The Influence of Fat and Protein on the Glycemic Index

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THE PANCREAPEDIA
Exocrine Pancreas Knowledge Base
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MOLECULE PAGE

GLP-1

John A. Williams

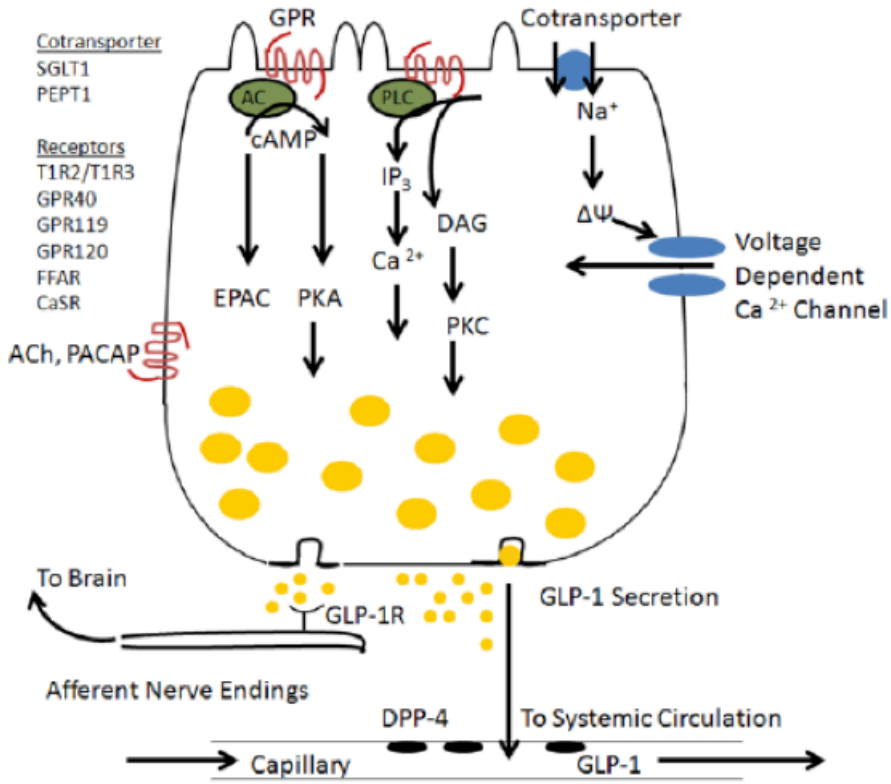

Figure 2. Regulation of GLP-1 secretion by nutrients acting via G protein coupled receptors and transporters. Nutrient receptors are located on the apical surface where exposed to luminal contents and secretion occurs at the basolateral pole where secreted GLP-1 can activate receptors on vagal afferent nerve endings or enter capillaries and travel through the systemic circulation to reach the islets. GLP-1 secretion may also be regulated by neurotransmitters such as ACh and PACAP.

American Physiological Society

AMERICAN JOURNAL OF PHYSIOLOGY
Gastrointestinal and Liver Physiology

Am J Physiol Gastrointest Liver Physiol. 2013 Feb 1; 304(3): G271–G282.
Published online 2012 Nov 29. doi: 10.1152/ajpgi.00074.2012

PMCID: PMC3566511

Sensing of amino acids by the gut-expressed taste receptor T1R1-T1R3 stimulates CCK secretion

Kristian Daly,[1] Miran Al-Rammahi,[1] Andrew Moran,[1] Marco Marcello,[2] Yuzo Ninomiya,[3] and Soraya P. Shirazi-Beechey[1]

"In summary, we have shown that T1R1-T1R3, expressed in endocrine CCK-containing cells (I cells) of mouse proximal intestine, is directly activated by a number of l-amino acids (but not their d-isomers), stimulating a pathway leading to CCK release."

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INVITED REVIEW

Pharmacology and physiology of gastrointestinal enteroendocrine cells

O. J. Mace, B. Tehan & F. Marshall

Pharma Res Per, 3(4), 2015, e00155, doi: 10.1002/prp2.155

Table 1. The principle location, EEC GPCR expression, and physiological function of gut hormones.

EEC	Hormone	GPCR(s) expressed	Location(s)	Target	Physiological function(s)
A	Ghrelin	T1R1 + T1R3, T2Rs	Stomach		Appetite control, food intake, growth hormone release
D	Somatostatin	GPBAR1, GPRC6A	Stomach, small intestine		Gastrin release (stomach)
G	Gastrin	LPAR5, GPRC6A	Stomach (pyloric antral)	Neuroendocrine cells of the gastric gland (enterochromaffin-like cells, parietal cells)	Gastric acid secretion, mucus growth; gastric contraction
I	CCK	T2Rs, FFA1, GPR120, GPBAR-1, CaSR	Proximal small intestine	Gall bladder, pancreas, gastric smooth muscle	Gallbladder contraction, inhibits stomach emptying, pancreatic enzyme secretion and food intake, stimulates pancreatic enzyme and HCO_3^- secretion
K	GIP	GPR119, GPR120, GPR40	Proximal small intestine	Pancreatic β-cells	Insulin release, gastric acid secretion, LPL activity in adipose
L	GLP-1, GLP-2, PYY, oxyntomodulin	T2Rs, T1R2 + T1R3, GPR40, GPR41, GPR43, GPR119, GPBAR-1, GPR120, CaSR, GPRC6A, SSTR5	Distal small intestine, colon	Endocrine pancreas	Nutrient uptake, intestinal motility, appetite regulation, insulin release, inhibits glucagon release, slows gastric emptying
M	Motilin	GPBAR-1	Small intestine	Smooth muscle of stomach and duodenum	Regulation of migrating myoelectric complex in pig, dog and human, gut motility
N	Neurotensin	GPR40, GPR41, GPR43, GPR120	Small (distal) and large intestine		Gastric acid secretion, biliary secretion, intestinal mucosal growth, intestinal peristalsis
P	Leptin	Nutrient receptors	Stomach		Appetite regulation; food intake
S	Secretin	Potential acid receptor	Proximal small intestine	Pancreas, stomach	Bicarbonate release, gastric acid secretion, colonic contraction, motility, pancreatic growth

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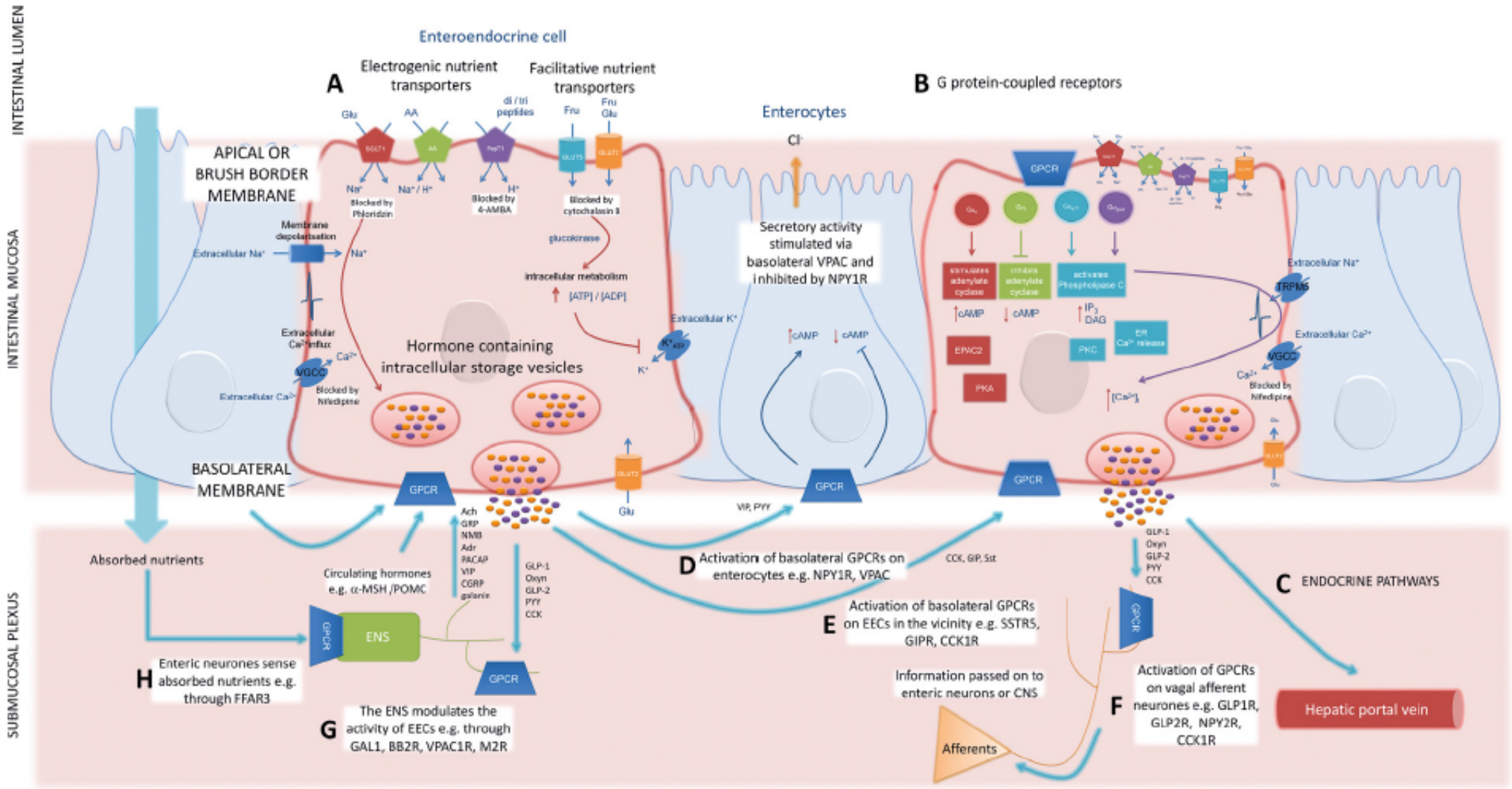

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INVITED REVIEW

Pharmacology and physiology of gastrointestinal enteroendocrine cells

O. J. Mace, B. Tehan & F. Marshall

Pharma Res Per, 3(4), 2015, e00155, doi: 10.1002/prp2.155

" "Roux-en-Y" in a pill remains the holy grail of harnessing the enteroendocrine system for the treatment of metabolic disease."

Synergism by individual macronutrients explains the marked early GLP-1 and islet hormone responses to mixed meal challenge in mice

L. Ahlkvist [a,*], J. Vikman [a], G. Pacini [b], B. Ahrén [a]

Regulatory Peptides 178 (2012) 29–35

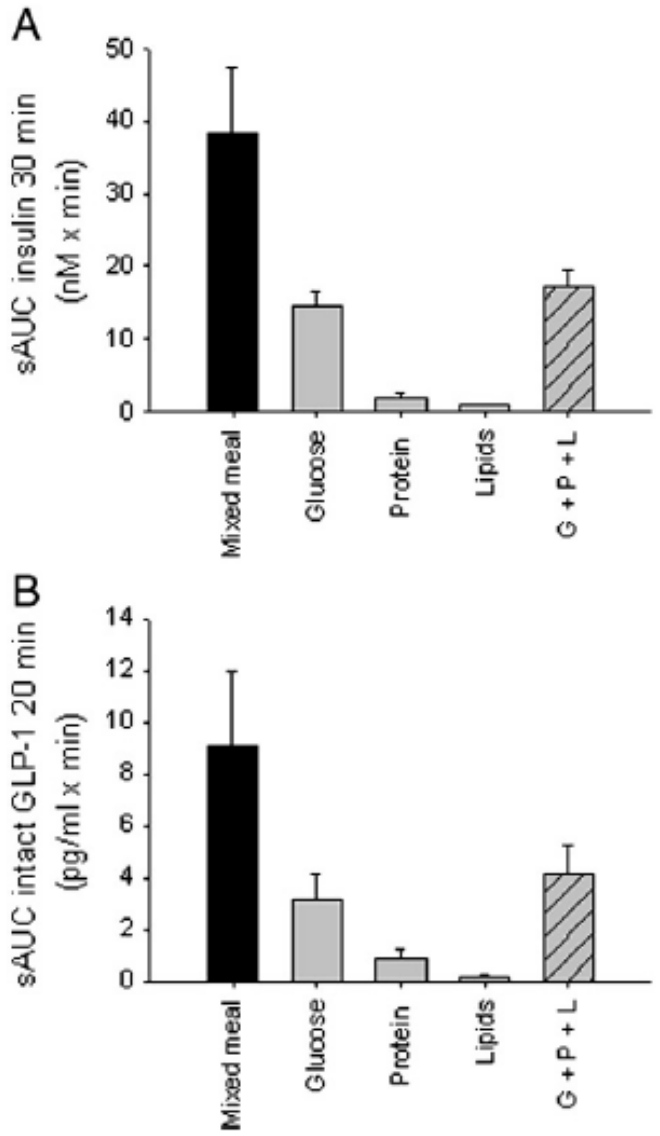

Fig. 4. Suprabasal area under the curve (sAUC) of insulin (A, 0–30 min) and intact GLP-1 (B, 0–20 min) after oral gavage of mixed meal (0.285 kcal) versus the sum of individual responses to glucose (0.171 kcal), protein (0.057 kcal) and lipids (0.057 kcal) in 5 h fasted and anesthetized C57BL/6J mice. Means±S.E.M. are shown, n=10–12 mice per group.

Prevention and management of type 2 diabetes: dietary components and nutritional strategies

Sylvia H Ley, Osama Hamdy, Viswanathan Mohan, Frank B Hu

Lancet 2014; 383: 1999–2007

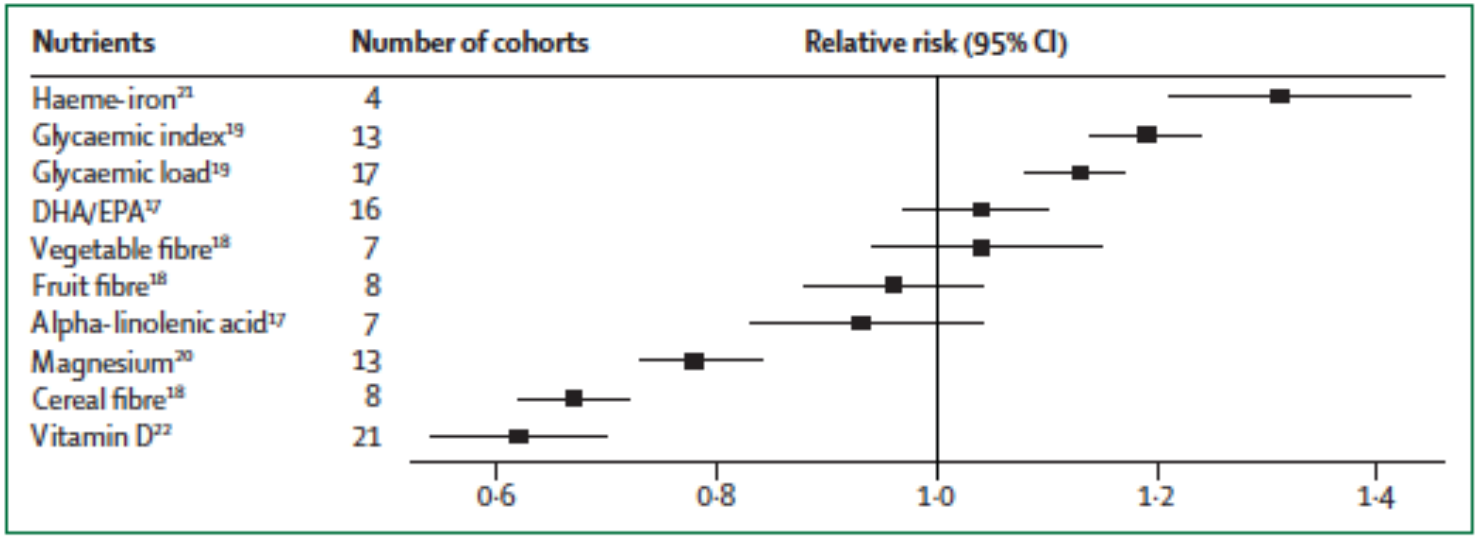

Figure 2: **Summary of meta-analyses of prospective cohort studies of nutrient intake and glycaemic variables and type 2 diabetes**

DHA=docosahexaenoic acid. EPA=eicosapentaenoic acid. Relative risks are a comparison of extreme categories, except for DHA/EPA (per 250 mg per day increase) and alpha-linolenic acid (per 0·5 g per day). All nutrients and glycaemic variables were assessed from dietary intake, except vitamin D for which blood 25-hydroxyvitamin D was used.

Prevention and management of type 2 diabetes: dietary components and nutritional strategies

Sylvia H Ley, Osama Hamdy, Viswanathan Mohan, Frank B Hu

Lancet 2014; 383: 1999–2007

	Main components	Diabetes prevention	Diabetes management
Mediterranean diet	High consumption of minimally processed plant-based foods; olive oil as the principal source of fat; low-to-moderate consumption of dairy products, fish, and poultry; low consumption of red meat; and low-to-moderate consumption of wine with meals	Mediterranean dietary patterns were associated with lower risk of type 2 diabetes in prospective cohort studies and RCTs[38,39,42,43]	Mediterranean diets compared with a conventional diet for diabetes management improved glycaemic control and insulin sensitivity, and reduced risk of CVD[43–46]
DASH	Rich in vegetables, fruits, and low-fat dairy products, including wholegrains, poultry, fish, and nuts; lower in saturated fat, red meat, sweets, and sugar containing beverages; and reduced in sodium	Adherence to the DASH diet was associated with lower risk of diabetes[47,48]	The DASH diet with 2400 mg per day sodium restriction had beneficial effects on glycaemic control and CVD risk factors[48,50]
Vegetarian and vegan	Vegan, diets devoid all animal-derived products; vegetarian diets, diets devoid of some animal products including lacto-ovo (consuming dairy or eggs), pesco (consuming fish, eggs, or dairy), semi (consuming all but no red meat and poultry)	Vegan, lacto-ovo, and semi-vegetarian diets were associated with lower risk of type 2 diabetes[51]	Improved glycaemic control or CVD risk was not consistently reported,[52,53] and the effect of vegetarian diets was difficult to isolate because calorie-restriction was often implemented
Dietary guidelines (AHEI)	Indices of the diet quality created on the basis of foods and nutrients predictive of chronic disease risk, including greater intake of vegetables and fruits, wholegrains, nuts and legumes, long-chain omega-3 fatty acids, and PUFAs; lower intake of sugar-sweetened beverages and fruit juice, red/processed meat, trans-fat, sodium; and moderate alcohol consumption	Adherence to high-quality diet assessed by AHEI was strongly associated with lower risk of diabetes[54]	NA
Prudent pattern	Dietary patterns higher in fruits, vegetables, wholegrains, legumes, and vegetable fats and lower in red meats, refined grains, and sugared soft drinks	Prudent dietary patterns over Western dietary patterns were associated with lower type 2 diabetes risk[55–60]	NA
Moderately low carbohydrate diet	Dietary patterns that restrict consumption of carbohydrates by increasing intake of fats and protein from animal or plant food sources	A diet moderately low in total carbohydrate but high in plant-based protein and fat was associated with lower diabetes risk, but a diet low in carbohydrate and high in animal fat and protein was associated with higher risk[14]	Carbohydrate restrictions improved glycaemic control and blood lipids and led to greater weight loss compared to conventional control diets[52]

RCT=randomised controlled trial. CVD=cardiovascular disease. DASH=dietary approaches to stop hypertension. AHEI=alternate healthy eating index. PUFA=polyunsaturated fatty acid. NA=not available.

Table 1: **Summary of observational and intervention studies on dietary patterns for diabetes prevention and management**

frontiers in Endocrinology

ORIGINAL RESEARCH
published: 16 September 2015
doi: 10.3389/fendo.2015.00139

Effects of a macro-nutrient preload on type 2 diabetic patients

*Chun-Jun Li[1], Gunnar Norstedt[2], Zhao-Gian Hu[1], Pei Yu[1], Dai-Qing Li[1], Jing Li[1], Qian Yu[1], Magnus Sederholm[3] and De-Min Yu[1]**

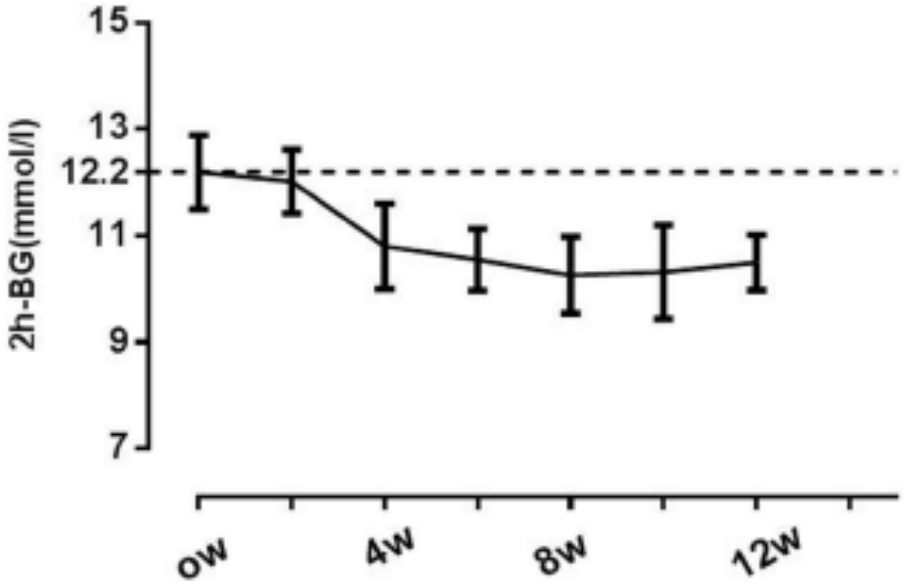

FIGURE 2 | Changes in postprandial glucose throughout the study. A lowering of 2 h-BG of ≥1.9 mmol/L was used as a cut-off separating 67% of the subjects as responders. Responders ($n = 19$) are indicated with -♦-. Non-responders ($n = 8$) are indicated with -▲-.

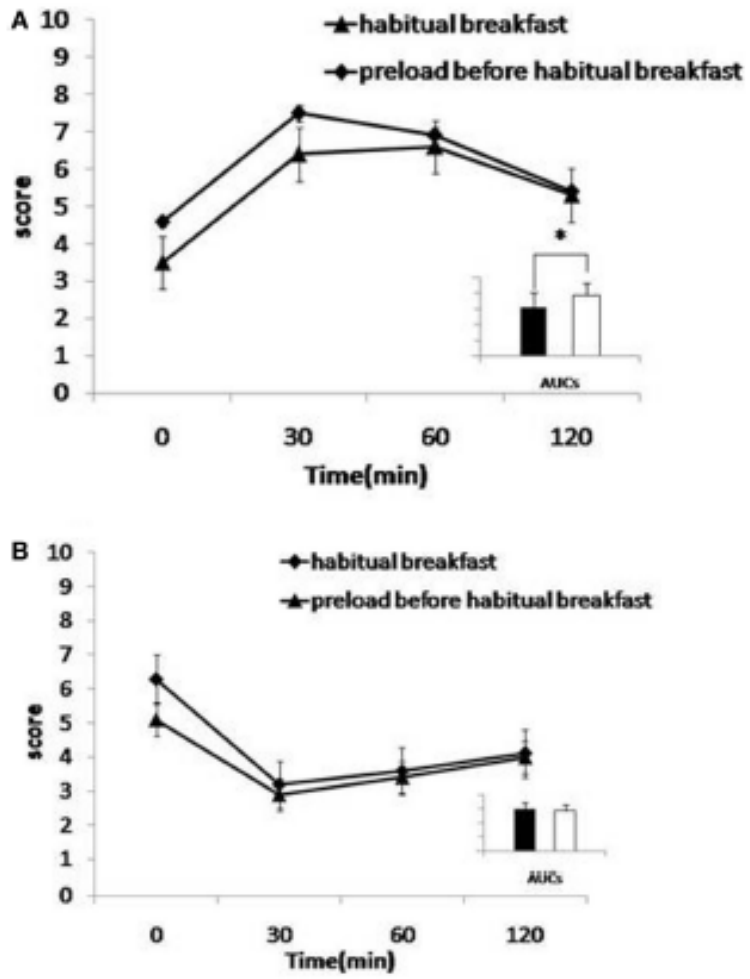

FIGURE 1 | (A,B) Effects of preload on satiety **(A)** and hunger **(B)**. Mean visual analog scale (VAS) subjective scores for satiety **(A)** and hunger **(B)** for habitual breakfast. Habitual breakfast is indicated by -♦- and Preload before habitual breakfast by -▲-. Inserts: area under the curve histograms for 0–120 min are shown, habitual breakfast (open bars), and preload before habitual breakfast (filled bars). The time-by-interaction was statistically significant for satiety ($p < 0.05$, 0–120 min).

Available online at www.sciencedirect.com
ScienceDirect
Journal of Nutritional Biochemistry 25 (2014) 36–43
Journal of Nutritional Biochemistry

Mechanism of action of pre-meal consumption of whey protein on glycemic control in young adults☆,☆☆

Tina Akhavan[a], Bohdan L. Luhovyy[a], Shirin Panahi[a], Ruslan Kubant[a], Peter H. Brown[b], G. Harvey Anderson[a,*]

Table 1
Mean plasma concentrations of glucose, insulin, C-peptide, and amylin after the preloads[1]

Biomarkers		Control	10 g Glucose	20 g Glucose	10 g WP	20 g WP	*P (two-way ANOVA)*		
							Preload	Time	Interaction
Glucose (mmol/L)	Pre-meal[2]	5.0±0.1^{c}	6.5±0.2^{b}	6.8±0.3^{a}	5.1±0.1^{c}	5.3±0.1^{c}	<.0001	<.0001	<.0001
	Post-meal[3]	6.0±0.1^{a}	5.7±0.1^{b}	6.0±0.1^{b}	5.7±0.1^{b}	5.6±0.1^{b}	.0006	<.0001	<.005
	Total[4]	5.7±0.1^{b}	6.0±0.1^{a}	6.0±0.1^{a}	5.5±0.1^{c}	5.5±0.1^{c}	<.0001	<.0001	<.0001
Insulin (pmol/L)	Pre-meal	36.4±3.8^{d}	153.1±16.3^{b}	207.9±24.3^{a}	82.8±9.1^{c}	106.0±13.6^{c}	<.0001	<.0001	<.0001
	Post-meal	229.8±11.5^{bc}	240.5±11.8^{ab}	266.6±13.4^{a}	218.1±11.3^{bc}	208.5±9.4^{c}	.0003	<.0001	NS
	Total	170.3±11.9^{c}	213.6±10.4^{b}	248.6±12.1^{a}	176.5±10.3^{c}	177.0±9.0^{c}	<.0001	<.0001	<.0001
C-peptide (pmol/L)	Pre-meal	530.7±24.2^{d}	1081.8±73.8^{b}	1280.3±112.3^{a}	772.4±50.1^{c}	847.8±48.9^{c}	<.0001	<.0001	<.0001
	Post-meal	1604.7±47.7^{bc}	1725.8±45.7^{b}	2024.9±63.4^{a}	1589.8±44.4^{c}	1558.2±40.7^{c}	<.0001	<.0001	.03
	Total	1274.2±59.4^{c}	1527.6±48.6^{b}	1795.8±65.0^{a}	1338.3±50.6^{c}	1339.6±45.3^{c}	<.0001	<.0001	<.0001
Amylin (pM)	Pre-meal	18.5±2.6^{b}	27.3±3.5^{a}	28.7±3.6^{a}	21.3±2.2^{b}	26.7±3.5^{a}	<.0001	.0004	.002
	Post-meal	35.7±2.8	38.2±3.1	39.5±3.5	36.4±2.6	35.8±3.3	NS	.006	NS
	Total	28.3±2.3^{c}	33.5±2.4^{a}	34.9±2.6^{a}	29.9±2.0^{bc}	31.9±2.5^{ab}	.0002	<.0001	<.005

[1] All values are± S.E.M. n=8. Data were analyzed for pre-meal, post-meal and total for preload, time, and preload x time interaction by 2-factor ANOVA (Proc Mixed) and significance was assessed using Tukey's post hoc (means in the same row with different superscripts^{a,b,c} are significantly different, P<.05 for all). NS (not significant).
[2] Pre-meal values are means of all plasma concentrations before the test meal and calculated from 0–30 min.
[3] Post-meal values are means of all plasma concentrations after the test meal and calculated from 50–230 min for plasma glucose, insulin and C-peptide and from 60–230 for plasma amylin.
[4] Total values are means of all plasma concentrations before and after the test meal and calculated from 0–230 min.

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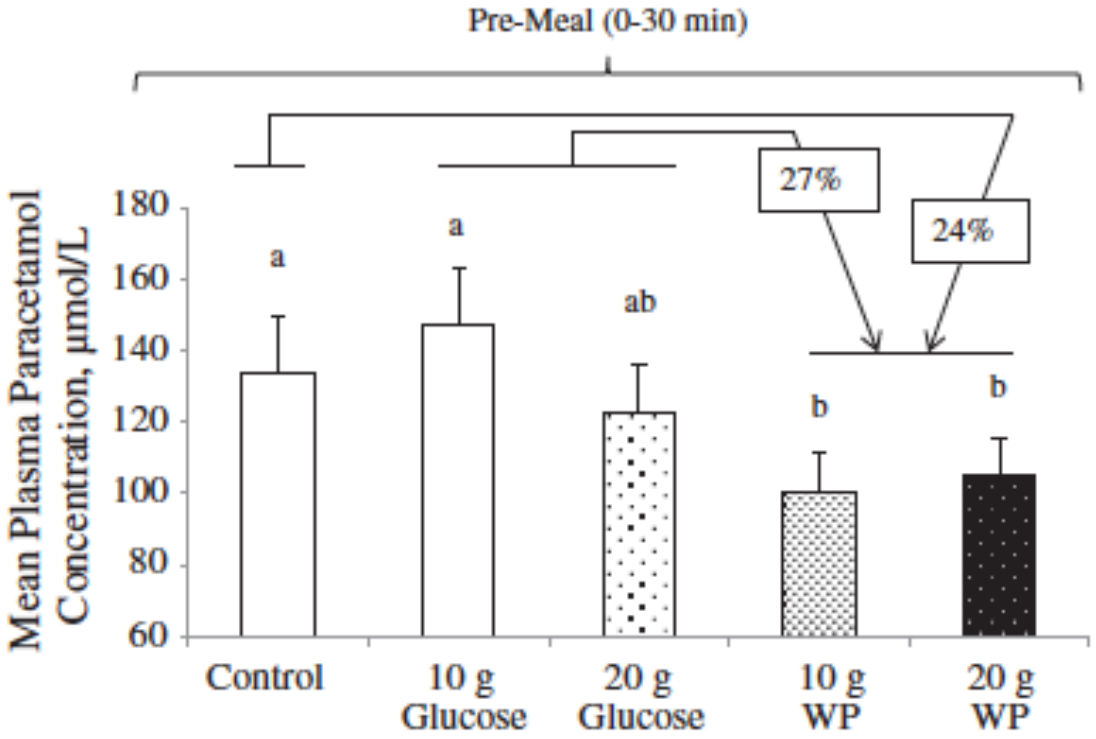
Mechanism of action of pre-meal consumption of whey protein on glycemic control in young adults☆,☆☆

Tina Akhavan[a], Bohdan L. Luhovyy[a], Shirin Panahi[a], Ruslan Kubant[a], Peter H. Brown[b], G. Harvey Anderson[a,*]



Pre-meal (0-30 min), Two-way ANOVA, Treatment, $P < .0001$, Time, $P < .0001$, Time by Treatment, *NS*

Fig. 4. Mean (±S.E.M.) pre-meal plasma concentrations of paracetamol after the whey protein and glucose preload consumption ($n=8$). Two-factor repeated-measures ANOVA followed by Tukey's post hoc was used to compare the effect of preloads (means with different superscripts at pre-meal (0–30 min) are different, $P < .0001$) and time ($P < .0001$), but no interaction effect.

Effect of a low dose whey/guar preload on glycemic control in people with type 2 diabetes-a randomised controlled trial

Peter M Clifton[1*], Claire Galbraith[2] and Leah Coles[2]

Clifton *et al. Nutrition Journal* 2014, **13**:103

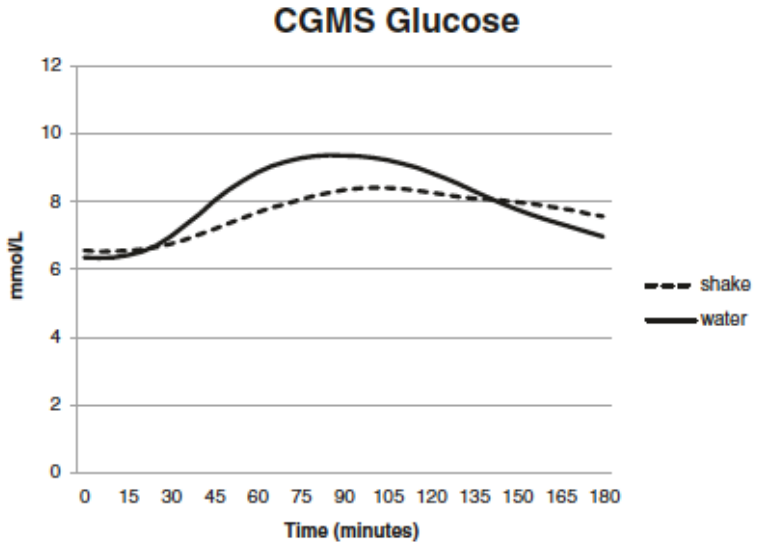


Figure 2 Blood glucose over 180 min by continuous glucose monitoring. Blood glucose values were calculated every 5 minutes. The two control and two treatment test days were averaged. The repeated measures ANOVA was significantly different (Treatment $p < 0.001$, time $p < 0.001$, time by treatment $p < 0.001$).

Conclusions: An 80 kcal whey protein/fibre preload can lower average glucose over 3 hours by 0.8 mmol/L. If used long term before at least two carbohydrate-rich meals/day this preload could lower HbA1c by up to 1%.

A protein-enriched low glycemic index diet with omega-3 polyunsaturated fatty acid supplementation exerts beneficial effects on metabolic control in type 2 diabetes

Simone M. Moosheer[a], *Wolfgang Waldschütz*[b], *Bianca K. Itariu*[a], *Helmut Brath*[b], *Thomas M. Stulnig*[a,*]

PRIMARY CARE DIABETES 8 (2014) 308–314

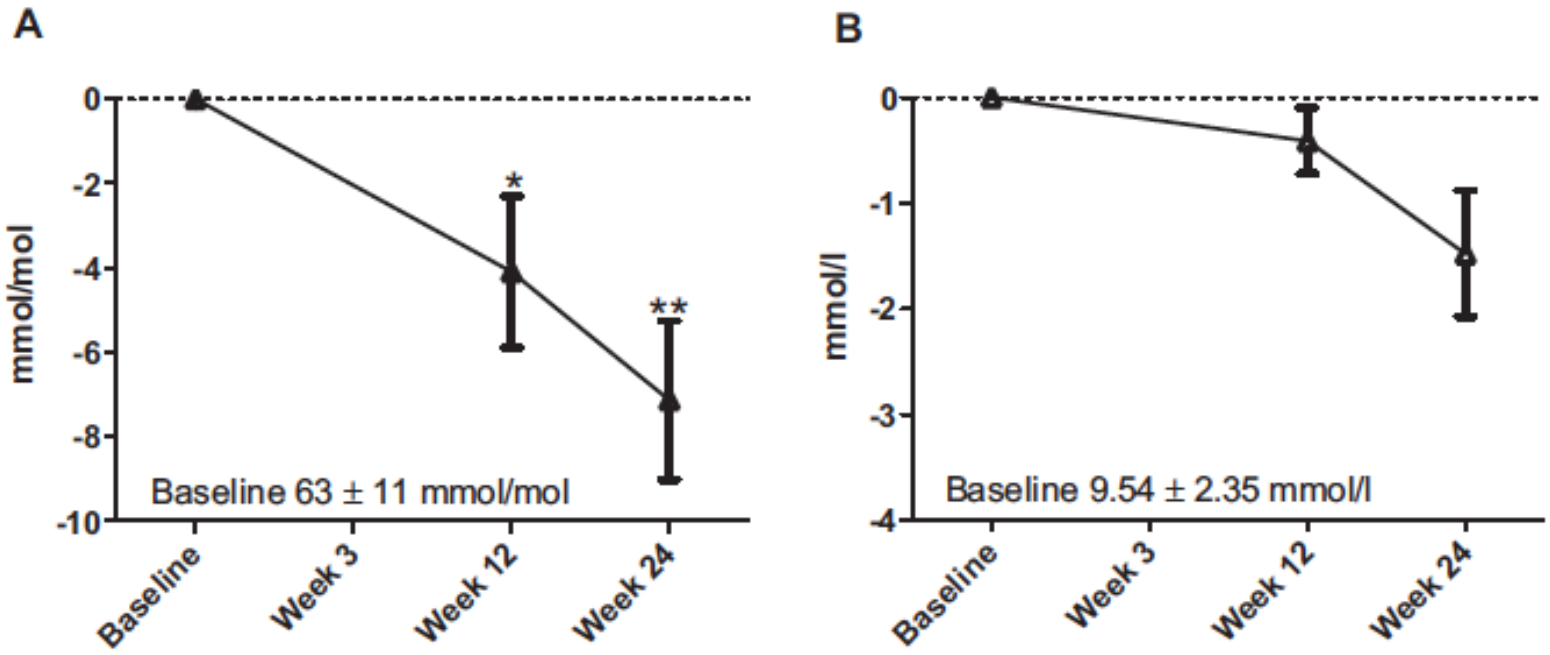
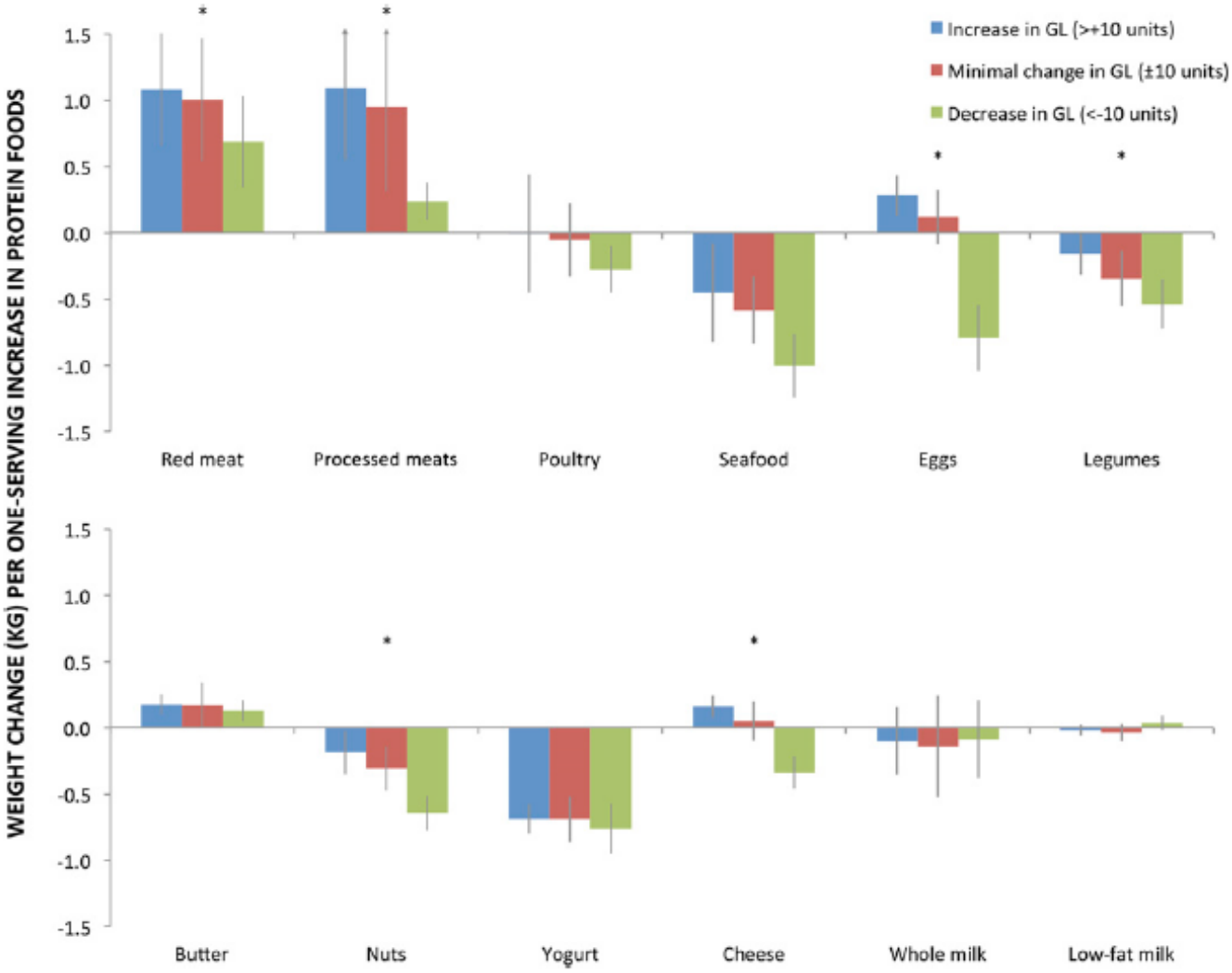


Fig. 1 – Changes in glycemic control. Differences ± SEM to baseline are given for the primary efficacy parameter HbA1c (A) and fasting plasma glucose (B). Statistical significance is indicated by asterisks with *, $P < 0.05$; **, $P < 0.01$.

Changes in intake of protein foods, carbohydrate amount and quality, and long-term weight change: results from 3 prospective cohorts[1–4]

Jessica D Smith, Tao Hou, David S Ludwig, Eric B Rimm, Walter Willett, Frank B Hu, and Dariush Mozaffarian

Am J Clin Nutr 2015;101:1216–24.



European Journal of Clinical Nutrition (2014) **68**, 1055–1059

www.nature.com/ejcn

ORIGINAL ARTICLE

Estimating insulin demand for protein-containing foods using the food insulin index

KJ Bell[1], R Gray[2], D Munns[2], P Petocz[3], G Howard[2], S Colagiuri[1] and JC Brand-Miller[1]

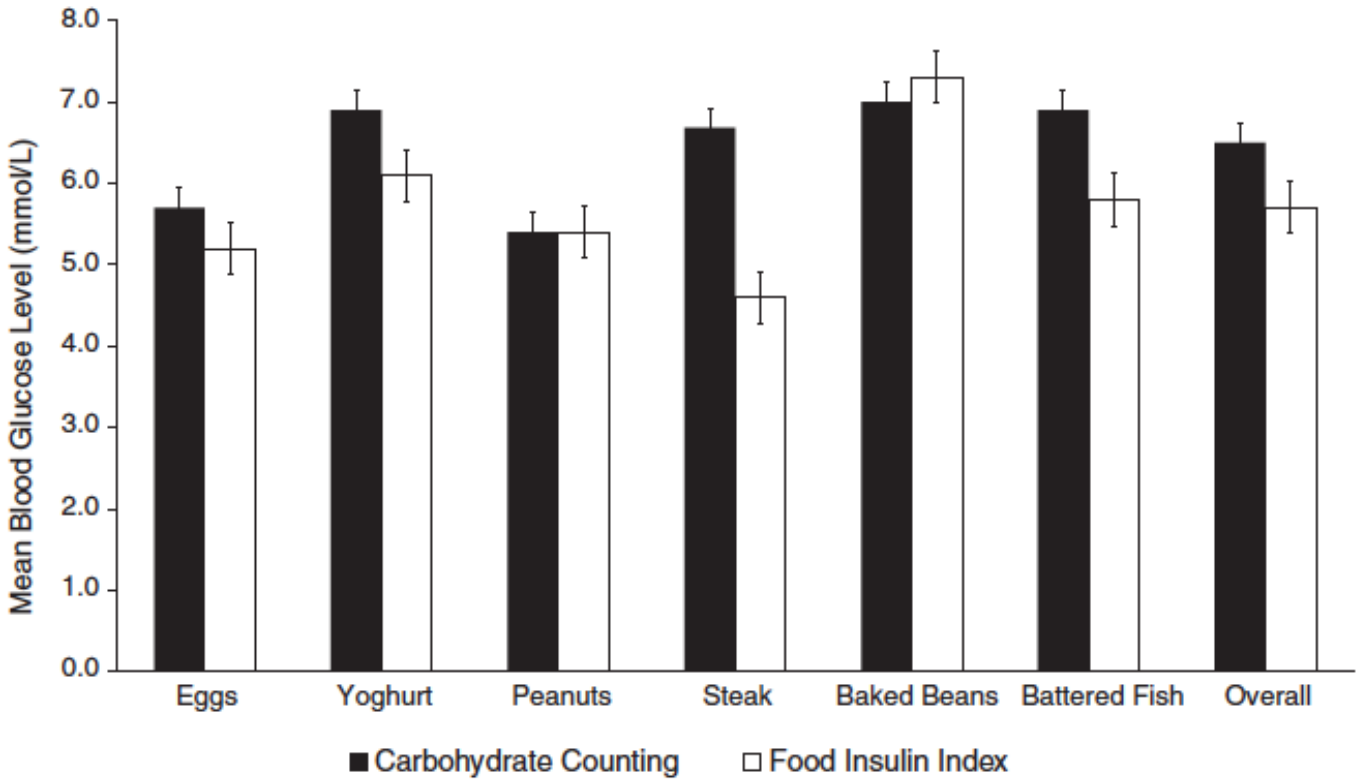


Figure 1. Mean ± s.e.m. blood glucose level after consumption of six foods in 11 subjects with type 1 diabetes.

OPEN

International Journal of Obesity (2015) 39, 721–726

www.nature.com/ijo

REVIEW

The role of higher protein diets in weight control and obesity-related comorbidities

A Astrup[1], A Raben[1] and N Geiker[2]

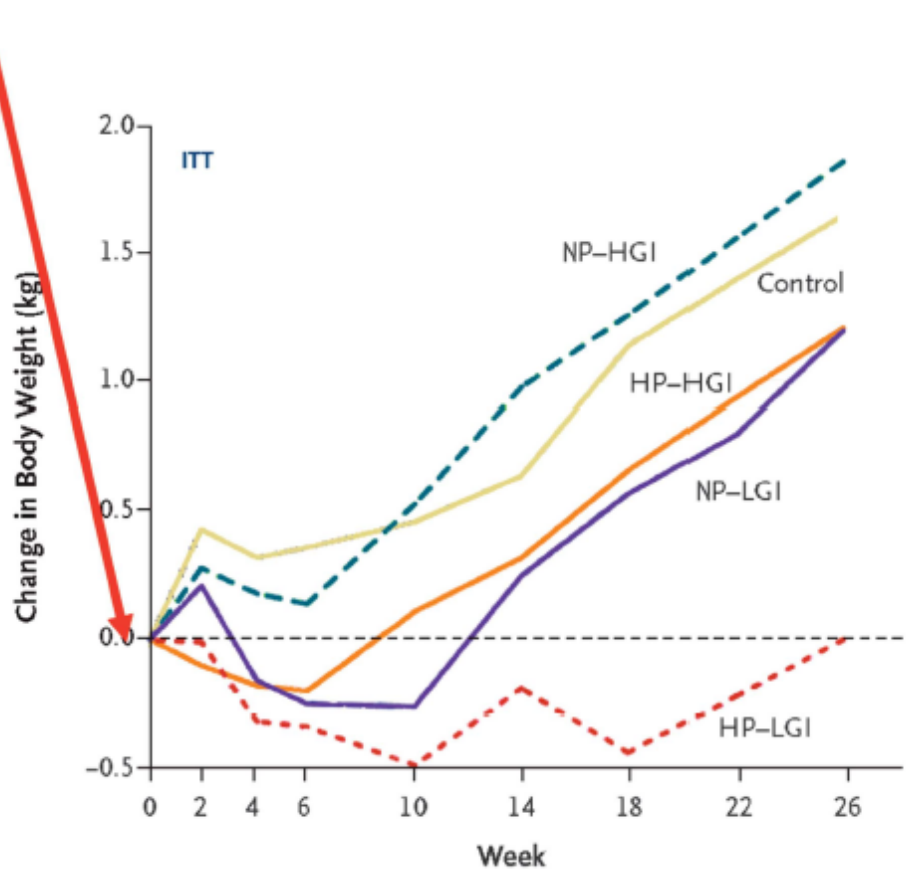


Figure 1. After an ~11 kg weight loss among the adult obese parents achieved by a 8-week 800 kcal/day diet, the entire family was randomized to different *ad libitum* diets with either low or high glycemic index (LGI or HGI), in combination with either normal or high protein (NP or HP). Both LGI and HP reduced weight regain significantly, and the combination of LGI and HP exerted an additive effect that completely prevented weight regain during the 6 months following the initial weight loss. The overweight and obese children in the LGI-HP group lost body fat spontaneously without adverse effect of growth or risk factors.

Conclusions

- The influence of individual macronutrients upon glycaemia is the result of a very complex interplay of receptors, second messengers, neurotransmitters and hormones.
- Protein and fat alter the glycaemic response of a carbohydrate meal.
- This action may favor diabetic patients and reduce the likelihood of developing metabolic disease in healthy individuals

Conclusions

- Pasta meals that contain fat and some protein may further improve on the already low glycemic index of this carbohydrate-rich food.

- This type of synergistic interaction between nutrients is best put to practice in dietary patterns such as the Mediterranean diet.

Food synergy: an operational concept for understanding nutrition[1–4]

David R Jacobs Jr, Myron D Gross, and Linda C Tapsell

Am J Clin Nutr 2009;89(suppl):1543S–8S.

In this way, once it is clear that deficiency diseases are being avoided, and as scientists continue to discuss nutrition from a nutrient perspective, the public may be better served by focusing on whole foods than on nutrient interpretations of them.