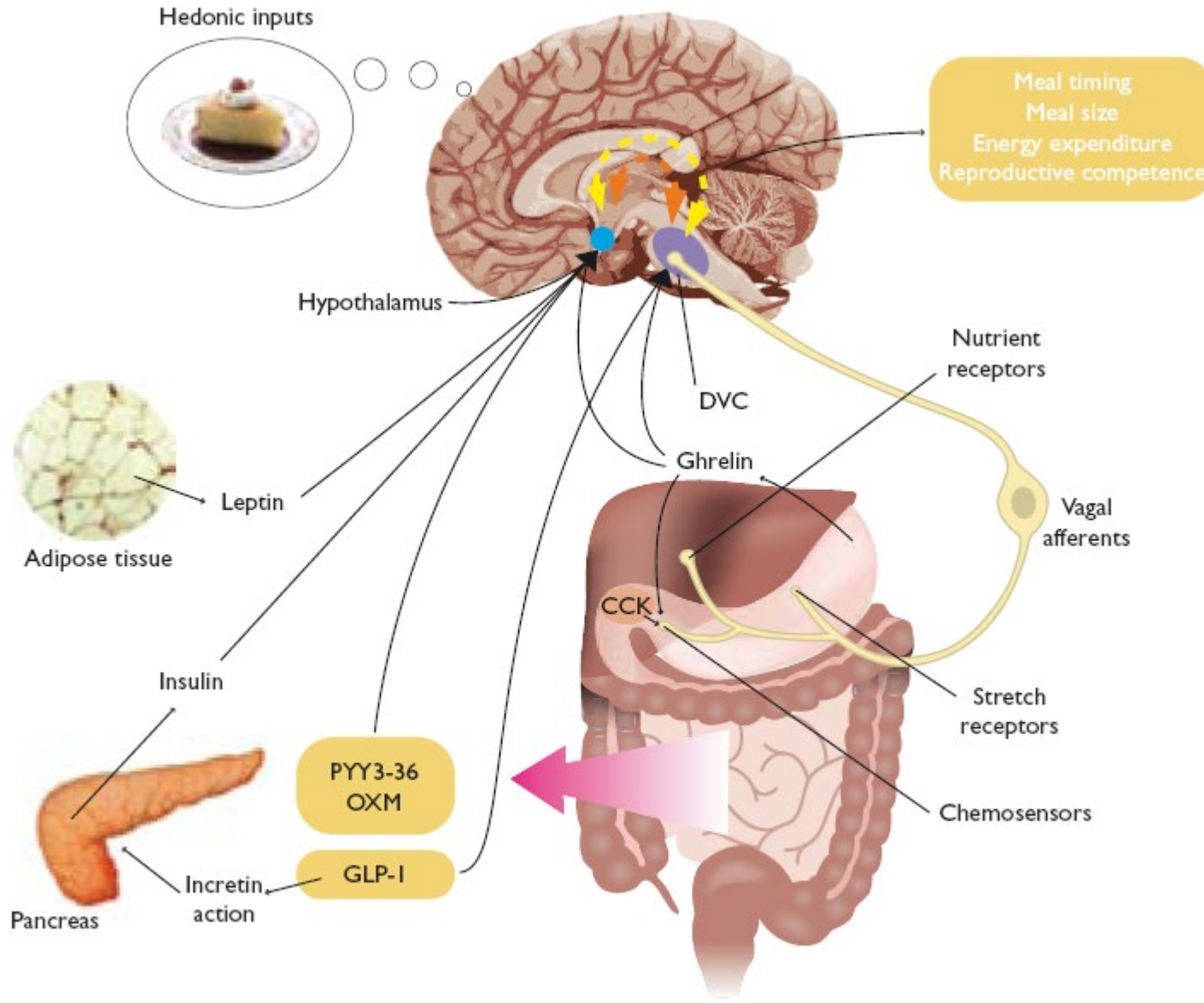
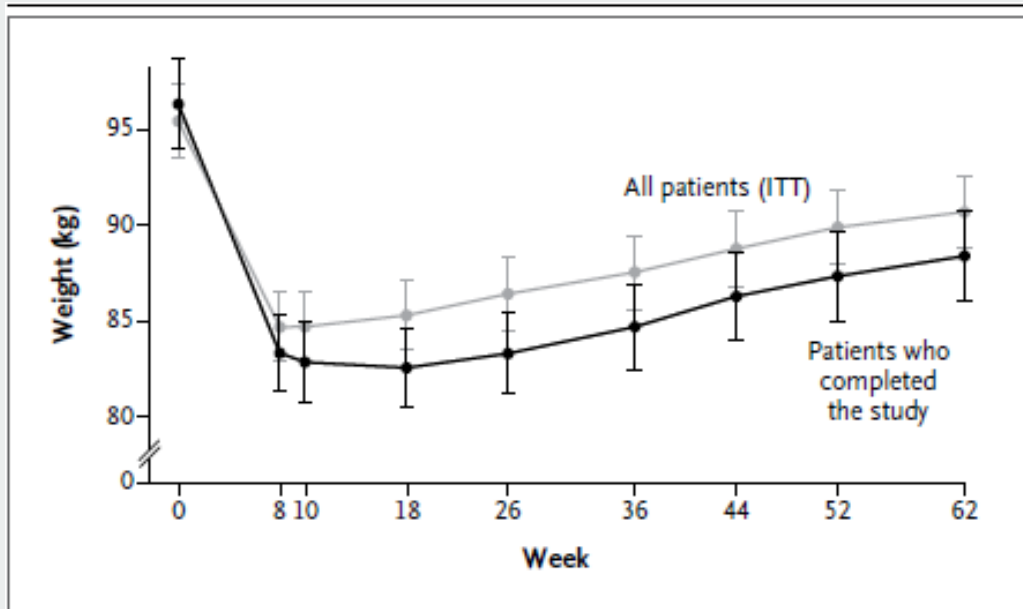
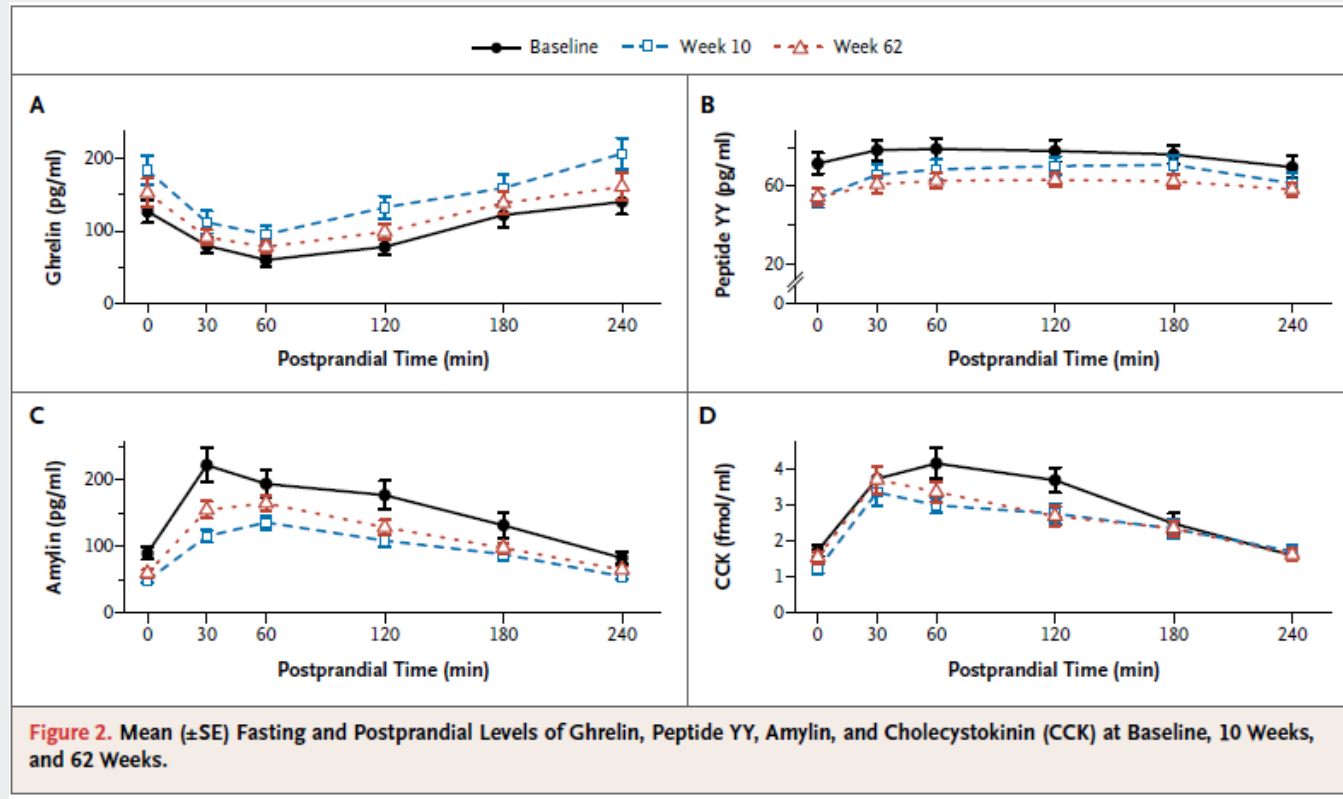


Figure 4: Neuro-physiological regulation of food intake (adapted from 17)

# Systems compensate

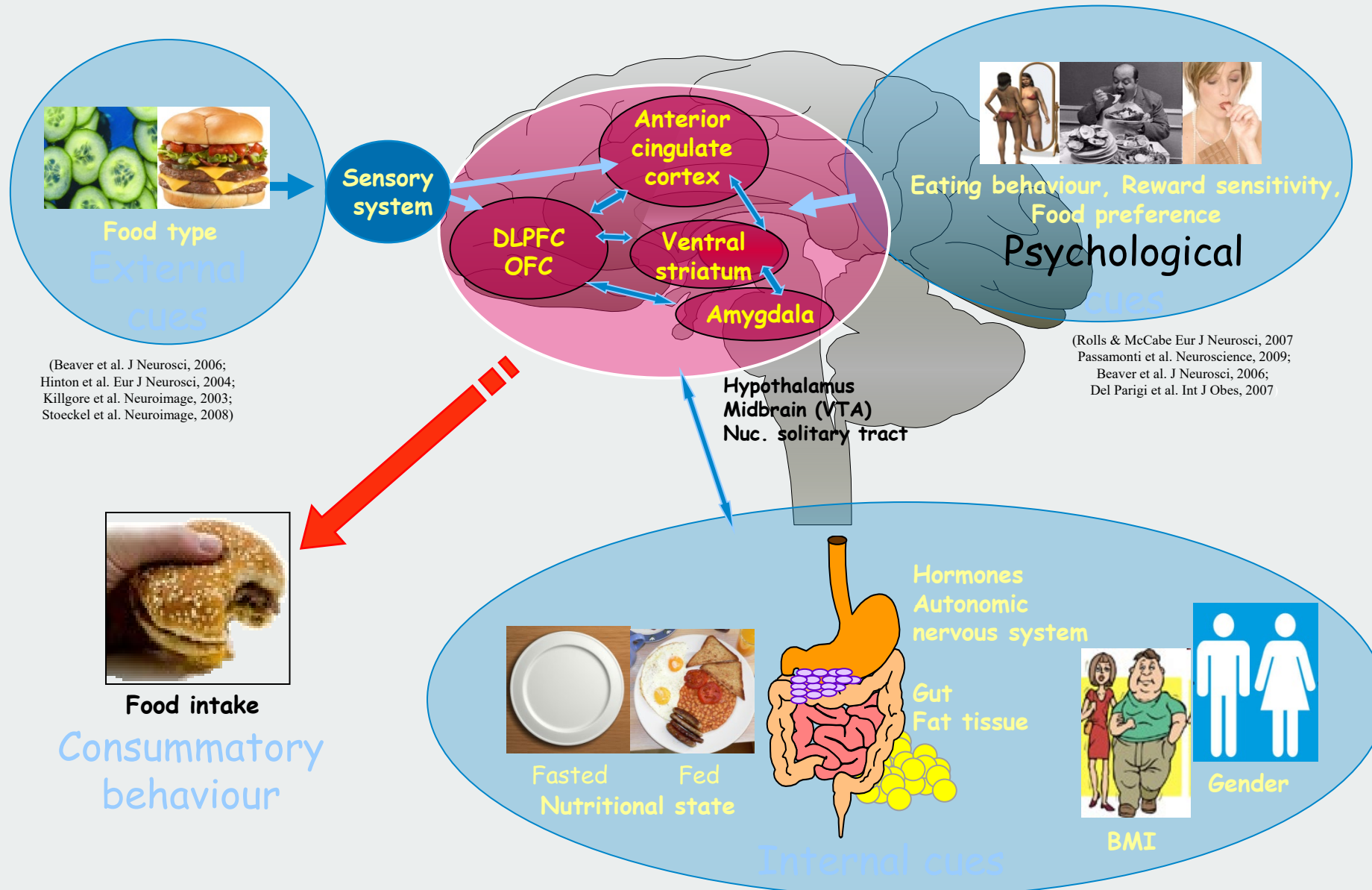


**Figure 1.** Mean ( $\pm$ SE) Changes in Weight from Baseline to Week 62. The weight-loss program was started at week 0 and completed at week 10. ITT denotes intention to treat.



**Figure 2.** Mean ( $\pm$ SE) Fasting and Postprandial Levels of Ghrelin, Peptide YY, Amylin, and Cholecystokinin (CCK) at Baseline, 10 Weeks, and 62 Weeks.

# Brain Food Reward Systems with thanks to Dr Goldstone



(Beaver et al. J Neurosci, 2006;  
Hinton et al. Eur J Neurosci, 2004;  
Killgore et al. Neuroimage, 2003;  
Stoeckel et al. Neuroimage, 2008)

(Rolls & McCabe Eur J Neurosci, 2007  
Passamonti et al. Neuroscience, 2009;  
Beaver et al. J Neurosci, 2006;  
Del Parigi et al. Int J Obes, 2007)

# Macronutrients

Lipids

Carbohydrates

Proteins

LCFAs

Monosaccharides, SCFAs

Amino acids, other proteolytic products

## 7TM chemosensors

Amino acids	GPRC6A
	CaSR
	Taste Rs
Peptides	GPR93
SCFAs	FFAR2
	FFAR3
LCFAs	FFAR1
	FFAR4
OEA	GPR119

## GI tract hormones

- PYY
- GLP-1
- GLP-2
- Oxyntomodulin
- Glicentin
- CCK
- Ghrelin
- Motilin
- GIP
- Gastrin

Paracrine effects

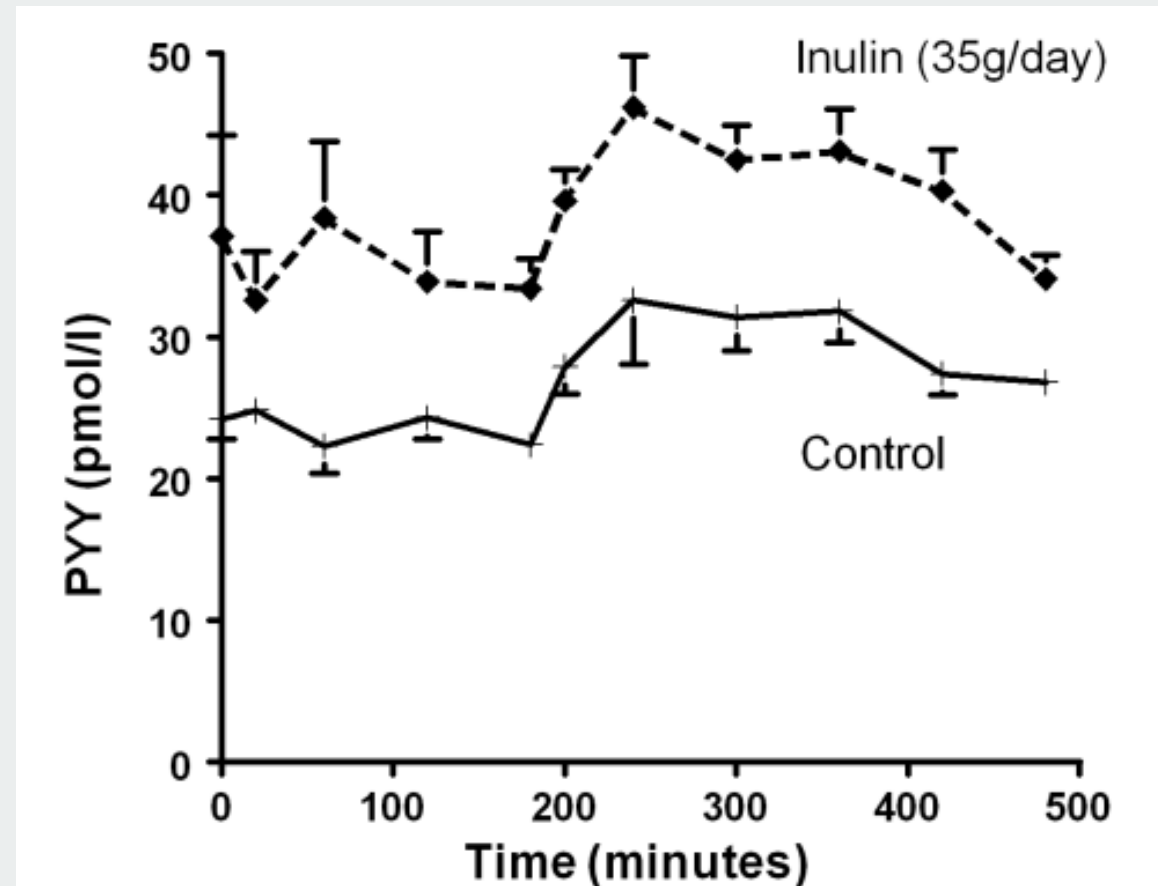
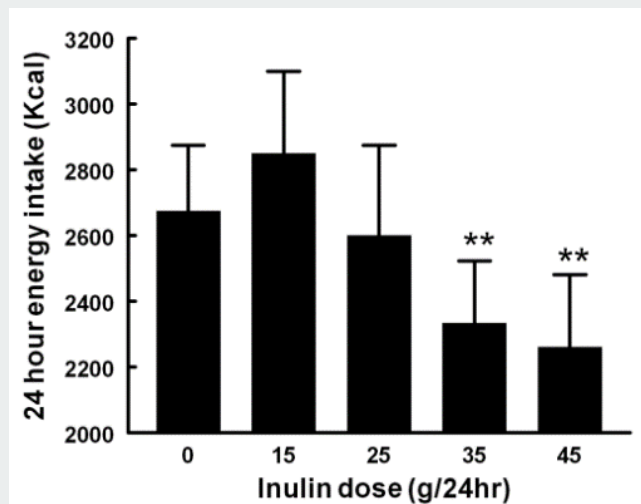
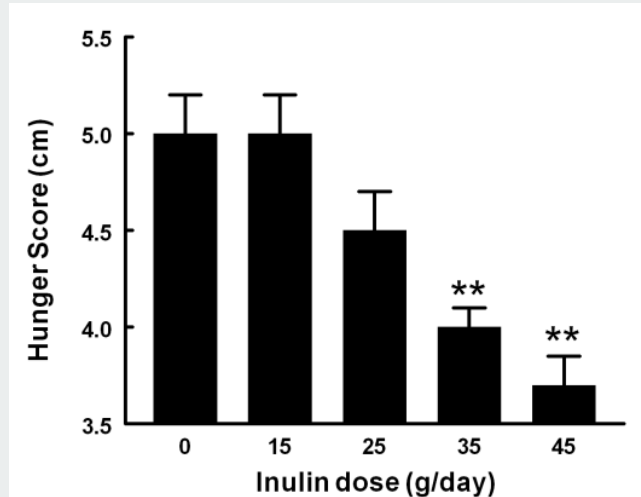
Modulation of neuronal function

Endocrine effects



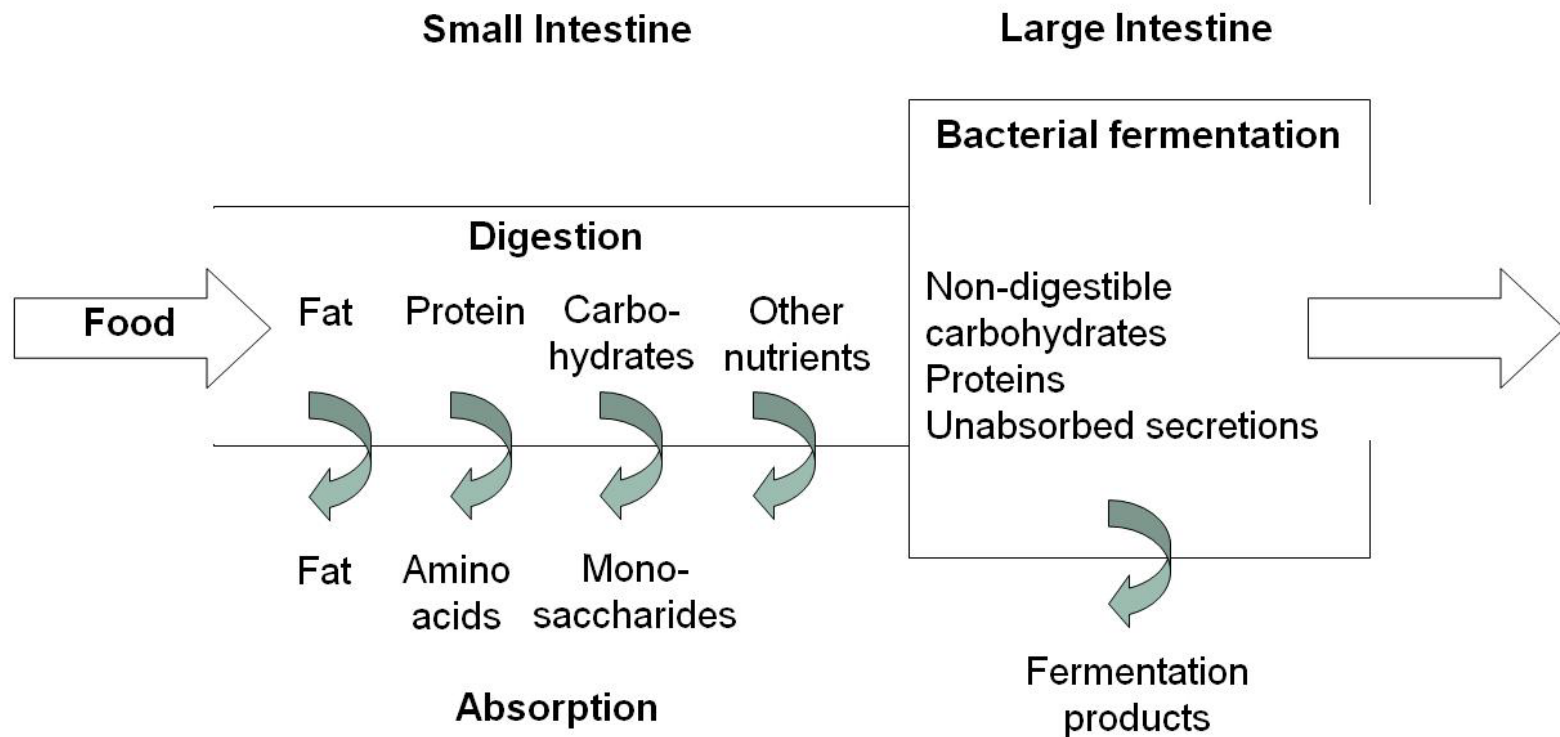


# Inulin and Appetite



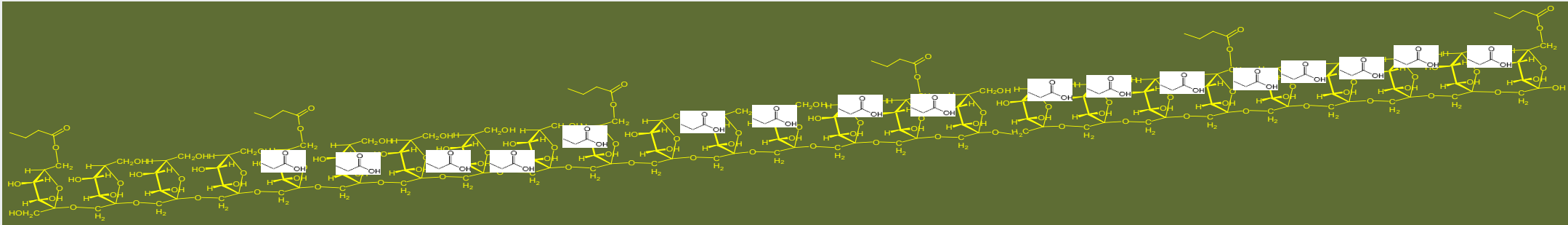
# Where do short chain fatty acids come from?

Transit of nutrients through human gastrointestinal tract:

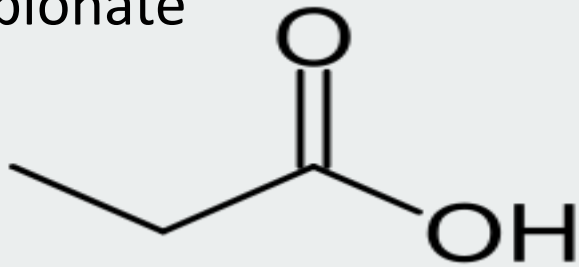


# Functional fibre: Propionate inulin ester

Inulin

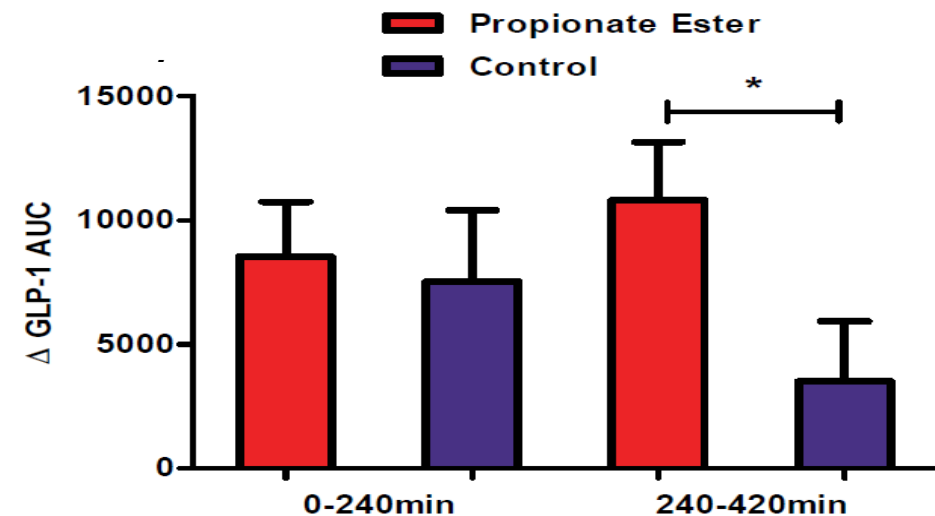
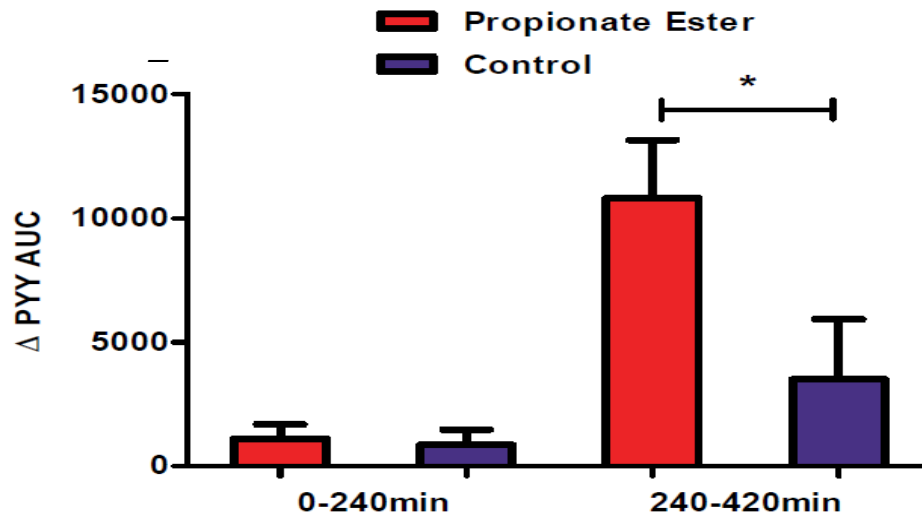
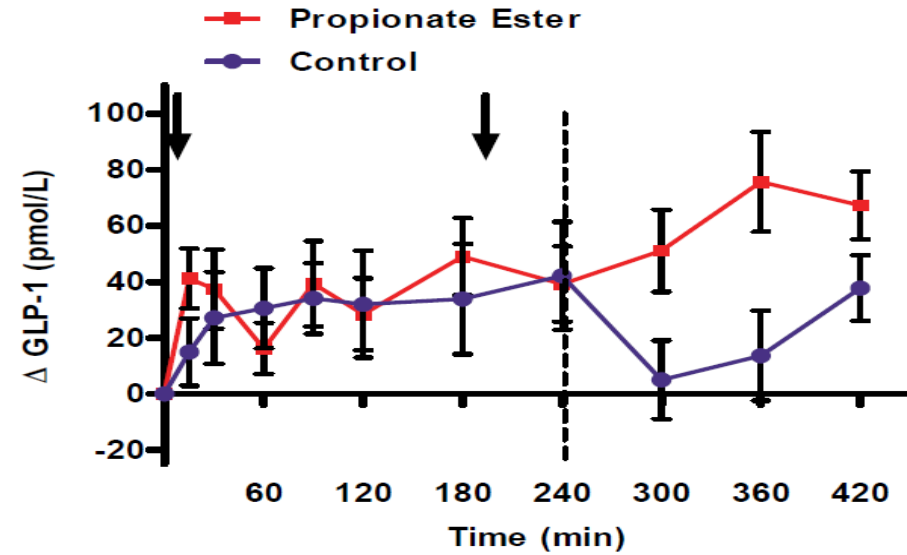
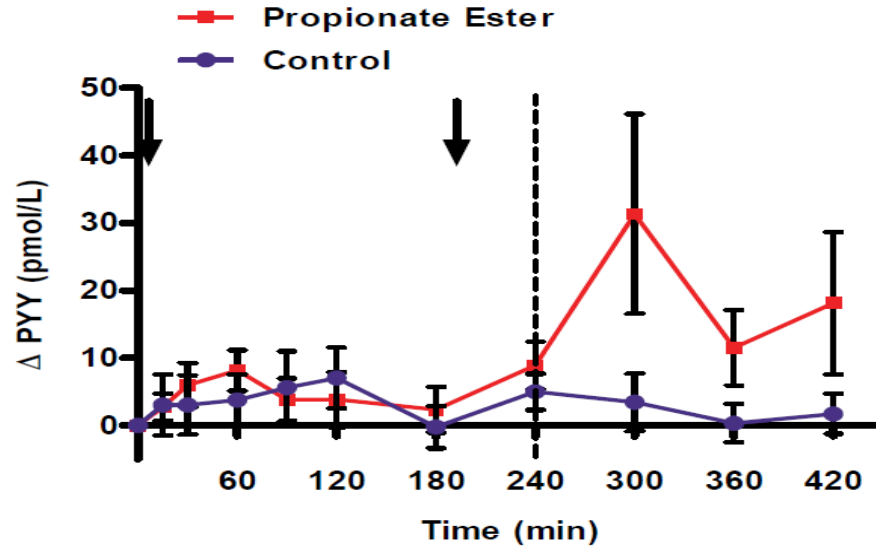


Propionate

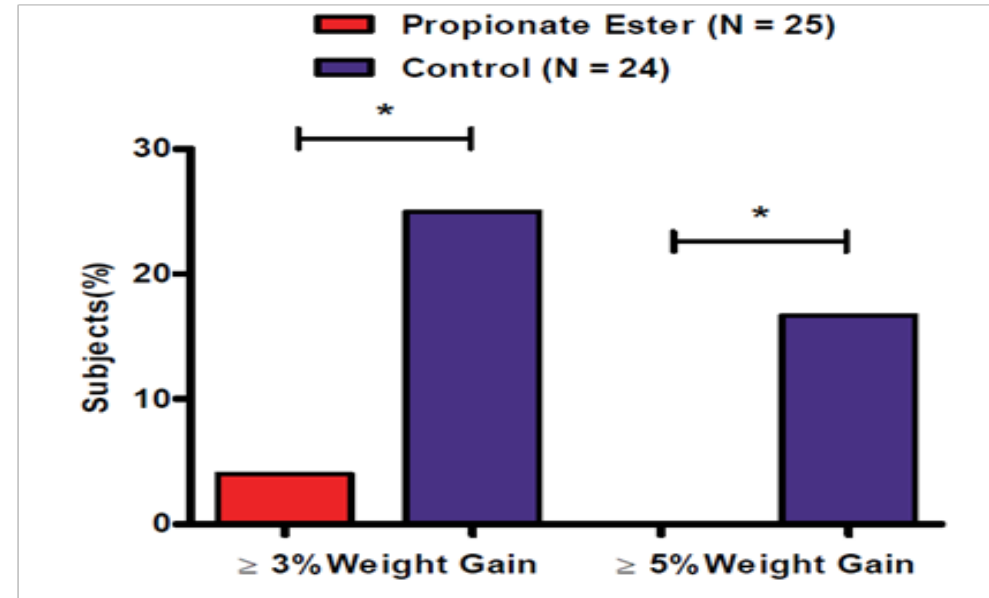
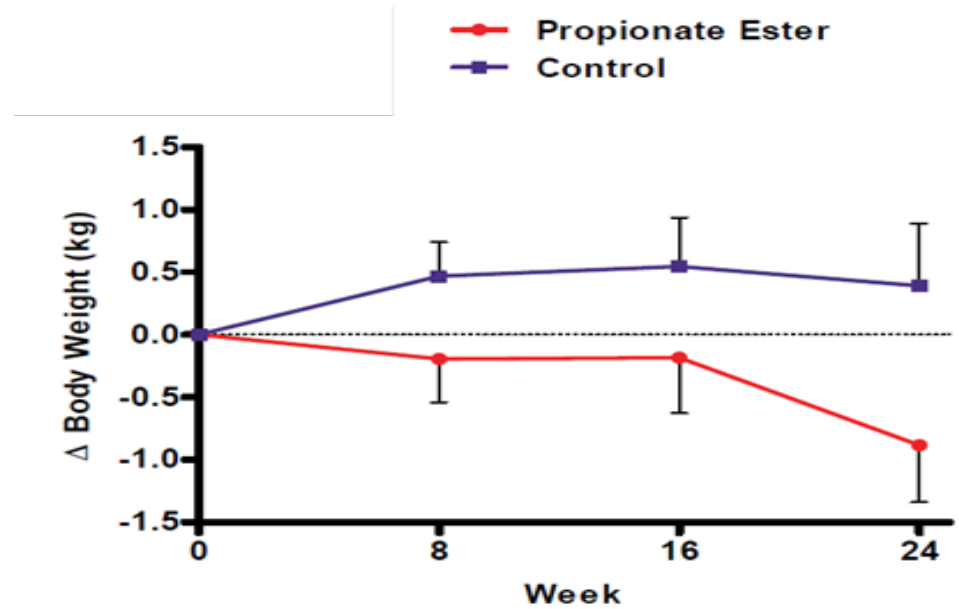


Douglas Morrison and Tom Preston  
University of Glasgow

# Acute Supplementation: Results



# Randomised Controlled Trial: Results

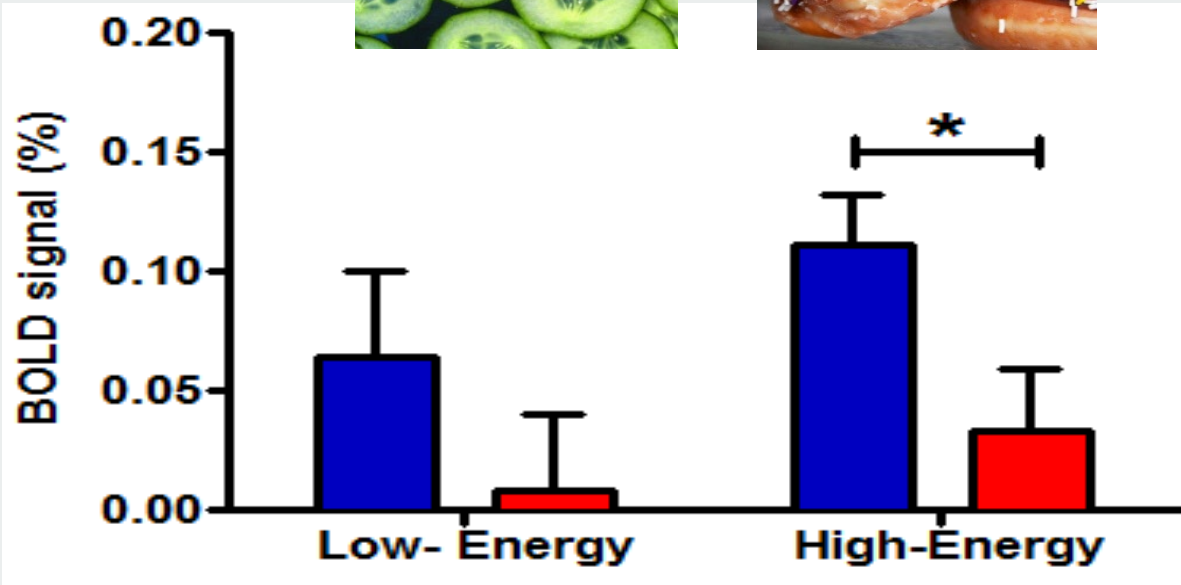
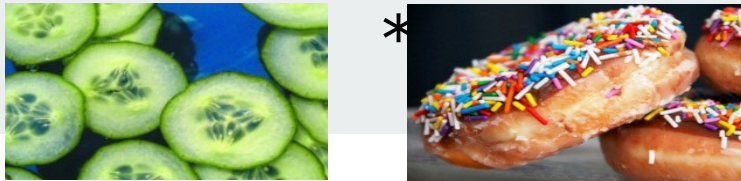


# BOLD responses

**Inulin-Control**  
**Inulin-Propionate Ester**

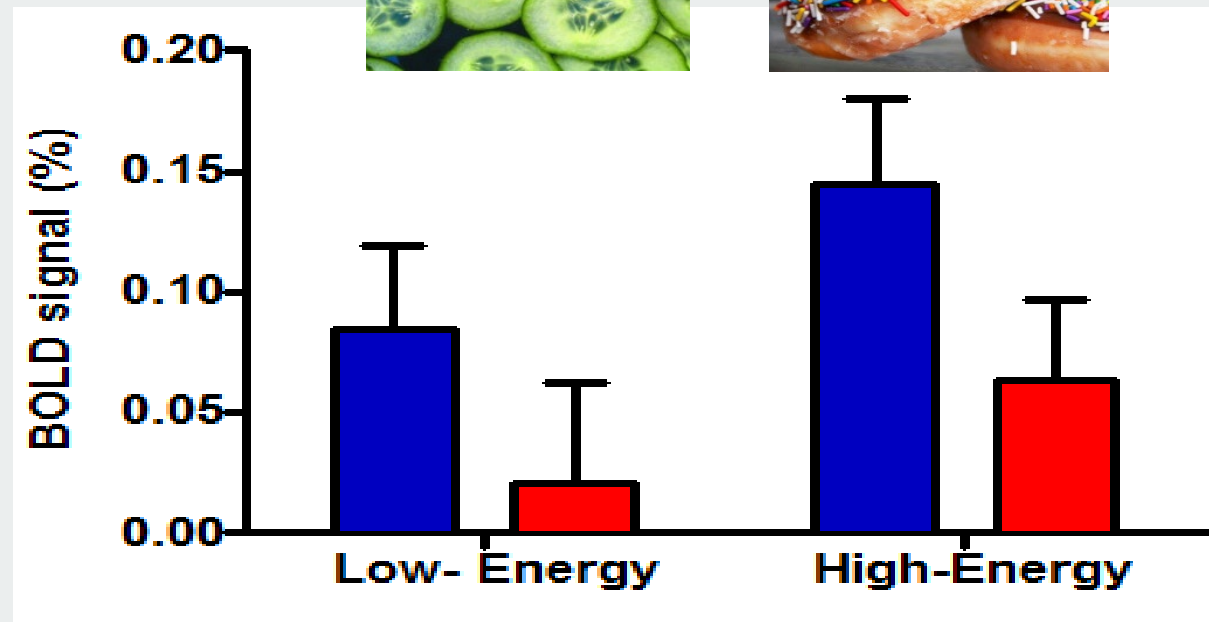
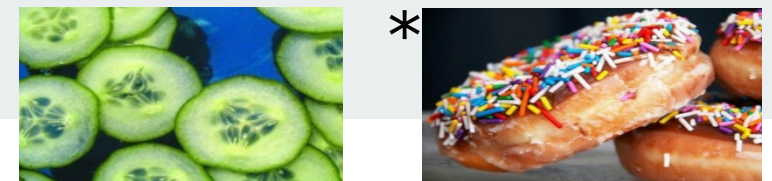
## Caudate

Interaction:  $P=0.009$



## Nucleus Accumbens

Interaction:  $P=0.005$

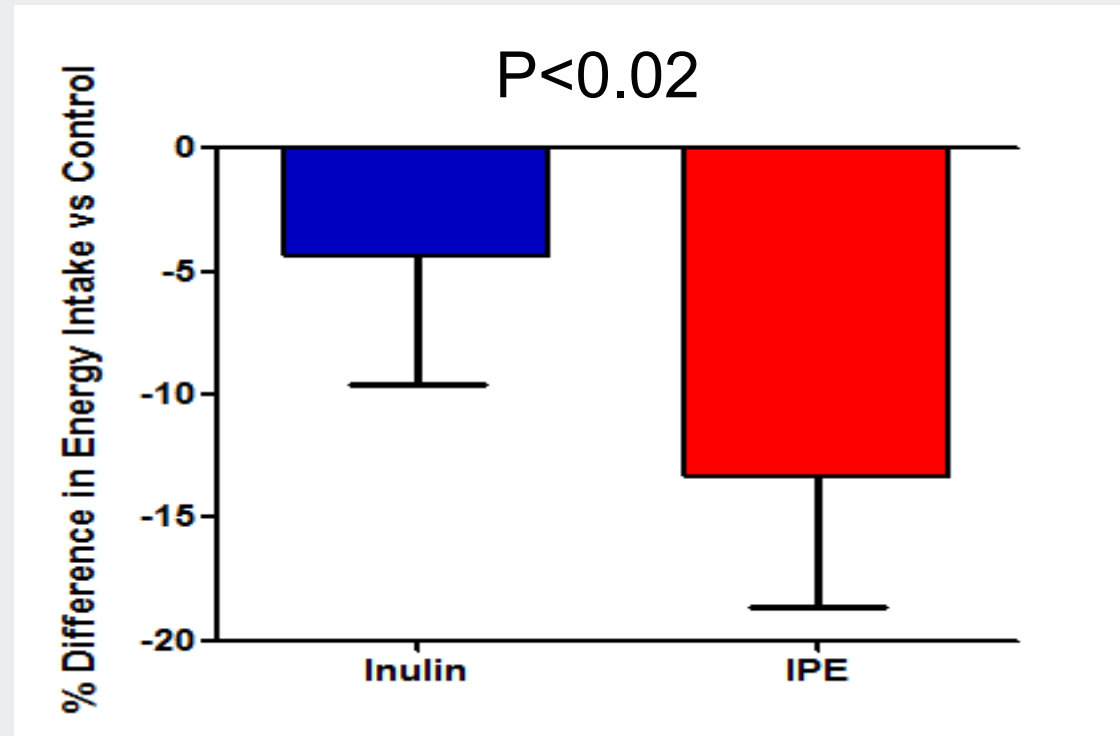


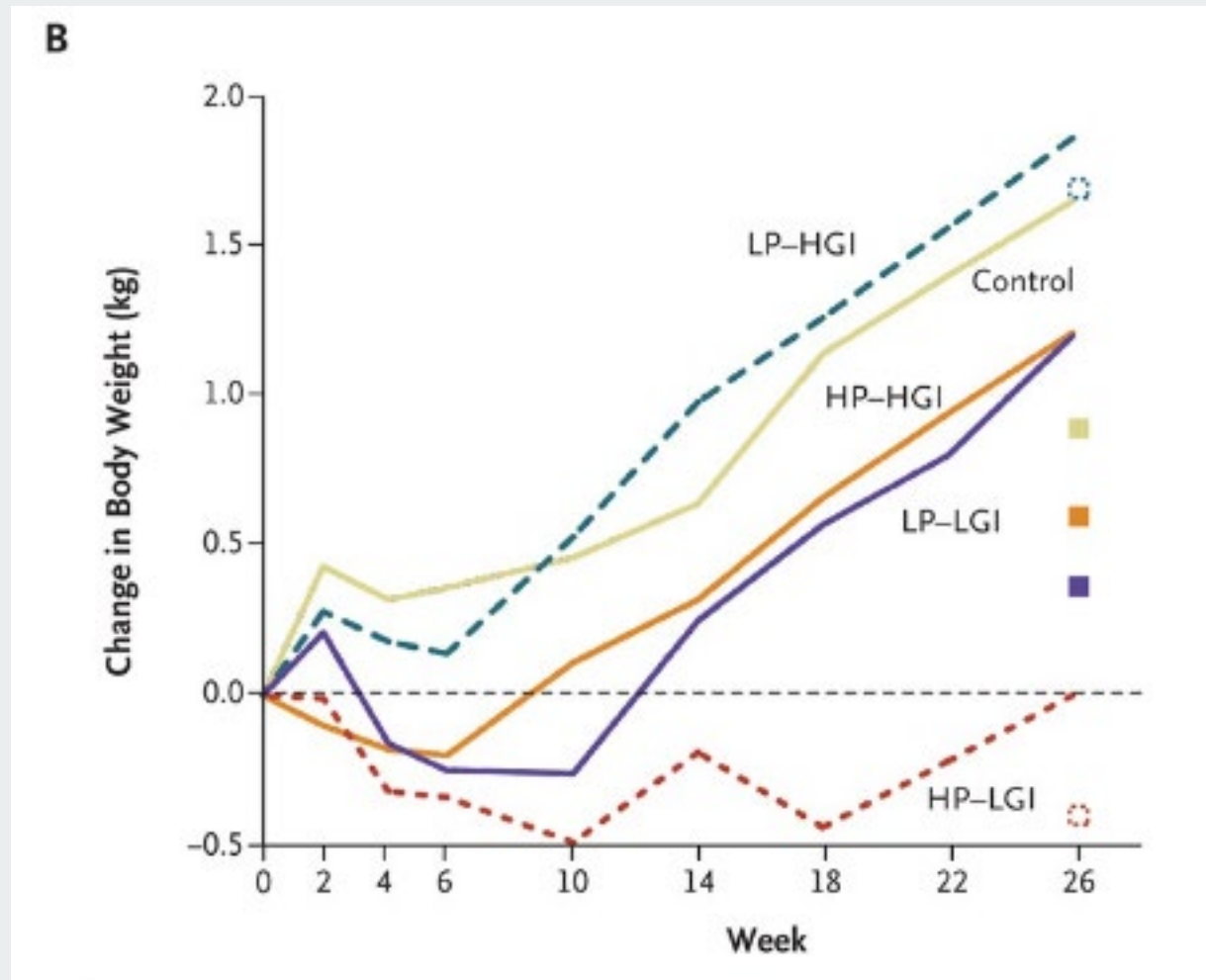
Data expressed as mean  $\pm$  SEM,  $n = 18$

P values represent treatment  $\times$  energy density interaction

BOLD signal food – object picture contrast

# % Difference in Energy Intake vs Control







## Summary

- Long-term maintenance of lost weight is the primary challenge of obesity treatment.
  - Biological, behavioural, and environmental factors conspire to resist weight loss and promote regain.
  - Realistic long-term weight loss magnitude is significantly lower than patient and healthcare provider expectations.
  - Can we bring knowledge about human physiology and biological effect of food together to enhance weight loss maintenance
  - Treatment of obesity requires ongoing attention and support, and weight maintenance-specific counselling, to improve long-term weight management.
-