

How the gut talks to the brain

Carel le Roux

Diabetes

Complications

Research Centre

University College

Dublin

Imperial College

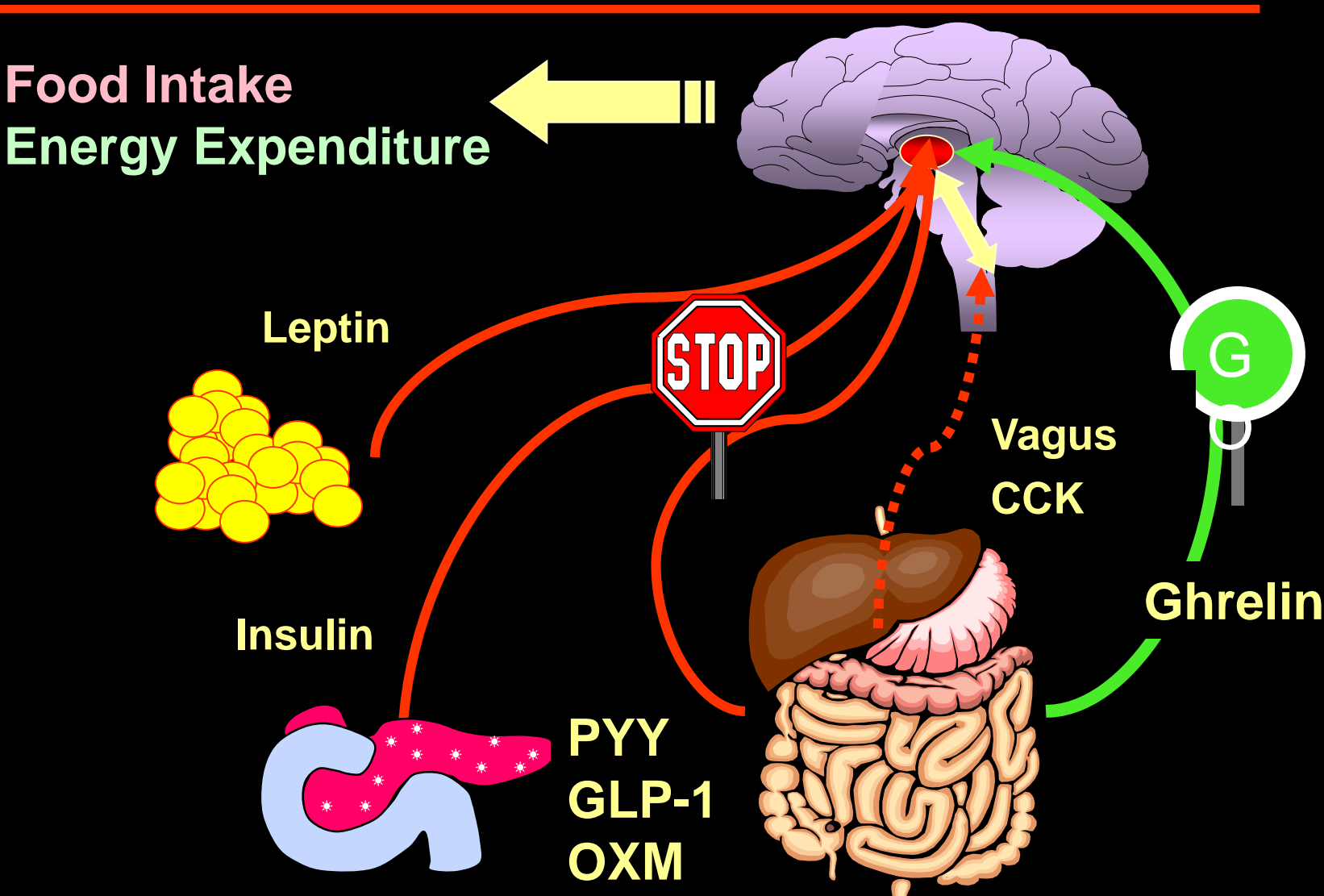
London



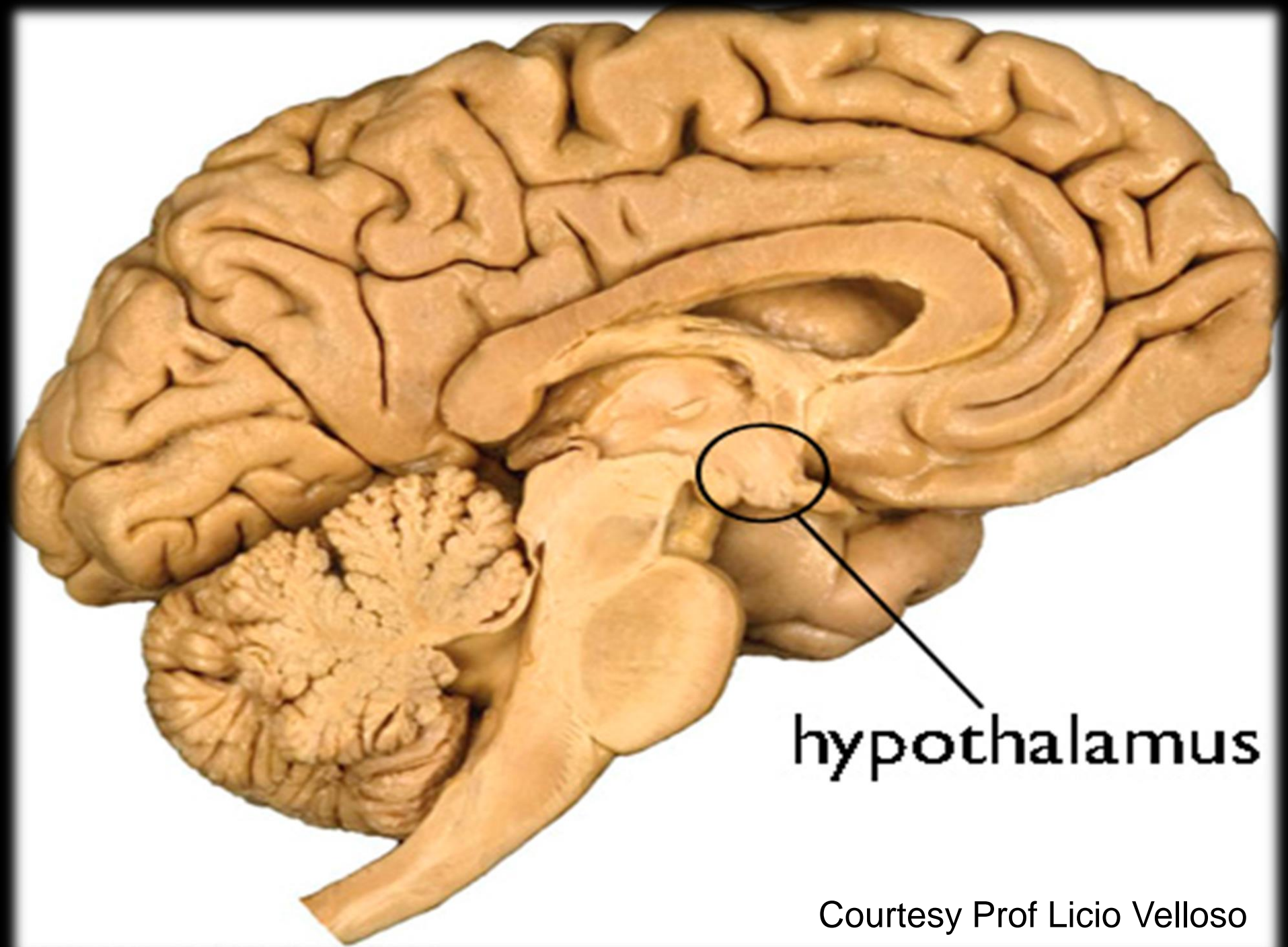
Conflict of interest

NovoNordisk,
Johnson & Johnson,
ONO pharmaceuticals,
Covidien,
Fractyl,
GI Dynamics,
Roche,
AstraZeneca
Lilly
Boehringer Ingelheim

Afferent factors in appetite regulation



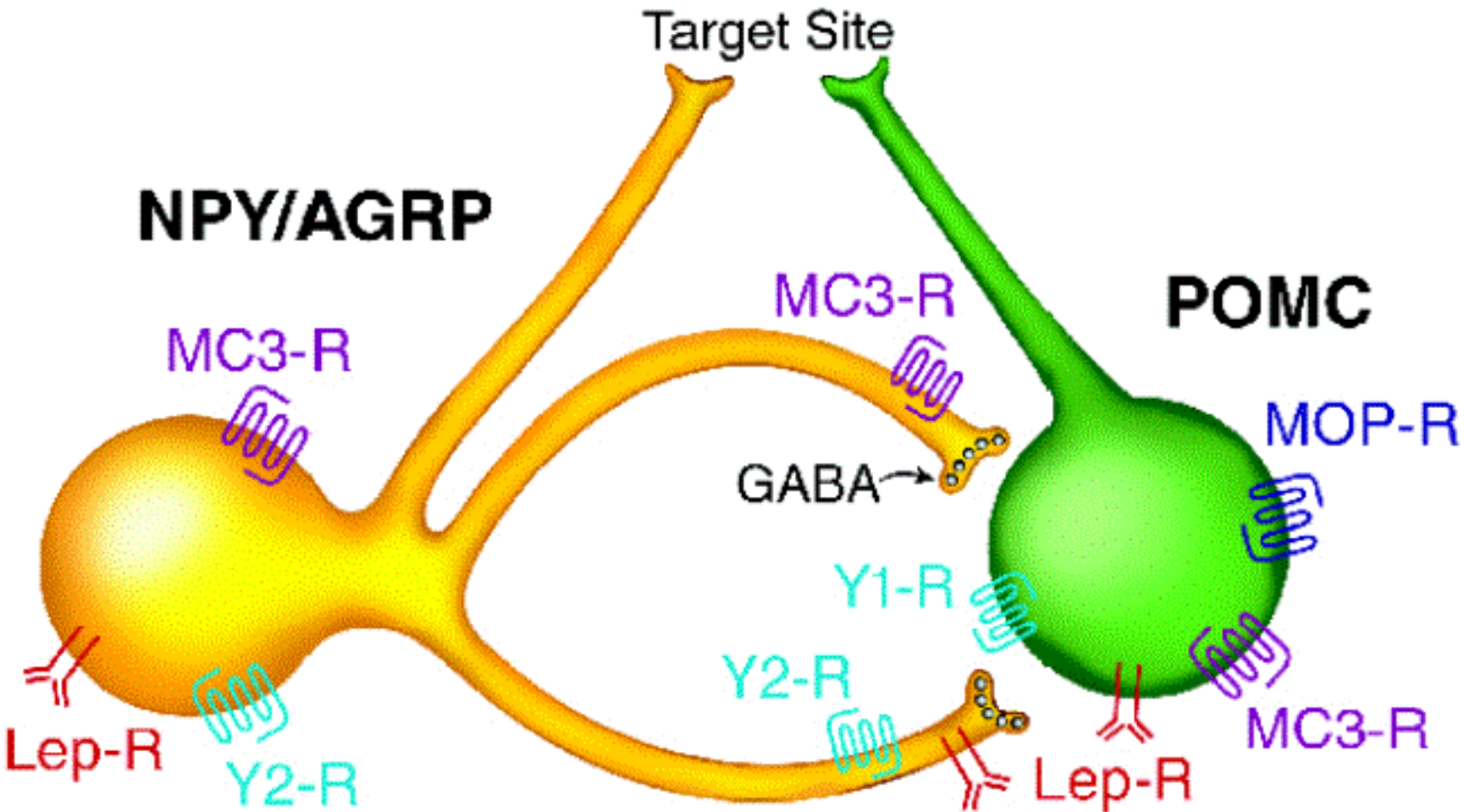
Vincent, le Roux et al. Nature Clin Practice Gastro & Hepatology 2008



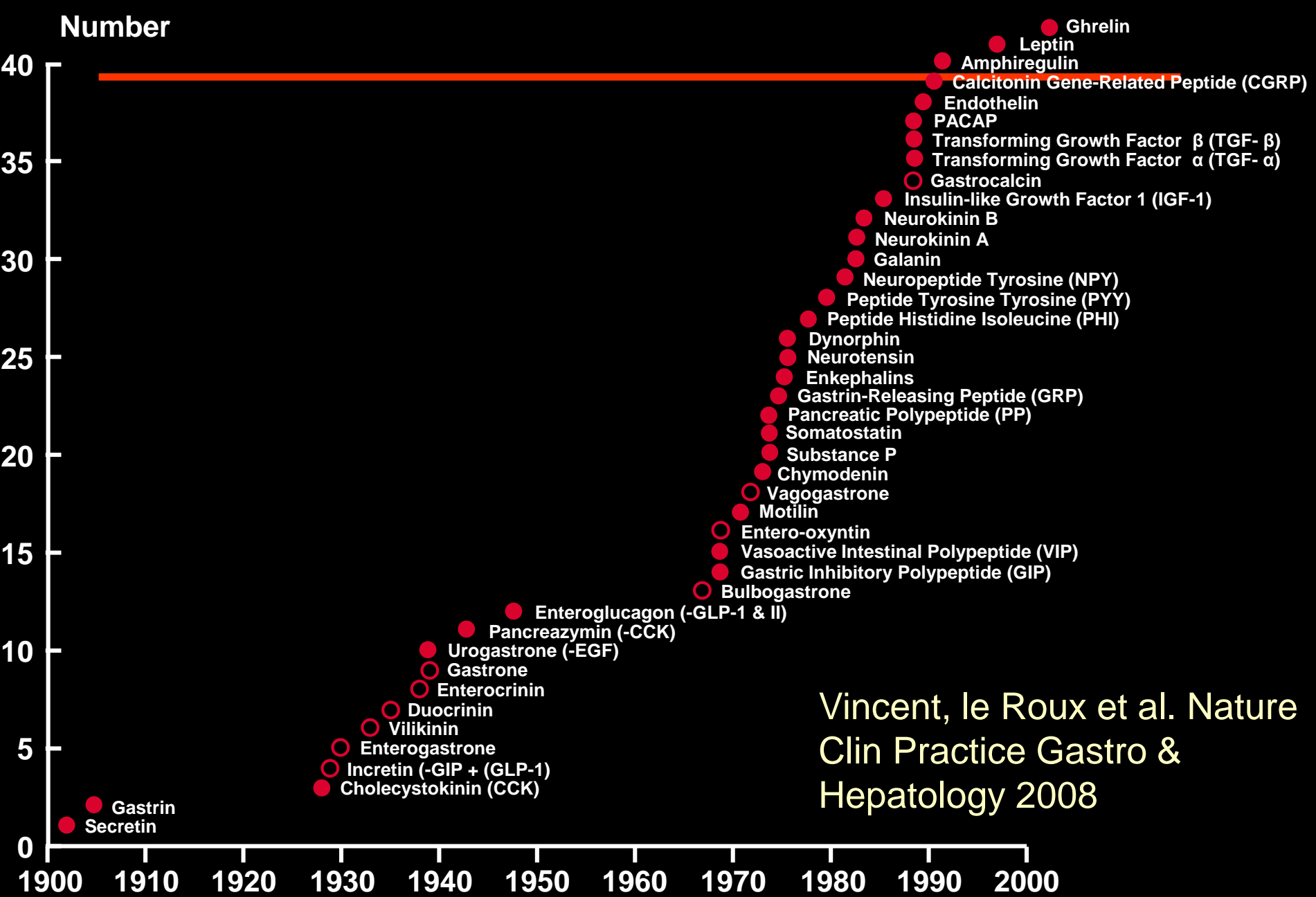
hypothalamus

Courtesy Prof Licio Velloso

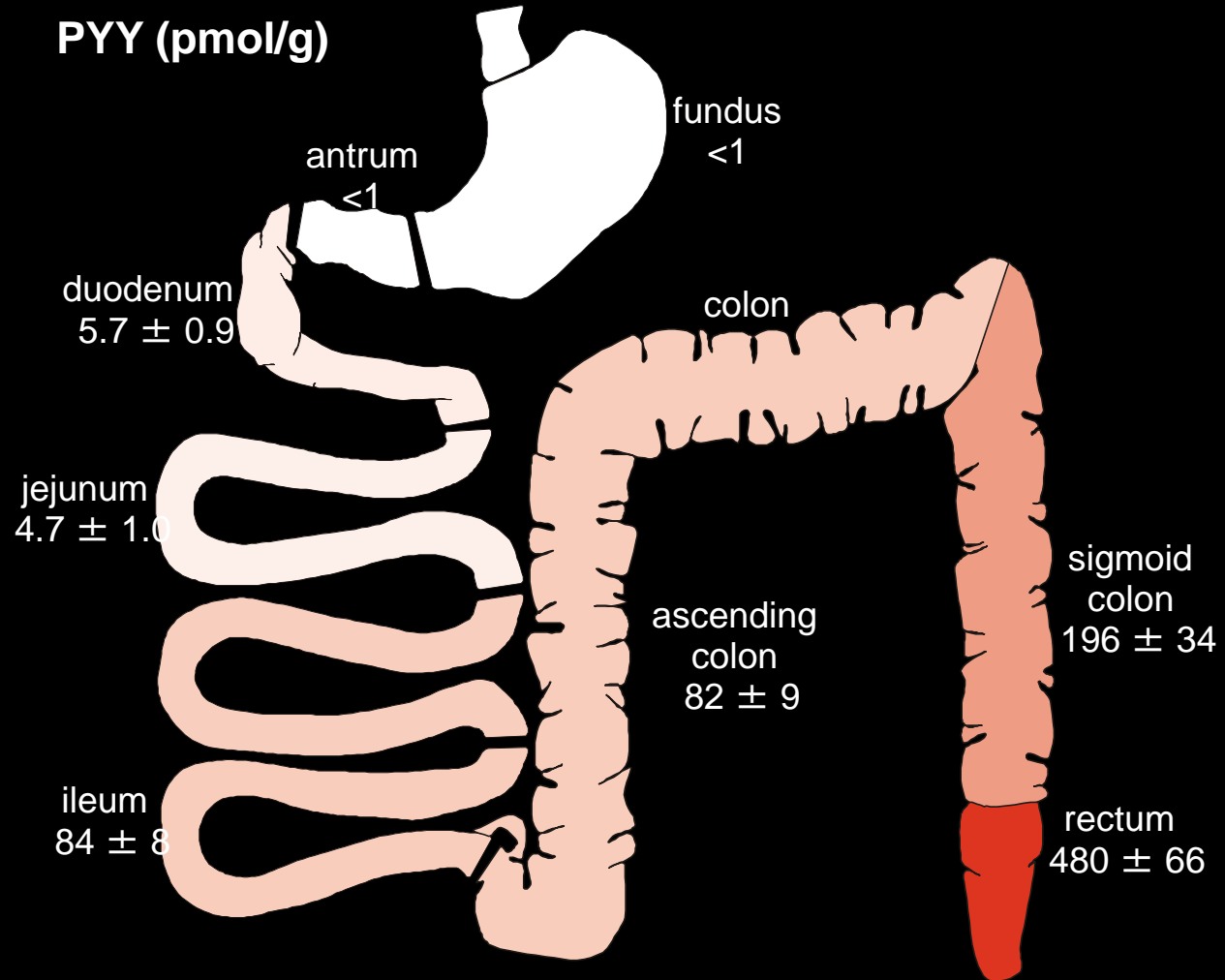
Arcuate nucleus



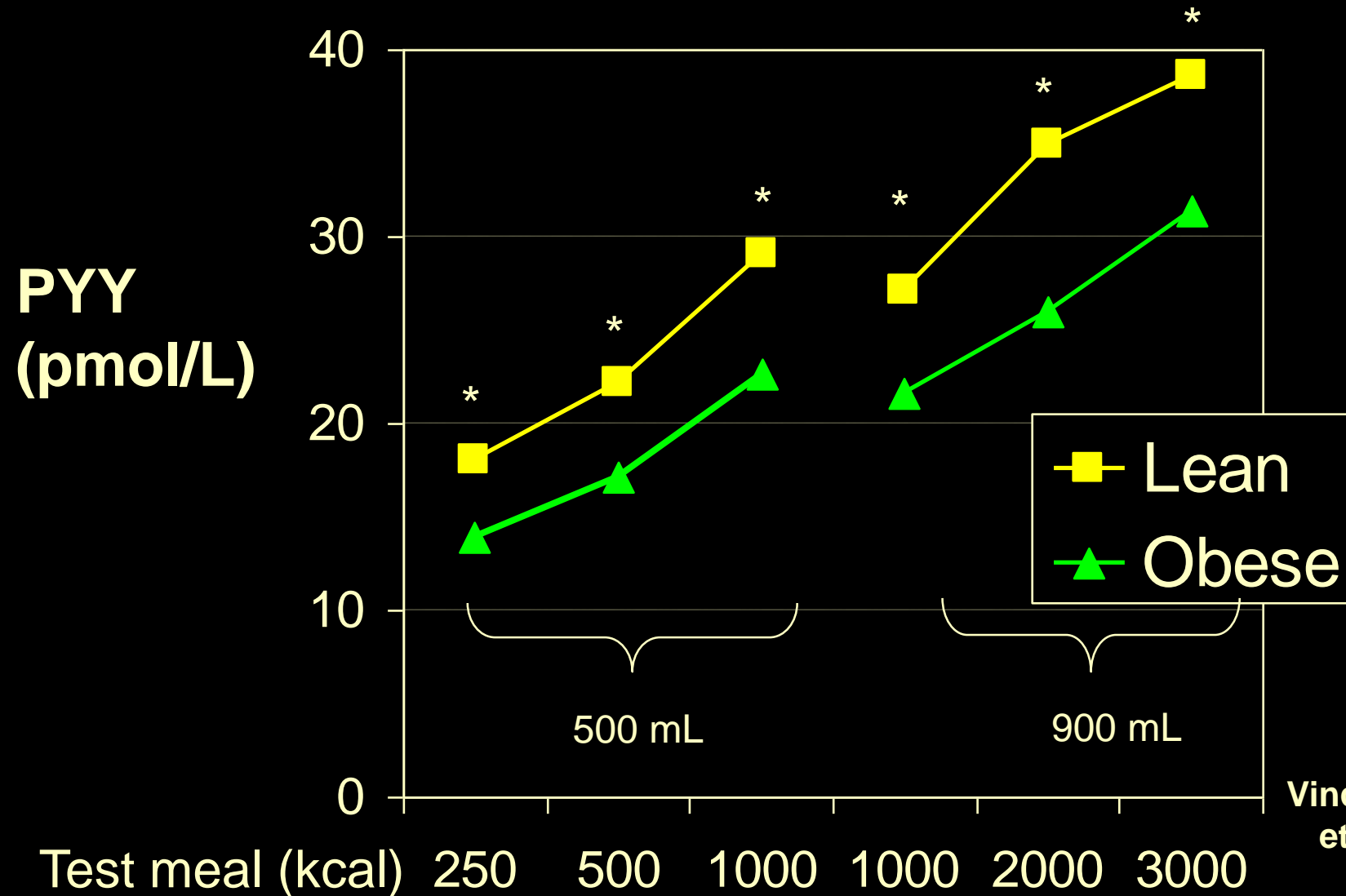
Discovery of gastrointestinal hormones



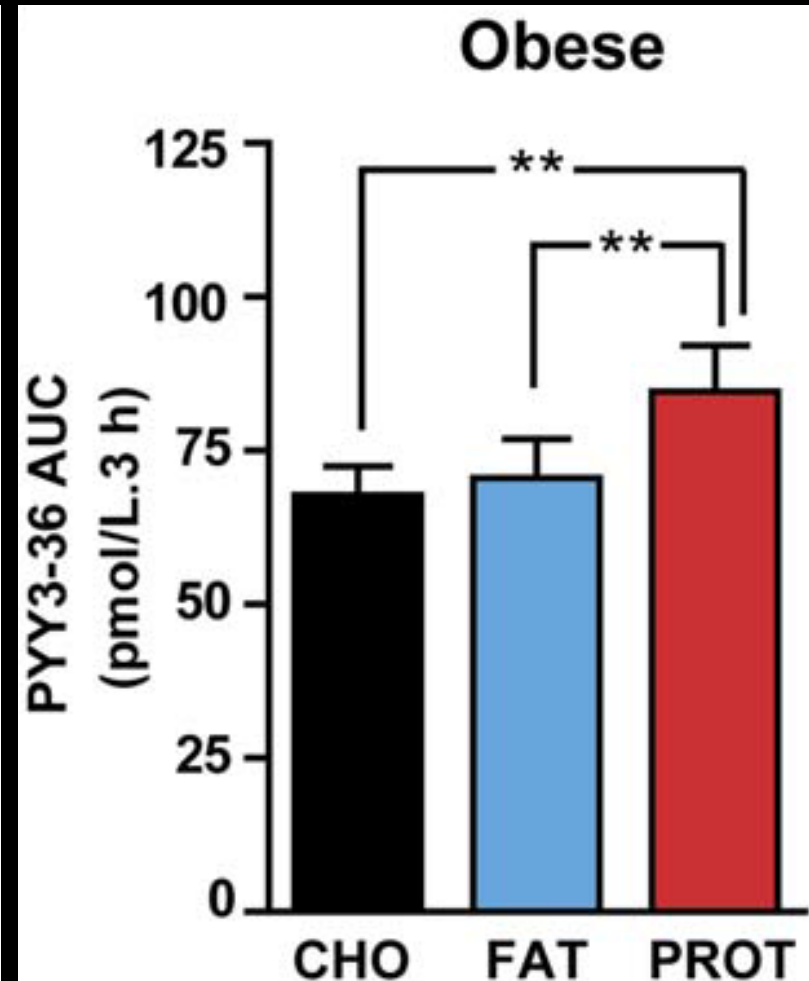
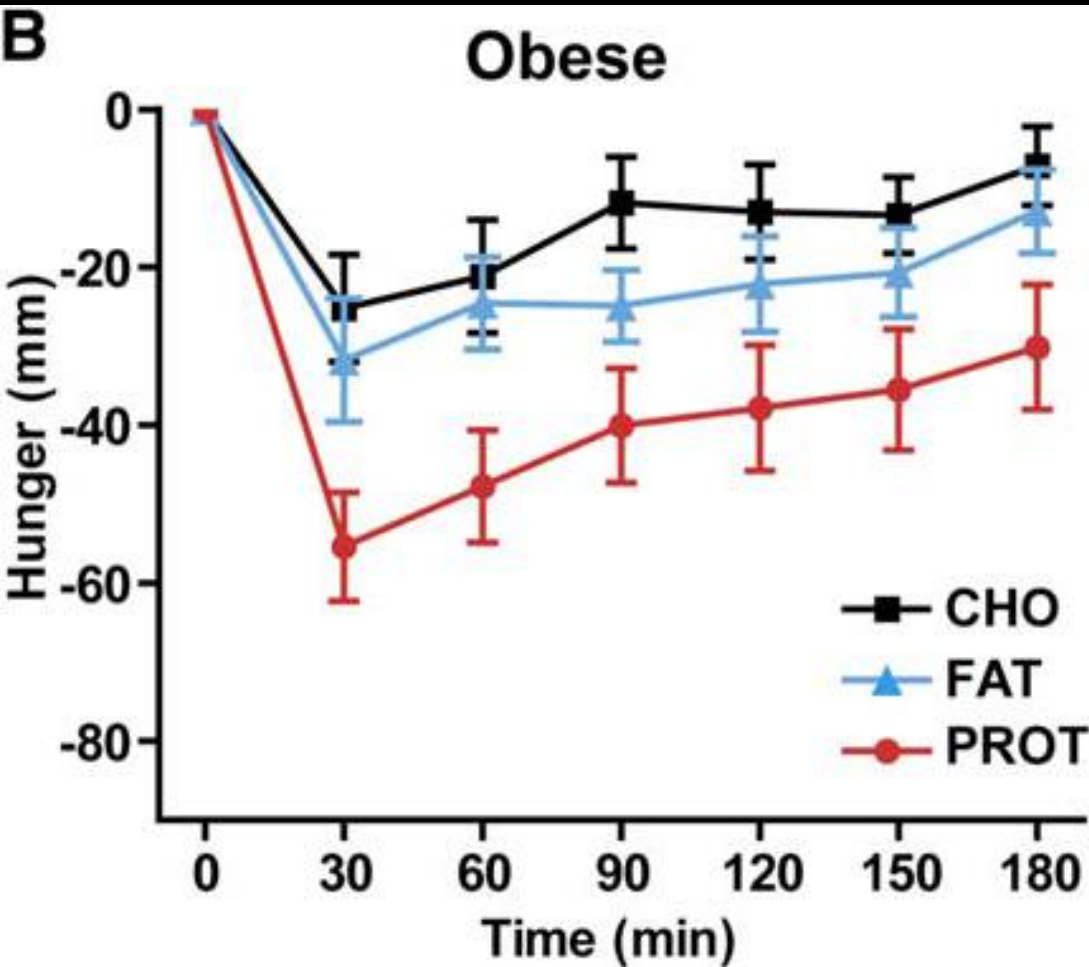
PYY distribution



Calorie Intake vs PYY dose response

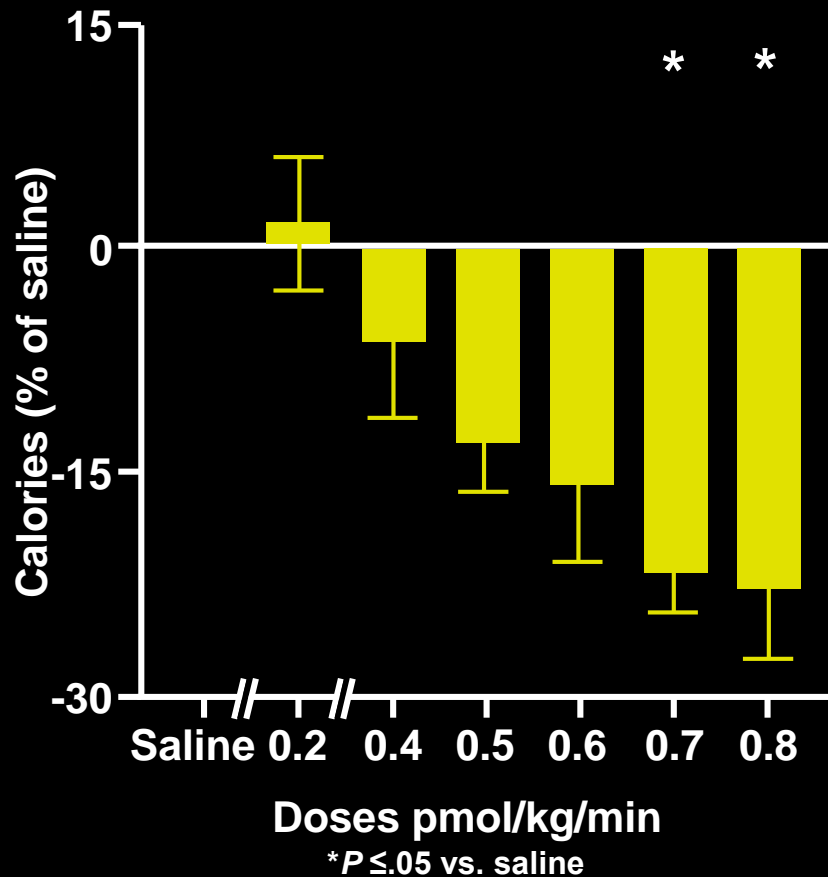


Protein reduces hunger and stimulates satiety gut hormones

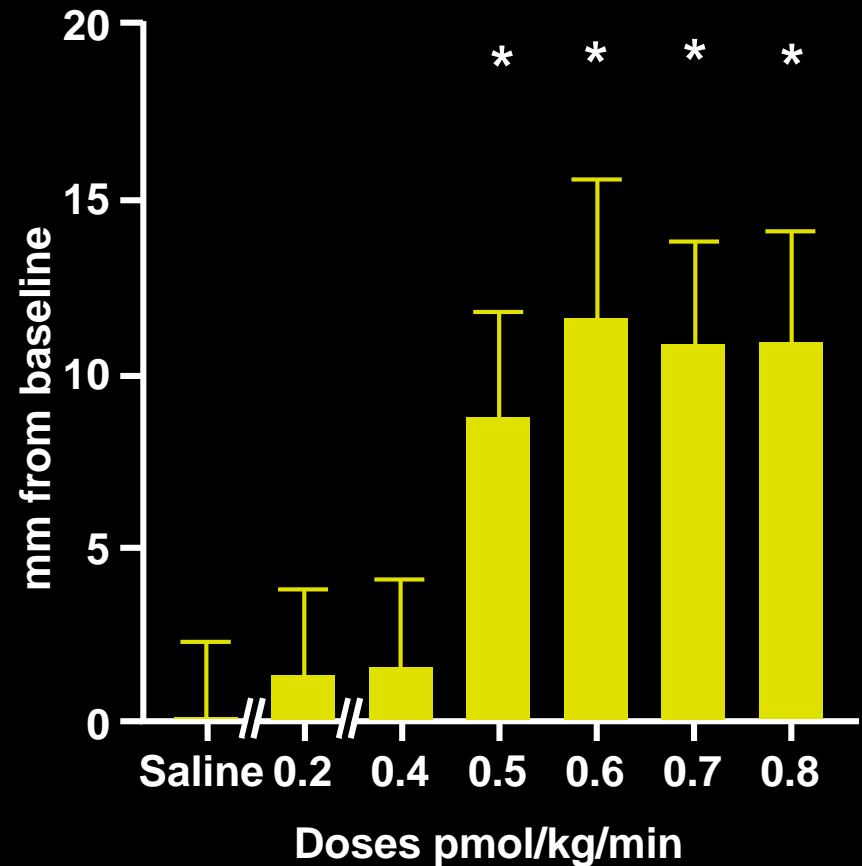


PYY3-36 dose response in humans

Calorie intake

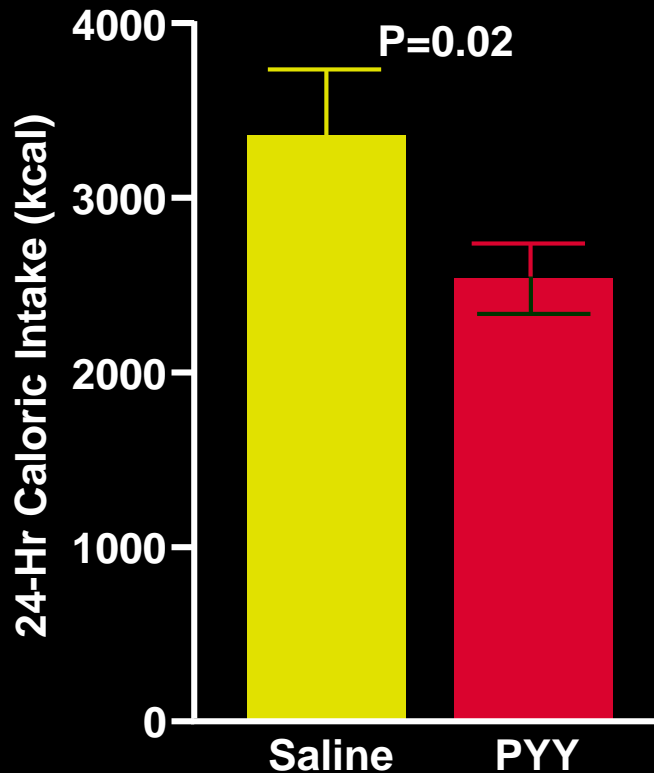


Satiety

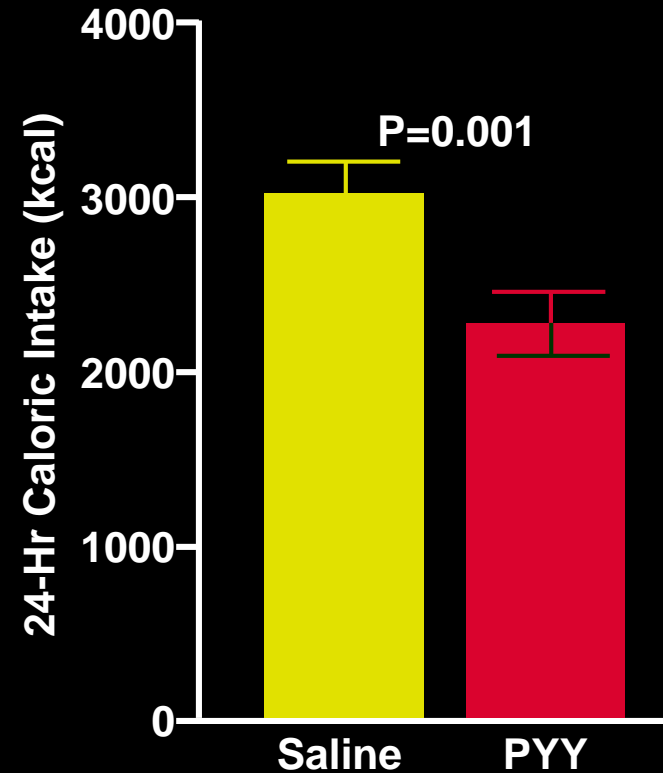


Effect of PYY3-36 on food intake

Obese



Lean



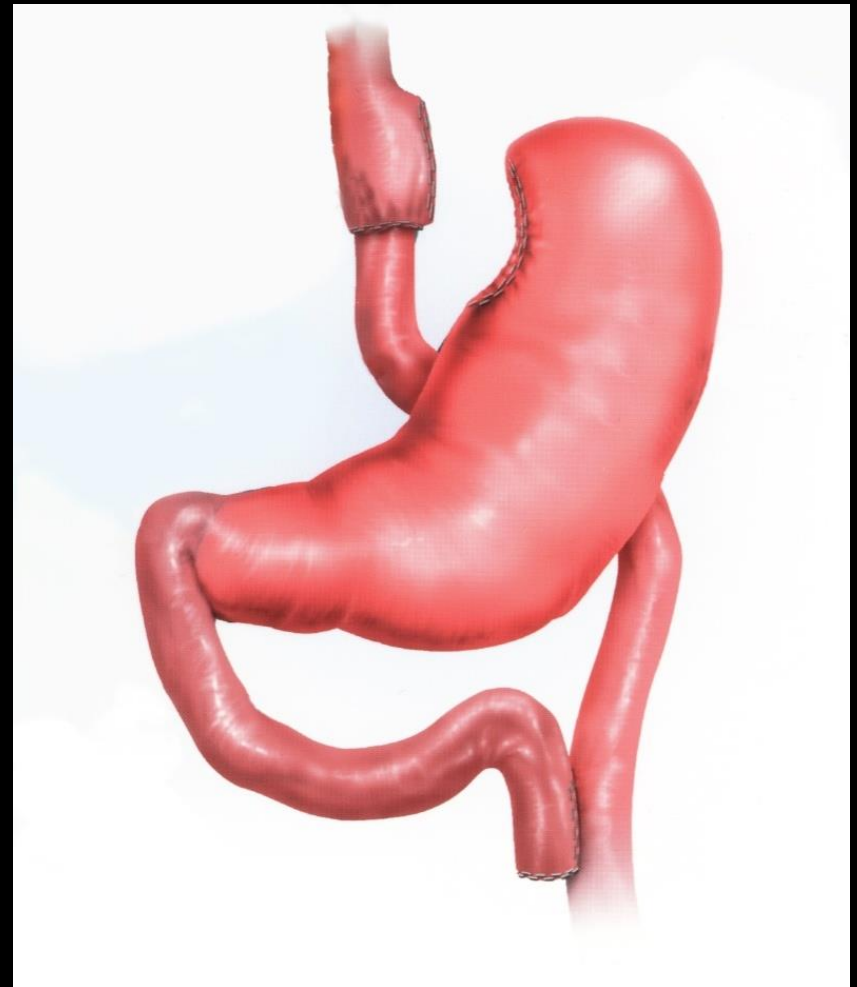
Surgical principles

Tadross, le Roux et al. Int J Obes 2009

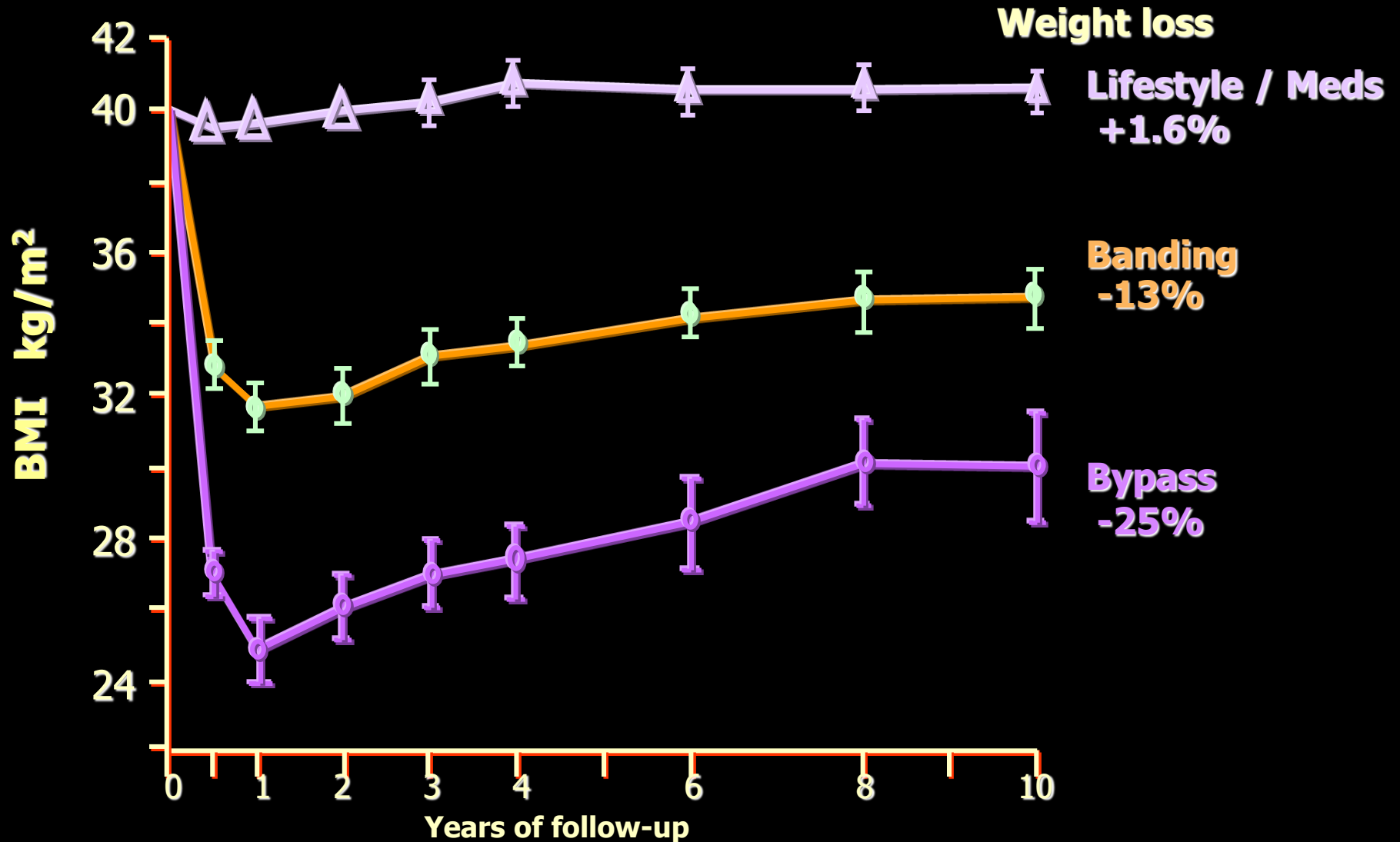
“Banding”



“Bypass”

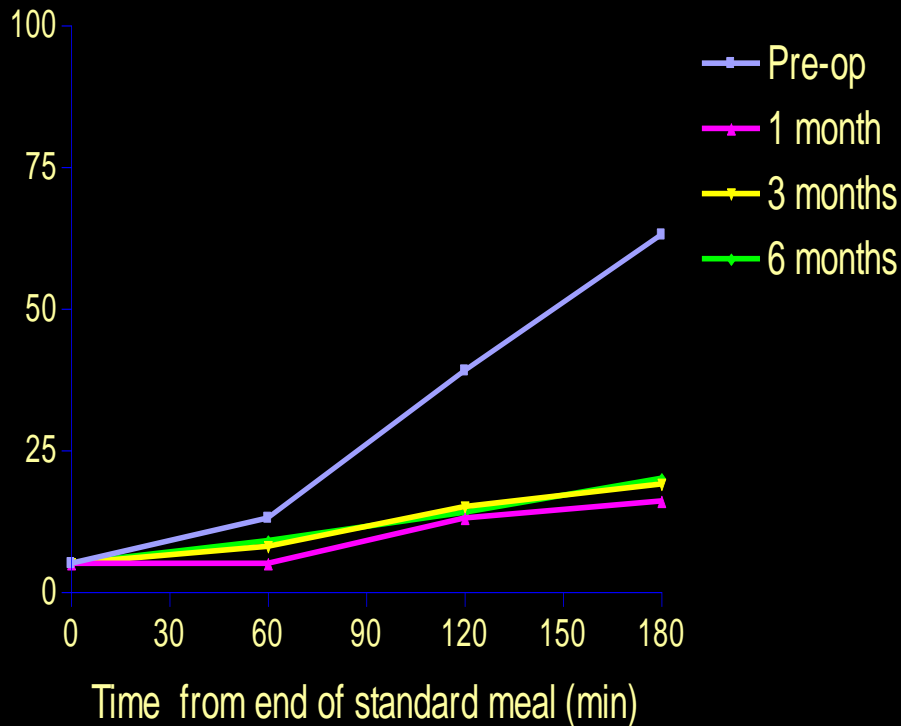


Long term weight loss maintenance

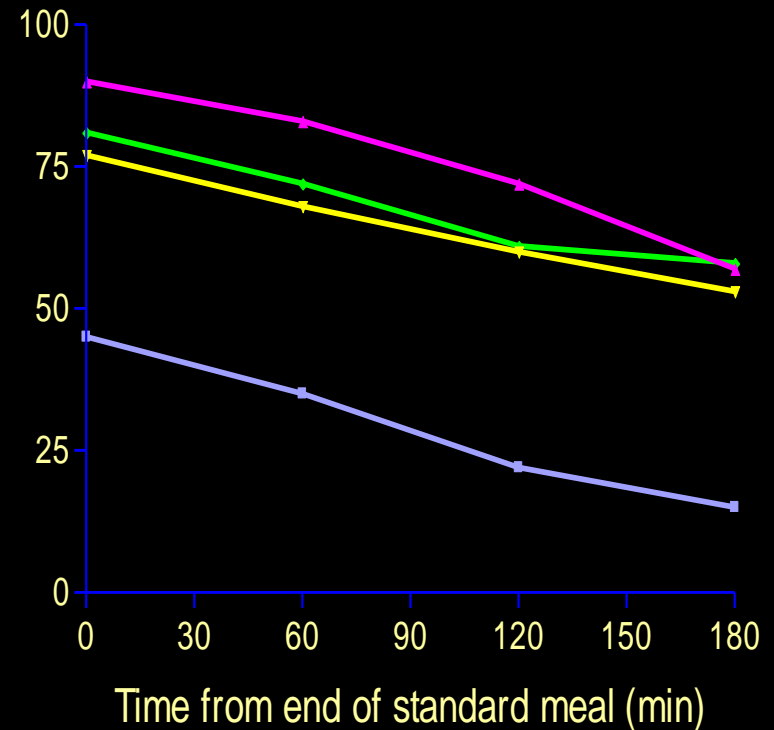


Visual analogue scores

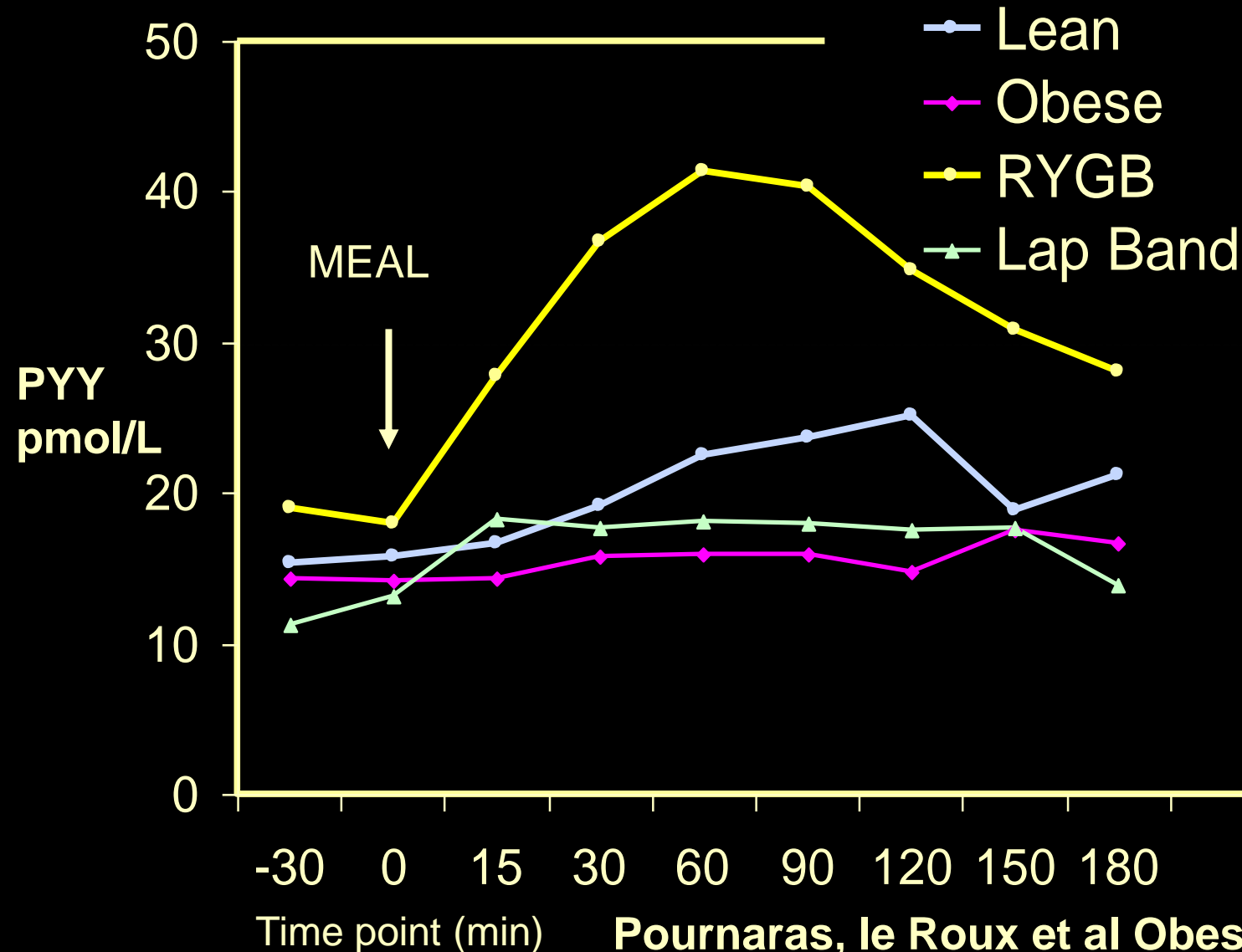
VAS - How hungry are you?



VAS - How full are you?

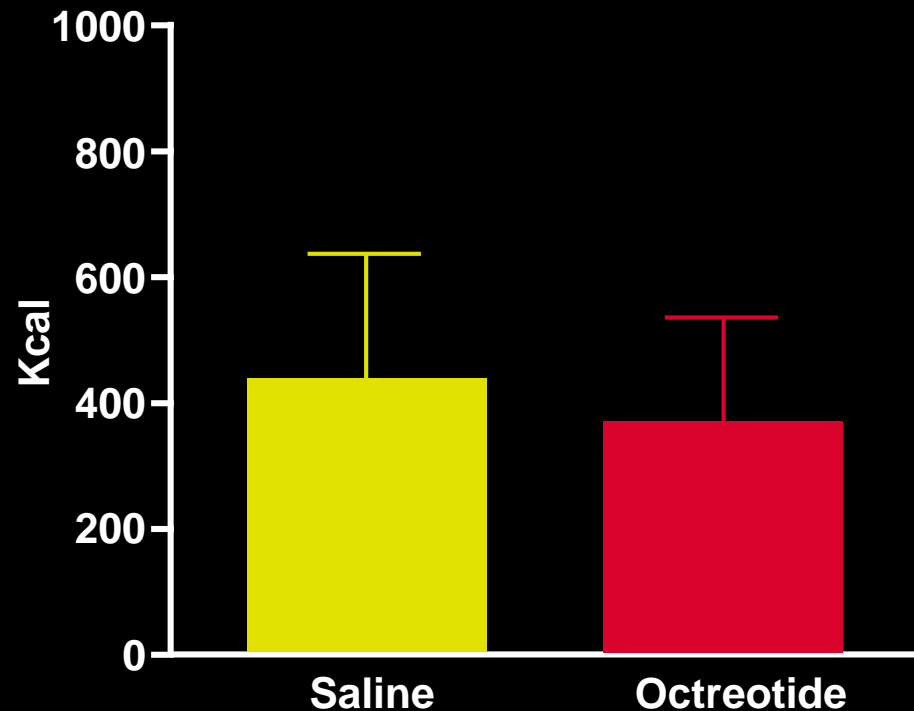


PYY response after bariatric surgery

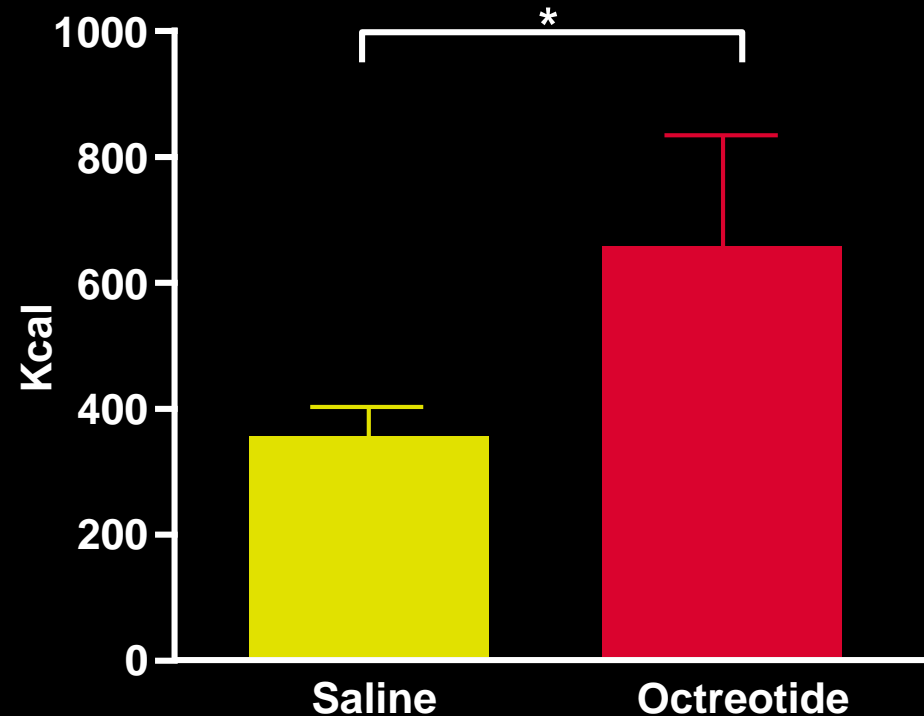


Blocking gut hormones with octreotide

Gastric banding



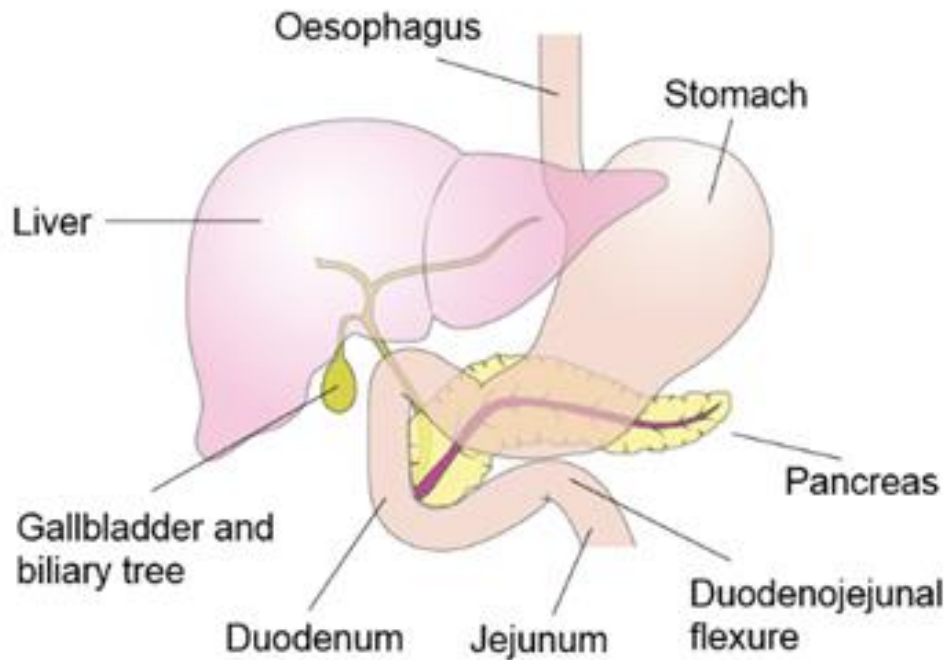
Gastric bypass



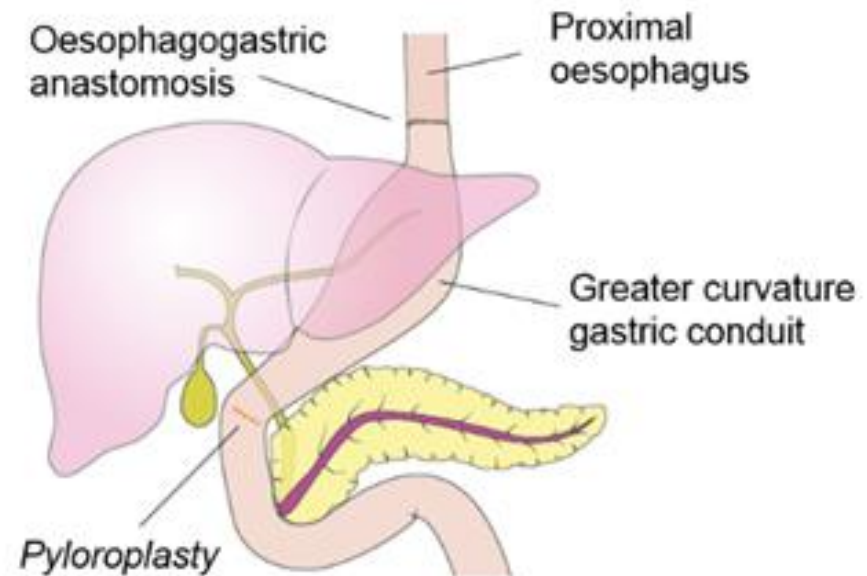
* $P < 0.05$

Oesophagectomy for cancer

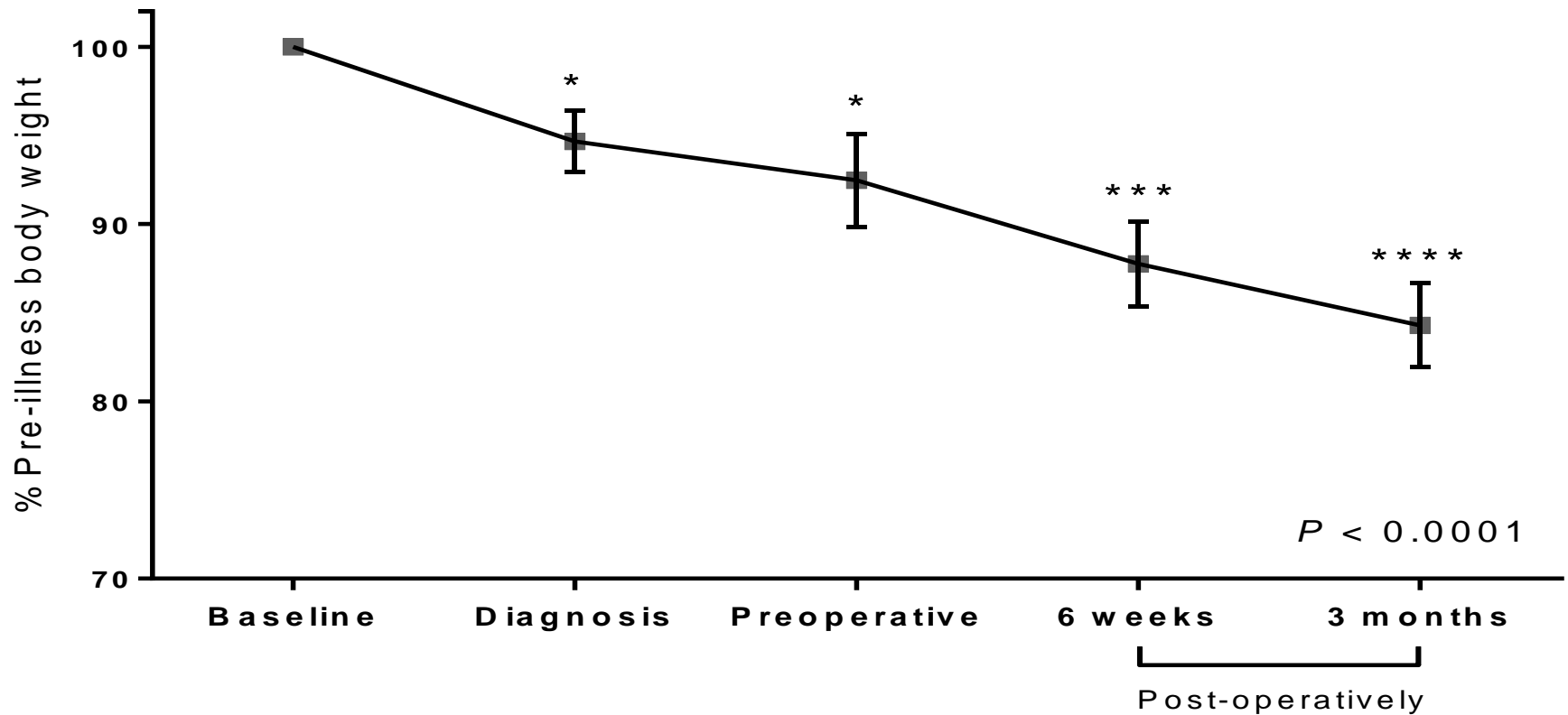
A Normal anatomy



B Oesophagectomy with gastric conduit reconstruction



Weight loss after oesophagectomy

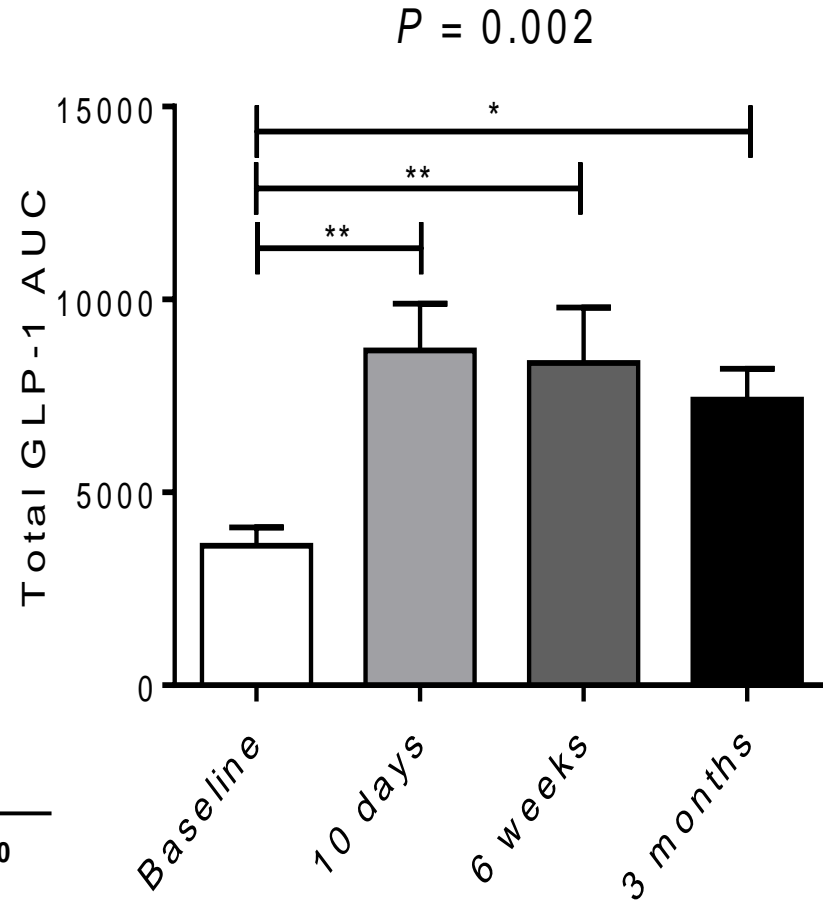
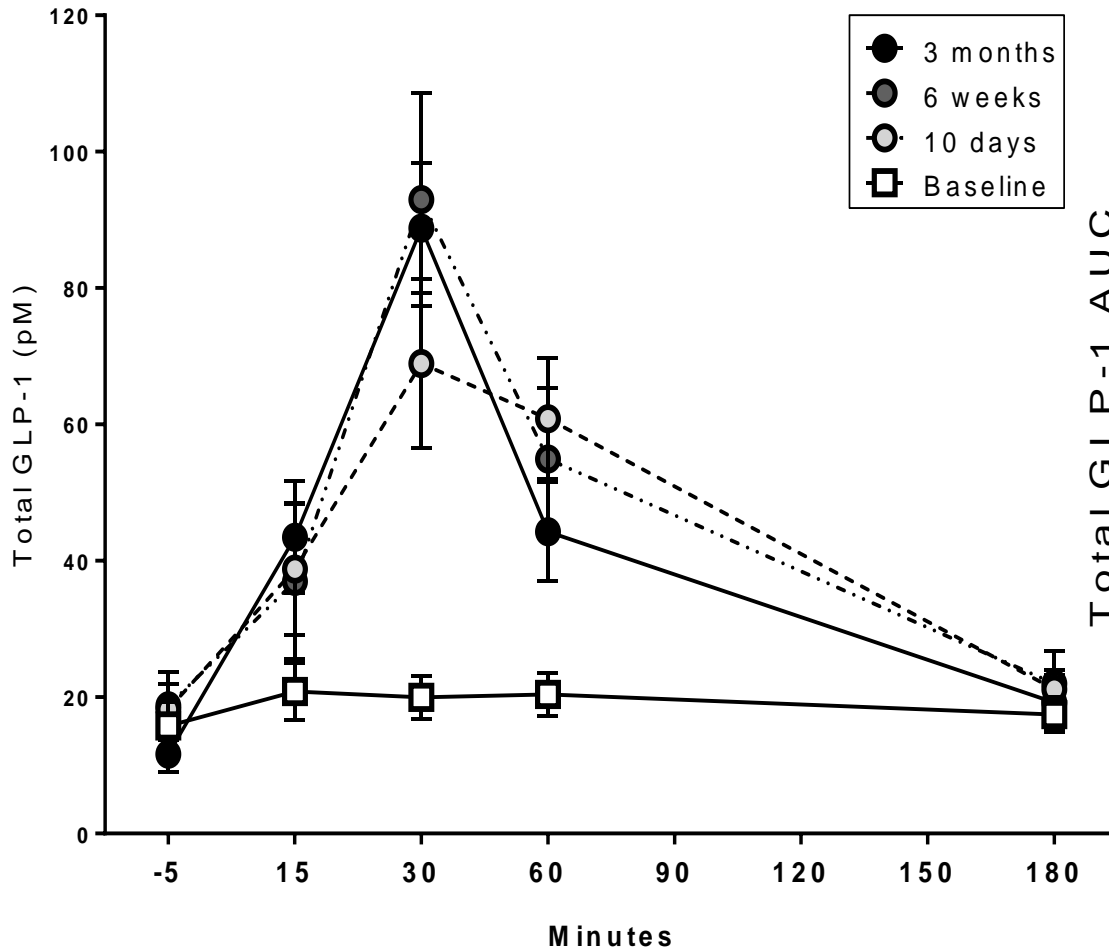


| Weight, kg | 88 | 79 | 81 | 76 | 72 |
|----------------|----------|----------|---------|---------|---------|
| Median (range) | (63–124) | (63-102) | (65-96) | (60-91) | (60-92) |

3 month %BWL = 14.3% (3.8 – 30.7%)

le Roux et al. Annals of Surgery 2016

Post-prandial GLP-1 after oesophagectomy



↑
400 kcal meal

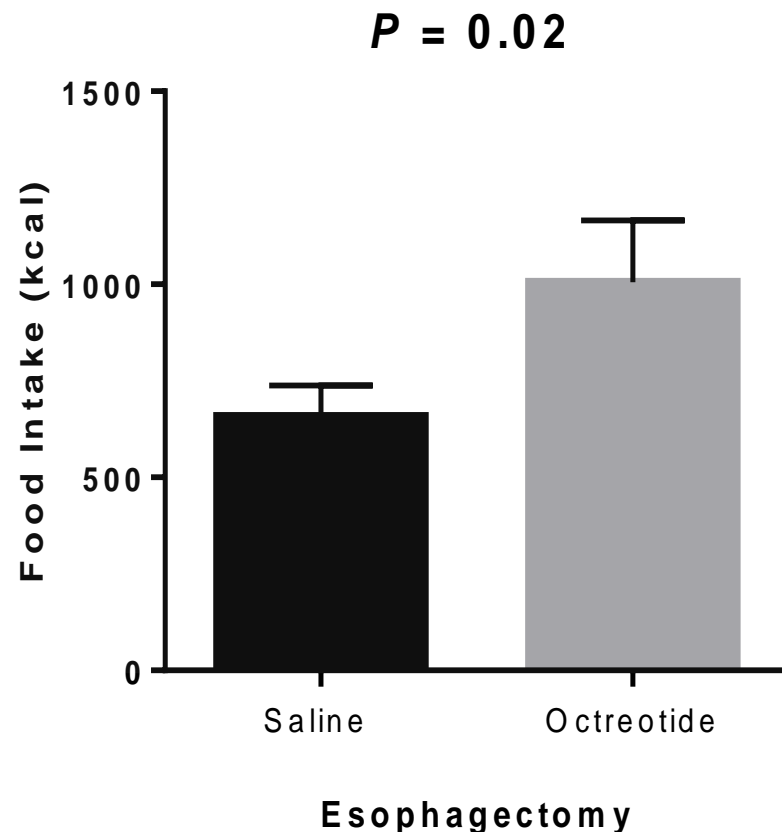
le Roux et al Ann Surg 2016

Octreotide increased food intake after oesophagectomy

A

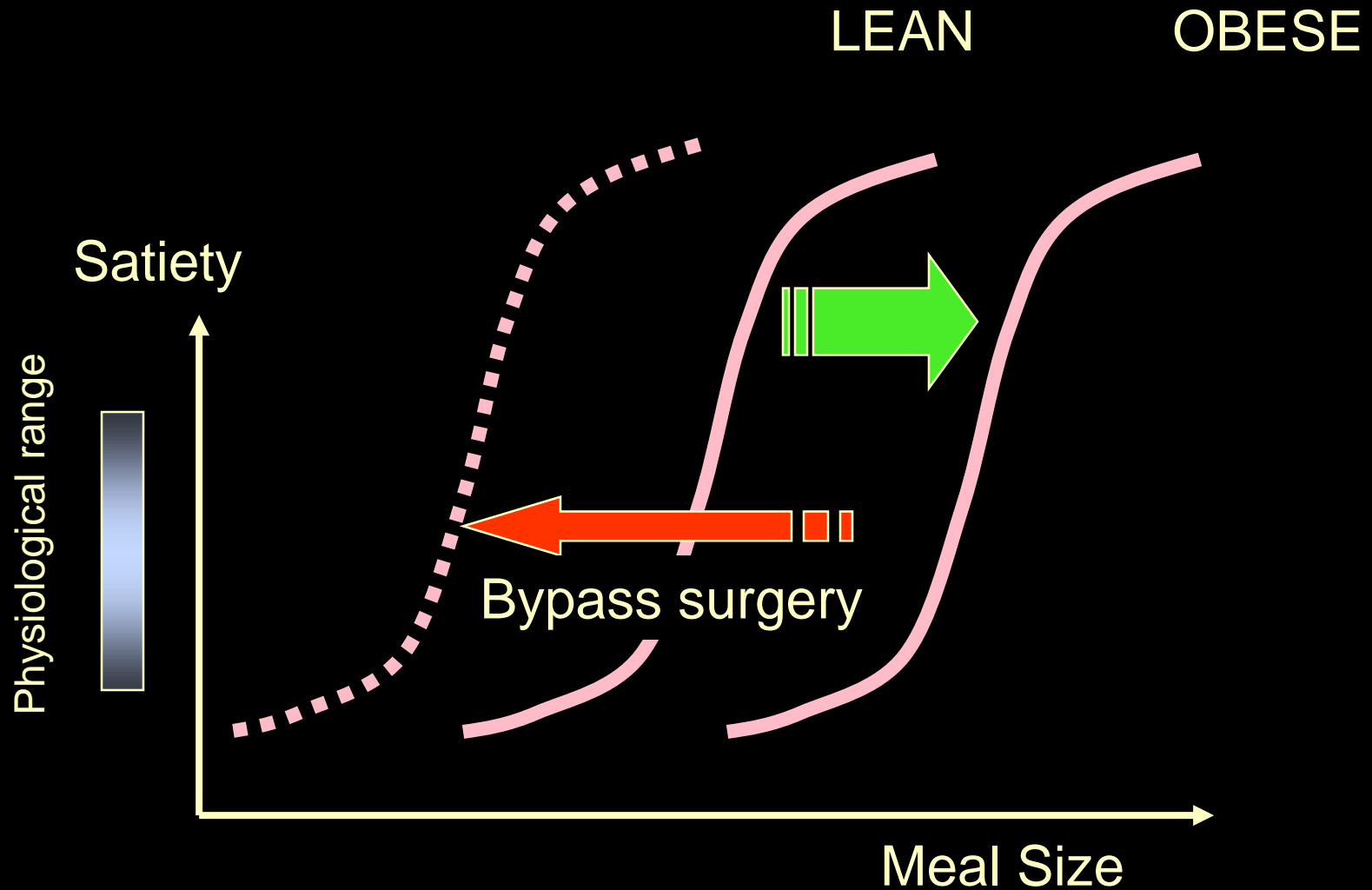


B



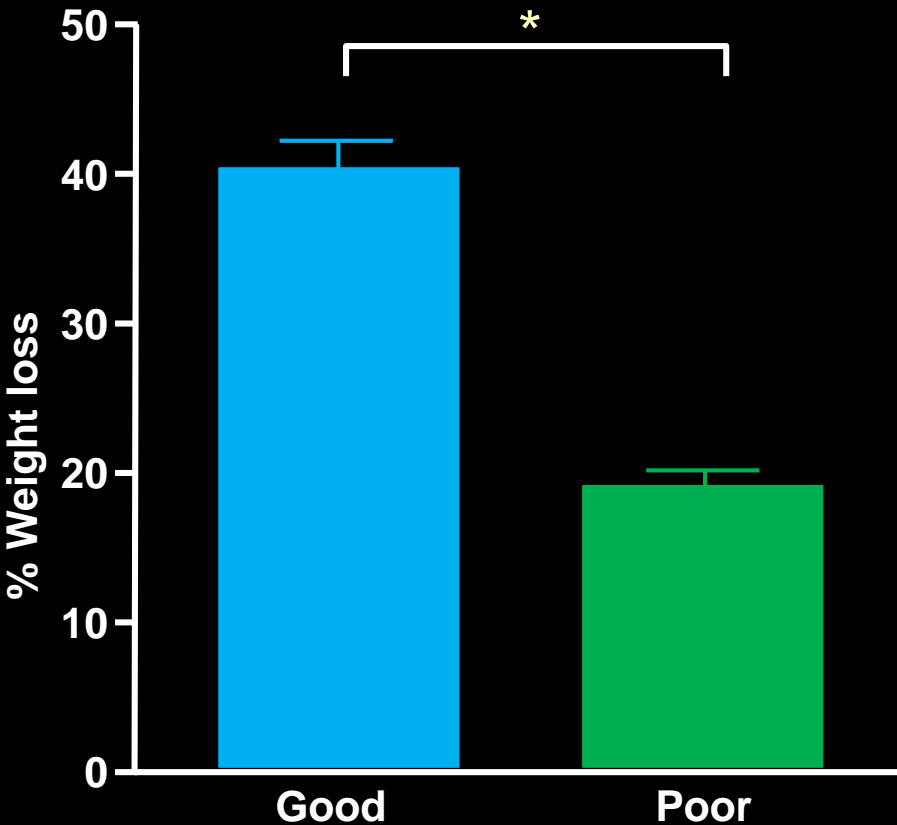
Trend towards lower calorie intake in OES group on saline day ($P = 0.085$)
No difference in calorie intake between groups on octreotide day ($P = 0.51$)

Dose response curve

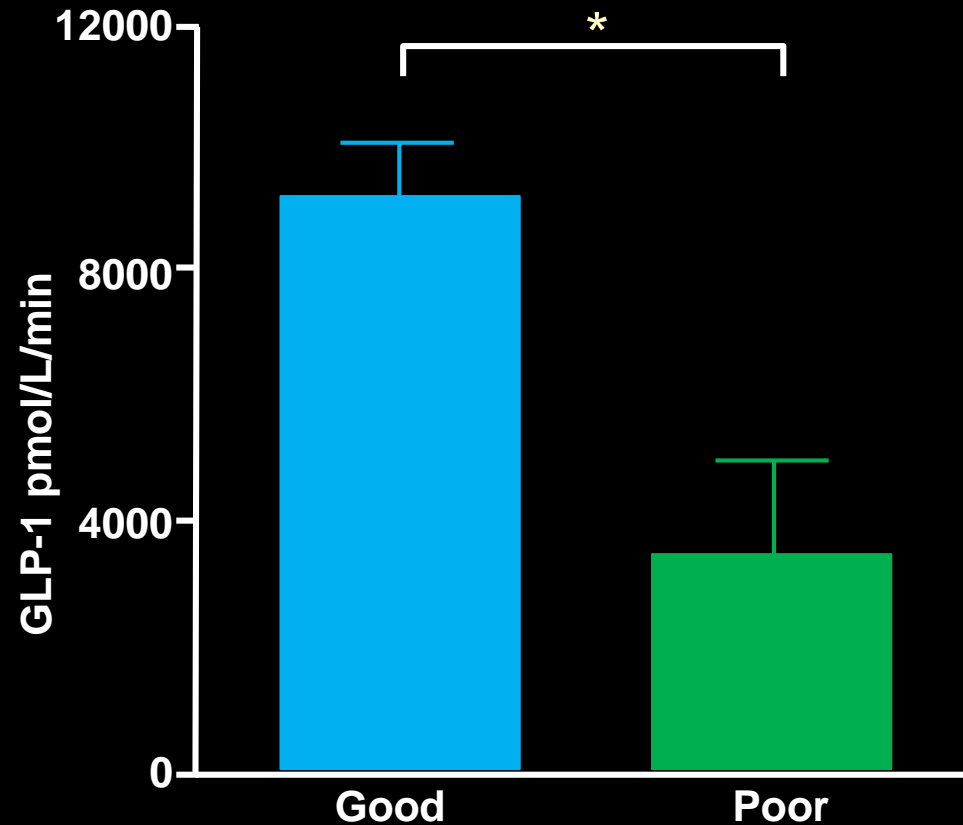


Good and poor weight loss after RYGB

Weight loss

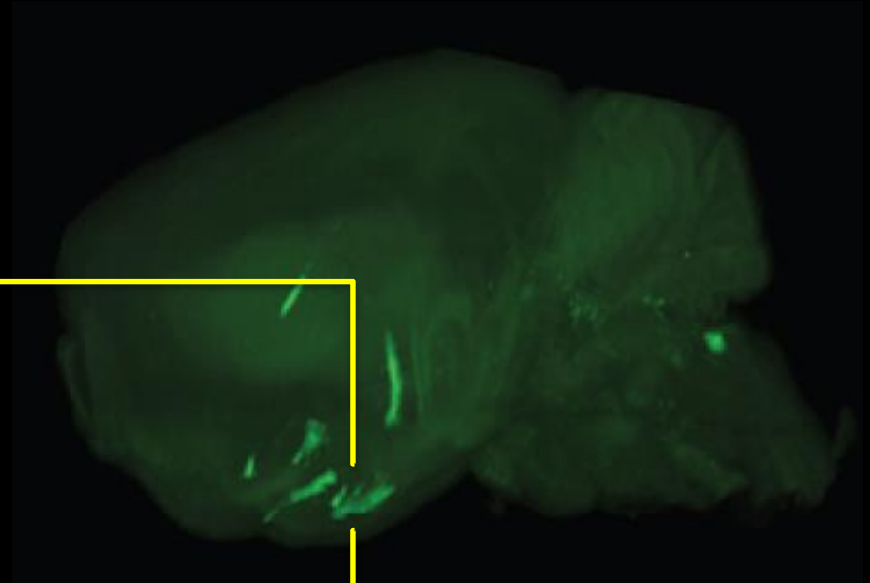


GLP-1



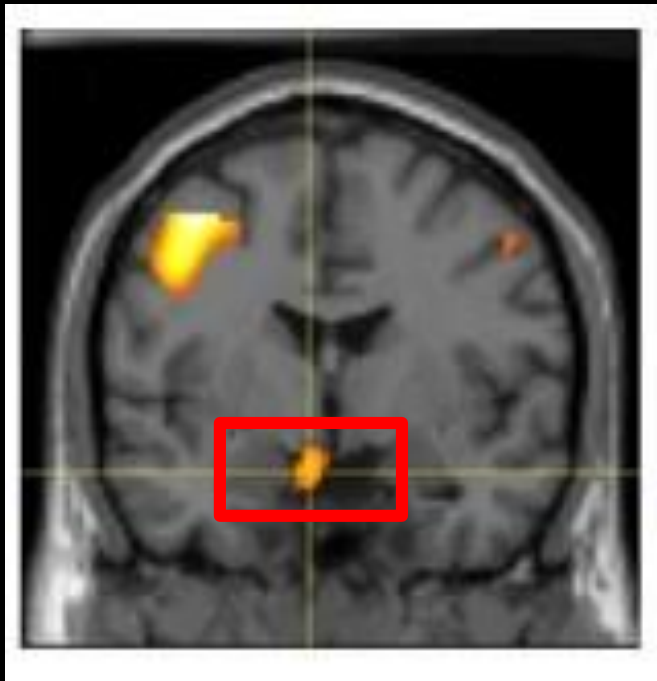
* $P < 0.05$

Liraglutide binds PVN and ARC in the brain

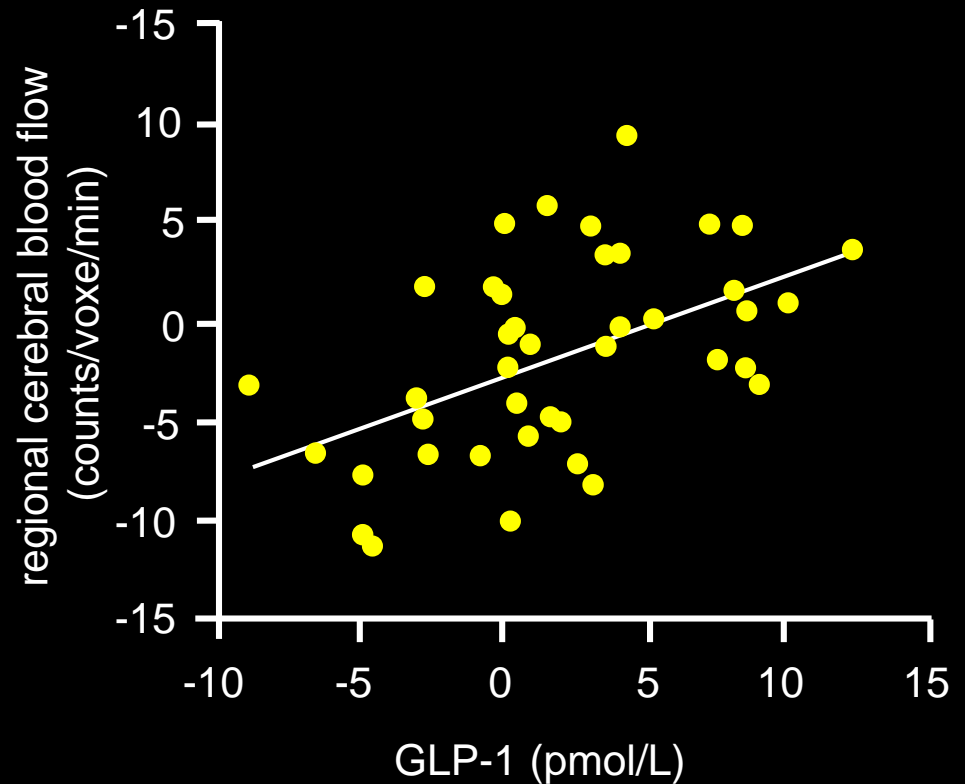


GLP-1 activates brain areas that regulate food intake

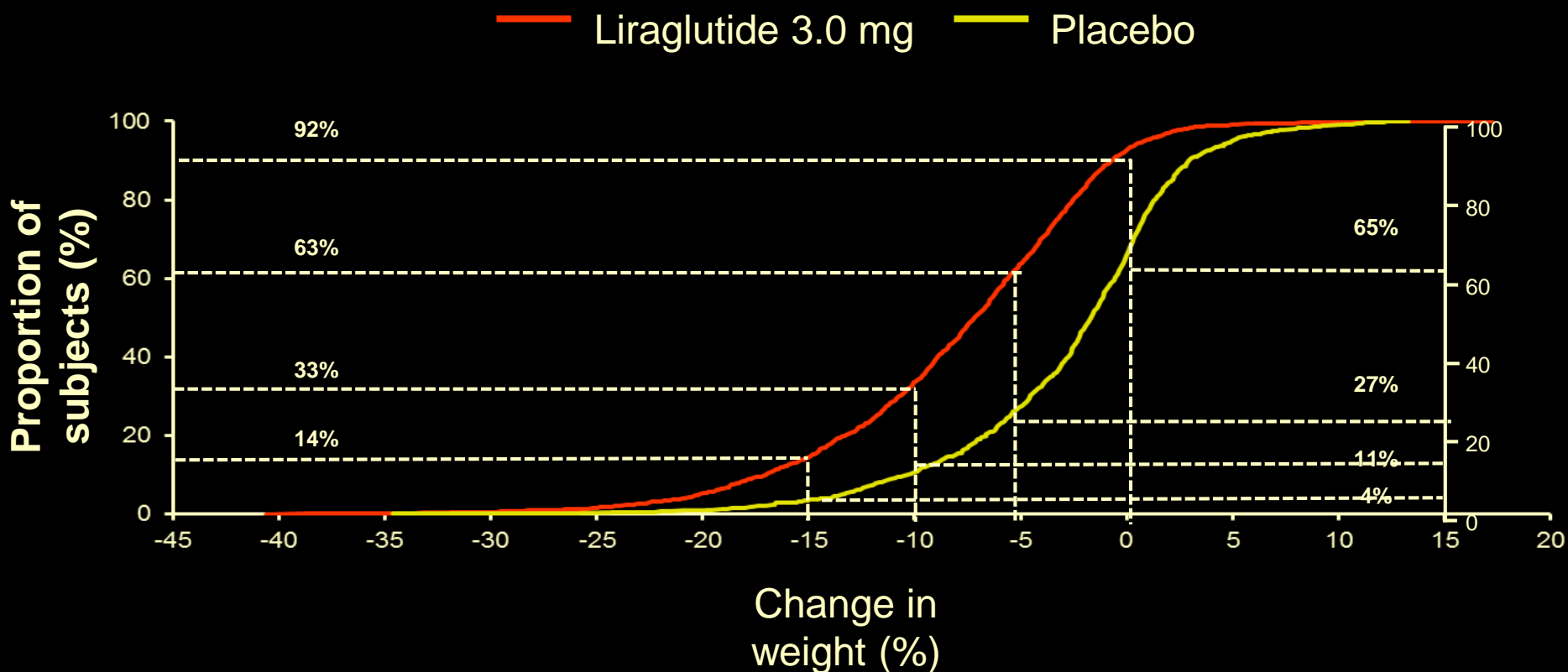
PET scan of the hypothalamus



Left dorsolateral prefrontal cortex; left middle and inferior frontal gyri, also activated

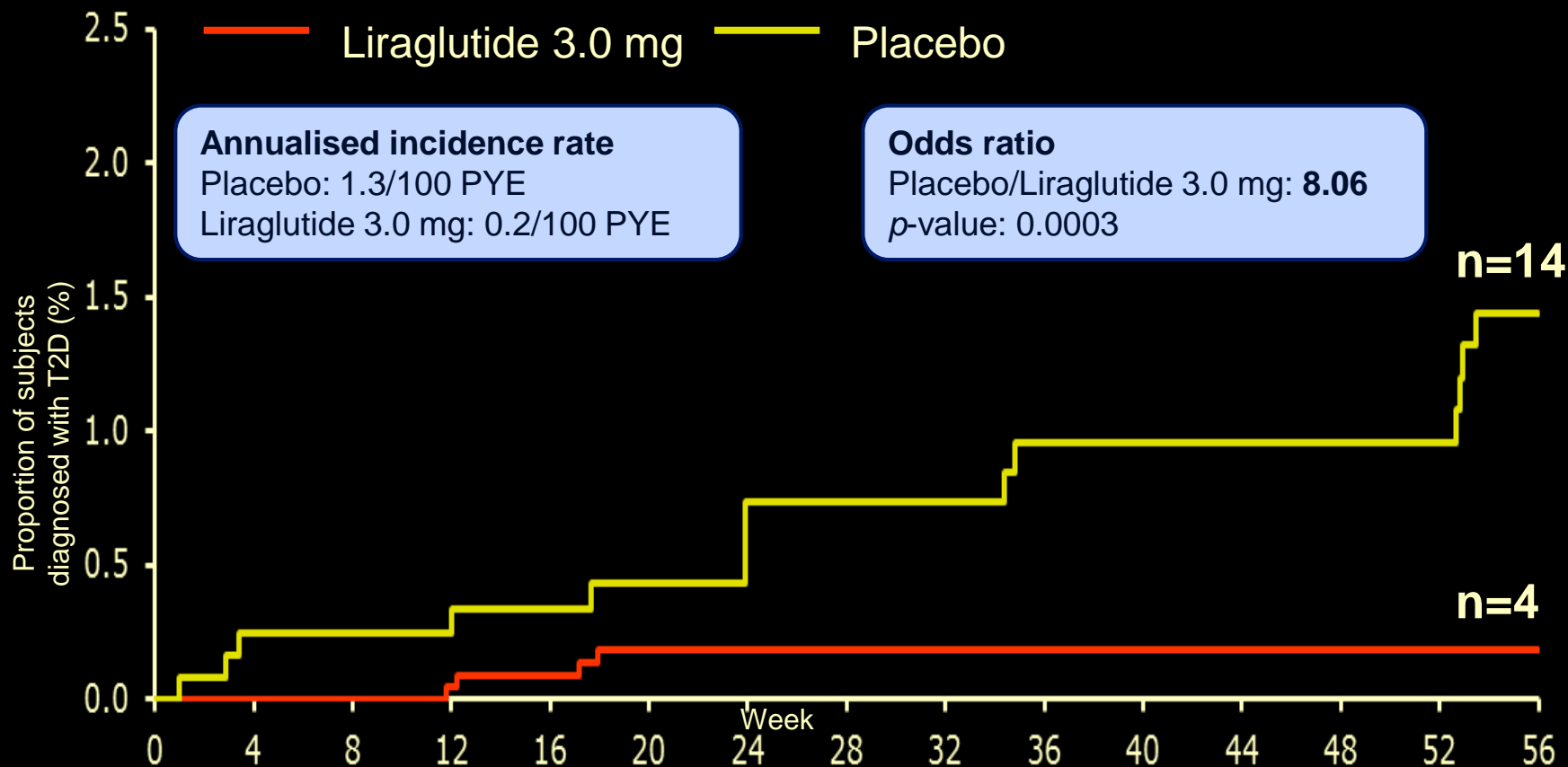


Distribution of weight loss on liraglutide 3mg Week 0–56



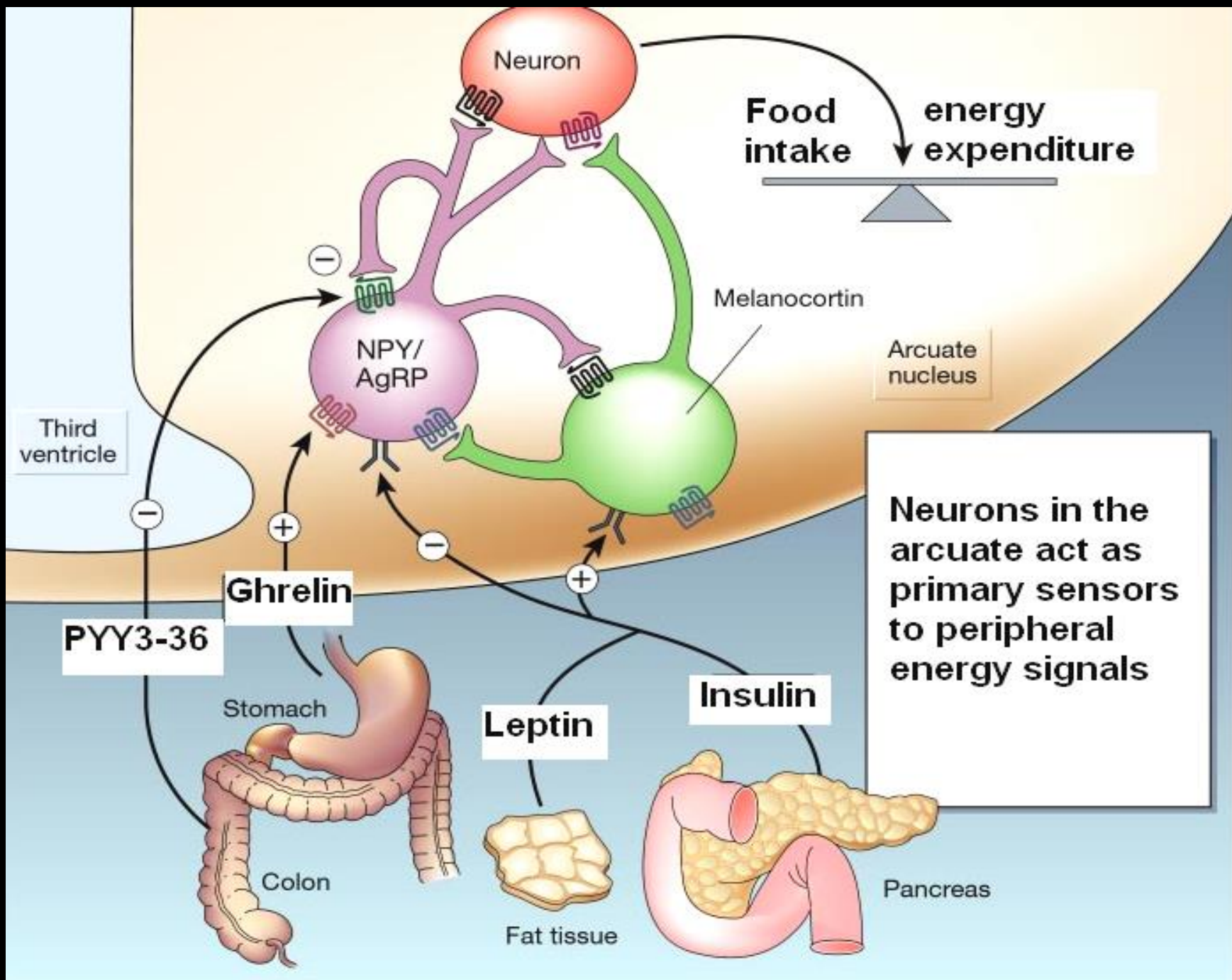
FAS, fasting visit data only, LOCF. Graphs are empirical cumulative distribution functions.
FAS, full analysis set; LOCF, last observation carried forward

Proportion of subjects diagnosed with T2D over 56 Weeks



FAS. Graph is observed proportions. Odds ratios describe the odds for diagnosis on liraglutide compared to the odds for diagnosis on placebo.

FAS, full analysis set; PYE, patient years exposure; T2D, type 2 diabetes





**METABOLIC
MEDICINE**

HEROES

Acknowledgements

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