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Carbohydrates and satiety

S. D. Poppitt, University of Auckland, New Zealand

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Abstract: Carbohydrates (CHO) provide a large percentage of our daily energy and are consumed in a wide variety of forms. Under isoenergetic conditions there is evidence of a macronutrient hierarchy for satiety (protein > CHO > fat), energy density (ED) plays a major role, but the causal relationships and underpinning mechanisms of the macronutrients are still being elicited. Effects of CHOs on food intake are greatly complicated by the wide variety of forms in which CHO is consumed. Numerous theories have been proposed as to the effect of CHO on satiety, with conflicting recommendations made both for increase and decrease in our daily diet, and these are discussed in this chapter. Hypotheses include effects on circulation and storage CHOs, including Mayer's original glucostatic theory of low circulating blood glucose and Flatt's glycogenostatic theory of low glycogen stores in liver and muscle both triggering hunger, and the glycaemic index (GI) theory of 'fast release' available CHO causing rapid high spikes and rebound low troughs in blood glucose to also stimulate hunger. Conversely, there are the peptide theory of CHO-driven secretion of circulating satiety biomarkers and/or peptides, and the high-fibre theory wherein foods with a high fibre content and/or a low GI and/or enhanced large bowel microbiota suppress hunger. In addition, low ED theory supports complex/fibrous CHO/low energy foods for suppression of hunger, whilst the low CHO theory, wherein total CHO intake is restricted, predicts suppression of both GI and hunger.

Key words: carbohydrate, glucose, fructose, glycaemic index, fibre, wholegrain foods, microbiota, beverages.

9.1 Introduction

This chapter aims to review the current evidence which links CHO in our diet to satiety, satiation and the regulation of food intake, and to investigate

Disclaimer: S. D. Poppitt holds the Fonterra Chair in Human Nutrition at the University of Auckland, Auckland, New Zealand.

some of the mechanisms which may underpin this relationship. The role of CHOs in weight loss has long been controversial[1–5] and much of this debate continues,[6,7] and clearly the effect of CHOs on appetite and food intake is central to this debate. CHOs provide a large percentage of our daily energy and are consumed in a wide variety of forms. For the purposes of this review, it is convenient to divide them into the available CHOs, which are digested and absorbed in the small intestine (SI), and the unavailable CHOs, which pass through into the large bowel for fermentation into short chain fatty acids (SCFA) and which may provide a nutrient source for the resident microbiota. The sections below will briefly review the macronutrient hierarchy and the satiety effects of CHO compared with lipids and proteins, and the relative effects of CHO composition when consumed as both a food and a beverage. In particular there will be focus on the differences between the mono/disaccharides glucose, fructose (including high fructose corn syrup, HFCS) and sucrose, low and high GI foods, CHOs targeted to the distal SI, and dietary fibres, whole grains and other fermentable CHO sources within the large bowel. In addition, the chapter will review both short and long term CHO interventions for satiety, and possible mechanisms of action. There have been many theories proposed as to the effect of dietary CHOs on satiety, leading to conflicting recommendations for both an increase and decrease in their daily intake. Some of these theories include dietary CHOs affecting levels of circulating and storage CHOs, including Mayer's original glucostatic theory of low circulating CHO (blood glucose) triggering hunger[8] and Flatt's glycogenostatic theory of low CHO stores (liver and muscle glycogen) triggering hunger[9,10]; the GI theory, wherein 'fast release' available CHO is hypothesised to generate rapid high spikes and rebound low troughs in blood glucose and hence trigger hunger[11]; the peptide theory, wherein dietary CHOs drive enhanced secretion of circulating 'satiety' biomarkers and/or peptides; the high-fibre theory, wherein foods with a high fibre content and/or a low GI suppress hunger, and wherein prebiotic CHOs may enhance number or activity of large bowel bacteria; the low ED theory, wherein high-CHO, low energy, high bulk foods suppress hunger; and the low CHO theory, wherein a low total CHO intake suppresses both GI and hunger.

9.2 Macronutrients and satiety

Whilst the format and composition of macronutrients are clearly important, under isoenergetic conditions there is evidence for a hierarchy in satiety,[12–17] although the underpinning mechanisms still remain unclear. Per MJ of energy ingested, the hierarchy (protein > CHO > lipid) has been hypothesised to be most pronounced under conditions wherein a fixed load of >1–1.5 MJ is fed and where fat is disproportionately energy dense.[18] Isoenergetically dense loads of high-fat, high-CHO and high-protein foods may exert less pronounced

differences. Alcohol, in turn, may engender lower satiety than any of the food macronutrients, due in part to its liquid form and disinhibiting nature, neither of which is conducive to suppression of appetite.[19,20] Much of this evidence originates from short postprandial studies, wherein a fixed energy, variable macronutrient preload is fed and eating behaviour at a subsequent *ad libitum* test meal is measured. In longer term fully *ad-lib* studies, wherein participants are free to eat as they choose and the energy intake (EI) of the manipulated item or meal is unrestricted, ED has been confirmed as a strong driver of EI, and it is clear that high-ED foods or meals promote greater intake.[18,21–23] The primary determinants of ED are lipid (increases ED) and water (decreases ED),[18] but whilst CHO *per se* does contribute less to this dietary ED seesaw, high-CHO foods are typically of lower ED than high-fat foods and hence have been hypothesised to suppress EI.[24] Conversely, manipulation of diets in order to promote high-ED, high-CHO foods may promote excess EI,[25] and it is notable that these changes in *ad-lib* intake can also be abolished if ED is kept constant in the face of changing CHO content.[26] In these longer term studies individuals tend to eat a relatively constant weight of food, hence high-ED foods promote EI.[18] The intriguingly simple finding that ED drives EI as a consequence of individuals eating a constant weight of food each day may be a result in these experiments of the abolition of learned behavioural cues that drive our habitual eating patterns. Covertly altering foods and removing all food choices certainly may alter our usual eating behaviours, and whether ED is such a strong driver of EI in our habitual environment of almost unlimited food choice is less well understood.

It should be recognised that the variable study design and the uncontrolled nature of long term appetite and/or weight control studies can make this literature difficult to interpret, and that not all longer term studies support the satiety hierarchy. For example, in a recent weight loss trial with >800 obese individuals, changes in CHO, fat and protein composition did not result in any macronutrient specific enhancement of satiety after 6 months or 2 years.[27] The inability to manipulate a single macronutrient such as CHO without in turn altering that of protein or fat further complicates the interpretation of these studies.[28] In general, the most consistent effect is that of high-protein suppressing intake,[29–31] although again not all high-protein studies report greater satiety,[27,32] whilst the effects of high vs low CHO diets on EI is less clear.[33] Part of this confusion may be due to the highly variable composition of diets considered 'high-CHO', and partly may be due to the composition of the replacement macronutrient(s) in 'low CHO' diets. The Atkins Diet is an example of a well-publicised low CHO diet regime which unexpectedly resulted in successful weight loss at 1 year follow-up when compared with a public health recommended low-fat diet.[1,2] Replacement of CHO in large part with dietary protein in these studies may lead to the conclusion that a likely mechanism underpinning this effect is protein-enhanced suppression of EI.

9.3 Available carbohydrates (small bowel effects) and satiety

Dietary CHOs are commonly defined as either 'available', those which are absorbed in the SI and hence available as a rapid response energy source, or 'unavailable', those which transit the SI undigested/absorbed and arrive in the large bowel for fermentation by the host bacteria. Available CHOs typically comprise the mono- and disaccharide 'simple sugars' and the starch polysaccharides, whilst unavailable CHOs comprise resistant starch (RS), non-starch polysaccharide (NSP) 'fibres' and other more minor components. The available CHOs may in turn be slowly or rapidly digested and absorbed in the SI, resulting in different postprandial glycaemic responses and possibly different appetitive responses. 'Slow' CHOs lower glycaemia relative to rapidly digested 'fast' CHOs, and this effect on circulating glucose has been proposed to suppress appetite[34,35] although it is a far from universal finding.[36,37] In a recent study Peters and colleagues measured postprandial glucose, insulin and appetitive responses to glucose polymer drinks that differed only in rate and extent of digestibility, and found no significant difference in appetite responses between maltodextrin ('fast') and pullunan ('slow') CHO sources.[11] The authors concluded that glycaemic responses *per se* have minimal effect on appetite when only CHO digestibility rate and extent are altered. It is not only CHOs in circulation that may alter appetitive response. Changing the levels of storage glycogen through diet and/or exercise has long been of interest to those investigating the role that dietary CHO has on appetite. The leading proponent of the 'glycogenostatic' theory of energy and body weight control was Professor J.P. Flatt, who hypothesised that depletion of the body's relatively small glycogen storage pool through either prolonged exercise or dietary CHO restriction would stimulate hunger and drive EI[10] as the body recognises and attempts to replenish the depleted stores. Conversely, studies measuring macronutrient intake, oxidation and balance have shown that rather than increase the motivation to eat, glycogen depletion may result in a repartitioning of oxidised substrates and the gradual re-establishment of CHO balance and replenishment of glycogen stores without an immediate increase in either CHO or EI.[38,39] A recent review of this area[40] concluded that there may be some evidence to suggest that CHO balance is involved in the short term regulation of food intake,[41,42] but that the evidence is limited and equivocal.[43,44]

9.3.1 Simple sugars: glucose, fructose, high fructose corn syrup, sucrose

There is a wide literature investigating the effects of various forms of available CHO on satiety, driven at least in part by the wide use of mono- and di-saccharide sweeteners in packaged foods. The global intake of sucrose (table sugar), a disaccharide composed of the monosaccharides glucose and fructose, has risen logarithmically since 1800.[45] Fructose and HFCS in

particular have raised concern in recent years[46] with hepatic *de novo* lipogenesis, lipotoxicity and oxidative stress all proposed as mechanisms responsible for adverse metabolic effects.[45,47] HFCS has undergone extensive investigation, a consequence of its ubiquitous use within the US diet, used increasingly as a replacement for other sweeteners first in beverages and, more recently, as a replacement for sugar in many processed and packaged foods.[48] HFCS is made by converting glucose into fructose using enzymes grown in bacteria and then diluting the fructose to provide the commercially required concentrations. The monosaccharides fructose and glucose, whilst identical in chemical formula ($C_6H_{12}O_6$), differ in a number of important ways including rate of emptying from the stomach, gastrointestinal absorption, hormone responses and metabolic fates. Fructose has almost complete hepatic extraction and rapid hepatic conversion into glucose, glycogen, lactate and to a lesser degree fat. Hence it would not be unexpected should they engender different signalling pathways and have divergent effects on satiety and eating behaviour. An extensive comparison of mono- and disaccharide CHOs was carried out by Akhavan and Anderson[49] in a postprandial study comparing mixed glucose/fructose beverages, HFCS, and a sucrose beverage with a zero-energy sweetener and water control, but found no significant differences in VAS assessed satiety or EI at a subsequent ad-lib test meal between any of these available CHO forms. A review of the literature by Moran[50] concluded that there was no compelling evidence in support of lower satiety when comparing fructose with glucose, or when comparing HFCS with sucrose. In a recent meta-analysis Sievenpiper and colleagues concluded that fructose does not cause weight gain when substituted on an isoenergetic basis for other CHOs[51] and that free fructose increases body weight only when given at high doses and when providing excess dietary energy, hence not supporting the hypothesis of an energy independent fructose-specific effect.

9.3.2 Glycaemic index (GI) or glycaemic load (GL): low vs high GI foods and blood glucose as a marker of hunger

The expression GI was originally coined to allow diabetic patients to classify the various forms of dietary CHO on the basis of their effect on postprandial glycaemia, and has long been of interest with respect to diabetes and wider health implications.[52] The GI of a food is calculated relative to a standard glucose load by comparing the 2 h glycaemic response of 50 g of available CHO from the test food with 50 g of available CHO from glucose.[53] The GL of a test food can then be calculated based on the total amount of available CHO in that food. It has been clearly shown that predicting the GI or GL of a food or meal results in poor outcomes, and that determining high or low GI requires clinical testing.[54] The poor predictive nature of these CHO foods may have led to some confusion in the literature as to whether dietary interventions have in fact achieved their desired high or low GI status. For example, equating diets high in fibre with also being low GI may have been

incorrect and misleading.[54] In light of this, perhaps it is not surprising that the evidence for enhanced satiety from low GI foods or diets is very mixed,[34,55–58] with a body of studies showing no effect of GI on satiety.[7,56,59–61] There is no doubt that GI has been controversial. As long ago as 2002, when the question 'should obese patients be counselled to follow low GI diets' was posed, it generated both strongly supportive[4] and strongly opposing[3] views. A more recent Cochrane review of GI and weight loss showed 1.09 kg greater weight loss with low GI diets,[35] although it is notable that only six studies fulfilled the requisite criteria and were included in the meta-analysis. A recent pan-European eight-country study has shown that a low GI diet, in combination with a higher protein intake, may enhance weight loss maintenance in overweight and obese men and women. The DIOGENES study randomised >700 individuals who had lost at least 8% of their baseline body weight through a prior LED into a 26-week dietary intervention,[6] and showed that a modest increase in protein content accompanied by a modest decrease in GI resulted in better maintenance of weight loss. Many questions are still to be resolved. Are diets that induce a lower glycaemic response and enhance weight loss more satiating? Is low GI an independent marker of satiety? And if so, what is the mechanism of action?

A review of possible mechanisms must start with Mayer's 1953 classical 'glucostatic theory'.[8] Mayer hypothesised that low blood glucose concentrations are a key factor in the trigger for hunger and hence also the initiation of eating. This theory has gradually led to the development of the 'GI theory' of appetite regulation, which proposes that the consumption of high GI foods causes both rapid high spikes and rebound low troughs in blood glucose, and that these exaggerated low troughs then trigger hunger and the initiation of an eating occasion. In turn, it is hypothesised that low GI foods, which by definition result in a muted postprandial glycaemic response, fail to trigger feelings of hunger and hence do not initiate eating. Teasing out the effects of low and high GI foods with appetite regulation is difficult, not least because GI responses are linked to such important dietary components as the total CHO content, the dietary fibre content and ED. In opposition to the GI theory of appetite regulation, the 'high-fibre theory' proposes that for many commonly eaten foods a low glycaemic response is associated with a high fibre content, and that it is the fibre content of the food or meal which is the primary hunger suppressor, and not low GI *per se*.[62,63] Clearly, fibres do attenuate the postprandial glycaemic response to high-CHO foods. For example the soluble fibre dextrin, when present within CHO-based beverages, has been shown to suppress glycaemia by ~50%.[64] More recently, however, it has been purported that the fibre content of many foods is actually a poor predictor of the glycaemic response to that food,[54] and that in turn the satiety response to a low GI food is not driven solely or even primarily by the fibre content of that food. Also in opposition to the GI theory of appetite regulation, the 'ED theory' proposes that there is an association between a low GI response and foods with a low ED, and that since ED has long been shown to be important

in the suppression of hunger and food intake[21,23] it is this characteristic of a food or meal which attenuates appetite, and not low GI *per se*. Finally, there is the 'low CHO theory', which proposes that since the glycaemic response to a set food item is driven by both its GI and also the total grams of CHO in the food (i.e. its GL), an association between satiety and a low glycaemic response may simply be a consequence of low total CHO content. Diets where CHO is replaced by dietary protein, arguably the best known of which is the Atkins Diet where CHO intake is significantly restricted, have long been shown to suppress intake and also to promote weight loss, at least in the short term.[1,2]

There is a large body of literature investigating the efficacy of low GI diets on satiety, including the evidence presented earlier in this chapter showing that glycaemic responses *per se* have minimal effect on appetite. Conversely, short term feeding studies in children,[65] obese adolescents[58] and overweight women[57] have shown prolongation of satiety after low vs moderately high GI meals and beverages. A number of longer term interventions have failed to find differences between low and high GI foods on satiety and EI,[7,66] and a review presented as part of a recent UK symposium on the dietary management of disease also concluded that whilst acute meal studies may point towards an effect of GI on appetite regulation, longer term interventions remain inconclusive.[67]

9.3.3 Carbohydrate and the ileal brake

A further mechanism proposed for enhanced satiety, acting through distal small bowel effects on gut motility, is the ileal brake.[68] It is hypothesised that exposure of the ileum to nutrients not usually delivered into the distal SI activates a feedback loop which puts a 'brake' on eating. This ileal feedback mechanism was initially discovered as an inhibition in small intestinal motility and transit after ileal fat exposure, and more recently has been shown to have effects on satiety and food intake.[69–71] There is some evidence from animal studies that CHOs may also induce the ileal brake and suppress food intake.[72–74] Whilst delivering nutrients to this area of the gut is clearly a challenge which has yet to be fully met, even with dietary lipids,[75,76] it remains an area of considerable interest.

9.4 Unavailable or fermentable carbohydrates (large bowel effects) and satiety

Epidemiological studies show dietary fibre and whole grains to be associated with a lower risk of overweight or obesity,[77,78] and early studies showed high-fibre foods to enhance satiety.[79,80] Fibre occurs in several forms within the diet, but for ease of classification in this review it can be defined as two main forms, soluble and insoluble.

9.4.1 Soluble fibre

Soluble fibre absorbs water in the GI tract to become a gelatinous, viscous substance and undergoes fermentation by bacteria in the large bowel to generate SCFAs. Many of the soluble fibres are also defined as 'viscous' as they induce thickening when mixed with liquids. These include the gums, pectins, aliginates and β-glucans. Soluble fibres may alter satiety by a number of mechanisms including lowering the ED of foods, since fibre is not absorbed in the SI and hence contributes less energy per gram than available CHOs. Viscous soluble fibres absorb large amounts of water from the GI tract and as a result increase in volume and may act as a 'bulking' agent within the gut. It has been proposed that these fibres may increase gastric distension[81] and possibly also the rate of gastric emptying, both of which may alter appetitive responses. They may also prolong transit time within the SI, the absorption rate of nutrients, and in turn the release of appetite-suppressing GI peptides such as cholecystokinin (CCK) from the proximal and GLP-1 and PYY from the distal SI.[69] Whether dietary fibre plays a role in the ileal brake, as described earlier in this chapter, is also under conjecture. Colonic fermentation of fibre and exposure of the large bowel to increased levels of SCFA is also a proposed mechanism for enhanced satiety.[82]

9.4.2 Insoluble fibre

Conversely, insoluble fibre acts as a bulking agent in the colon and is not a major prebiotic source of nutrients for the microbiota population. Fibre type may well be important in eliciting a satiety response, as may administration of fibre in isolation or within a mixed meal.[83] A recent review of the effect of soluble, viscous fibre on appetite regulation by Kristensen and Jensen[84] concluded that the majority of studies[63,85,86] but not all[83,87] do show enhanced satiety and/or suppression of food intake with viscous dietary fibre-enriched beverages. The dose required, however, appears to be high, with the explanation for some 'no effect' studies being insufficient intake of fibre,[84,87] with a possible threshold effect when intake reaches 8 g.[88] Clearly the format of fibre administration is important. Studies using insoluble fibre have also shown suppressed food intake,[62,89] the mechanisms for which are likely to be increased bulking and decreased ED of the food items or meals.

9.4.3 Wholegrain foods

Wholegrain foods have been suggested as an important constituent of the diet, due to their high fibre content, low ED and increased volume and particle size; however, outcomes are mixed for effects on weight loss. Some observational studies have shown an association with lower risk of weight gain,[90] but whether satiety or food intake is altered is unknown. Wholegrain foods are those in which the starchy endosperm, germ and bran (intact, ground,

cracked or flaked) are present in the product as they are in the original intact plant. Studies have shown that postprandial hunger and fullness may be altered by some wholegrain products such as wholemeal wheat bread[91] and some barley foods[92] but longer term studies have failed to find effects on EI or body weight.[93] Further research is needed to develop consensus as to whether wholegrains influence satiety and EI.

9.4.4 Gut microbiota; fermentation, SCFA, prebiotics

Growing and intriguing evidence that gut microbiota resident within the large bowel may differ between lean and obese individuals[94] has led to the microbiome being proposed as an environmental factor responsible for both weight gain and altered energy metabolism of obesity.[95,96] The microbiota, which includes viruses, archaea and some unicellular eukaryotes as well as bacteria, is present throughout the human body but in greatest numbers (~10^{12} microorganisms/mL) in the large bowel. As described earlier, unavailable CHOs undergo fermentation by the host microbiota to generate SCFAs. These in turn have been termed 'bacterial dietary metabolites' and hypothesised to have biological activities which may regulate various host functions,[95] including suppression of food intake.[82] One proposed anorectic mechanism is the enhancement by SCFA of colonic 'satiety' peptide GLP-1 released from enteroendocrine L-cells of the large bowel.[97] Exogenous administration of GLP-1 analogues such as liraglutide[98] clearly do suppress appetite and EI, although whether sufficiently high concentrations can be achieved through dietary manipulation such as increased prebiotic substrate is yet to be demonstrated.[99] An increase in large bowel bifidobacteria numbers in particular has been associated with enhanced intestinal health[100] but whether this association can be extrapolated to obesity is not known. Human obesity has been associated with both a low[94,96] and high[82] abundance of bacteria from the phylum Bacteroidetes relative to Firmicutes, but other studies show no parallel relationship[101] or find no difference between phyla at all.[102] The role that prebiotic CHOs, which stimulate the growth or activity of the gut bacteria, may have in this relationship is equally unclear.

9.5 Form of carbohydrate (liquid vs solid): sugar sweetened beverages

There is a growing literature to support the belief that food rheology and food matrix effects are of great importance to the satiating or satiety effects of all of the macronutrients, not least dietary CHOs.[103] Comparative effects of liquid vs solid foods are dealt with in detail in Chapter 10, but it is useful to give a brief summary of the evidence as it pertains to sugary drinks here. Liquid CHOs, and particularly the sugar sweetened beverages, are of especial interest

and relevance since global intake by adults and children has dramatically increased in recent years. The issue has been of particular concern in the US, where approximately one-half of the population consumes sugar-containing drinks on any given day, and has led to dietary guidelines issued in 2010 recommending a limit on consumption of beverages with added sugars.[104] Whilst the energy content of a food is clearly an important driver of satiety, a body of studies,[103,105] although not all,[106] have shown that consumption of liquid CHO may be poorly recognised and engender less compensation than an isoenergetic high-CHO solid meal. Whether this is a consequence of the sweet nature of CHO beverages or simply the food form remains under debate.[103] A recent study by Mattes and colleagues confirmed water based, energy-containing beverages to increase the risk of positive energy balance,[107] and in turn growing evidence has linked intake of higher energy beverages with weight gain.[108,109]

9.6 Conclusion and future trends

Dietary CHOs provide a significant proportion of our daily intake and are consumed in a wide variety of forms. The effect of the various available and unavailable forms of CHO on appetite and the mechanisms by which they may underpin the regulation of food intake and hence body weight remain remarkably controversial. Whilst is has become clear that the contribution of CHO in attaining a lower ED diet is likely to suppress intake, the ideal composition of that CHO is less well understood. Conversely, low CHO diets have seen some success in appetite suppression and weight loss, and whether these effects may be attributed more to a substitution for dietary protein rather than an effect of CHO removal *per se* can be debated. Certainly there is a convincing argument for restricting the intake of sweet, high-CHO beverages since added energy from any source within a drink setting may engender low levels of energy compensation and drive overconsumption. The role of GI in appetite control also remains to be fully elucidated with evidence both in support of and refuting the use of low GI foods for hunger suppression, and there is considerable on-going work in this area. Whilst unavailable CHOs in the form of soluble and insoluble dietary fibre have long been purported to suppress food intake, new relationships between obesity, the large bowel microbiome and prebiotic CHOs have engendered some intriguing hypotheses which, with the aid of modern 'omics' technologies, may in the near future prove to be of growing relevance.

9.7 References

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