

Food Processing and Gut Metabolic Responses

By **Gabor Erdosi**

MSc Molecular Biology, MBA; R&D Consultant

Background in metabolic profiling, industrial biotech (food processing), surgical procedures

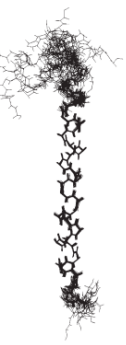
Food As Medicine Lecture Series, Harvard Medical School, January 26th 2021

Primary concepts

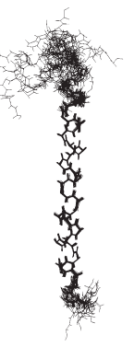
Speed and small intestinal region of food absorption largely determine metabolic, and eventually, health outcomes. The presentation is arranged around this principle.

When talking about food processing, an argument against its role is that 'processing' cannot be properly defined. Another one that often comes up is that humans have been processing their food for hundreds of thousands of years. Some of the main questions raised by this presentation therefore will be:

- Are all kinds of processing created equal?
- What has changed about processing over the last few hundred years or so, and do these changes have to do anything with the epidemic of metabolic diseases humanity has been experiencing lately?



What have we done?



Industrial food processing can involve

- Disruption of original structure, e.g. milling/grinding, juicing, (cooking)
- Predigestion: partial or full hydrolysis of polysaccharides, proteins.
- Use of additives: emulsifiers, stabilizers, shelf life improving compounds, antioxidants, texture improvers, etc. (E968: erythritol)
- Complete reformulation from the ingredients generated above.

Efforts to identify the effects of (ultra-)processing

It has been long suspected that the departure from natural food forms influences metabolism and health (metabolic health). However, there are vested interests and a huge complexity of food matrices and food-microbiota-host (immunity) interactions at play. Arbitrary systems have been developed to attempt classification of foods. The NOVA system. These are not based on the mechanisms of mentioned complex interactions. No wonder that associations with higher intake yield any strength in observational studies, from barely existing to sometimes rather strong ones. I have been trying to identify actual mechanisms for several years.

NOVA NOVA NOVA NOVA



Includes milling, juicing, cooking? Really?

- Group 1 - Unprocessed or minimally processed foods
- Group 2 - Processed culinary ingredients
- Group 3 - Processed foods
- Group 4 - Ultra-processed food and drink products

Endocrine anatomy of the GI system

Open Access Review

Enteroendocrine Hormone Secretion and Metabolic Control: Importance of the Region of the Gut Stimulation

by [Cong Xie](#)¹, [Karen L. Jones](#)^{1,2}, [Christopher K. Rayner](#)^{1,3} and [Tongzhi Wu](#)^{1,2,4,*}

¹ Adelaide Medical School and Centre of Research Excellence (CRE) in Translating Nutritional Science to Good Health, The University of Adelaide, Adelaide 5005, Australia

² Endocrine and Metabolic Unit, Royal Adelaide Hospital, Adelaide 5005, Australia

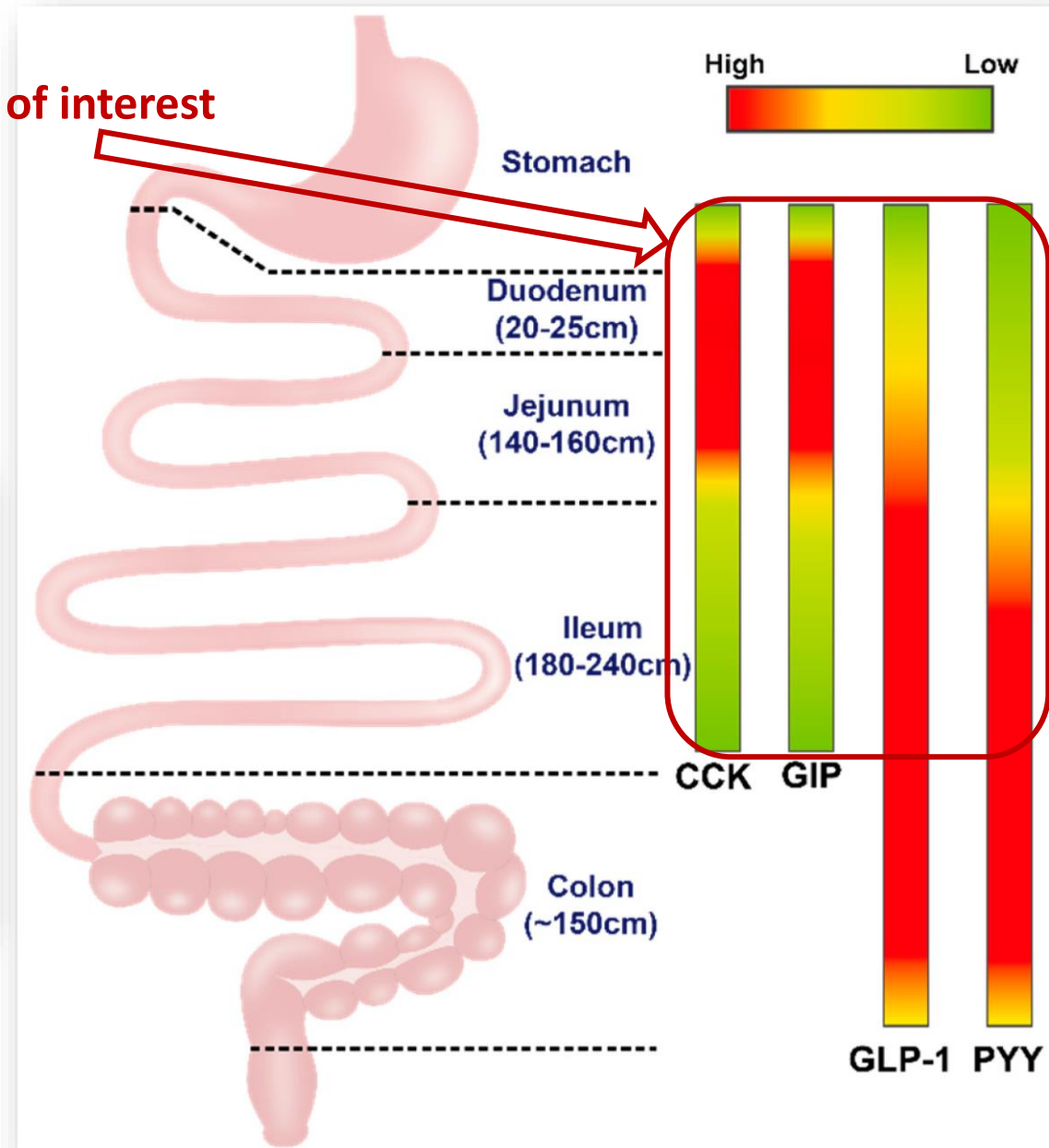
³ Department of Gastroenterology and Hepatology, Royal Adelaide Hospital, Adelaide 5005, Australia

⁴ Institute of Diabetes, School of Medicine, Southeast University, Nanjing 210009, China

* Author to whom correspondence should be addressed.

Pharmaceutics **2020**, *12*(9), 790; <https://doi.org/10.3390/pharmaceutics12090790>

Zone of interest



Nutrient sensing in the GI system

Mechanisms underlying glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 secretion

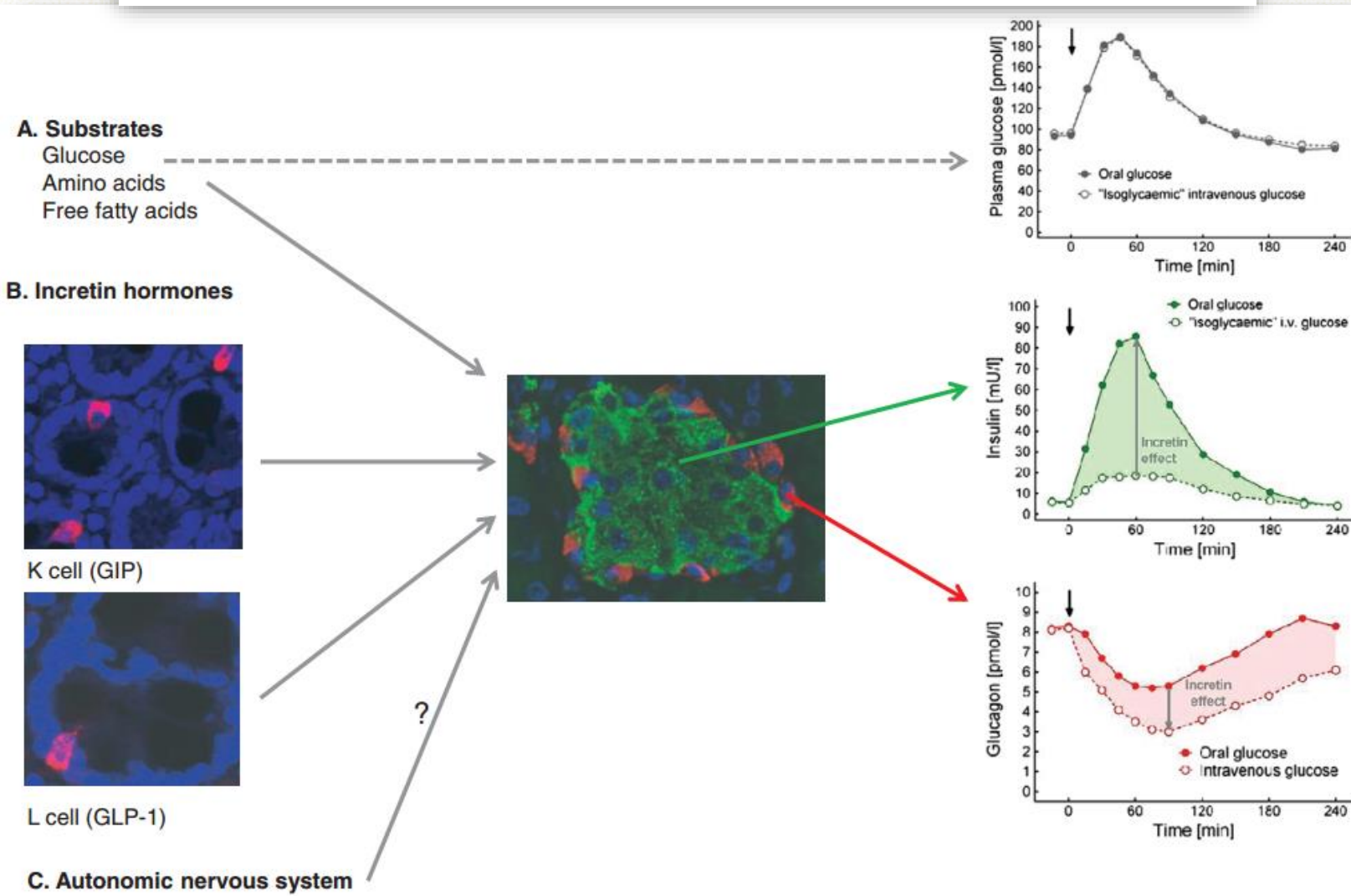
Frank Reimann Fiona M Gribble

First published: 14 March 2016 | <https://doi.org/10.1111/jdi.12478> | Cited by: 10

K/L cell distribution		Enteroendocrine stimulus	EEC Transporter/ ion channel	EEC Receptor	
		Small intestine	Monosaccharide	SLC5A1 (SGLT1)	Tas1R2/3 (?)
		Long chain fatty acid		FFAR1, FFAR4	
		Mono-acyl glycerol, acyl-ethanolamide		GPR119, CB1	
		Amino acid	B0AT1 (SLC6A19) ATA2 (SLC38A2)	CASR, GPRC6A	
		Di/tripeptide	SLC15A1 (PEPT1)	CASR	
		Bile acid		GPBAR1	
		Colon	Short chain fatty acid		FFAR2, FFAR3
		Bile acid		GPBAR1	
		Indole	Kv channels		

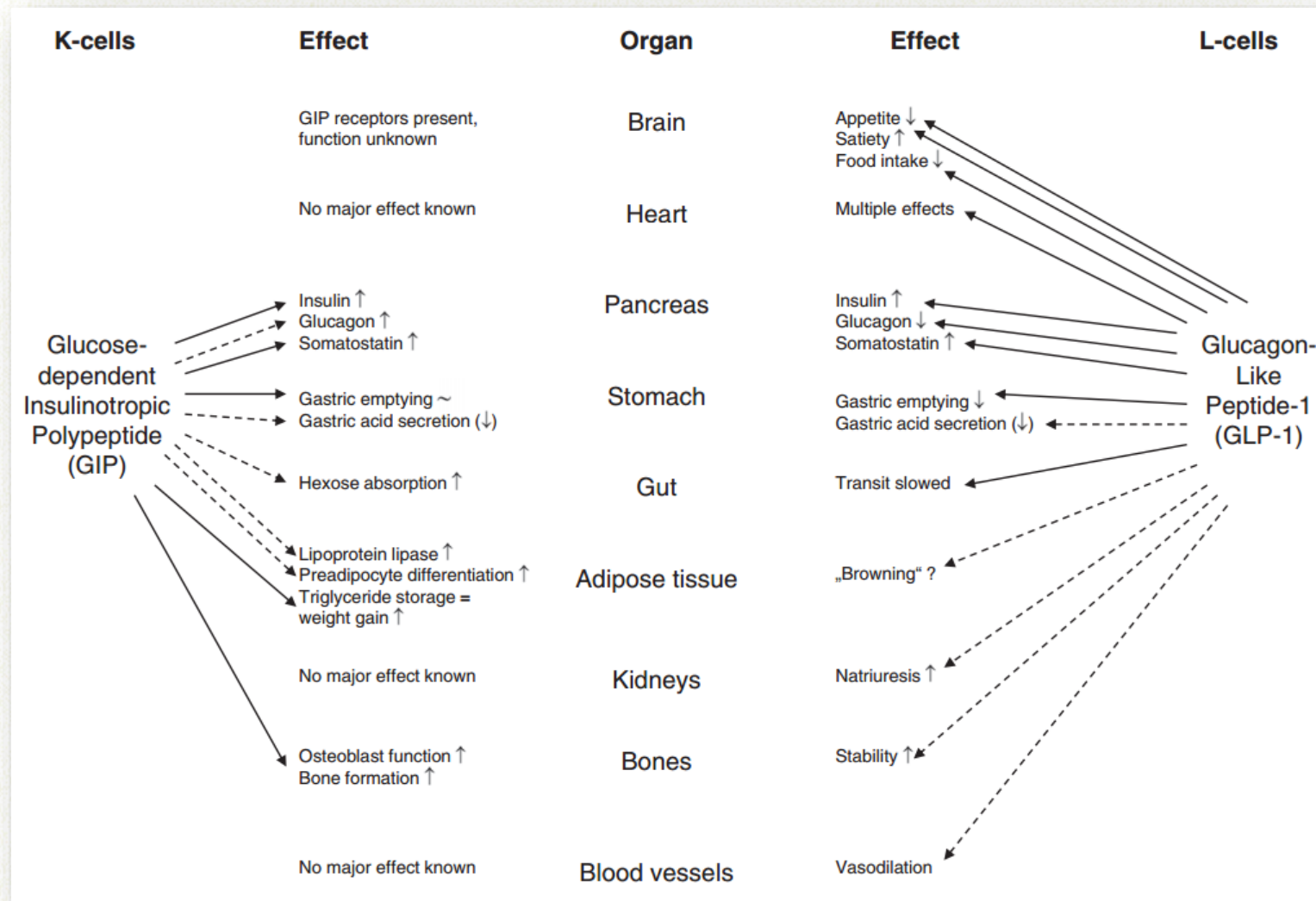
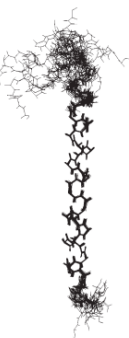
Incretin hormones: Their role in health and disease

Michael A. Nauck MD  | Juris J. Meier MD 



Incretin hormones: Their role in health and disease

Michael A. Nauck MD  | Juris J. Meier MD 

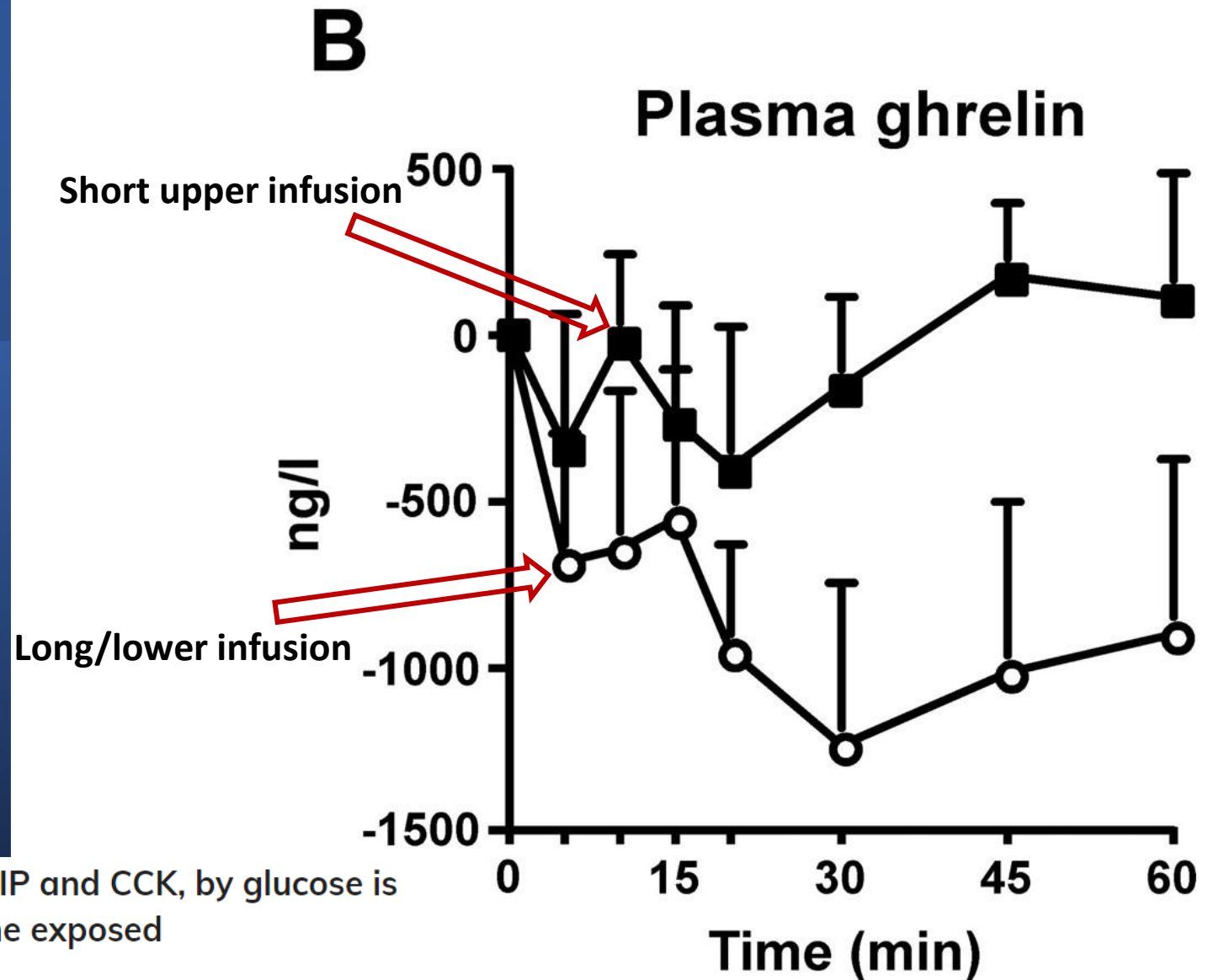


Effects of intestinal hormones on hunger-satiety signaling

<i>Gut hormone</i>	<i>Site of synthesis</i>	<i>Food intake-regulating receptor</i>	<i>Peripheral effect on food intake</i>
CCK	Intestinal L-cells	CCK _A	Decrease
Ghrelin	Stomach	GHS	Increase
PP	Pancreas/colon	Y4R	Decrease
PYY	Intestinal L-cells	Y2R	Decrease
GLP-1	Intestinal L-cells	GLP1R	Decrease
OXM	Intestinal L-cells	GLP1R?	Decrease

Abbreviations: CCK, cholecystokinin; CCK_A, cholecystokinin receptor subtype A; GHS, growth hormone secretagogue receptor; GLP-1, glucagon-like peptide-1; GLP1R, GLP-1 receptor; OXM, oxyntomodulin; PP, pancreatic polypeptide; PYY, peptide YY; Y2R, PYY Y2 receptor; Y4R, PP Y4 receptor.

Effects of intestinal hormones on hunger-satiety signaling (cont.)

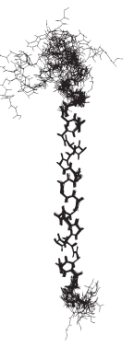


The release of GLP-1 and ghrelin, but not GIP and CCK, by glucose is dependent upon the length of small intestine exposed

Tanya J. Little, Selena Doran, James H. Meyer, Andre J. P. M. Smout, Deirdre G. O'Donovan,

... See all authors

01 SEP 2006 // <https://doi.org/10.1152/ajpendo.00099.2006>



Let us examine the effects of

- Cooking
- Juicing, milling/grinding
- Reformulation, i.e., combining refined (macro)nutrients (the only manipulation that counts as [ultra-]processed in the NOVA system)

Next, look at potential mechanisms, starting already in the gut

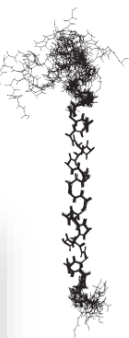
- Imbalance in hormonal signaling, disconnected from energy content.
- AAA: Accelerated appearance and absorption of nutrients driven by structural disruption of food. Profound influence on hunger-satiety signaling, nutrient/energy partitioning, inflammatory signaling.

The Effect of Cooking vs. Raw Food on Weight

Table 2
Body Mass Index by diet type^a.

% raw food	Sex	Diet type	Mean or median age (y)	n	BMI	Reference
Cooked	F	“Typical American diet”	53	7	25.4	Fontana et al., 2005
Mostly cooked	F	Mixed diet (not vegetarian)	45	23,147	24.2	Rosell et al., 2005
Mostly cooked	F	Vegetarian since birth	43	257	23.7	Rosell et al., 2005
Mostly cooked	F	Vegetarian starting between 1 and 9 years old	33	257	23.9	Rosell et al., 2005
Mostly cooked	F	Vegetarian starting between 10 and 14 years old	25	1042	23.8	Rosell et al., 2005
Mostly cooked	F	Vegetarian starting between 15 and 19 years old	27	2226	23.6	Rosell et al., 2005
Mostly cooked	F	Vegetarian starting after 19 years old	39	7880	23.5	Rosell et al., 2005
Mostly raw	F	Vegan; includes cooked vegetables	53	87	21.5	Donaldson, 2001
All raw	F	Vegetarian and raw for mean of 3.6 years	56	7	20.1	Fontana et al., 2005
All raw	F	Vegetarian			20	Hobbs, 2005
Cooked	M	“Typical American diet”	52	11	25.5	Fontana et al., 2005
Mostly cooked	M	Mixed diet (not vegetarian)	48	6103	25.2	Rosell et al., 2005
Mostly cooked	M	Vegetarian since birth	47	122	24.2	Rosell et al., 2005
Mostly cooked	M	Vegetarian starting between 1 and 9 years old	42	71	25.4	Rosell et al., 2005
Mostly cooked	M	Vegetarian starting between 10 and 14 years old	30	118	24.4	Rosell et al., 2005
Mostly cooked	M	Vegetarian starting between 15 and 19 years old	30	538	24.2	Rosell et al., 2005
Mostly cooked	M	Vegetarian starting after 19 years old	41	3011	24.3	Rosell et al., 2005
Mostly raw	M	Vegan, includes cooked vegetables	57	54	22.9	Donaldson, 2001
All raw	M	Vegetarian and raw for mean of 3.6 years	53	11	20.7	Fontana et al., 2005
All raw	M	Vegetarian			21.0	Hobbs, 2005
70–79% raw	F + M	Overall sample: 44.2% meat-eaters, 32.2% vegetarian, 23.6% vegan	Adult	66	21.1	Koebnick et al., 1999
80–89% raw	F + M	“	Adult	103	21.0	Koebnick et al., 1999
90–99% raw	F + M	“	Adult	248	20.2	Koebnick et al., 1999
100% raw	F + M	“	Adult	96	19.3	Koebnick et al., 1999

^a In studies by Rosell et al. (2005), ages are medians. Body Mass Indices (BMI) for studies by Koebnick et al. (1999) were read off a graph. For all raw-foodists in the Koebnick et al. (1999) study, the mean percentage of raw food eaten was 91% (obtained by self-report), age-adjusted BMI was 20.1 (female) and 20.7 (male).



Cooking Carbohydrate Rich Foods

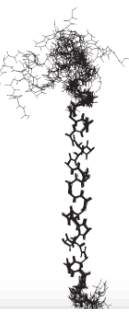


Table 3
Ileal digestibility of starch (%) in relation to processing^a.

Starch type	Starch source	<i>In vivo</i>		<i>In vitro</i>		Change in digestibility from raw to cooked	Reference
		Raw	Cooked	Raw	Cooked		
A	Wheat	71.2	96.0			+34%	Muir et al., 1995
A	Oats			74.5	95.7	+28%	Muir and O’Dea, 1992
A	Barley	93	99			+6%	Sun et al., 2006 (pigs)
B	Green banana	47.3	98.8	45.8		+109%	Langkilde et al., 2002
B	Green banana	49.4	96.9			+96%	Muir et al., 1995
B	Plantain			53.6	100	+87%	Englyst and Cummings, 1986
B	Potato		96.7	50.7		(+91%)	Englyst and Cummings, 1987
B	Potato	32–47	98			+108–206%	Sun et al., 2006 (pigs)
C	Pea	80	91			+14%	Sun et al., 2006 (pigs)

^a Data are for humans unless otherwise stated. Studies *in vivo* used collections of ileal fluids in ileostomy patients or cannulated pigs. Studies *in vitro* measure resistant starch (RS) as starch that is not hydrolysed following six hours of enzymatic hydrolysis. Silvester et al. (1995) showed that 97% of RS assayed in foods was recovered in ileal fluids.

What is the underlying mechanism? Starch liquefaction/solubilization.

Cooking lipid and protein rich foods

Cooking Increases Net Energy Gain From a Lipid-Rich Food

Emily E. Groopman,^{1,2*} Rachel N. Carmody,^{1,3} and Richard W. V.

¹Department of Human Evolutionary Biology, Peabody Museum, Harvard

²Columbia College of Physicians and Surgeons, New York, NY 10032

³FAS Center for Systems Biology, Harvard University, Cambridge, MA 0

KEY WORDS dietary fat; nuts; oil bodies; food processing

ABSTRACT Starch, protein, and lipid are three major sources of calories in the human diet. The unique and universal human practice of cooking has been demonstrated to increase the energy gained from foods rich in starch or protein. Yet no studies have tested whether cooking has equivalent effects on the energy gained from lipid-rich foods. Using mice as a model, we addressed this question by examining the impact of cooking on the energy gained from peanuts, a lipid-rich oilseed, and compared this impact against that of nonthermal processing (blending). We found that **cooking consistently increased the energy gained per calorie**, whereas blend-

ing had no fecal fat ex when peanut microstructure integrity of that otherwise effects were observed with tance of cooking humans, bo 000:000–000

Evenepoel, Pieter, Dirk Claus, Benny Geypens, Martin Hiele, Karen Geboes, Paul Rutgeerts, and Yvo Ghoo.

Amount and fate of egg protein escaping assimilation in the small intestine of humans. *Am. J. Physiol. 277 (Gastrointest. Liver Physiol. 40): G935–G943, 1999.*—Studies attempting to evaluate protein assimilation in humans have hitherto relied on either ileostomy subjects or intubation techniques. The availability of stable isotope-labeled protein allowed us to determine the amount and fate of dietary protein escaping digestion and absorption in the small intestine of healthy volunteers using noninvasive tracer techniques. Ten healthy volunteers were studied once after ingestion of a cooked test meal, consisting of 25 g of ¹³C-, ¹⁵N-, and ²H-labeled egg protein, and once after ingestion of the same but raw meal. Amounts of 5.73% and 35.10% ($P < 0.005$) of cooked and raw test meal, respectively, escaped digestion and absorption in the small intestine. A significantly higher percentage of the malabsorbed raw egg protein was recovered in urine as fermentation metabolites. These results 1) confirm that substantial amounts of even easily digestible proteins may escape assimilation in healthy volunteers and 2) further support the hypothesis that the metabolic fate of protein in the colon is affected by the amount of protein made available.

Energetic consequences of thermal and nonthermal food processing

Rachel N. Carmody^{a,1}, Gil S. Weintraub^a, and Richard W. Wrangham^{a,b}

^aDepartment of Human Evolutionary Biology, Peabody Museum, Harvard University, Cambridge, MA 02138; and ^bStellenbosch Institute for Advanced Study (STIAS), Wallenberg Research Centre at Stellenbosch University, Stellenbosch 7600, South Africa

Edited by James O'Connell, University of Utah, Salt Lake City, UT, and approved October 6, 2011 (received for review July 26, 2011)

NAS

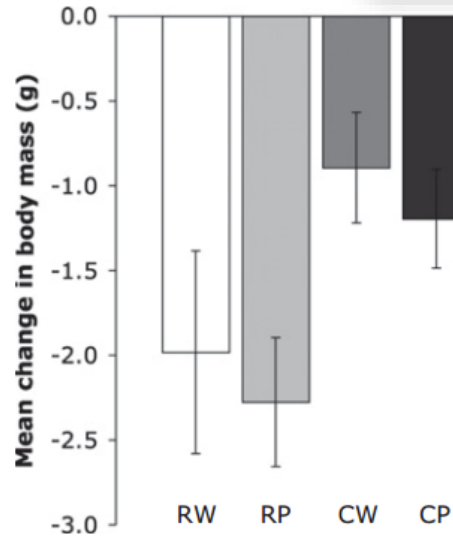


Fig. 3. Changes in body mass on meat diets. Mean cumulative change in body mass ($\pm 95\%$ CI) over 4 d in mice ($n = 16$) fed standardized ad libitum diets of organic beef (*B. taurus*) eye round served raw and whole (RW), raw and pounded (RP), cooked and whole (CW), and cooked and pounded (CP). Diets were administered based on a counterbalanced within-subjects study design.

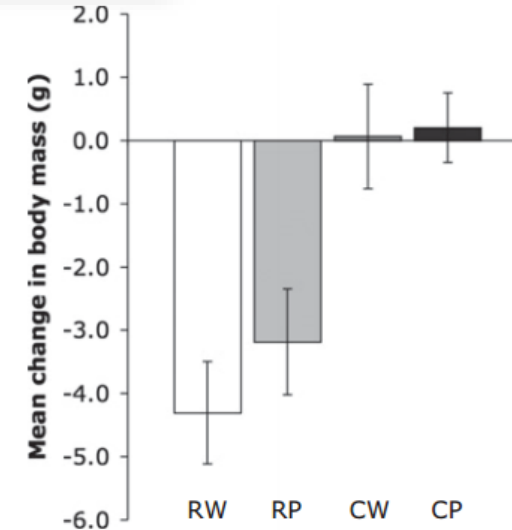
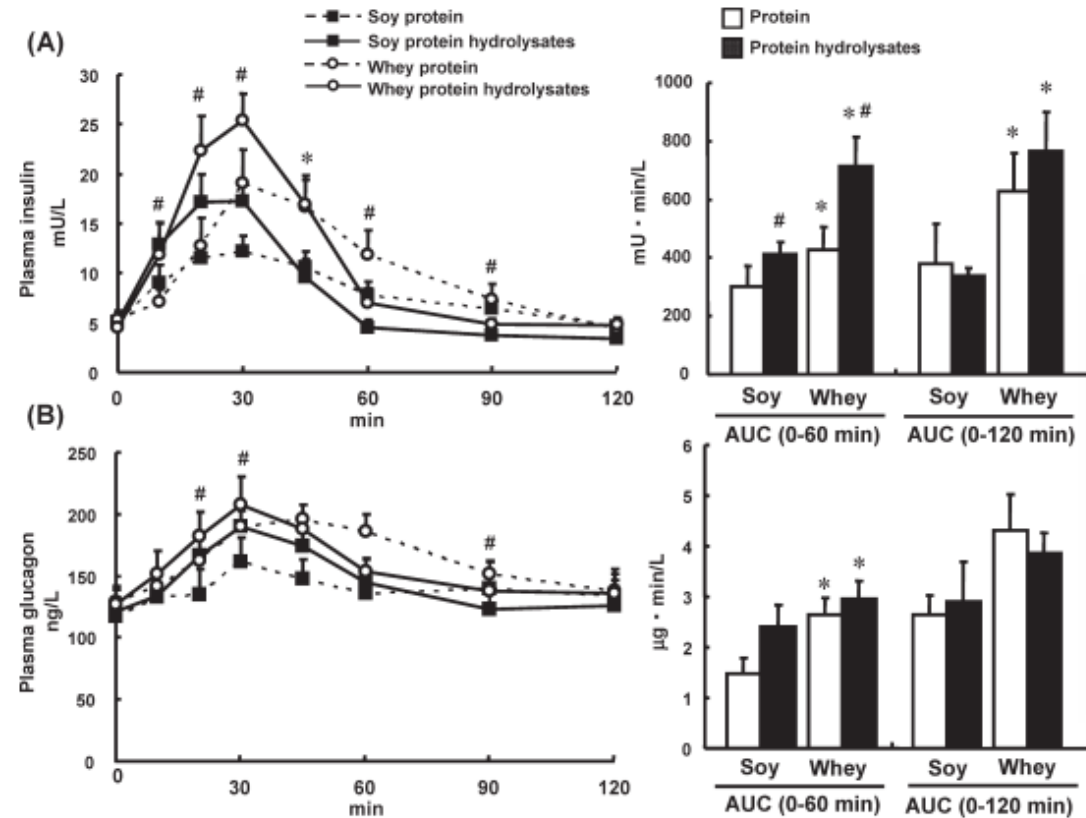
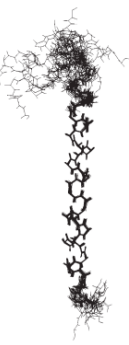


Fig. 1. Changes in body mass on tuber diets. Mean cumulative change in body mass [$\pm 95\%$ confidence interval (CI)] over 4 d in mice ($n = 17$) fed standardized ad libitum diets of organic sweet potato (*I. batatas*) served raw and whole (RW), raw and pounded (RP), cooked and whole (CW), and cooked and pounded (CP). Diets were administered based on a counterbalanced within-subjects study design.

„our results indicate that human dieters who count calories and eat similar mixed diets but cook them to different extents would experience different weight gain outcomes at comparable levels of physical activity. This prediction is consistent with recent long-term data indicating that preparation-specific factors affect the relationship between caloric consumption and weight gain in humans.”

Hydrolyzing protein



Comparison of Different Sources and Degrees of Hydrolysis of Dietary Protein: Effect on Plasma Amino Acids, Dipeptides, and Insulin Responses in Human Subjects

Masashi Morifuji*†§, Mihoko Ishizaka†, Seigo Baba†, Kumiko Fukuda†, Hitoshi Matsumoto†, Jinichiro Koga†, Minoru Kanegae† and Mitsuru Higuchi#

† Food and Health R&D Laboratories, Meiji Seika Kaisha Ltd., Saitama 350-0289, Japan

§ Graduate School of Sport Sciences

Faculty of Sport Sciences

Waseda University, Saitama 359-1192, Japan

J. Agric. Food Chem., 2010, 58 (15), pp 8788–8797

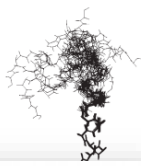
DOI: 10.1021/jf101912n

Publication Date (Web): July 8, 2010

Cite this: *J. Agric. Food Chem.* 58, 15, 8788–8797

RIS Citation

Figure 5. Plasma (A) insulin and (B) glucagon concentrations. The left-hand graphs show the plasma concentration of insulin over the 120 min study period. The right-hand graphs show the area under the curve (AUC) for the 0–60 and 0–120 min periods. Values are expressed as means ± SEM, $n = 5/\text{group}$. #, $P < 0.05$ significant difference between nonhydrolyzed protein and protein hydrolysates; *, $P < 0.05$ significant difference between dietary protein source.



Pureeing and juicing apples

The rebound fall in plasma-glucose which occurred during the second and third hours after juice, and to a lesser extent after purée, was in striking contrast to the practically steady level after apples. This finding indicates that dietary fibre plays a role in glucose homeostasis and that, after fibre-depleted food these homeostatic mechanisms may be disturbed. The purée data indicate that, surprisingly, this may also apply to foods in which fibre has merely been physically disrupted.

THE LANCET, OCTOBER 1, 1977

DEPLETION AND DISRUPTION OF DIETARY FIBRE EFFECTS ON SATIETY, PLASMA-GLUCOSE, AND SERUM-INSULIN

G. B. HABER* K. W. HEATON
D. MURPHY

University Departments of Medicine and Chemical Pathology,
Royal Infirmary, Bristol

L. F. BURROUGHS
Long Ashton Research Station, Bristol

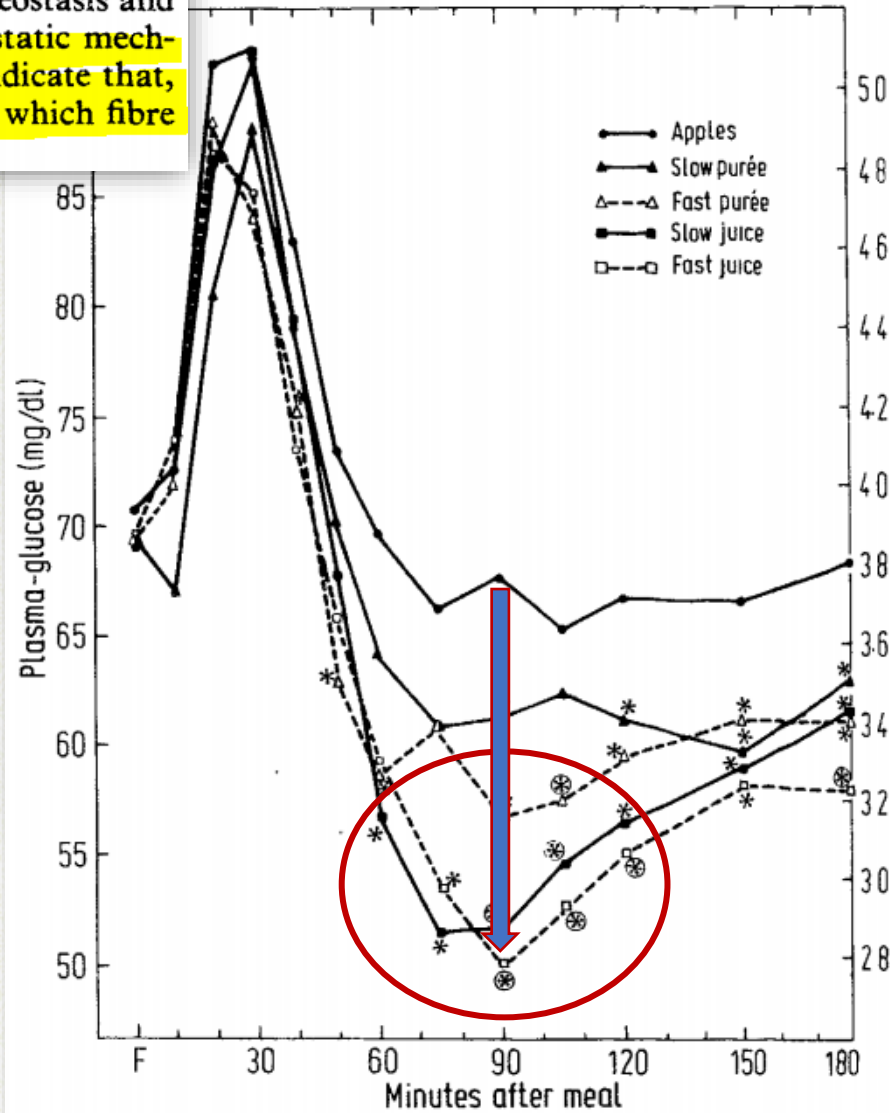


Fig. 3—Mean plasma-glucose levels in nine normal subjects after ingesting 60 g carbohydrate as whole apples, apple purée, and apple juice.

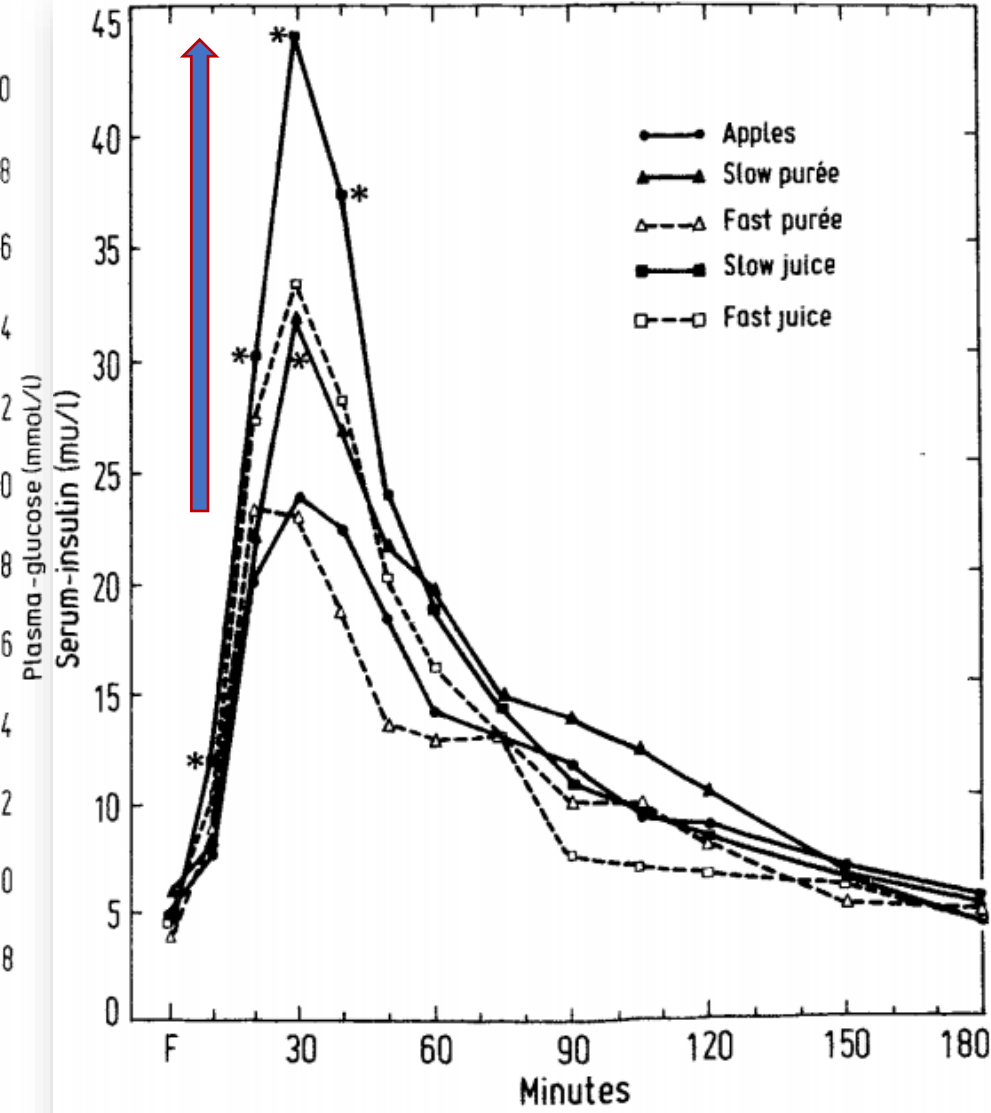


Fig. 4—Mean serum-insulin levels in nine normal subjects after ingesting 60 g carbohydrate as whole apples, purée (fast and slow), and juice (fast and slow) (see legend to fig. 3).

DEPLETION AND DISRUPTION OF DIETARY FIBRE EFFECTS ON SATIETY, PLASMA-GLUCOSE, AND SERUM-INSULIN

G. B. HABER* K. W. HEATON
D. MURPHY

University Departments of Medicine and Chemical Pathology,

Juicing apples and the (much) later discovery of ghrelin

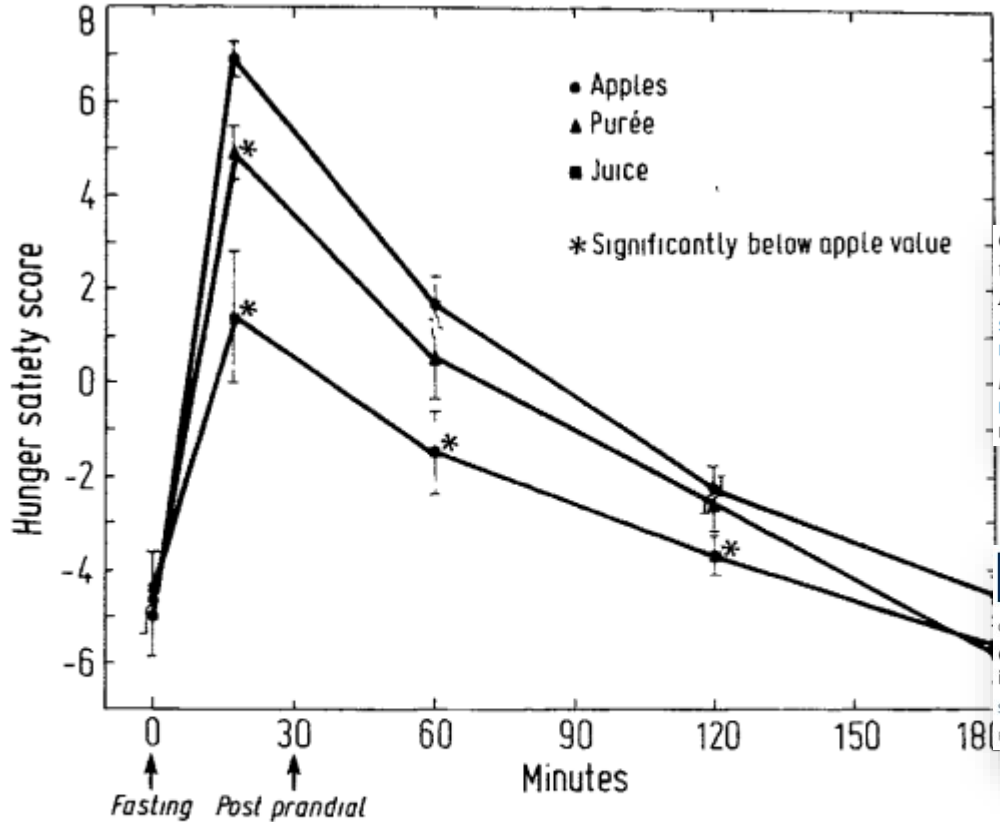
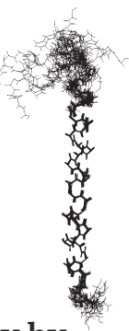


Fig. 2—Mean hunger/satiety scores in ten normal subjects before and after the three test meals, when all were ingested in the same number of minutes.

Glucose Availability Predicts the Feeding Response to Ghrelin in Male Mice, an Effect Dependent on AMPK in AgRP Neurons ^{FREE}

Sarah H Lockie, Romana Stark, Mathieu Mequinion, Sarah Ch'ng, Dong Kong, David C Spanswick, Andrew J Lawrence, Zane B Andrews

Endocrinology, Volume 159, Issue 11, November 2018, Pages 3605–3614, <https://doi.org/10.1210/en.2018-00536>

Published: 10 September 2018 Article history

Journal of Neuroendocrinology

ORIGINAL ARTICLE

Glucose availability regulates ghrelin-induced food intake in the ventral tegmental area

Sarah H. Lockie, Romana Stark, David C. Spanswick, Zane B. Andrews

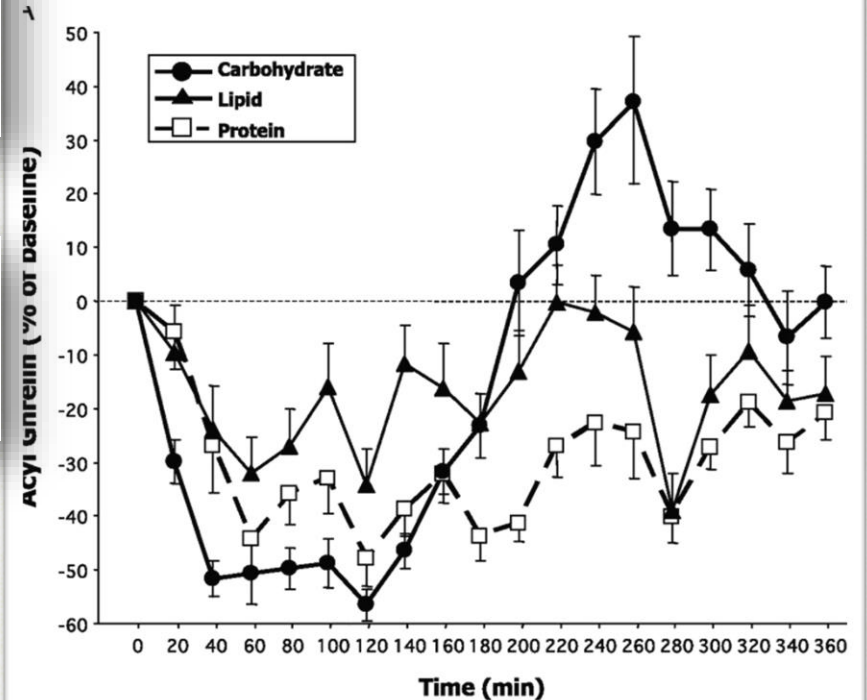
First published: 11 February 2019 | <https://doi.org/10.1111/jne.12696> | Citations: 2

Acyl and Total Ghrelin Are Suppressed Strongly by Ingested Proteins, Weakly by Lipids, and Biphatically by Carbohydrates ^{FREE}

Karen E. Foster-Schubert, Joost Overduin, Catherine E. Prudom, Jianhua Liu, Holly S. Callahan, Bruce D. Gaylinn, Michael O. Thorner, David E. Cummings

The Journal of Clinical Endocrinology & Metabolism, Volume 93, Issue 5, 1 May 2008, Pages 1971–1979, <https://doi.org/10.1210/jc.2007-2289>

Published: 01 May 2008 Article history



Grinding grains: 1) Wheat

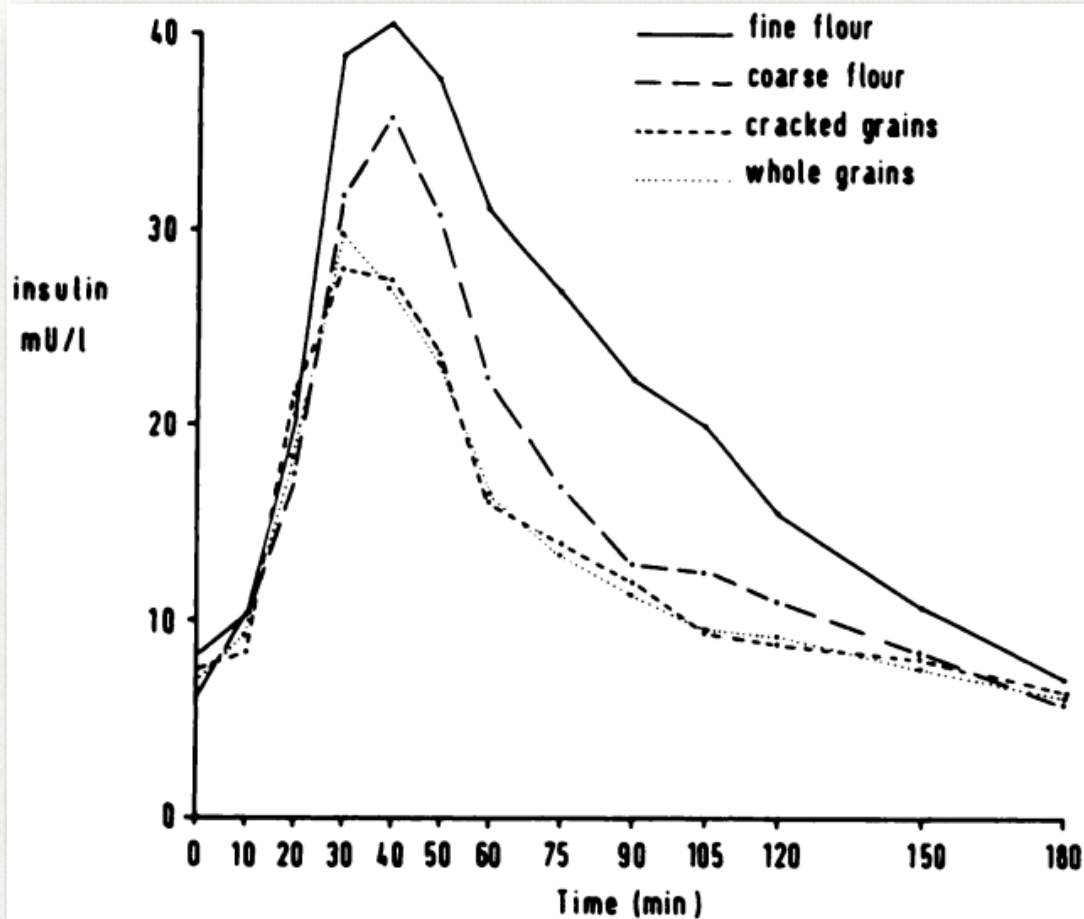


FIG 2. Mean plasma insulin concentration in 10 normal subjects after four isocaloric whole-wheat meals of different particle size. (1 mU/L = 7.175 pmol/L.)

Particle size of wheat, maize, and oat test meals: effects on plasma glucose and insulin responses and on the rate of starch digestion in vitro¹⁻³

Kenneth W Heaton, MD; Samuel N Marcus, MD; Pauline M Emmett, BSc; and Colin H Bolton, PhD

ABSTRACT When normal volunteers ate isocaloric wheat-based meals, their plasma insulin responses (peak concentration and area under curve) increased stepwise: whole grains < cracked grains < coarse flour < fine flour. Insulin responses were also greater with fine maize meal than with whole or cracked maize grains but were similar with whole groats, rolled oats, and fine oatmeal. The peak-to-nadir swing of plasma glucose was greater with wheat flour than with cracked or whole grains. In vitro starch hydrolysis by pancreatic amylase was faster with decreasing particle size with all three cereals. Correlation with the in vivo data was imperfect. Oat-based meals evoked smaller glucose and insulin responses than wheat- or maize-based meals. Particle size influences the digestion rate and consequent metabolic effects of wheat and maize but not oats. The increased insulin response to finely ground flour may be relevant to the etiology of diseases associated with hyperinsulinemia and to the management of diabetes. *Am J Clin Nutr* 1988;47:675-82.

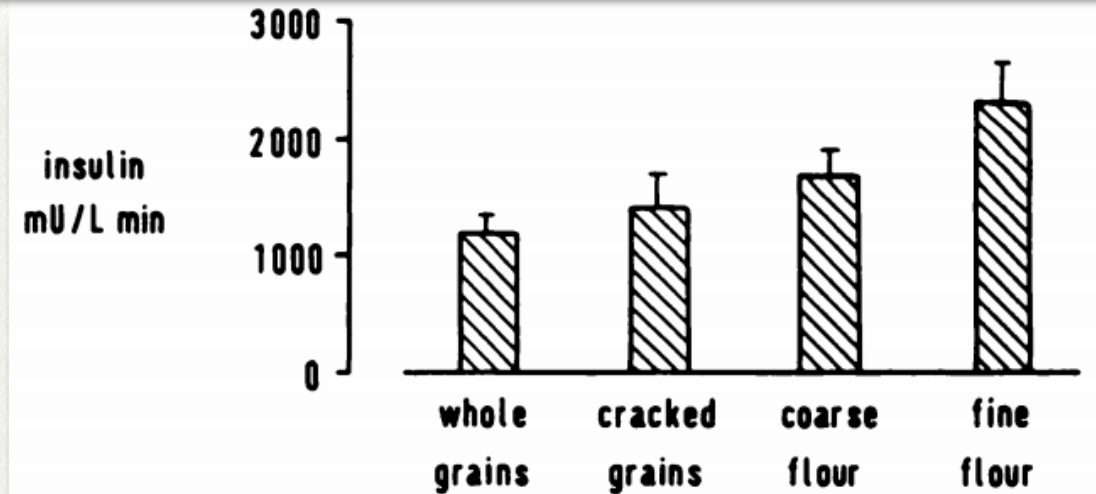


FIG 3. Area under plasma insulin concentration curve (mean \pm SEM) after four isocaloric whole-wheat meals. Significant differences as follows: fine flour > all others, coarse flour > whole grains.

Grinding grains: 2) Rice

Physical factors influencing postprandial glucose and insulin responses to starch¹

Kerin O'Dea,³ Ph.D., Paul J. Nestel, M.D., F.R.A.C.P., and Lynne Antonoff

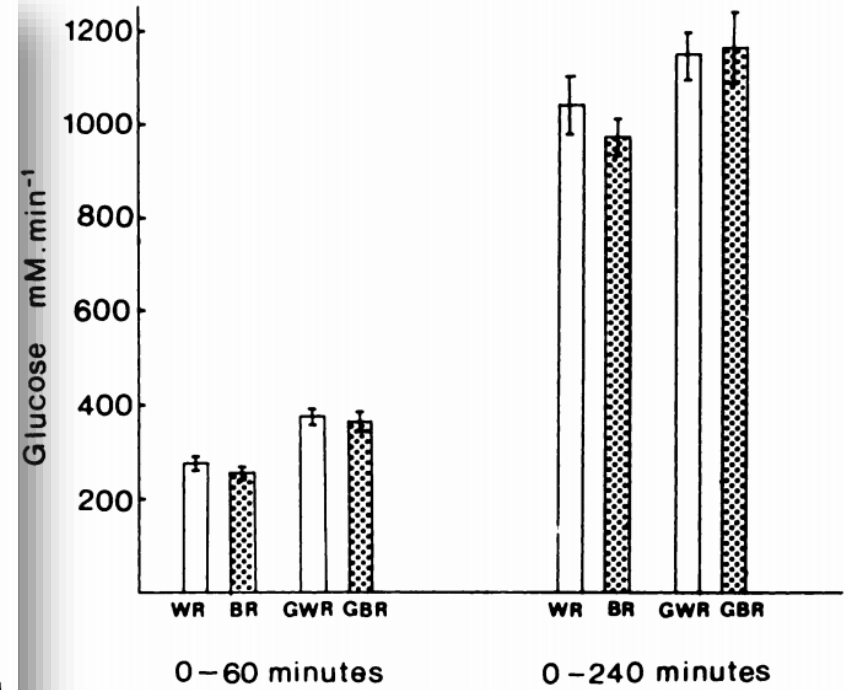
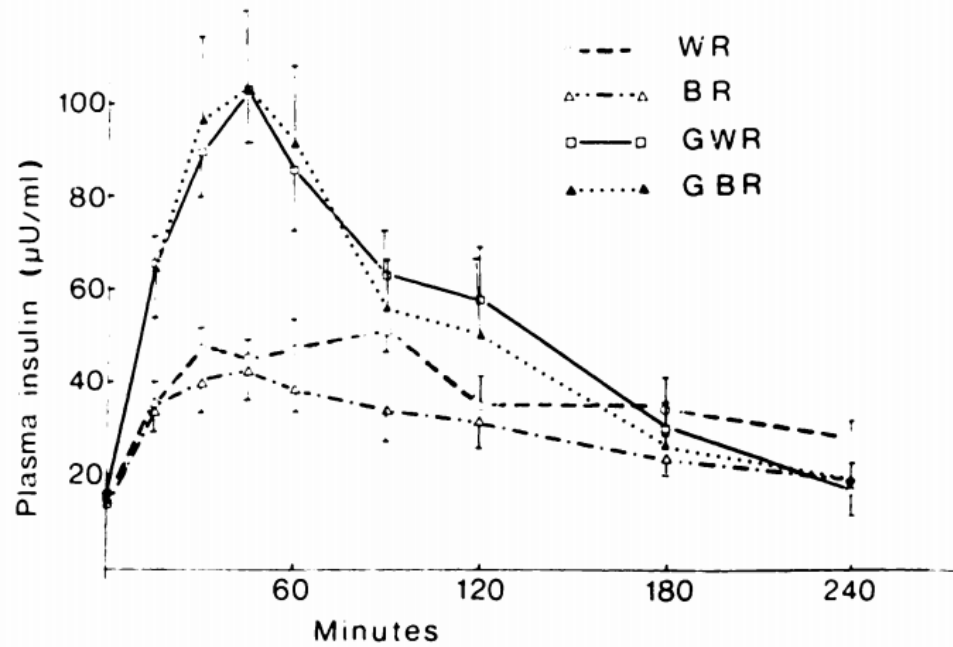
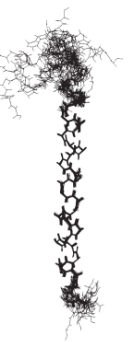


FIG. 2. Plasma insulin responses to white rice (WR), brown rice (BR), ground white rice (GWR), and ground brown rice (GBR). Mean \pm SEM (n = 6). Statistics: GWR > WR: 15 min ($P < 0.005$), 30 min ($P < 0.005$), 45 min ($P < 0.001$), and 60 min ($P < 0.005$); GBR > BR: 15 min ($P < 0.025$), 30 min ($P < 0.005$), 45 min ($P < 0.005$), 60 min ($P < 0.005$), and 90 min ($P < 0.025$).

...der the blood glucose curves during the first 60 min (0 to 60) and for the entire test period (0 to 240 min) for white rice (WR), brown rice (BR), ground white rice (GWR), and ground brown rice (GBR). Mean \pm SEM (n = 6). Statistics: 0 to 60 min: GWR > WR, $P < 0.01$, GBR > BR, $P < 0.001$.

Postprandial glucose, insulin, and incretin responses to grain products in healthy subjects

FREE

Katri S Juntunen ✉, Leo K Niskanen, Kirsi H Liukkonen, Kaisa S Poutanen, Jens J Holst, Hannu M Mykkänen

The American Journal of Clinical Nutrition, Volume 75, Issue 2, 1 February 2002, Pages 254–262, <https://doi.org/10.1093/ajcn/75.2.254>

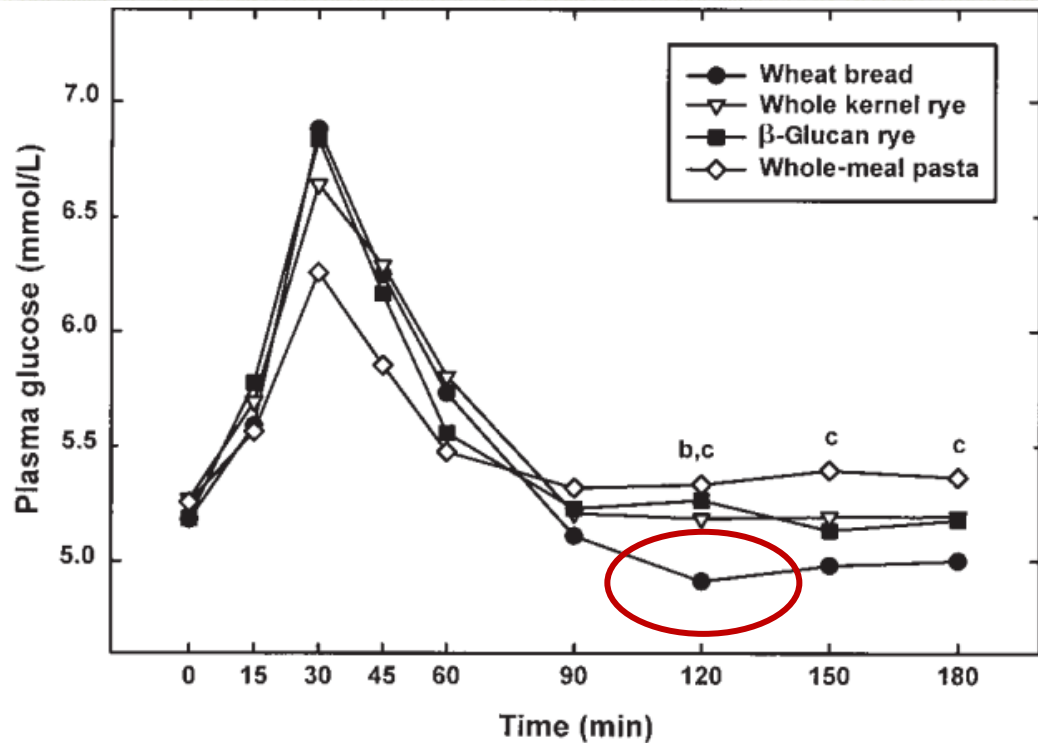


FIGURE 2. Mean fasting and postprandial glucose responses to rye and wheat products over 180 min ($n = 20$). Postprandial glucose responses to β -glucan rye bread (b) and pasta (c) were significantly different from those to wheat bread, $P < 0.05$. The pooled SEM was 0.9 for the whole-kernel rye bread, 0.9 for the β -glucan rye bread, 0.6 for the pasta, and 0.8 for the white wheat bread.

„The results indicate that the lower insulinemic response to the rye breads and pasta than to the wheat bread is not explained by the fiber content, type of cereal, or rate of gastric emptying, but by the structural properties of the food.”

„Our findings agree with those of Järvi et al, who compared diets with identical nutrient compositions and type and amount of fiber and produced differences in the glycemic index mainly by altering the structure of the starchy foods. They found that consumption of a diet with a low glycemic index and a preserved food structure improved glucose and insulin responses.”

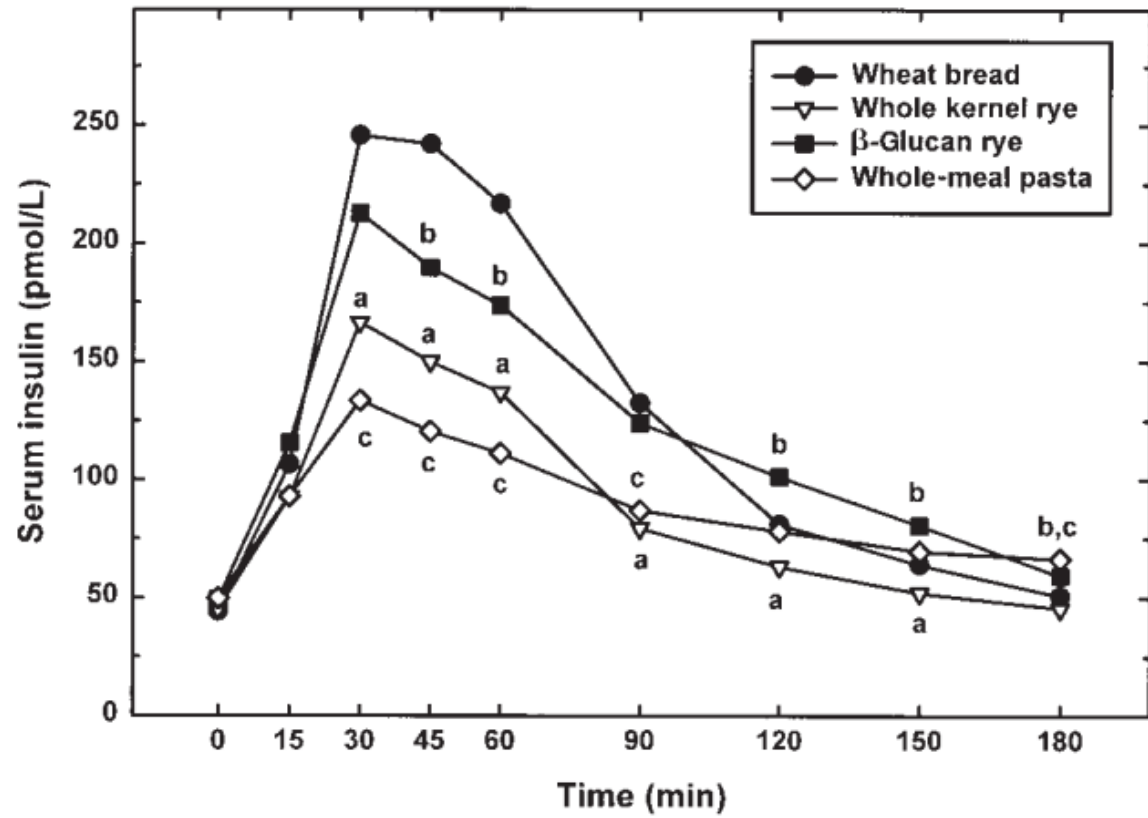


FIGURE 3. Mean fasting and postprandial insulin responses to rye and wheat products over 180 min ($n = 20$). Postprandial insulin responses to whole-kernel rye bread (a), β -glucan rye bread (b), and pasta (c) were significantly different from those to white wheat bread, $P < 0.05$. The pooled SEM was 40.5 for the whole-kernel rye bread, 56.3 for the β -glucan rye bread, 36.3 for the pasta, and 73.8 for the white wheat bread.

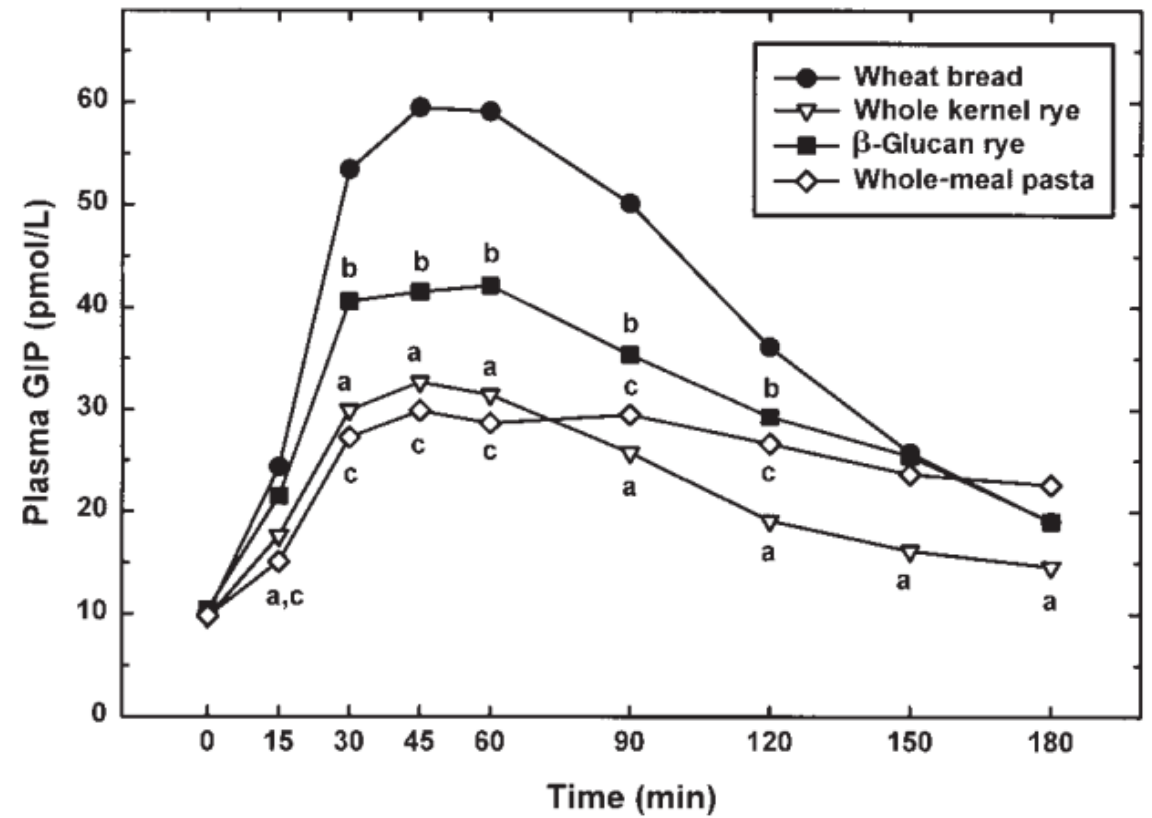


FIGURE 4. Mean fasting and postprandial glucose-dependent insulinotropic polypeptide (GIP) responses to rye and wheat products over 180 min ($n = 20$). Postprandial GIP responses to whole-kernel rye bread (a), β -glucan rye bread (b), and pasta (c) were significantly different from those to white wheat bread, $P < 0.05$. The pooled SEM was 7.6 for the whole-kernel rye bread, 11.1 for the β -glucan rye bread, 8.9 for the pasta, and 12.1 for the white wheat bread.

Structural differences between rye and wheat breads but not total fiber content may explain the lower postprandial insulin response to rye bread FREE

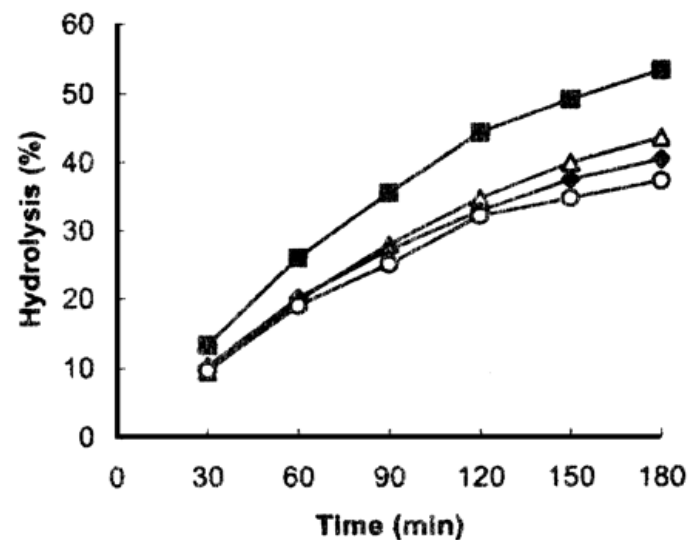
Katri S Juntunen ✉, David E Laaksonen, Karin Autio, Leo K Niskanen, Jens J Holst, Kari E Savolainen, Kirsi-Helena Liukkonen, Kaisa S Poutanen, Hannu M Mykkänen

The American Journal of Clinical Nutrition, Volume 78, Issue 5, 1 November 2003, Pages 957–964, <https://doi.org/10.1093/ajcn/78.5.957>

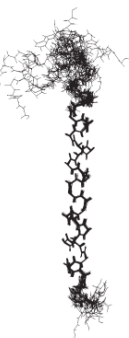
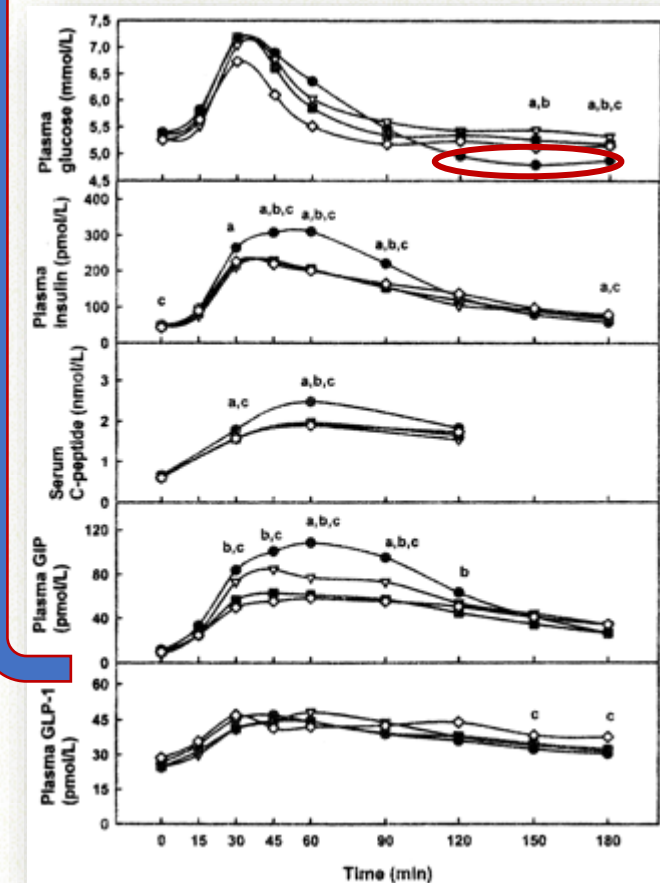
In vitro starch hydrolysis

In vitro starch hydrolysis differed among the test breads ($P = 0.029$; **Figure 2**). Hydrolysis indexes of 82 ± 3 , 76 ± 2 , and 71 ± 4 were obtained for the endosperm, traditional, and high-fiber rye breads, respectively.

FIGURE 2



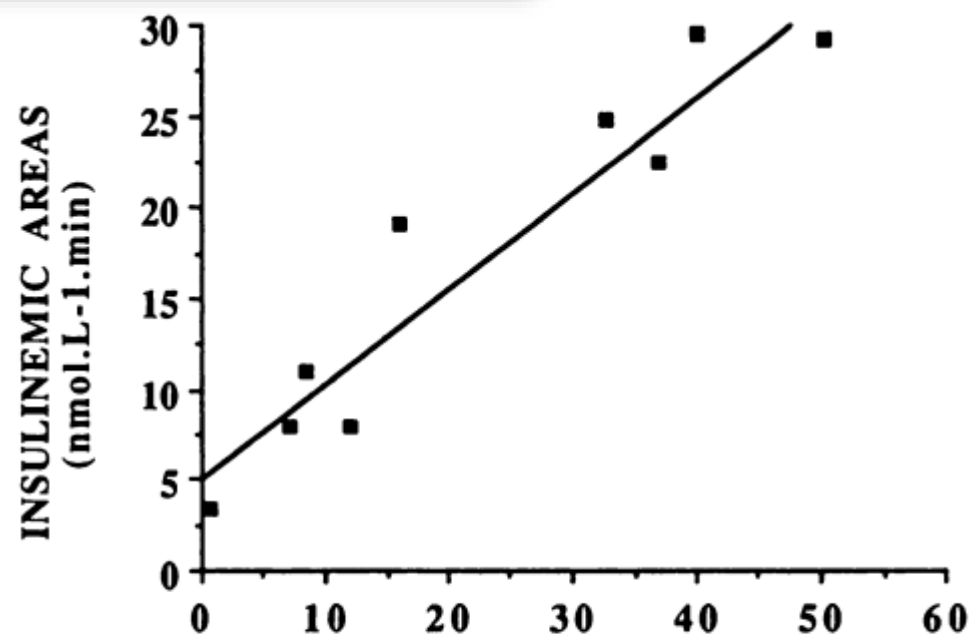
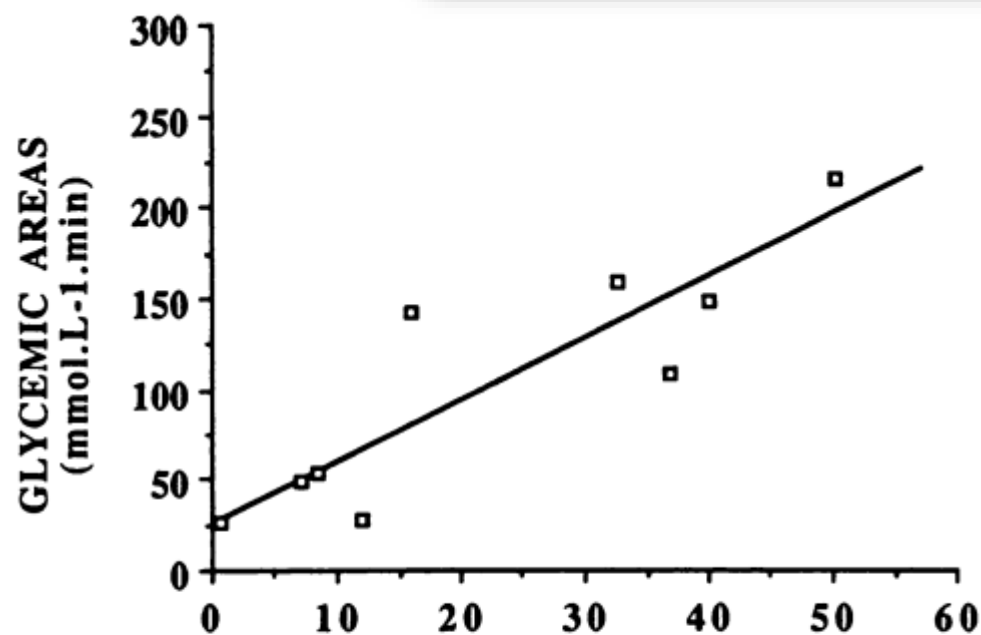
Hormones \ Breads	AUC			
	Refined wheat	Endosperm rye	Traditional rye	High fiber rye
GIP (pmol · min/L)	10496	8347	6357	6506
GLP-1 (pmol · min/L)	2089	2557	2309	2141
GIP/GLP-1	5.02	3.26	2.75	3.04



Insulin and glycemic responses in healthy humans to native starches processed in different ways: correlation with in vitro alpha-amylase hydrolysis

F R Borner, A M Fontvieille, S Rizkalla, P Colonna, A Blayo, C Mercier, G Slama

The American Journal of Clinical Nutrition, Volume 50, Issue 2, 1 August 1989, Pages 315–323, <https://doi.org/10.1093/ajcn/50.2.315>



STARCH HYDROLYSIS (%) AT 30 MINUTES

FIG 4. Correlations between ratio of in vitro starch hydrolysis within 30 min and mean areas ($\text{mmol} \cdot \text{L}^{-1} \cdot \text{min}^{-1}$) under the 0–180-min plasma glucose variations (\square) ($y = 3.4x + 26.7$; $r = 0.88$, $p < 0.01$) and mean areas under the 0–180-min plasma insulin variations (\blacksquare) ($y = 0.54x + 5.1$; $r = 0.95$, $p < 0.001$).

Contributions of fat and protein to the incretin effect of a mixed meal

Guillaume Carrel, Léonie Egli, Christel Tran, Philippe Schneiter, Vittorio Giusti, David D'Alessio, and Luc Tappy

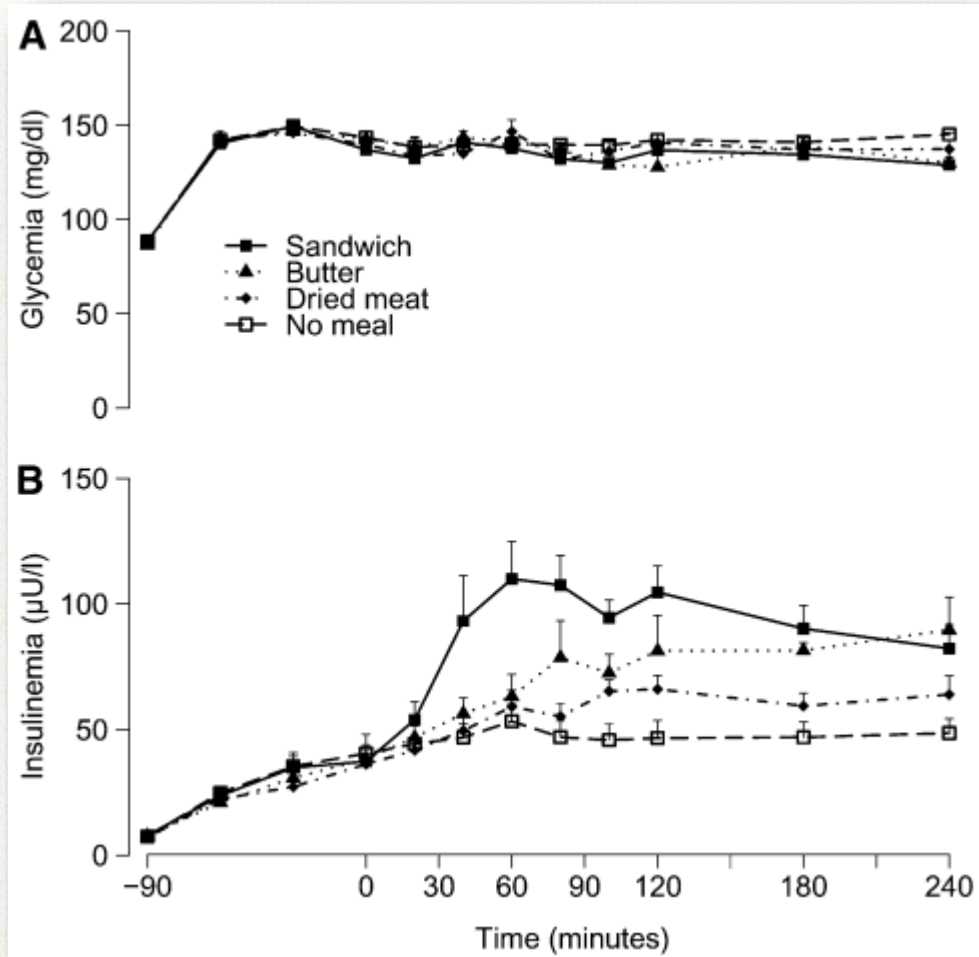
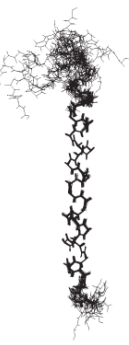


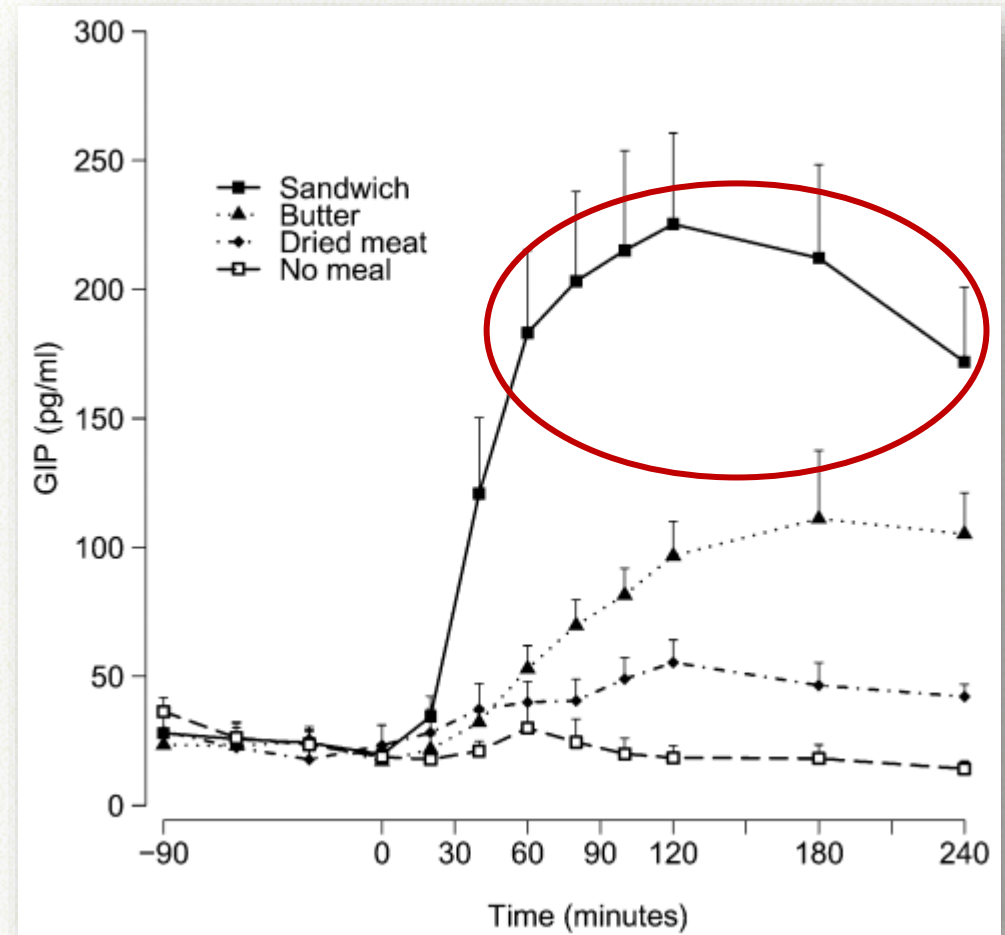
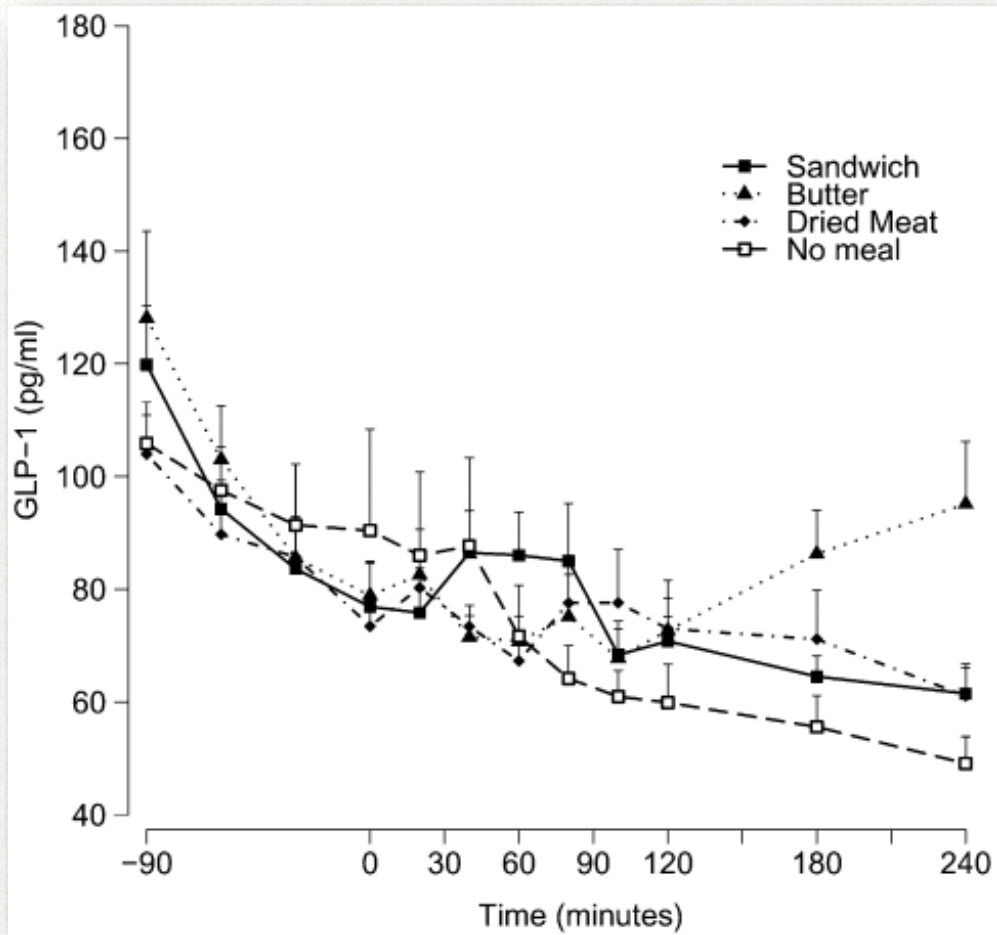
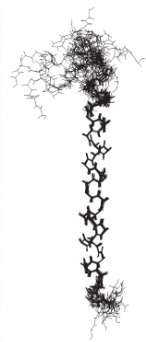
TABLE 1

Composition of the different test meals

Meal content	Proteins	Lipids	Carbohydrates
	<i>g</i>	<i>g</i>	<i>g</i>
Sandwich			
120 g White bread	10.9	1.1	63.2
20 g Butter	0.1	16.4	0.1
10 g Dried meat	3.9	0.5	0.1
Total	14.9	18.0	63.4
Dried meat alone			
40 g Dried meat	15.4	2.0	0.2
Butter alone			
20 g Butter	0.1	16.4	0.1

Contributions of fat and protein to the incretin effect of a mixed meal

Guillaume Carrel, Léonie Egli, Christel Tran, Philippe Schneiter, Vittorio Giusti, David D'Alessio, and Luc Tappy



Plant-rich mixed meals based on Palaeolithic diet principles have a dramatic impact on incretin, peptide YY and satiety response, but show little effect on glucose and insulin homeostasis: an acute-effects randomised study

H. Frances J. Bligh (a1), Ian F. Godsland (a2), Gary Frost (a3), Karl J. Hunter (a1) ...

<https://doi.org/10.1017/S0007114514004012> Published online: 09 February 2015

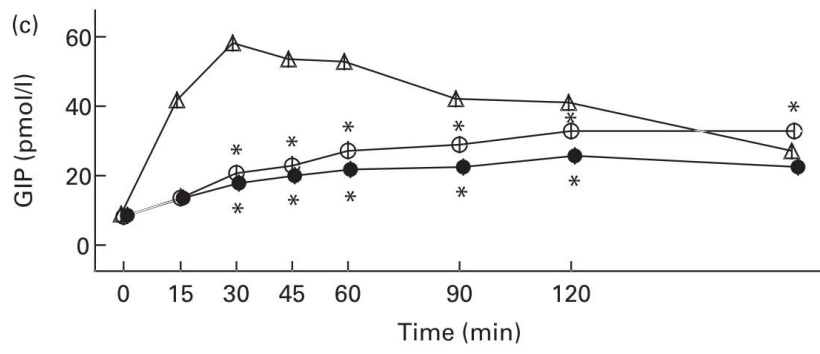
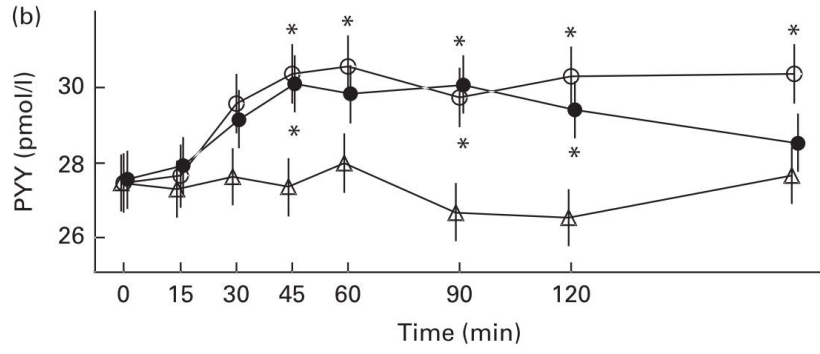
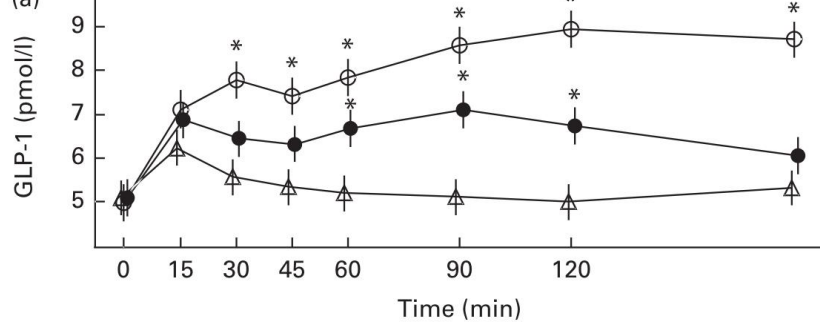
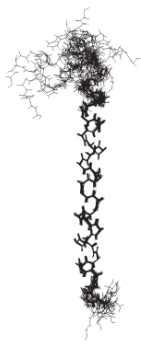


Fig. 2. Postprandial plasma glucagon-like peptide 1 (GLP-1) (a) peptide YY (PYY) (b) and glucose-dependent insulinotropic peptide (GIP) (c) responses after consumption of Palaeolithically inspired PAL1 (○) and PAL2 (●), and a reference meal (REF). Values are means, with standard errors represented by vertical bars. * Mean value was significantly different from that of the reference meal ($P < 0.05$). A Bonferroni adjustment was used to preserve the 0.05 error rate within each time point. The mean AUC for 180 min for GLP-1 were 1494 (SE 66.1) min × pmol/l for PAL1, 1180 (SE 64.4) min × pmol/l for PAL2 and 980 (SE 63.3) min × pmol/l for the REF (PAL1 v. REF $P < 0.001$; PAL2 v. REF $P = 0.003$).

Table 1. Macronutrients and ingredients for the three test meals*

	Reference	PAL1	PAL2
Available carbohydrate, desired target (g)	50	50	50
Available carbohydrate, analysed (g)	46.1	43.3	44.2
Fibre, calculated (g)	3	12	10
Total carbohydrates, calculated target† (g)	53	66	65
Energy, calculated (kJ)	1602	2326	1606
Total carbohydrates, calculated (g (% of energy))	57 (60)	65 (43)	66 (60)
Fat, calculated (g (% of energy))	11 (25)	18 (28)	11 (25)
Protein, calculated (g (% of energy))	13 (15)	41 (29)	16 (15)
Total phenolics (mg GAE per meal)	4.47	57.2	86.1
Rice, white, long-grain, regular, cooked‡§ (g)	90		
Strawberries, raw (g)		100	120
Apples, raw, with skin (g)		110	110
Peppers, sweet, yellow, raw (g)		100	100
Fish, haddock, cooked, dry heat‡ (g)		90	
Onions, sweet, raw (g)		60	60
Mango, frozen (g)	65		
Carrots, cooked, boiled, drained, without salt‡ (g)	50		
Eggplant, raw (g)		50	50
Mushrooms, white, raw (g)		50	50
Fish, salmon, Atlantic, farmed, cooked, dry heat‡ (g)	39	39	39
Raisins, seedless (g)		25	25
Nuts, almonds, blanched (g)		14	
Oil, olive, salad or cooking (g)	4		
Courgettes (g)		150	150
Cinnamon (g)		5	5
Capers (g)		5	5
Flax seed oil (g)		4	4
Total meal weight, uncooked (g)	248	802	718

PAL1, Palaeolithic meal 1; PAL2, Palaeolithic meal 2; GAE, equivalents of gallic acid.



Disrupting food texture vs. 'high-fat diet'. Fat is dispensable?

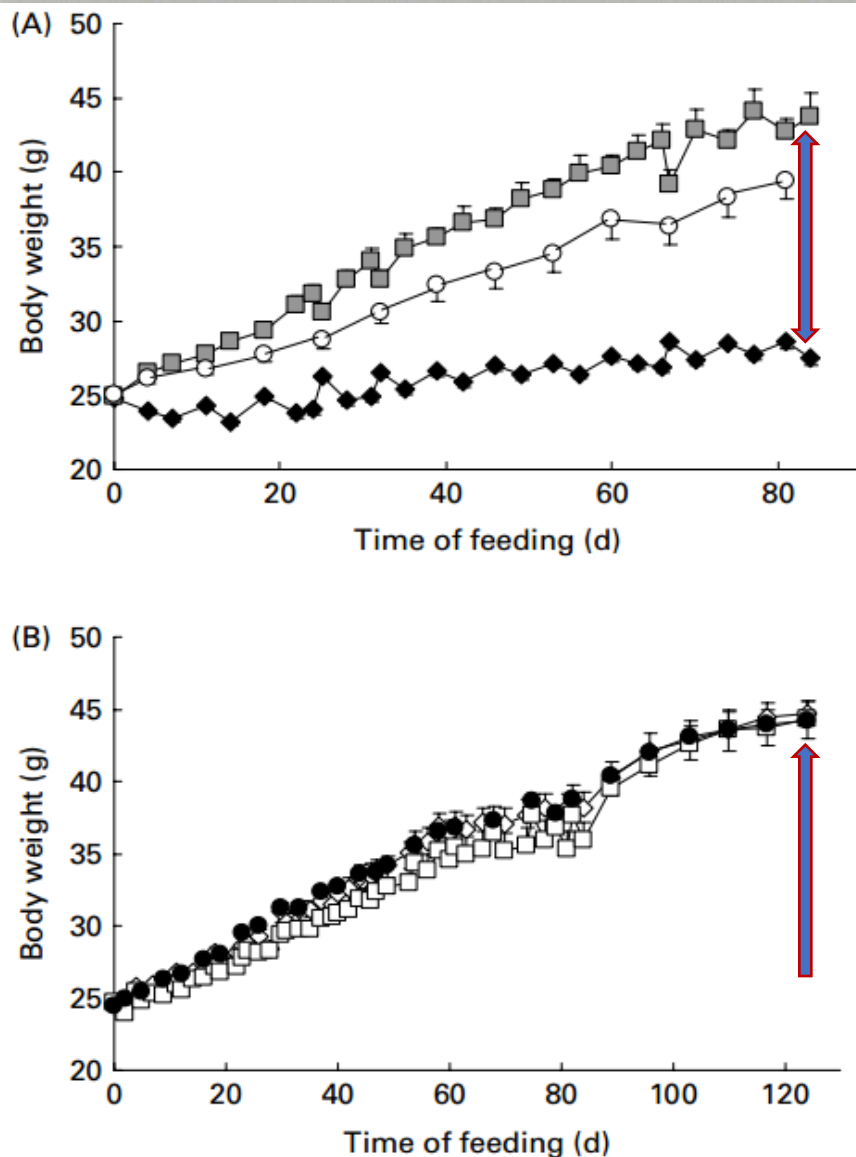


Fig. 1. Body-weight changes in mice receiving the different diets. (A) Body-weight development in mice receiving the different diets provided as pellets (cohorts 1 and 3). Values are means, with their standard errors represented by vertical bars (C-H (◆): *n* 20; HF-H (■): *n* 20; W-H (○): *n* 12). (B) Body-weight development in mice receiving the different powder diets (cohorts 2 and 3). Values are means, with their standard errors represented by vertical bars (C-S (◇): *n* 20; HF-S (□): *n* 19; W-S (●): *n* 12).

Volume 109, Issue 8 28 April 2013, pp. 1518-1527

Cited by 15

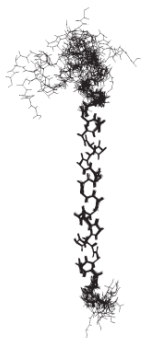
Access

Diet-induced obesity in *ad libitum*-fed mice: food texture overrides the effect of macronutrient composition

Charles Desmarchelier^(a1), Tobias Ludwig^(a2), Ronny Scheundel^(a1), Nadine Rink^(a3) ...

<https://doi.org/10.1017/S0007114512003340> Published online: 06 August 2012

„Here, we show for the first time that a pellet-based high carbohydrate/starch diet fails to trigger obesity, whereas the same diet given in powder form produces an obese phenotype similar to a HF or W diet. While all mice receiving the high-carbohydrate C diets ingested very similar amounts of food and lost similar quantities of energy through faeces, they displayed quite different body-weight gains. The most striking difference, however, was that feed efficiency was 4-fold higher in the powder diet compared with the pellet variant.”



What else the flooding of the proximal small intestine with simple sugars (and additives) can negatively impact?

- Small intestinal microbiota composition and function
- Lipid absorption and chylomicron secretion
- Bile acid quantity as well as composition

Carbohydrate Intake as a Risk Factor for Biliary Sludge and Stones During Pregnancy

Wong, Alan C. MD, MPH; Ko, Cynthia W. MD, MS [Author Information](#) ©

Journal of Clinical Gastroenterology: September 2013 - Volume 47 - Issue 8 - p 700-705
doi: 10.1097/MCG.0b013e318286fdb0

Published: 19 January 2012

Integrated genomics and post-genomics approaches in microbial ecology

The human small intestinal microbiota is driven by rapid uptake and conversion of simple carbohydrates

Erwin G Zoetendal [✉](#), Jeroen Raes, Bartholomeus van den Bogert, Manimozhiyan Arumugam, Carien CGM Booijink, Freddy J Troost, Peer Bork, Michiel Wels, Willem M de Vos & Michiel Kleerebezem

The ISME Journal 6, 1415–1426(2012) | [Cite this article](#)

Glucose and GLP-2 (Glucagon-Like Peptide-2) Mobilize Intestinal Triglyceride by Distinct Mechanisms

Priska Stahel, Changting Xiao, Xenia Davis, Patrick Tso, Gary F. Lewis [✉](#)

Originally published 11 Jul 2019 | <https://doi.org/10.1161/ATVBAHA.119.313011> | Arteriosclerosis, Thrombosis, and Vascular Biology. 2019;39:1565–1573

[Gut](#). 1983 Jan; 24(1): 2–6.

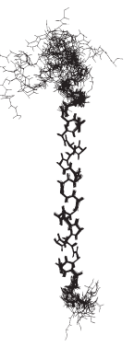
doi: [10.1136/gut.24.1.2](https://doi.org/10.1136/gut.24.1.2)

PMCID: PMC1419917

PMID: [6293939](https://pubmed.ncbi.nlm.nih.gov/6293939/)

Diet and gall stones: effects of refined and unrefined carbohydrate diets on bile cholesterol saturation and bile acid metabolism.

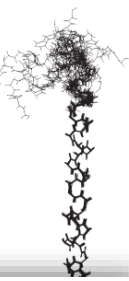
[J R Thornton](#), [P M Emmett](#), and [K W Heaton](#)



Other lines of supporting evidence for the mechanism (of AAA)

- Bariatric surgery
- Meal placement
- Meal frequency
- Observed effects of incretin imbalance
 - The biological literacy test: explain differences between sucrose and isomaltulose observed in metabolic effects

Meal size and meal frequency



Incretin Secretion in Relation to Meal Size and Body Weight in Healthy Subjects and People with Type 1 and Type 2 Diabetes Mellitus FREE

T. Vilsbøll ✉, T. Krarup, J. Sonne, S. Madsbad, A. Vølund, A. G. Juul, J. J. Holst

The Journal of Clinical Endocrinology & Metabolism, Volume 88, Issue 6, 1 June 2003, Pages 2706–2713, <https://doi.org/10.1210/jc.2002-021873>

„it is possible to modulate the β -cell sensitivity to glucose in obese healthy subjects, and possibly also in type 2 diabetic patients, by giving them a large meal, compared with a small meal.”

Hypercaloric diets with increased meal frequency, but not meal size, increase intrahepatic triglycerides: A randomized controlled trial

Karin E. Koopman, Matthan W.A. Caan, Aart J. Nederveen, Anouk Pels, Mariette T. Ackermans, Eric Fliers, Susanne E. la Fleur, Mireille J. Serlie ✉

First published: 26 March 2014 | <https://doi.org/10.1002/hep.27149> | Cited by: 29

Incretin and Islet Hormone Responses to Meals of Increasing Size in Healthy Subjects FREE

Wathik Alsalim, Bilal Omar, Giovanni Pacini, Roberto Bizzotto, Andrea Mari, Bo Ahrén ✉

The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 2, 1 February 2015, Pages 561–568, <https://doi.org/10.1210/jc.2014-2865>

„Glucose profiles were similar after the two larger meals, whereas after the smaller meal, there was a postpeak reduction below baseline to a nadir of 3.8 ± 0.1 mmol/L after 75 minutes ($P < .001$). The AUC for GLP-1, GIP, insulin, and C-peptide were significantly higher by increasing the caloric load as was β -cell sensitivity to glucose. ... The adaptation at larger meals results in identical glucose excursions, whereas after a lower caloric lunch, the insulin response is [disproportionately] high, resulting in a postpeak suppression of glucose below baseline.”

Food order

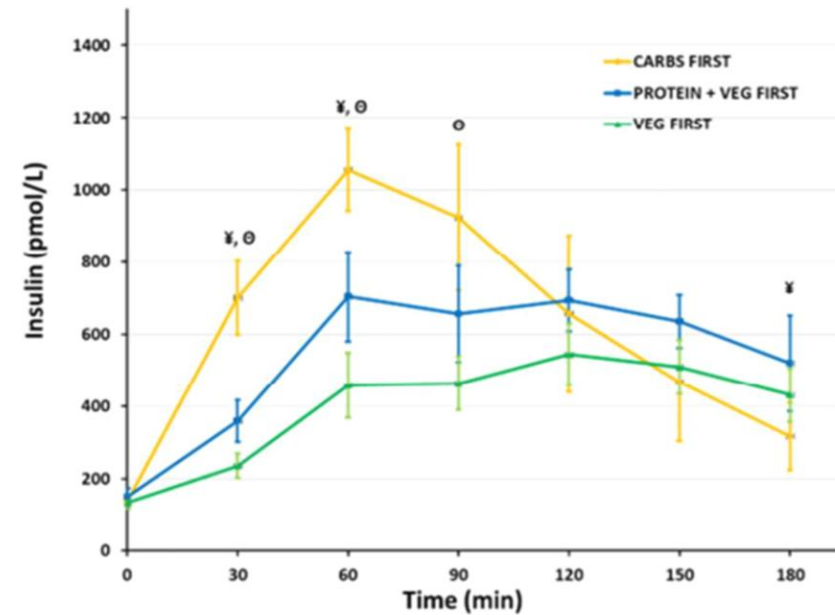
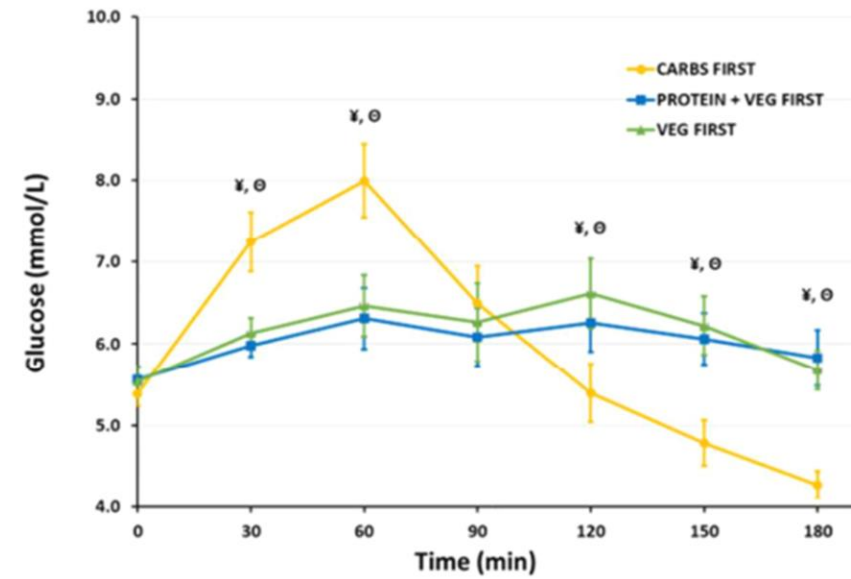
DIABETES, OBESITY AND METABOLISM
A JOURNAL OF PHARMACOLOGY AND THERAPEUTICS

BRIEF REPORT

The impact of food order on postprandial glycaemic excursions in prediabetes

Alpana P. Shukla MD✉, Morgan Dickison MS, Natasha Coughlin MS, Ampadi Karan, Elizabeth Mauer MS, Wanda Truong MS, Anthony Casper ... See all authors ✓

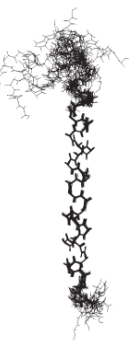
First published: 12 August 2018 | <https://doi.org/10.1111/dom.13503> | Citations: 6



Postprandial glucose and insulin levels following, carbohydrate-first, protein and vegetables-first and vegetables-first meal orders. Values are mean \pm SEM.


¥. Statistically significant differences ($p < 0.05$) between: Carbs-First vs. Protein and Vegetables-First

Ø. Statistically significant differences ($p < 0.05$) between: Carbs-First vs. Vegetables-First



Eating slowly

Eating Slowly Increases the Postprandial Response of the Anorexigenic Gut Hormones, Peptide YY and Glucagon-Like Peptide-1 FREE

Alexander Kokkinos , Carel W. le Roux, Kleopatra Alexiadou, Nicholas Tentolouris, Royce P. Vincent, Despoina Kyriaki, Despoina Perrea, Mohammad A. Ghatei, Stephen R. Bloom, Nicholas Katsilambros

The Journal of Clinical Endocrinology & Metabolism, Volume 95, Issue 1, 1 January 2010, Pages 333–337, <https://doi.org/10.1210/jc.2009-1018>

„Peptide YY area under the curve (AUC) was higher after the 30-min meal than after the 5-min meal (mean \pm SEM AUC 5 min meal: 4133 ± 324 , AUC 30 min meal: 5250 ± 330 pmol/liter \cdot min, $P = 0.004$), as was glucagon-like peptide-1 AUC (mean \pm SEM AUC 5 min meal: 6219 ± 256 , AUC 30 min meal: 8794 ± 656 pmol/liter \cdot min, $P = 0.001$).”

„Eating at a physiologically moderate pace leads to a more pronounced anorexigenic gut peptide response than eating very fast.”

Anorexigenic postprandial responses of PYY and GLP1 to slow ice cream consumption: preservation in obese adolescents, but not in obese adults

A E Rigamonti¹, F Agosti², E Compri², M Giunta^{1,2}, N Marazzi², E E Muller¹,

This Article

Published online before print
December 12, 2012, doi:
10.1530/EJE-12-0867

Eur J Endocrinol March 1, 2013
168 429-436

Eating rate is a heritable phenotype related to weight in children FREE

Clare H Llewellyn, Cornelia HM van Jaarsveld, David Boniface, Susan Carnell, Jane Wardle 

The American Journal of Clinical Nutrition, Volume 88, Issue 6, 1 December 2008, 1560–1566, <https://doi.org/10.3945/ajcn.2008.26175>

Proxies for carbohydrate processing: Glycemic load

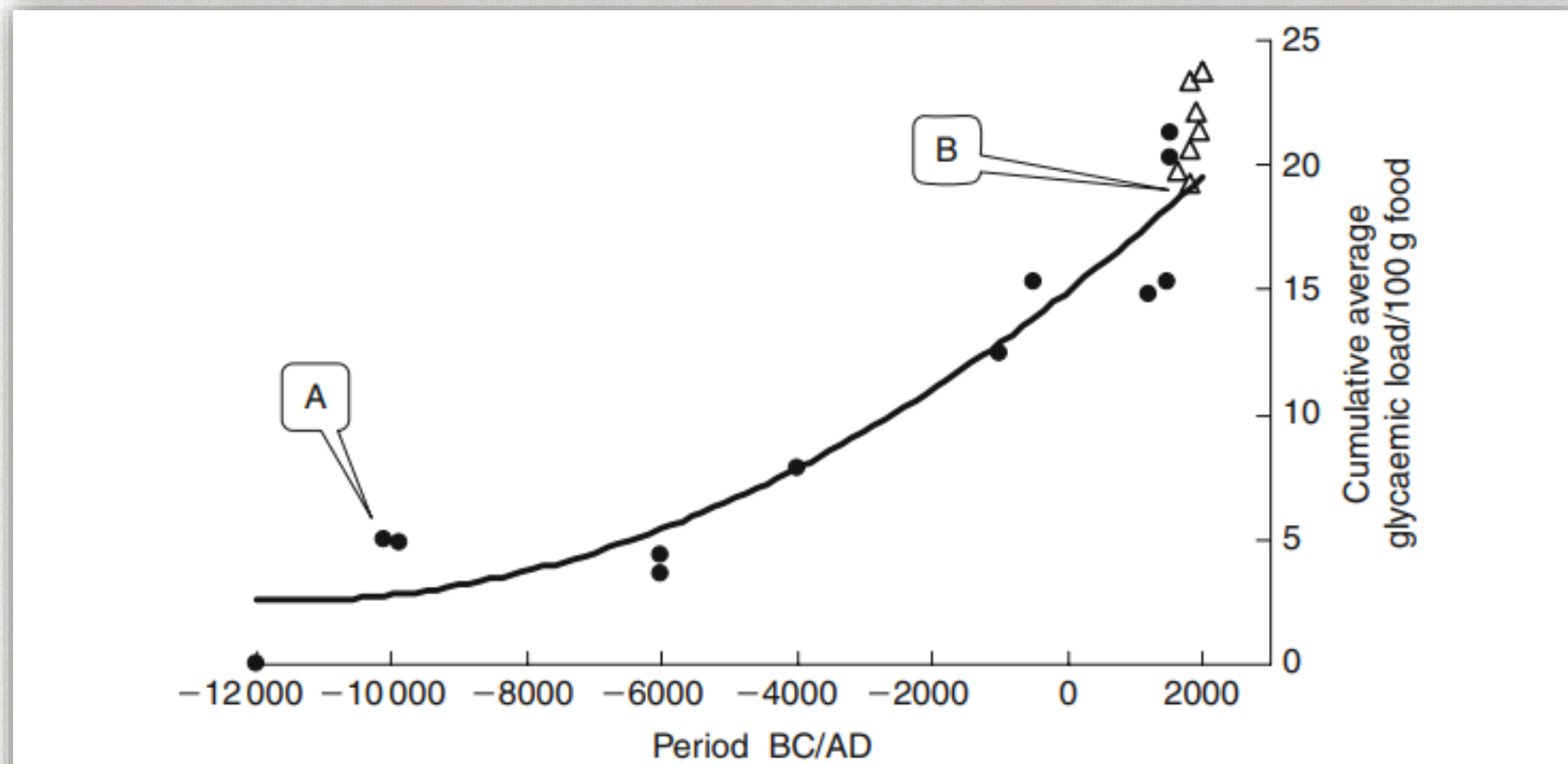
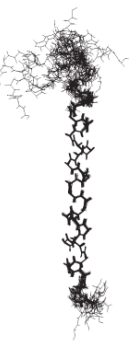


Fig. 1.1 Evolutionary adaptation to ancient diets of low glycaemic load may have left mankind genetically predisposed to non-communicable diseases provoked by today's high-glycaemic diets. Based on the history of foods in Europe,³² with calculations by this author (A, agricultural revolution; B, industrial revolution). Open symbols show values post the industrial revolution.

Increased consumption of refined carbohydrates and the epidemic of type 2 diabetes in the United States: an ecologic assessment FREE

Lee S Gross ✉, Li Li, Earl S Ford, Simin Liu

The American Journal of Clinical Nutrition, Volume 79, Issue 5, 1 May 2004, Pages 774–779, <https://doi.org/10.1093/ajcn/79.5.774>

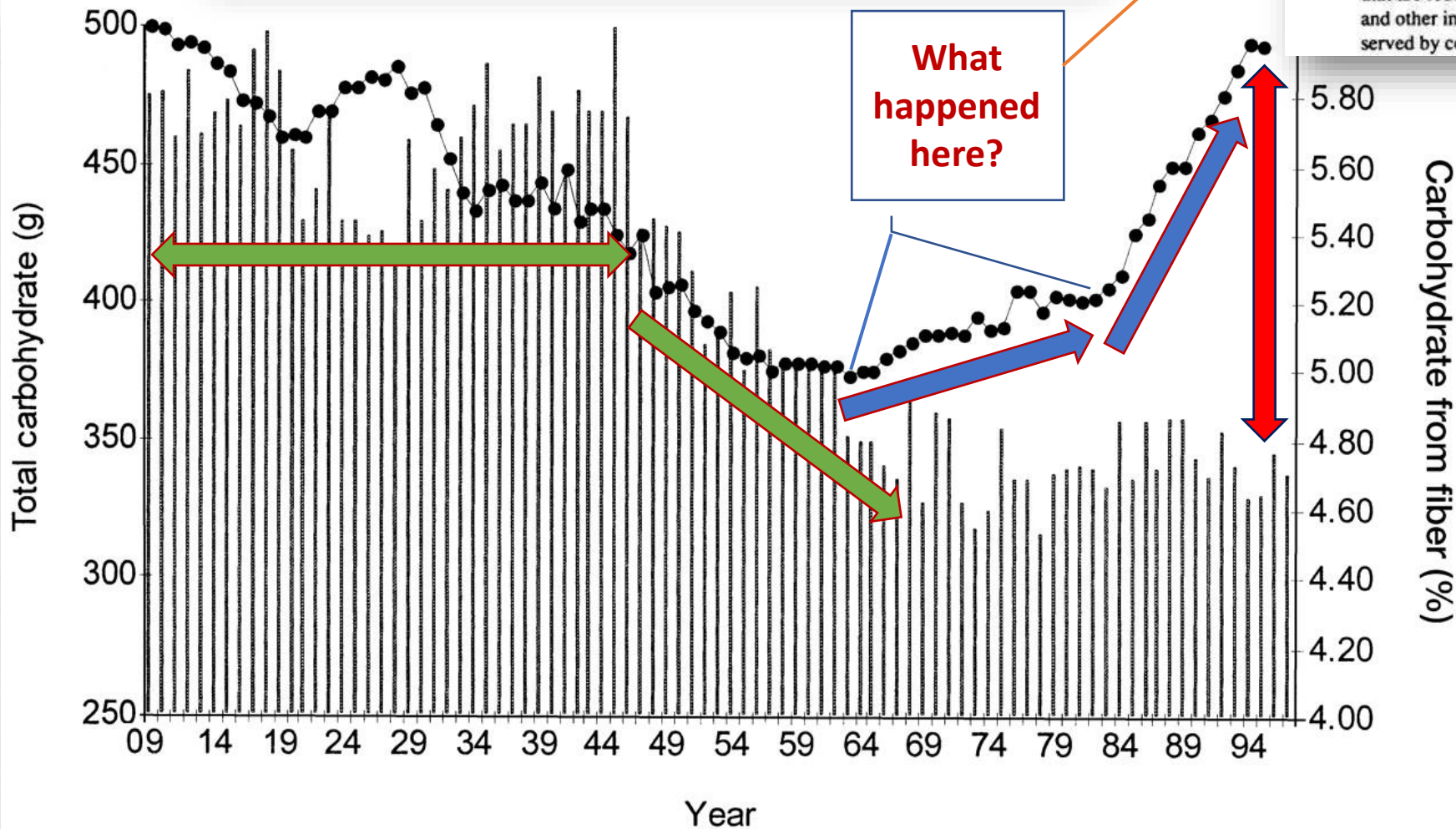
2.15

Increase to at least 5,000 brand items the availability of processed food products that are reduced in fat and saturated fat. (Baseline: 2,500 items reduced in fat in 1986)

Note: A brand item is defined as a particular flavor and/or size of a specific brand and is typically the consumer unit of purchase.

Baseline data source: Nielsen Company National Scantrack.

If Americans are to meet the objective for reduction of dietary fat and saturated fat in their diets by the year 2000 (see Objective 2.5), sufficient food choices must be available. Considerable progress has already been achieved in increasing the availability of processed food products with lowered sodium. It is equally important that a wide selection of lower fat and saturated fat foods be offered to the public. Processed food products that are reduced in fat and saturated fat should also be made more available to schools and other institutions, low-income families, and American Indians living on reservations served by commodity food programs.



Proxies for carbohydrate processing: Fiber


Structure and speed of absorption

Accelerated Intestinal Glucose Absorption in Morbidly Obese Humans: Relationship to Glucose Transporters, Incretin Hormones, and Glycemia FREE

Nam Q. Nguyen ✉, Tamara L. Debreceni, Jenna E. Bambrick, Bridgette Chia, Judith Wishart, Adam M. Deane, Chris K. Rayner, Michael Horowitz, Richard L. Young

The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 3, 1 March 2015, Pages 968–976, <https://doi.org/10.1210/jc.2014-3144>

The effect of dietary fibre on reducing the glycaemic index of bread

Francesca Scazzina ^(a1), Susanne Siebenhandl-Ehn ^(a2) and Nicoletta Pellegrini ^(a1) 
<https://doi.org/10.1017/S0007114513000032> Published online: 18 February 2013

„The reviewed literature suggests that the presence of intact structures not accessible to human amylases, as well as a reduced pH that may delay gastric emptying or create a barrier to starch digestion, seems to be more effective than dietary fibre *per se* in improving glucose metabolism, irrespective of the type of cereal.”

Results:

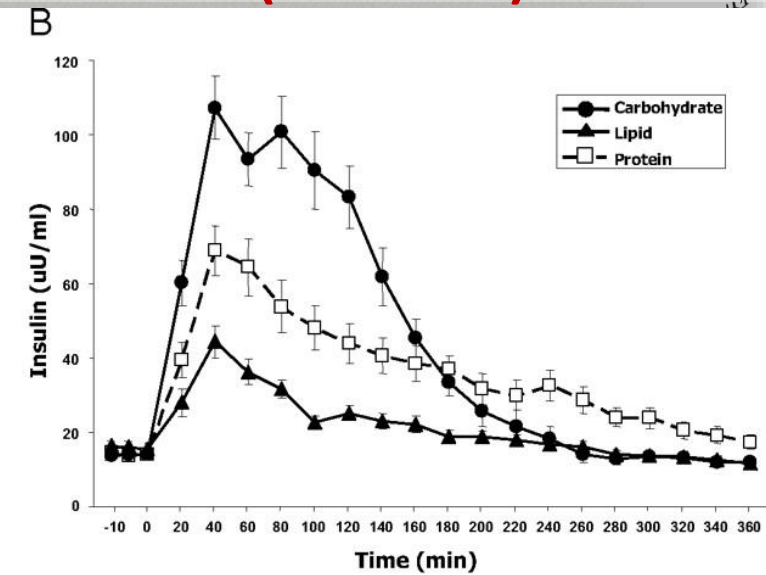
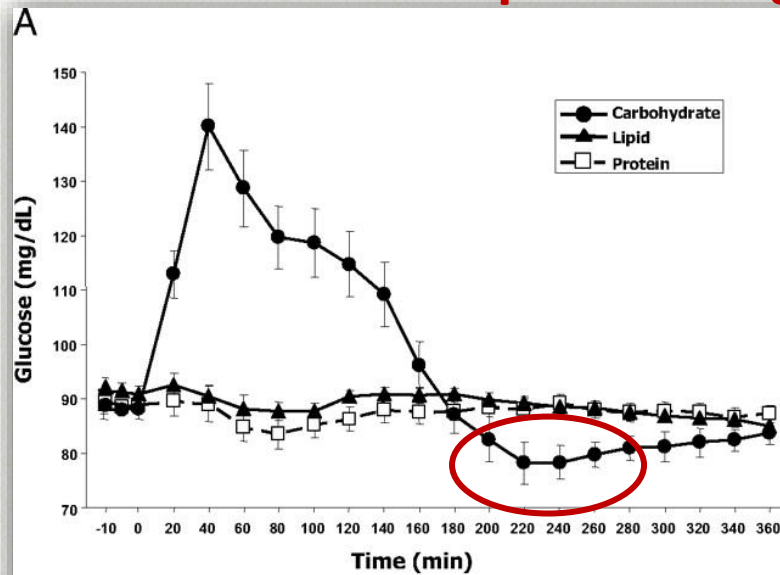
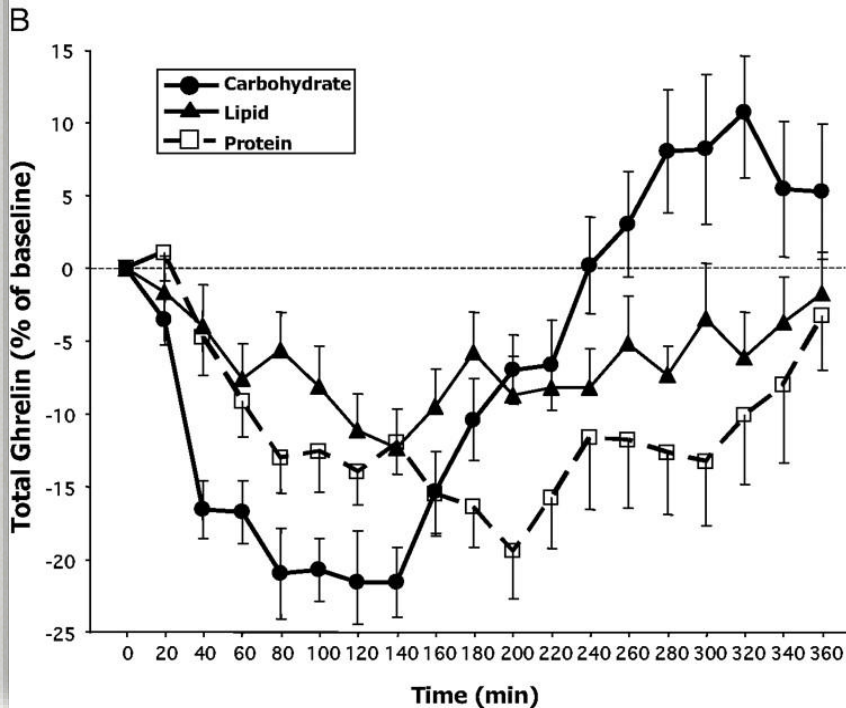
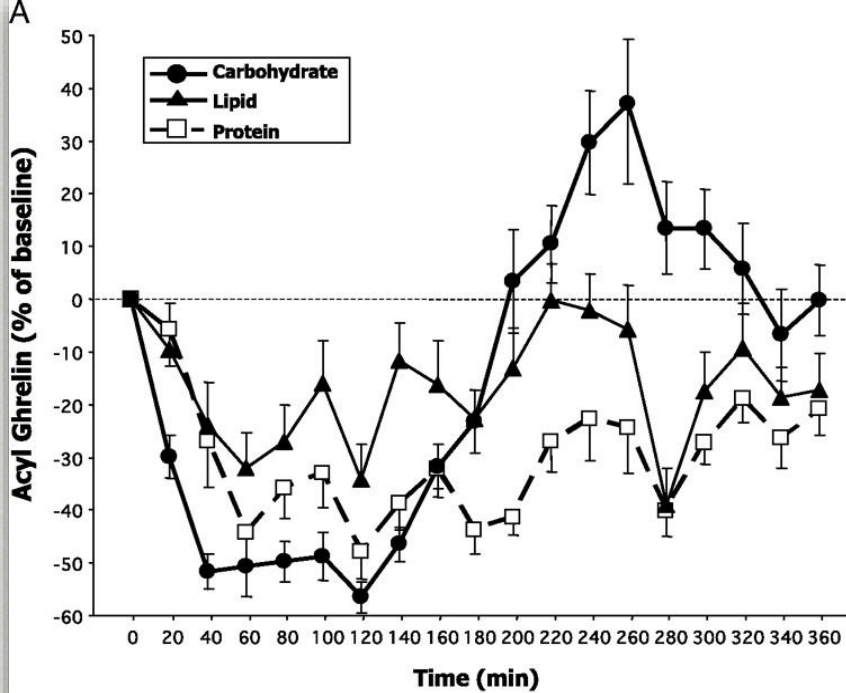
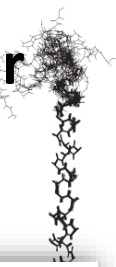
The increase in plasma 3-OMG ($P < .001$) and blood glucose ($P < .0001$) were greater in obese than lean subjects. Plasma 3-OMG correlated directly with blood glucose ($r = 0.78$, $P < .01$). In response to intraduodenal glucose, plasma GIP ($P < .001$), glucagon ($P < .001$), and insulin ($P < .001$) were higher, but GLP-1 ($P < .001$) was less in the obese compared with lean. Expression of SGLT-1 ($P = .035$), but not GLUT2 or T1R2, was higher in the obese, and related to peak plasma 3-OMG ($r = 0.60$, $P = .01$), GIP ($r = 0.67$, $P = .003$), and insulin ($r = 0.58$, $P = .02$).

Conclusions:

In morbid obesity, proximal intestine glucose absorption is accelerated and related to increased SGLT-1 expression, leading to an incretin-glucagon profile promoting hyperinsulinemia and hyperglycemia. These findings are consistent with the concept that accelerated glucose absorption in the proximal gut underlies the foregut theory of obesity and type 2 diabetes.

„All test beverages were equivalent in terms of their volume, total caloric content, and energy density.”

100 % purified ingredients! (80-10-10)



Acyl and Total Ghrelin Are Suppressed Strongly by Ingested Proteins, Weakly by Lipids, and Biphatically by Carbohydrates ^{FREE}

Karen E. Foster-Schubert ✉, Joost Overduin, Catherine E. Prudom, Jianhua Liu, Holly S. Callahan, Bruce D. Gaylinn, Michael O. Thorner, David E. Cummings

The Journal of Clinical Endocrinology & Metabolism, Volume 93, Issue 5, 1 May 2008, Pages 1971-1979, <https://doi.org/10.1210/jc.2007-2289>

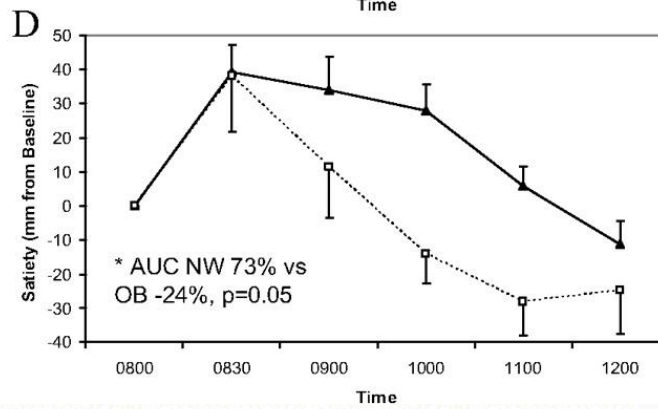
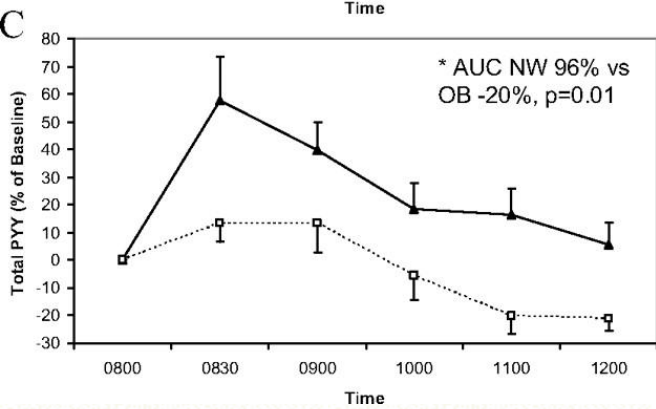
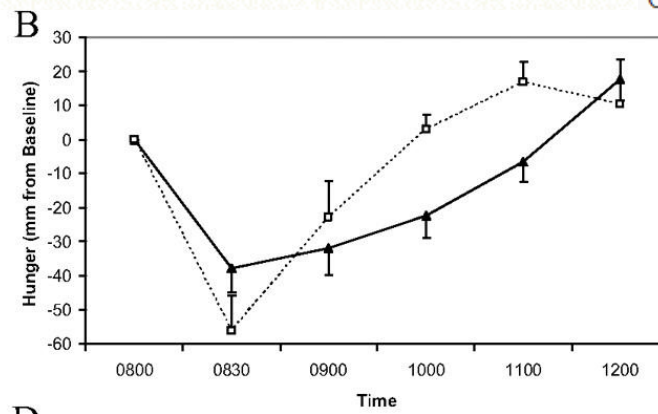
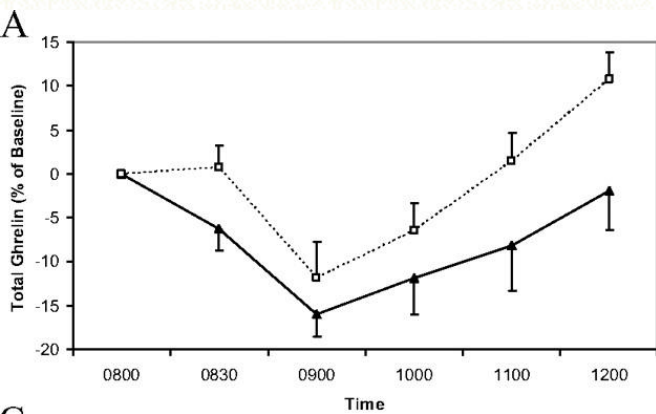


Table 2

Ghrelin, hunger, PYY, and satiety AUC comparisons within NW and OB groups to the three test meals

	Carbohydrate	Protein	Fat	P value
	88-2-10	36-44-20	17-2-81	
NW				
Ghrelin (%)	-36 ± 13	-61 ± 10	-42 ± 8	F (2, 27) = 1.5; P = 0.24
Hunger (mm)	-63 ± 17 ^a	-137 ± 27	-71 ± 27 ^b	F (2, 27) = 2.8; P = 0.08
PYY (%)	96 ± 30	130 ± 35	163 ± 36	F (2, 27) = 1.0; P = 0.39
Satiety (mm)	73 ± 23	122 ± 26	97 ± 31	F (2, 27) = 0.8; P = 0.44
OB				
Ghrelin (%)	-8 ± 10	-28 ± 7	-8 ± 10	F (2, 26) = 1.6; P = 0.22
Hunger (mm)	-22 ± 22 ^c	-158 ± 42	-63 ± 30 ^d	F (2, 26) = 4.7; P = 0.02
PYY (%)	-20 ± 27 ^e	181 ± 34	53 ± 31 ^f	F (2, 26) = 11.3; P = 0.0003
Satiety (mm)	-24 ± 41 ^g	170 ± 44	65 ± 36 ^h	F (2, 26) = 5.8; P = 0.008

Data are expressed as mean ± SE from baseline.

^a P = 0.04 vs. protein;

^b P = 0.06 vs. protein;

^c P = 0.006 vs. protein;

^d P = 0.05 vs. protein;

^e P < 0.0001 vs. protein

^f P = 0.007 vs. protein;

^g P = 0.002 vs. protein;

^h P = 0.08 vs. protein.

Effects of Meals High in Carbohydrate, Protein, and Fat on Ghrelin and Peptide YY Secretion in Prepubertal Children ^{FREE}

Jefferson P. Lomenick ✉, Maria S. Melguizo, Sabrina L. Mitchell, Marshall L. Summar, James W. Anderson

The Journal of Clinical Endocrinology & Metabolism, Volume 94, Issue 11, 1 November 2009, Pages 4463–4471, <https://doi.org/10.1210/jc.2009-0949>

„The high-carbohydrate meal consisted of one Fruit Roll-up, one low-fat Pop-tart, one package of Sunkist fruit chews, and one juice box (430 kcal, 88% carbohydrate, 2% protein, 10% fat).”

„In conclusion, our data show that the macronutrient content of foods has differential effects on ghrelin and PYY secretion and appetite ratings in prepubertal children and are consistent with the observed effectiveness of high-protein/low-carbohydrate diets.”

A high carbohydrate, but not fat or protein meal attenuates postprandial ghrelin, PYY and GLP-1 responses in Chinese men

Ehsan Parvaresh Rizi^{1,2}, Tze Ping Loh³, Sonia Baig¹, Vanna Chhay¹, Shiqi Huang⁴, Jonathan Caleb Quek¹, E. Shyong Tai^{1,2,5}, Sue-Anne Toh^{1,2,5,6}, Chin Meng Khoo^{1,2*}

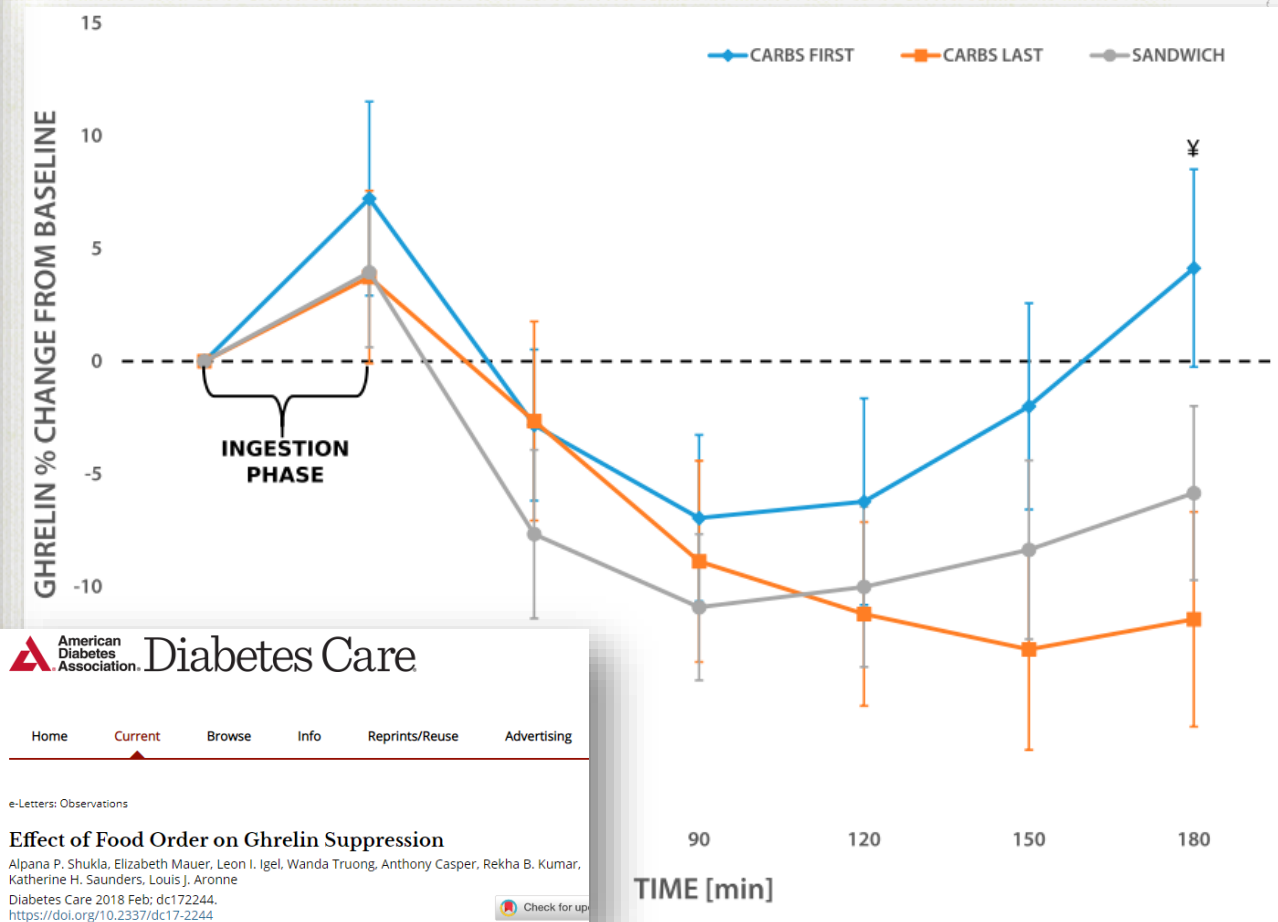
1 Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, **2** Department of Medicine, National University Health System, Singapore, **3** Department of Laboratory Medicine, National University Health System, Singapore, **4** Food Science and Technology Program, Department of Chemistry, Faculty of Science, National University of Singapore, Singapore, **5** Duke-National University of Singapore Medical School, Singapore, **6** Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, United States of America

*Chin Meng KHOO@nuhs.edu.sg

Abstract

It is known that the macronutrient content of a meal has different impacts on the postprandial satiety and appetite hormonal responses. Whether obesity interacts with such nutrient-dependent responses is not well characterized. We examined the postprandial appetite and satiety hormonal responses after a high-protein (HP), high-carbohydrate (HC), or high-fat (HF) mixed meal. This was a randomized cross-over study of 9 lean insulin-sensitive (mean \pm SEM HOMA-IR 0.83 \pm 0.10) and 9 obese insulin-resistant (HOMA-IR 4.34 \pm 0.41) young (age 21–40 years), normoglycaemic Chinese men. We measured fasting and postprandial plasma concentration of glucose, insulin, active glucagon-like peptide-1 (GLP-1), total peptide-YY (PYY), and acyl-ghrelin in response to HP, HF, or HC meals. Overall postprandial plasma insulin response was more robust in the lean compared to obese subjects. The postprandial GLP-1 response after HF or HP meal was higher than HC meal in both lean and obese subjects. In obese subjects, HF meal induced higher response in postprandial PYY compared to HC meal. HP and HF meals also suppressed ghrelin greater compared to HC meal in the obese than lean subjects. **In conclusion, a high-protein or high-fat meal induces a more favorable postprandial satiety and appetite hormonal response than a high-carbohydrate meal in obese insulin-resistant subjects.**

Satiety signaling based on macronutrients



American Diabetes Association. **Diabetes Care**

Home Current Browse Info Reprints/Reuse Advertising

e-Letters: Observations

Effect of Food Order on Ghrelin Suppression

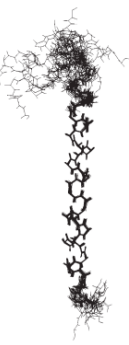
Alpana P. Shukla, Elizabeth Mauer, Leon I. Igel, Wanda Truong, Anthony Casper, Rekha B. Kumar, Katherine H. Saunders, Louis J. Aronne

Diabetes Care 2018 Feb; dc172244.
<https://doi.org/10.2337/dc17-2244>


Check for updates

Figure 1—Ghrelin percent change from baseline following carbohydrate-first (carbs first), carbohydrate-last (carbs last), and sandwich meal orders. Values are mean \pm SEM, $n = 16$. ¥Statistically significant difference ($P = 0.003$, linear mixed-effects model) between carbs first and carbs last at 180 min.

Placement of carbohydrates



High orange juice consumption with or in-between three meals a day differently affects energy balance in healthy subjects

Franziska A Hägele, Franziska Büsing, Alessa Nas, Julian Aschoff, Lena Gnädinger, Ralf Schweiggert, Reinhold Carle & Anja Bosy-Westphal 

Nutrition & Diabetes **8**, Article number: 19 (2018)

doi:10.1038/s41387-018-0031-3

[Download Citation](#)

Received: 07 September 2017

Revised: 21 December 2017

Accepted: 07 February 2018

Published: 25 April 2018

After BM-intervention, fat mass increased (+1.0 ± 1.8 kg; $p < 0.05$) and postprandial insulin sensitivity tended to decrease ($\Delta\text{Matsuda}_{\text{ISI}}$: -0.89 ± 2.3 ; $p = 0.06$). By contrast, after WM-intervention fat mass and gamma-glutamyl transferase (GGT) decreased (-0.30 ± 0.65 kg; -2.50 ± 3.94 ; both $p < 0.05$), whereas glucose variability was higher (ΔMAGE : $+0.45 \pm 0.59$, $p < 0.05$). Daylong glycaemia, insulin secretion, changes in basal insulin sensitivity, and triglycerides did not differ between WM- and BM-interventions (all $p > 0.05$). In young healthy adults, a conventional 3-meal structure with orange juice consumed together with meals had a favorable impact on energy balance, whereas juice consumption in-between meals may contribute to a gain in body fat and adverse metabolic effects.

Basic setup of the entero-insular axis



ELSEVIER

Biochimica et Biophysica Acta (BBA) - Gene Regulatory

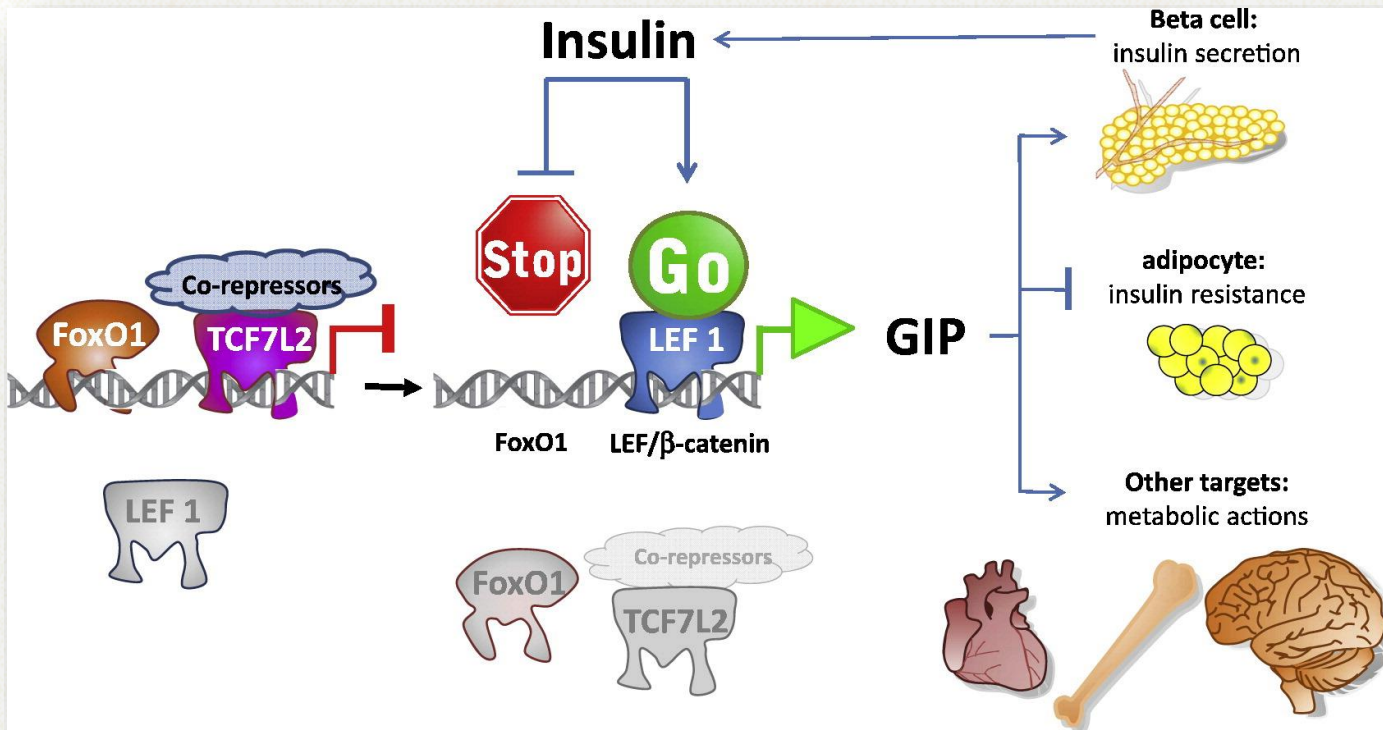
Mechanisms

Volume 1839, Issue 11, November 2014, Pages 1141-1150



Insulin drives glucose-dependent insulintropic peptide expression via glucose-dependent regulation of FoxO1 and LEF1/ β -catenin

Jose Manuel García-Martínez ^{a, 1, 2}, Ana Chocarro-Calvo ^{a, 1, 2, 3}, Antonio De la Vieja ^b, Custodia García-Jiménez



„...insulin stimulates the expression of the major human incretin, glucose-dependent insulintropic peptide (GIP) in enteroendocrine cells but requires glucose to do it.

...

Our results reveal a glucose-regulated feedback loop at the entero-insular axis, where glucose levels determine basal and insulin-induced *Gip* expression;”

Diet: Friend or Foe of Enteroendocrine Cells: How It Interacts with Enteroendocrine Cells FREE

Sofia Moran-Ramos, Armando R. Tovar, Nimbe Torres ✉ Author Notes

Advances in Nutrition, Volume 3, Issue 1, 1 January 2012, Pages 8–20,

GIP biological actions.

Although the prime physiological role of GIP is to increase insulin secretion induced by intestinally absorbed nutrients, the GIP receptor has been found in different tissues, suggesting that it has variable extra-pancreatic functions. Indeed, it has been shown that GIP modulates calcium deposition in bone and bone formation (26, 27) and has an important role in lipid metabolism. GIP has been reported to stimulate fat deposition in adipocytes by increasing the activity of lipoprotein lipase (28–30). Moreover, high fat-fed and *ob/ob* mice that are knocked-out for the GIP receptor, although mildly glucose intolerant, were protected against obesity (31). In the same line, GIP receptor antagonism reversed obesity and metabolic-associated abnormalities in high fat-fed rats (32). These and other data suggest that GIP as is a metabolically thrifty gene and postulate it as possible link between overnutrition and obesity (31, 33, 34).

Diabetologia (1999) 42: 1314–1323

Diabetologia

© Springer-Verlag 1999

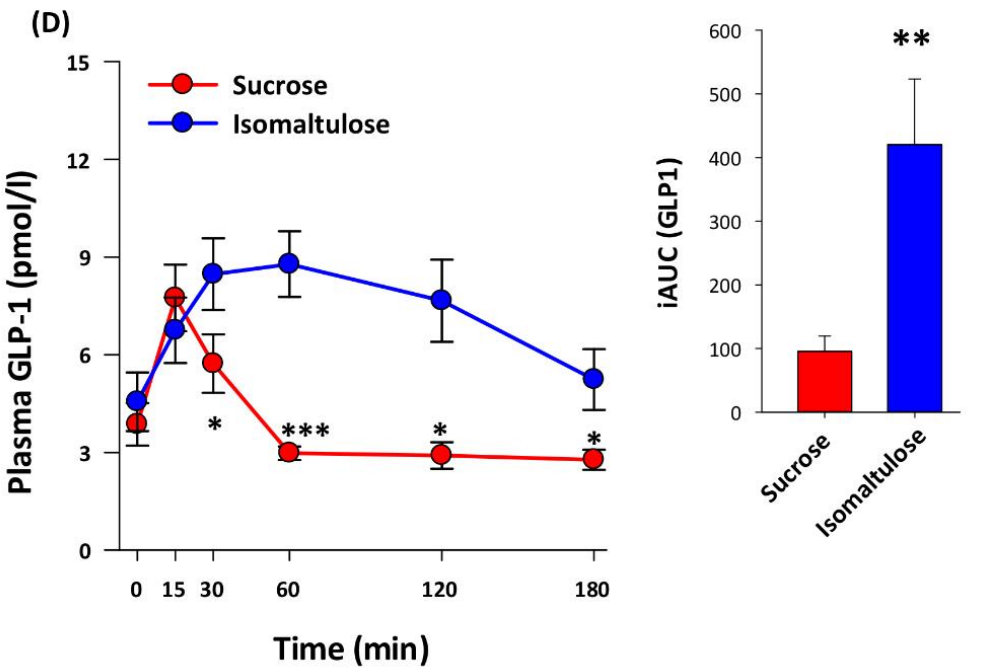
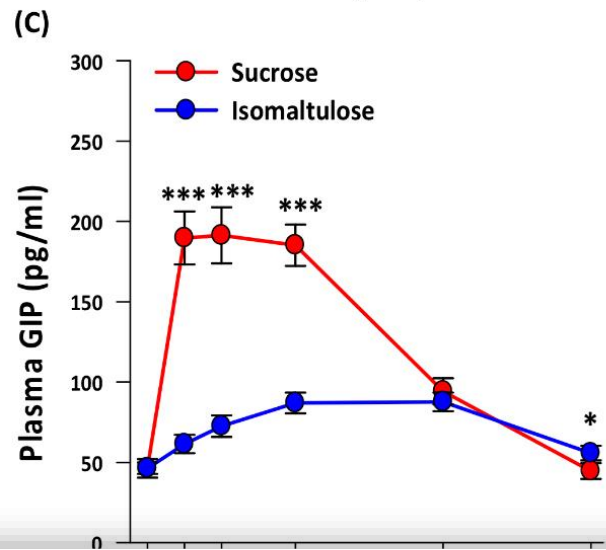
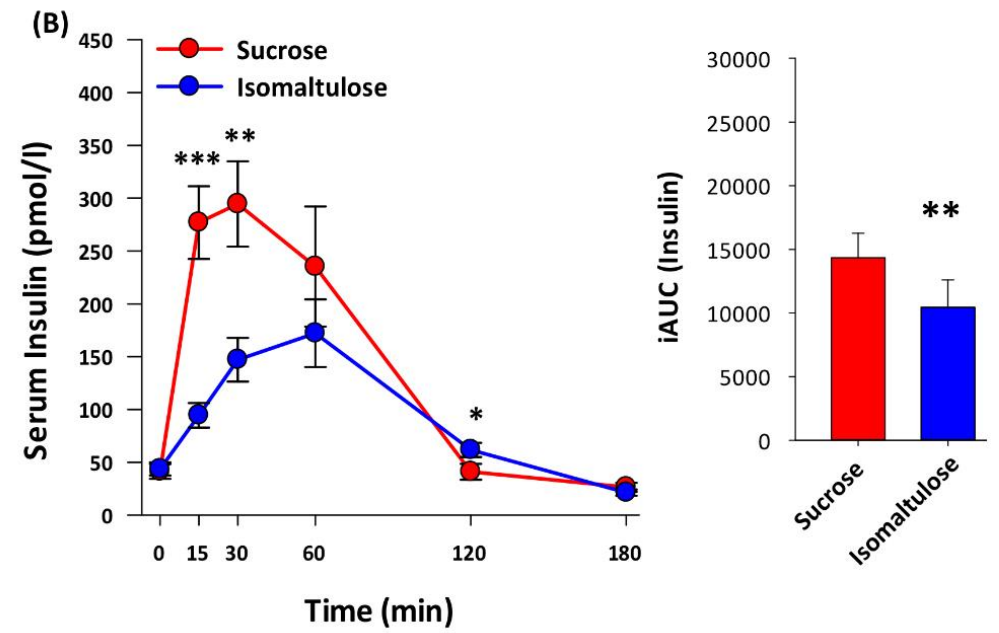
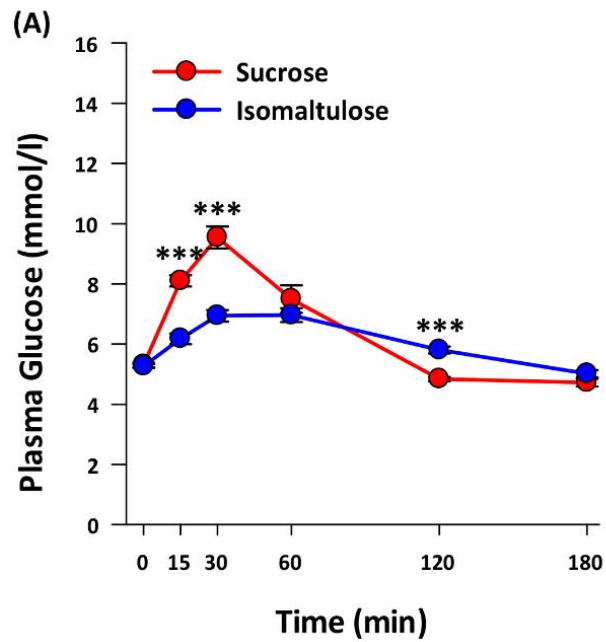
Twenty-four-hour insulin secretion rates, circulating concentrations of fuel substrates and gut incretin hormones in healthy offspring of Type II (non-insulin-dependent) diabetic parents: evidence of several aberrations

B. Nyholm¹, M. Walker², C.H. Gravholt¹, P.A. Shearing², J. Sturis³, K. G. M. M. Alberti², J.J. Holst⁴, O. Schmitz¹

in relatives and control subjects. During daytime (i.e. after meals, Fig.4) AUC for plasma GIP (46002 ± 3337 vs 35006 ± 3428 pmol · l⁻¹ · min, $p < 0.05$) was significantly increased in the relatives compared with control subjects, whereas AUC for plasma GLP-1 (23321 ± 3189 vs 18384 ± 1438 pmol · l⁻¹ · min, $p = 0.38$) remained similar in the two groups. The AUC for plasma GIP was significantly increased in the relatives after breakfast (12999 ± 886 vs 9986 ± 913 pmol · l⁻¹ · min, $p < 0.05$) and lunch (17842 ± 1698 vs 12272 ± 1311 pmol · l⁻¹ · min, $p < 0.05$) though barely statistical significant after dinner (15161 ± 1088 vs 12749 ± 1589 pmol · l⁻¹ · min, $p = 0.15$). In contrast, AUC for plasma GLP-1 did not differ between the two groups after any of the three meals (Fig.4). During night-time, neither

A nice model of the incretin imbalance:
Sucrose vs. Isomaltulose
 in healthy humans

Pure forms not only have a huge effect on incretins, but also on plasma glucose and insulin.

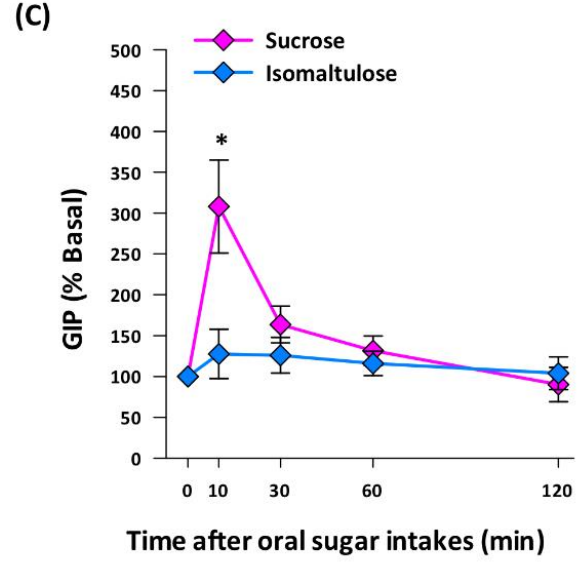
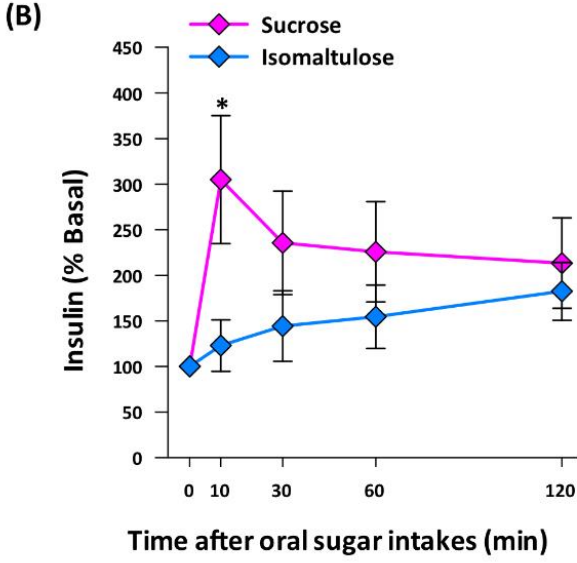
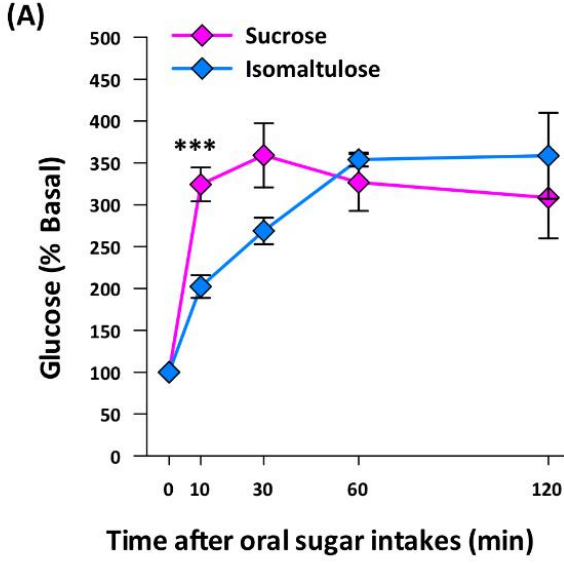


Trends Endocrinol Metab. 2018 May;29(5):289-299. doi: 10.1016/j.tem.2018.03.003. Epub 2018 Mar 27.

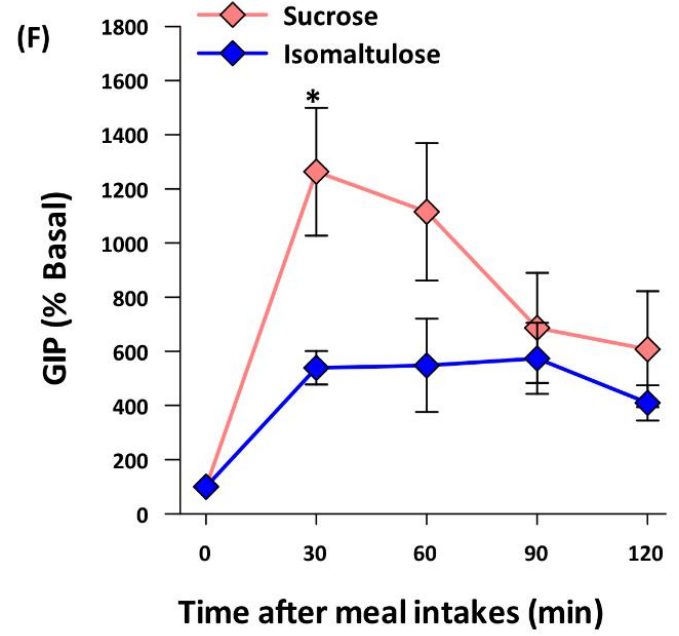
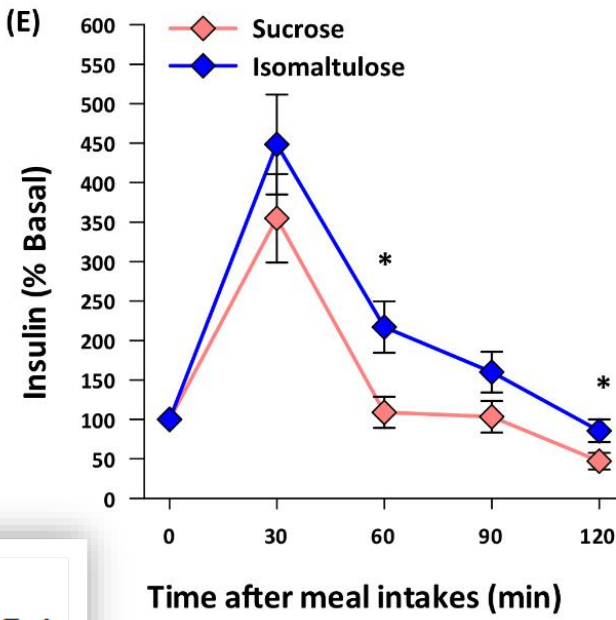
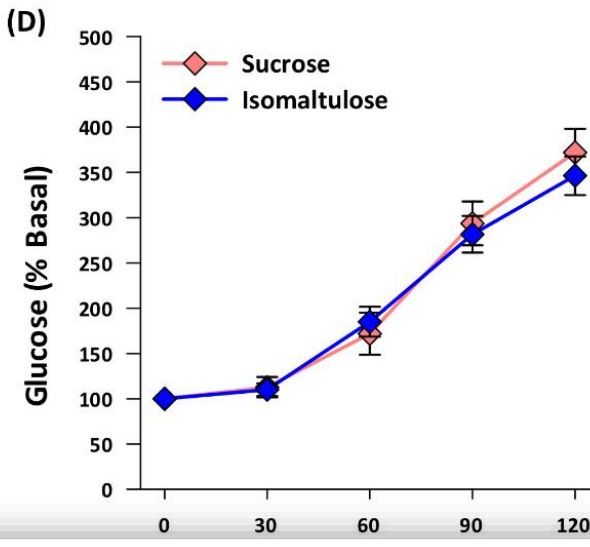
High Glycemic Index Metabolic Damage - a Pivotal Role of GIP and GLP-1.

Pfeiffer AFH¹, Keyhani-Nejad F².

Pure forms show the same response in mice. Sustained feeding with sucrose induces insulin resistance and fatty liver.



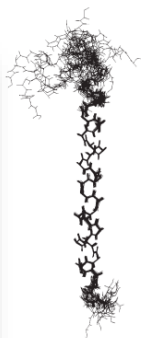
Mixed meal intake supplemented with these two sugars removes the effect on blood glucose and insulin, but it is even more pronounced on GIP. Fatty liver persists in the sucrose group.



Trends Endocrinol Metab. 2018 May;29(5):289-299. doi: 10.1016/j.tem.2018.03.003. Epub 2018 Mar 27.

High Glycemic Index Metabolic Damage - a Pivotal Role of GIP and GLP-1.

Pfeiffer AFH¹, Keyhani-Nejad F².



Boiled potato, low-fat veal and butter (50 g from CHO, protein and fat)

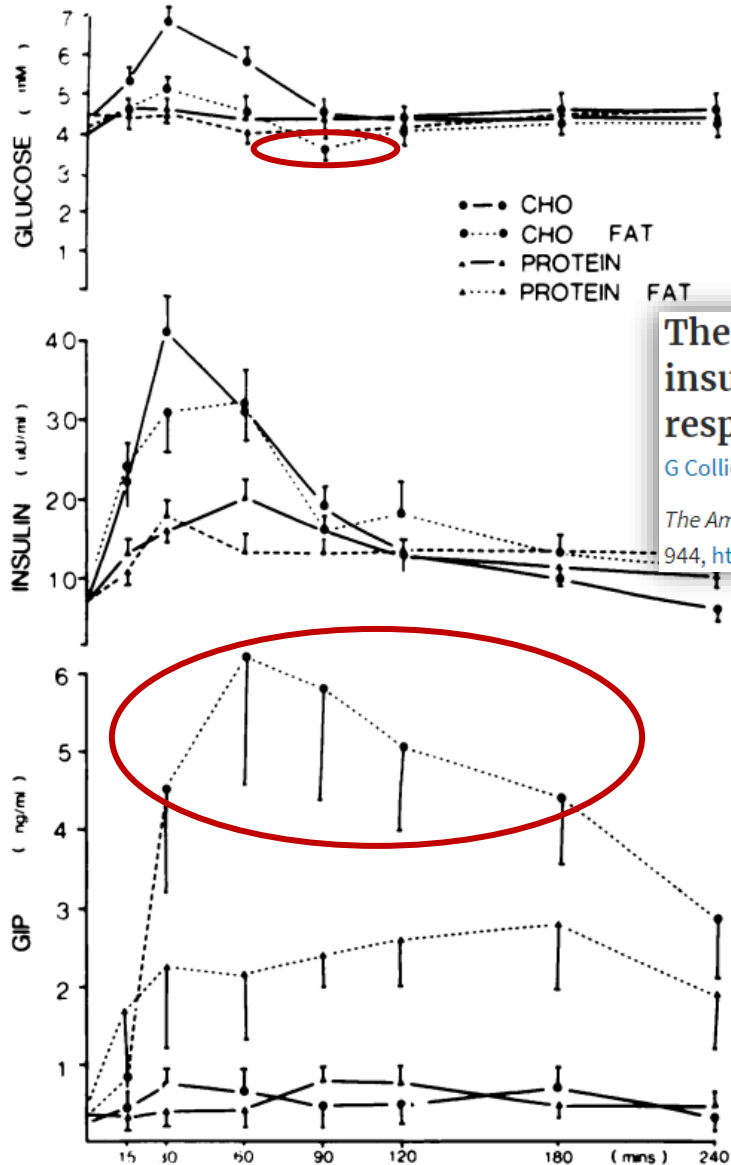


FIG 1. Plasma glucose, insulin, and GIP responses to 50 g carbohydrate \pm 50 g fat and 50 g protein \pm 50 g fat. Mean \pm SEM (n = 8).

The effect of coingestion of fat on the glucose, insulin, and gastric inhibitory polypeptide responses to carbohydrate and protein

G Collier, K O'Dea

The American Journal of Clinical Nutrition, Volume 37, Issue 6, 1 June 1983, Pages 941-944, <https://doi.org/10.1093/ajcn/37.6.941>

Perhaps it shouldn't be surprising that the only outlier is the combination that doesn't occur in nature? \Rightarrow Pre-digested carbohydrate with substantial amount of fat added on top.

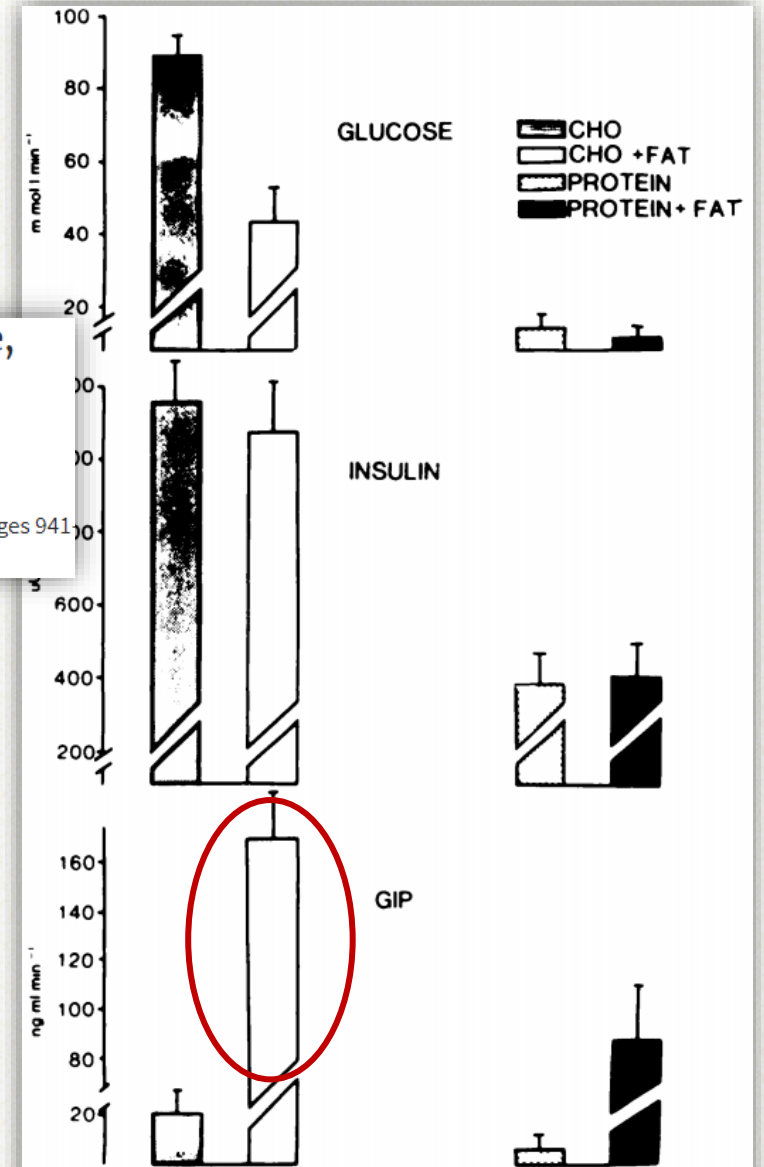
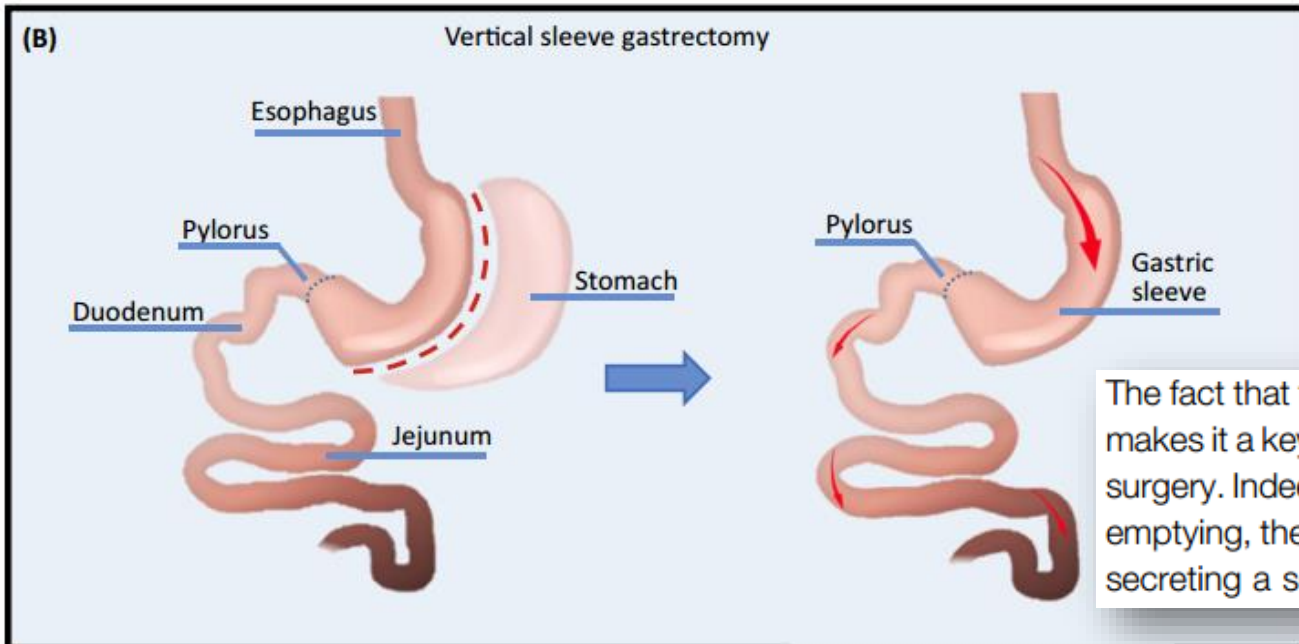
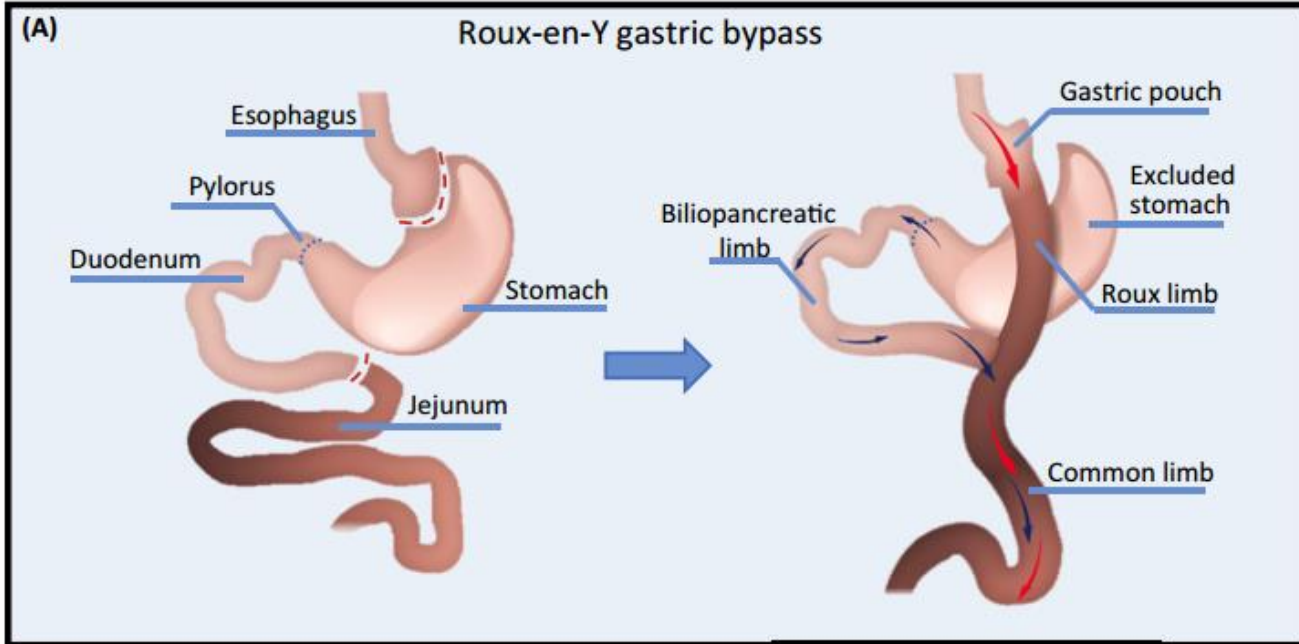


FIG 2. Areas under the incremental curves for glucose, insulin, and GIP for the 1st h after ingestion of 50 g carbohydrate \pm 50 g fat and 50 g protein \pm 50 g fat. Mean \pm SEM (n = 8).

Review

Intestinal Adaptations after Bariatric Surgery: Consequences on Glucose Homeostasis

Jean-Baptiste Cavin¹, André Bado¹, Maude Le Gall¹ ✉

Diabetes: How bariatric (bypass) surgery works

The fact that the gastrointestinal (GI) tract is the direct target of bariatric procedures potentially makes it a key player, although so far underestimated, in the metabolic changes observed after surgery. Indeed, the GI tract can play a direct role in glucose homeostasis by modulating gastric emptying, the digestion of carbohydrates, and absorption of glucose during meals, and also by secreting a set of hormones, including incretins that regulate the release of insulin [6].

Research Article

**Effect of Modified Roux-en-Y Gastric Bypass Surgery on
 GLP-1, GIP in Patients with Type 2 Diabetes Mellitus**

Shao-Wei Xiong,¹ Jing Cao,¹ Xian-Ming Liu,¹ Xing-Ming Deng,¹ Zeng Liu,¹ and Fang-Ting Zhang²

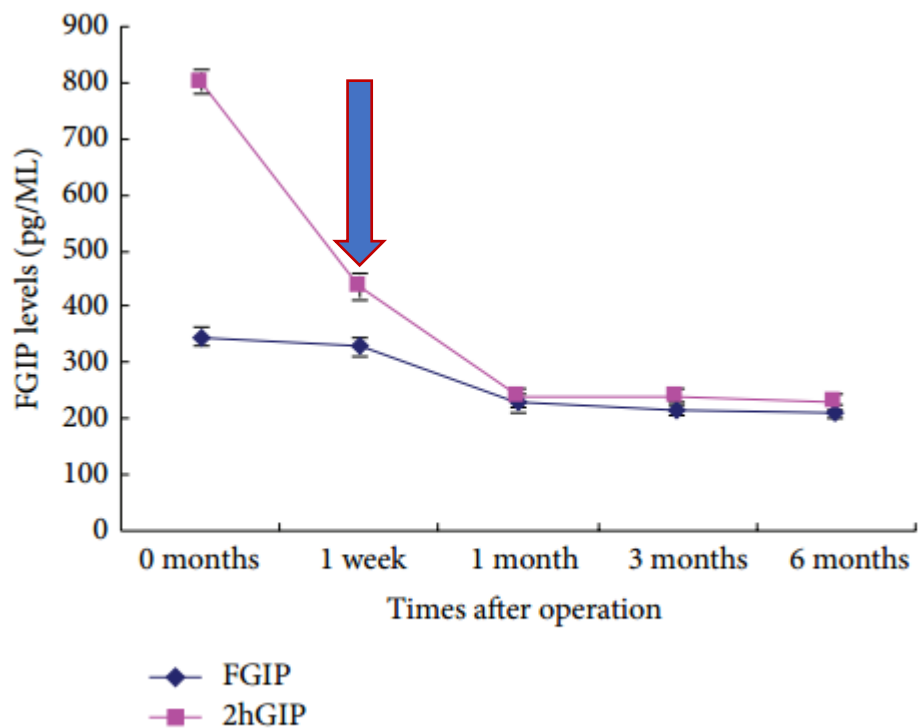


FIGURE 2: FGIP levels before and after the surgery.

TABLE 2: Comparison of GLP-1 and GIP levels before and after the surgery.

	<i>n</i>	FGLP-1	2hGLP-1	FGIP	2hGIP
0 mo	50	6.5 ± 1.3	11.9 ± 1.6*	347 ± 16	801 ± 21*
1 wk	50	9.3 ± 1.1*	19.7 ± 2.0 [▲] #	328 ± 15	436 ± 25 [▲]
1 mo	50	11.6 ± 1.7 [▲]	23.7 ± 1.9 [▲] #	229 ± 16*	238 ± 17 [▲]
3 mo	50	17.9 ± 1.9 [▲]	28.9 ± 2.1 [▲] #	217 ± 12*	241 ± 15 [▲]
6 mo	50	18.1 ± 1.8 [▲]	29.2 ± 2.2 [▲] #	213 ± 14*	230 ± 13 [▲]

Data are shown as mean ± SD, FGLP-1 and 2hFGLP-1 (pmol/L), FGIP, and 2hFGIP (pg/ML).

Compared with the before surgery (0 months) group **P* < 0.05, [▲]*P* < 0.01. Comparison of the same point in time #*P* < 0.01.

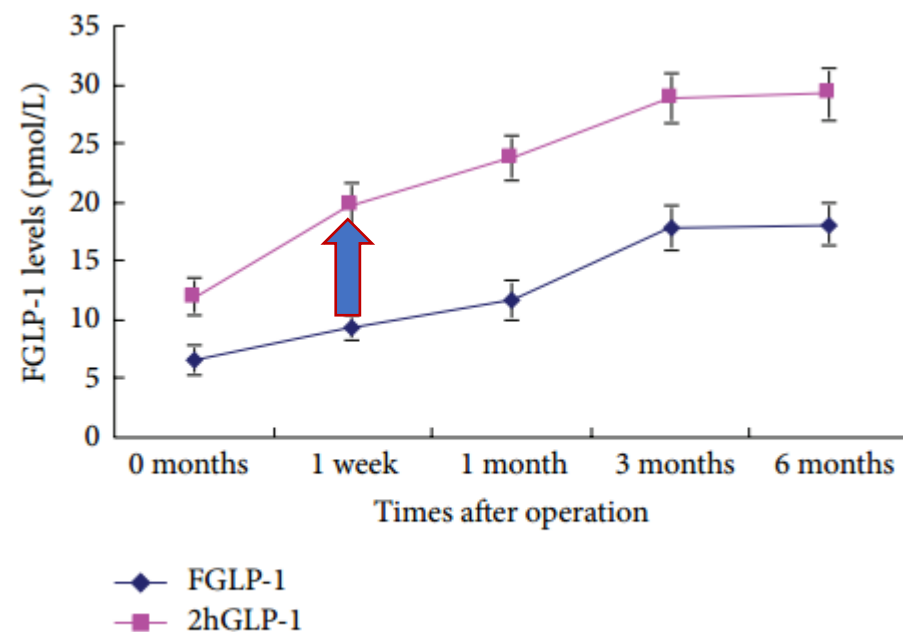



FIGURE 1: FGLP-1 levels before and after the surgery.

BPD/RYGB/SG short term effects

- Bypass surgery naturally decreases upper small intestinal SGLT1 stimulation (bypasses). Although subject to strong debate, it seems independent of caloric restriction.
- A strong effect on immune modulation was also reported in animal models
- Curiously enough, sleeve gastrectomy, which does not involve the bypass of intestinal segments, also decreases SGLT1 expression.

Identification of Proteins Associated with the Early Restoration of Insulin Sensitivity After Biliopancreatic Diversion

Cecilia Karlsson , Kristina Wallenius, Anna Walentinsson, Peter J Greasley, Tasso Miliotis, Mårten Hammar, Amerigo Iaconelli, Sofia Tapani, Marco Raffaelli, Geltrude Mingrone ... [Show more](#)

The Journal of Clinical Endocrinology & Metabolism, Volume 105, Issue 11, November 2020, Pages e4157–e4168,

<https://doi.org/10.1210/clinem/dgaa558>

Published: 24 August 2020 [Article history](#) ▼

Sleeve Gastrectomy and Roux-en-Y Gastric Bypass Attenuate Pro-inflammatory Small Intestinal Cytokine Signatures

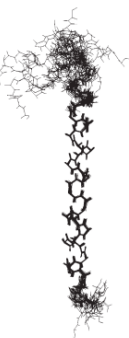
Renuka Subramaniam, Hassan Aliakbarian, Hina Y. Bhutta, David A. Harris, Ali Tavakkoli & Eric G. Sheu 

Obesity Surgery **29**, 3824–3832(2019) | [Cite this article](#)

Residual Gastric Dilatation Interferes with Metabolic Improvements Following Sleeve Gastrectomy by Upregulating the Expression of Sodium-Glucose Cotransporter-1

Jun Xia, Qian He, Ming He, Guiwen Xu, Yizhou Tang & Yixing Ren 

Obesity Surgery **29**, 3324–3333(2019) | [Cite this article](#)



First-Phase Insulin Secretion Restoration and Differential Response to Glucose Load Depending on the Route of Administration in Type 2 Diabetic Subjects After Bariatric Surgery

Serenella Salinari, DSC1, Alessandro Bertuzzi, DSC2, Simone Asnaghi, MSC1, Caterina Guidone, MD3, Melania Manco, MD4 and Geltrude Mingrone, MD, PHD3

+ Author Affiliations

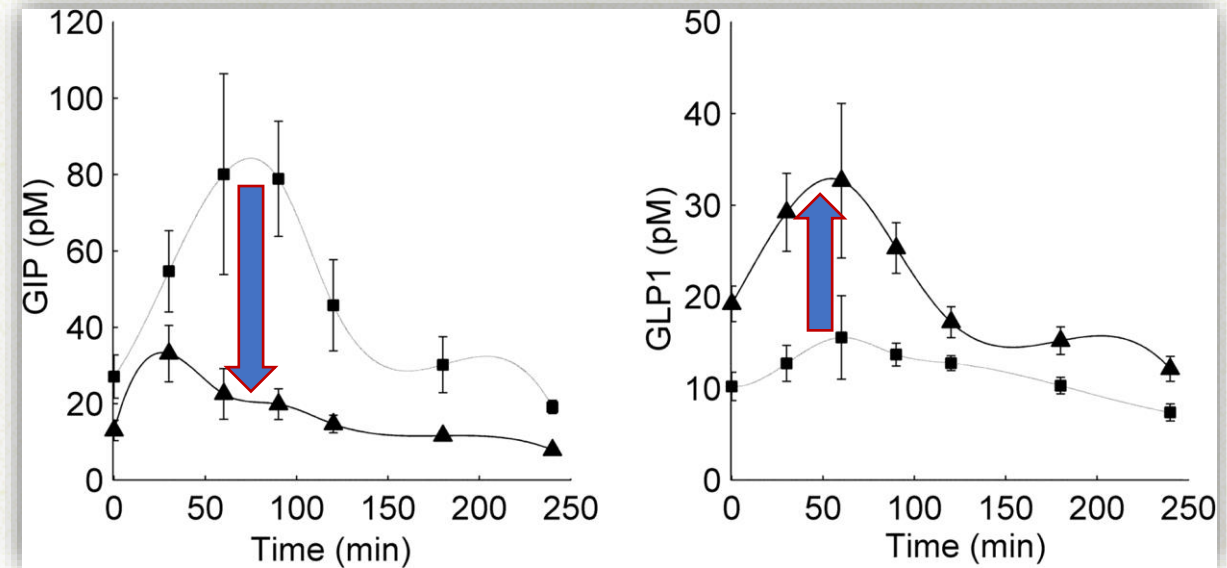
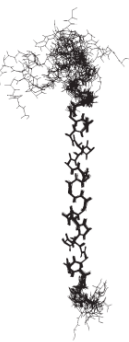
Corresponding author: Serenella Salinari, salinari@dis.uniroma1.it

Diabetes Care 2009 Mar; 32(3): 375-380. <https://doi.org/10.2337/dc08-1314>




RESULTS—The first phase of insulin secretion after the IVGTT was fully normalized after the operation. The disposition index from OGTT data was increased about 10-fold and became similar to the values found in control subjects, and the disposition index from IVGTT data increased about 3.5-fold, similarly to what happened after the euglycemic clamp. The area under the curve (AUC) for GIP decreased about four times (from $3,000 \pm 816$ to 577 ± 155 pmol \cdot l⁻¹ \cdot min, $P < 0.05$). On the contrary, the AUC for GLP1 almost tripled (from 150.4 ± 24.4 to 424.4 ± 64.3 pmol \cdot l⁻¹ \cdot min, $P < 0.001$). No significant correlation was found between GIP or GLP1 percent changes and modification of the sensitivity indexes independently of the route of glucose administration.

A reverse imbalance for reversing diabetes?



Effect of the Duodenal-Jejunal Bypass Liner on Glycemic Control in Patients With Type 2 Diabetes With Obesity: A Meta-analysis With Secondary Analysis on Weight Loss and Hormonal Changes

Pichamol Jirapinyo^{1,2}, Andrea V. Haas^{2,3} and Christopher C. Thompson^{1,2†}

 Author Affiliations

Corresponding author: Christopher C. Thompson, cthompson@hms.harvard.edu.

Diabetes Care 2018 May; 41(5): 1106-1115. <https://doi.org/10.2337/dc17-1985>

RESULTS

Primary outcomes were change in HbA_{1c} and HOMA of insulin resistance (HOMA-IR). Secondary outcomes were change in weight and gut hormones glucose-dependent insulinotropic peptide (GIP), glucagon-like peptide 1 (GLP-1), peptide YY (PYY), and ghrelin. Seventeen studies were included. At explant, HbA_{1c} decreased by 1.3% [95% CI 1.0, 1.6] and HOMA-IR decreased by 4.6 [2.9, 6.3]. Compared with control subjects, DJBL subjects had greater HbA_{1c} reduction by 0.9% [0.5, 1.3]. Six months after explant, HbA_{1c} remained lower than baseline by 0.9% [0.6, 1.2]. At explant, patients lost 11.3 kg [10.3, 12.2], corresponding to a BMI reduction of 4.1 kg/m² [3.4, 4.9], total weight loss of 18.9% [7.2, 30.6], and excess weight loss of 36.9% [29.2, 44.6]. The amount of weight loss remained significant at 1 year postexplantation. After DJBL, GIP decreased, whereas GLP-1, PYY, and ghrelin increased.


CONCLUSIONS

DJBL improves glycemic control and insulin resistance in T2D patients with obesity. DJBL also appears to induce significant weight loss in this population. Additionally, changes in gut hormones suggest mechanisms similar to RYGB. Study limitations included heterogeneity among studies.

DIABETES, OBESITY AND METABOLISM

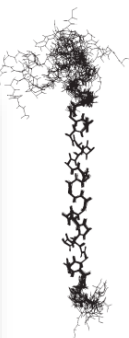
A JOURNAL OF PHARMACOLOGY AND THERAPEUTICS

Comparisons of the effects of 12-week administration of miglitol and voglibose on the responses of plasma incretins after a mixed meal in Japanese type 2 diabetic patients

T. Narita , H. Yokoyama, R. Yamashita, T. Sato, M. Hosoba, T. Morii, H. Fujita, K. Tsukiyama, Y. Yamada

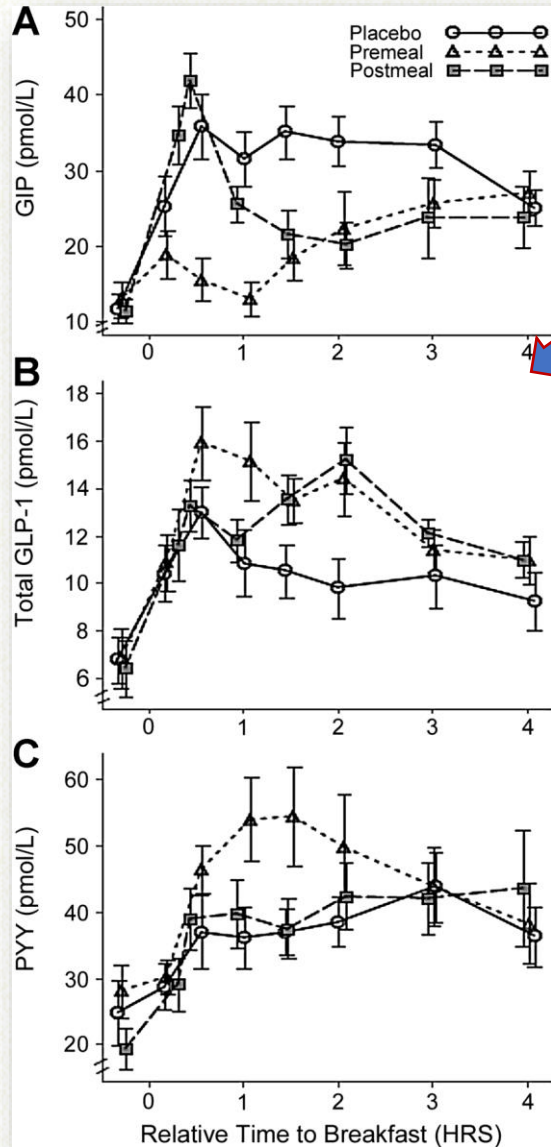
First published: 03 November 2011 | <https://doi.org/10.1111/j.1463-1326.2011.01526.x> | Cited by: 38

To compare the effects of miglitol [an alpha-glucosidase inhibitor (AGI) absorbed in the intestine] and voglibose (an AGI not absorbed) on plasma glucagon-like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP) levels, 26 and 24 Japanese type 2 diabetic patients were randomly assigned to receive miglitol or voglibose, respectively. After 12-week administration of both drugs, during 2-h meal tolerance test, plasma glucose, serum insulin and total GIP were significantly decreased and active GLP-1 was significantly increased. Miglitol group showed a significantly lower total GIP level than voglibose group. Miglitol, but not voglibose, significantly reduced body weight (BW). In all participants, the relative change in BW was positively correlated with that of insulin significantly and of GIP with a weak tendency, but not of GLP-1. In conclusion, both drugs can enhance postprandial GLP-1 responses and reduce GIP responses. The significant BW reduction by miglitol might be attributable to its strong GIP-reducing efficacy.



Selective sodium-dependent glucose transporter 1 inhibitors block glucose absorption and impair glucose-dependent insulinotropic peptide release

Robert L. Dobbins,¹ Frank L. Greenway,² Lihong Chen,¹ Yaping Liu,¹ Sharon L. Breed,¹ Susan M. Andrews,¹ Jeffrey A. Wald,¹ Ann Walker,¹ and Chari D. Smith¹



Gastric bypass surgery in a pill!

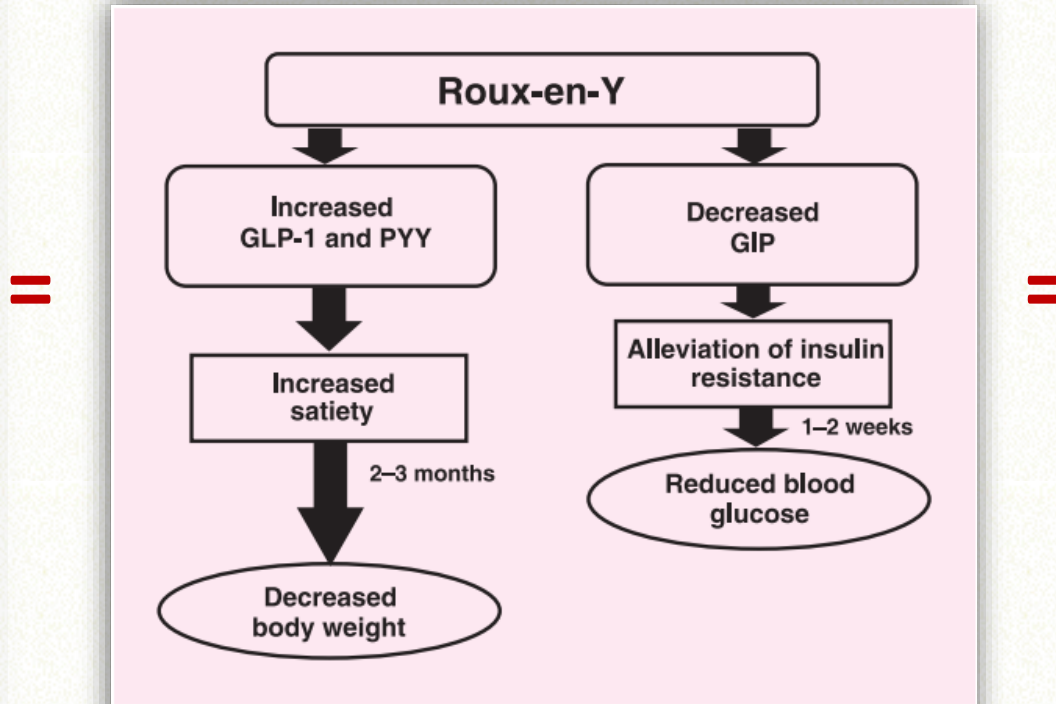
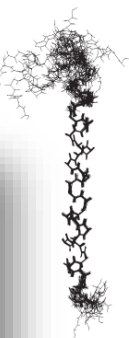
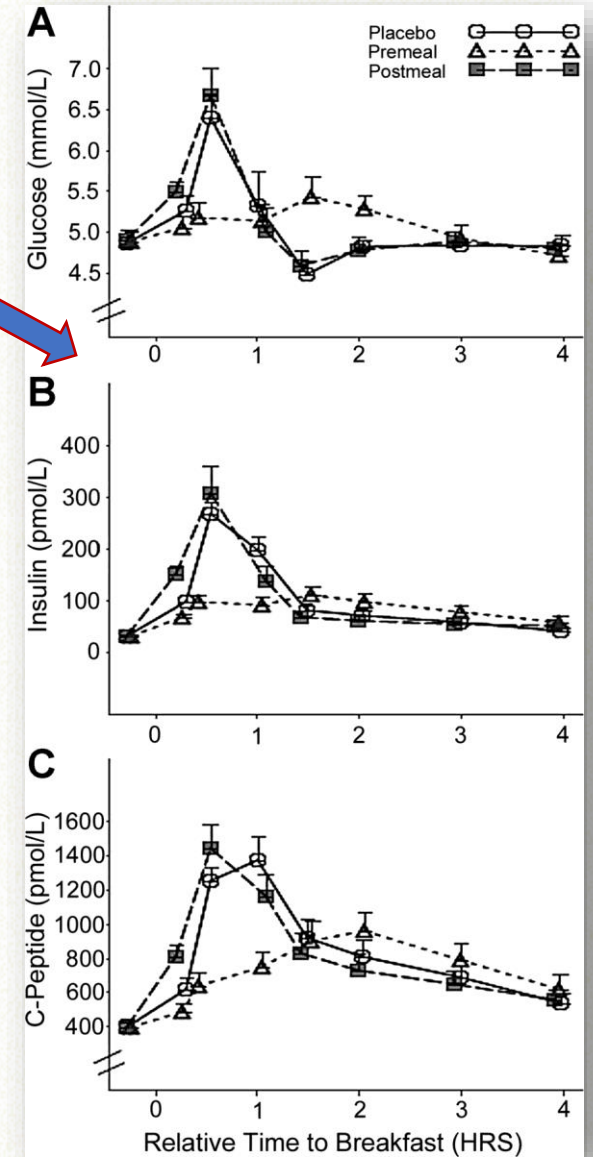
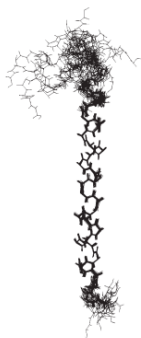


FIGURE 3 Role of endocrine changes in alleviation of insulin resistance, glucose intolerance, satiety and weight loss following Roux-en-Y bypass surgery. GIP, gastric inhibitory polypeptide; GLP-1, glucagon-like peptide 1; PYY, peptide YY.





Anything that interferes with starch-sugar digestion or slows absorption has the same beneficial effect

Natural SGLT1 and/or amylase inhibitors:

- Polyphenols
- Probiotics
- Moderate alcohol consumption
- Helminth therapy (!)

SGLT1/GIP variants

- SGLT1
- GIP

In vitro and animal studies

Alpha-amylase, α -glucosidase and lipase inhibiting activities of polyphenol-rich extracts from six common bean cultivars of Southern Italy, before and after cooking

Maria Neve Ombra , Antonio d'Acierno, Filomena Nazzaro, Patrizia Spigno, Riccardo Riccardi, Massimo Zaccardelli, ... show all

Pages 824-834 | Received 06 Sep 2017, Accepted 14 Dec 2017, Published online: 16 Jan 2018

 Download citation  <https://doi.org/10.1080/09637486.2017.1418845>  Check for updates

Journal of the Science of Food and Agriculture 

Research Article

Bifidobacterium from breastfed infant faeces prevent high-fat-diet-induced glucose tolerance impairment, mediated by the modulation of glucose intake and the incretin hormone secretion axis

Tong Li, Jianjun Yang, Hongxing Zhang, Yuanhong Xie, Junhua Jin 

First published: 27 February 2020 | <https://doi.org/10.1002/jsfa.10360>

PLOS ONE

 OPEN ACCESS  PEER-REVIEWED


RESEARCH ARTICLE

Role of Macrophages in the Altered Epithelial Function during a Type 2 Immune Response Induced by Enteric Nematode Infection


Luigi Notari, Diana C. Riera, Rex Sun, Jennifer A. Bohl, Leon P. McLean, Kathleen B. Madden, Nico van Rooijen, Tim Vanuytsel, Joseph F. Urban Jr., Aiping Zhao, Terez Shea-Donohue 



Published: January 23, 2014 • <https://doi.org/10.1371/journal.pone.0084763>

Moderate Alcohol Consumption Uniquely Regulates Sodium-Dependent Glucose Co-Transport in Rat Intestinal Epithelial Cells In Vitro and In Vivo

Molly Butts, Soudamani Singh, Jennifer Haynes, Subha Arthur, Uma Sundaram 

The Journal of Nutrition, Volume 150, Issue 4, April 2020, Pages 747-755,
<https://doi.org/10.1093/jn/nxz277>

Published: 26 November 2019 [Article history](#) 

 Journal of the American College of Cardiology 

Volume 72, Issue 15, 9 October 2018, Pages 1763-1773

Mini Focus on Diabetes
Original Investigation

Genetic Variants in *SGLT1*, Glucose Tolerance, and Cardiometabolic Risk

Sara B. Seidemann MD, PhD ^{a, b}, Elena Feofanova MS ^c, Bing Yu PhD ^c, Nora Franceschini MD ^d, Brian

AMERICAN JOURNAL OF PHYSIOLOGY
 **GASTROINTESTINAL AND LIVER PHYSIOLOGY**

JOURNAL HOME ISSUES  COLLECTIONS INFORMATION ABOUT  

 | Hormones and Signaling

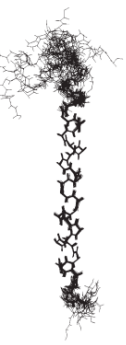
Common variants of *GIP* are associated with visceral fat accumulation in Japanese adults

Kazuhiro Nakayama , Kazuhisa Watanabe, Supichaya Boonvisut, Saho Makishima, ... See all authors 

01 DEC 2014 // <https://doi.org/10.1152/ajpgi.00282.2014>

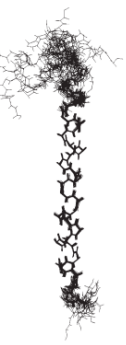
Scientific conclusions

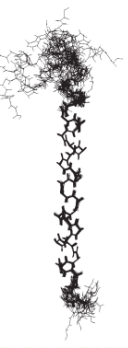
- Speed and zone of intestinal nutrient absorption is crucial in determining metabolic response to food.
- The greatest effect is seen with carbohydrate rich plant processing, thus retaining plant structure is critical.
- Diets high in ultra-refined, quick-absorbing food items plausibly result in an altered intestinal hormonal profile, hunger/satiety signaling, inflammatory signaling, and consequently, in higher food intake and increased meal frequency.
- This effect is exaggerated when ultra-processed carbohydrates are consumed in combination with significant amounts of fat. The „doughnut effect.”
- GIP may be part of a „thrifty machinery” in mammals.
 - Easily digestible, high energy density foods overstimulate it.
 - There is a negative feedback from acute elevations in insulin, but positive by chronic hyperinsulinemia, promoting further quick weight gain and IR.



Practical conclusions, takeaways

- Processing of food items high in protein and fat is mostly harmless, at least as far as short-term metabolic responses are concerned. Prioritize food items high in these macronutrients.
- Plant foods (carbohydrates) should be carefully selected based on their (dense) structure. Processing, especially industrial refining disrupts structure and accelerates absorption, resulting in reduced satiation. Excluding most carbohydrate sources also solves this problem...
- Consume carbohydrate rich foods at the end of meals (as dessert).
- Have fewer, larger meals vs. frequent small ones. Snacking is a bad idea.
- Eat your meal slowly to maximize satiation via the increased release of lower intestinal hormones.





Thank you for your attention!