British Journal of Nutrition (2013), **109**, 1539–1541

British Journal of Nutrition

Invited Commentary

Weight gain and insulin sensitivity: a role for the glycaemic index and dietary fibre?

(First published online 27 November 2012)

Since its first description by Jenkins *et al.*[1] in the 1980s, the glycaemic index (GI) has been used as a dietary tool to enhance the glycaemic control of people living with diabetes. The management of glycaemia is relevant today more than ever, with an estimated 2·9 million people currently affected by type 2 diabetes in the UK[2]. However, the GI as a concept has dipped in and out of scientific fashion. By its nature, the GI is highly complex in that it hinges on a number of physico-chemical properties of carbohydrates, such as the chemical structure of the carbohydrate, the surrounding food matrix and the processing it undergoes[3]. The fact that GI measurements are confounded by other food components within the diet serves as an additional layer of complexity[4]. Consequently, the concept of the GI has been met, at times, with scepticism and some have found it challenging to embrace. However, one could argue that the proof is in the eating. There are now two high-quality systematic reviews that demonstrate the clinical utility of the GI in the management of type 2 diabetes[5,6], and a 24-week randomised controlled trial demonstrating a 0·5 % fall in glycosylated Hb[7]. There is also a Cochrane systematic review which suggests that the GI may play a role in promoting weight loss[8]. Therefore, the literature, as it currently stands, presents a convincing case for the clinical application of the GI in the management of body weight and glucose homeostasis.

In this issue of the *British Journal of Nutrition*, Lagerpusch *et al.*[9] observed that in the dynamic phase of weight gain, a high-fibre, low-GI diet reduced daytime measurements of interstitial glucose when compared with an energy-matched low-fibre, high-GI diet. Furthermore, the deterioration in insulin sensitivity induced by refeeding was attenuated, though the effects of the two dietary interventions were resolved at the end of the refeeding phase. The authors claim that there is public health relevance to this, as many adults demonstrate short-term weight cycling, i.e. repeated cycles of weight loss and weight regain. Indeed, estimations of the prevalence of weight cycling are within the range of 18–34 and 20–55 % for men and women, respectively[10–12]. However, the health effects associated with weight cycling are largely unknown[13,14]. This study by Lagerpusch *et al.*[9] is the first to examine the impact of the GI on insulin sensitivity during and after weight regain in young healthy individuals using multiple indices of glucose and insulin homeostasis. The experimental diets differed not only in the GI (74 *v.* 40 GI units) but also in dietary fibre content (27 *v.* 64 g). The authors do not offer any suggestions as to which specific dietary manipulation they believe may be driving their observed improvements in glucose metabolism and insulin sensitivity. However, previous studies have attempted to answer this question.

In two large-scale epidemiological studies (the Nurses' Health Study and Health Professionals Follow-up Study), it has been demonstrated that the risk of developing type 2 diabetes increases with a concomitant increase in dietary glycaemic load (the GI multiplied by the amount of carbohydrate consumed) and a reduction in fibre consumption[15–17]. The uncoupling of these two aspects of the diet meant that the relationship disappeared or was significantly weaker. Furthermore, the Reading, Imperial, Surrey, Cambridge, and Kings (RISCK) study, a large multicentre dietary intervention in over 500 adults at risk of CVD, aimed to elucidate how dietary changes may influence insulin sensitivity and other CVD risk factors[18]. A surprising finding of the study was the absence of an improvement in insulin sensitivity following a low- *v.* high-GI diet. However, in this study, the total amount of fibre was matched in both the high- and low-GI groups. This raises the intriguing question of whether the dietary deconstruction seen in most nutritional interventions, in line with the current reductionist scientific approach, is actually detrimental. By controlling for every aspect of the diet, could we actually be missing important physiological effects that occur from dietary manipulations which often go hand-in-hand, like GI and dietary fibre?

The mechanisms underlying the beneficial effects of high-fibre, low-GI diets on insulin sensitivity are complex and multifactorial. In the gastrointestinal tract, low-GI diets with a high fibre content slow gastric emptying, reduce digesta transit rate and alter the luminal environment, all of which will ultimately delay glucose absorption and result in an ameliorated insulin response[19]. High-fibre, low-GI foods may also influence insulin sensitivity via mechanisms independent of actions within the upper gastrointestinal tract. For example, high-fibre, low-GI diets may promote insulin sensitivity by improving metabolic flexibility, i.e. the ability of an organism to modify fuel oxidation in response to changes in nutrient availability. Metabolic flexibility enables an efficient transition from lipid oxidation and high rates of fatty acid uptake during the fasted state, to suppression of lipid oxidation and increased glucose uptake and utilisation in response to insulin stimulation[20]. In the 1990s, it was demonstrated that exposure to a low-GI diet over a 4-week period increases

whole-body insulin sensitivity and suppresses circulating NEFA levels[21,22], an effect probably due to increased insulin-stimulated NEFA uptake at the level of the adipocyte[22]. In support of this, an elegant human study by Robertson *et al.*[23] subsequently demonstrated that consumption of a fermentable fibre improved insulin sensitivity and reduced adipose tissue lipolysis. This coincided with a rise in the plasma levels of SCFA, end products of bacterial fibre fermentation in the distal gut. Research into the metabolic effects of SCFA has been gaining momentum since the identification of the G-protein-coupled SCFA receptors GPR41 and GPR43. The expression profile of these receptors in the adipose tissue, colon, liver and pancreas provides a plausible network by which these products of fermentation may have an impact upon insulin sensitivity and metabolic flexibility[24]. Evidence from GPR43 knockout mice suggests that SCFA may directly suppress lipolysis from adipocytes and lower circulating NEFA levels *in vivo*, effects associated with improved insulin sensitivity[25]. Furthermore, SCFA are thought to promote the release of gut hormones such as glucagon-like peptide 1, an incretin which enhances first-phase insulin release, through the activation of GPR43.

The paper by Lagerpusch *et al.* attempts to further our understanding by bringing to light some interesting observations about complex high-fibre, low-GI diets and their ability to beneficially influence glucose homeostasis in the dynamic stages of weight regain, a relatively unexplored metabolic state. Important strengths of this study include the strictly controlled nutrition regimen and the comprehensive assessment of insulin sensitivity. However, this paper raises as many questions as it answers. With beneficial effects on glucose homeostasis being apparent only during the active weight-gain period and not seen at the end of the refeeding protocol, are the benefits of a high-fibre, low-GI diet largely acute? Similarly, does the lack of deterioration in any insulin sensitivity measurement between baseline and post-refeeding suggest that weight cycling is not detrimental to health, at least in terms of glucose metabolism? Are these findings in lean, healthy, young men directly applicable to higher-risk populations with existing glycaemic impairment? Lastly, can the methodological approach be taken a step further to unpick the mechanisms underlying the insulin-sensitising effects? The real strength of this paper is to act as a stimulus for further investigation into the complex physiological effects of a high-fibre, low-GI diet, the mechanisms underlying these effects and how they may be exploited to improve the management of glycaemia.

Acknowledgement

The authors declare no conflict of interest.

Michelle Sleeth
Arianna Psichas
Gary Frost

Nutrition and Dietetic Research Group
Division of Diabetes
Endocrinology and Metabolism
6th Floor
Commonwealth Building
Imperial College Hammersmith Campus
Du Cane Road
London W12 ONN
UK
email g.frost@imperial.ac.uk

doi:10.1017/S0007114512005016

References

1. Jenkins DJ, Wolever TM, Jenkins AL, *et al.* (1983) The glycaemic index of foods tested in diabetic patients: a new basis for carbohydrate exchange favouring the use of legumes. *Diabetologia* **24**, 257–264.
2. Diabetes UK (2012) Diabetes in the UK 2012. Key statistics on diabetes. http://www.diabetes.org.uk/Documents/Reports/Diabetes-in-the-UK-2012.pdf (accessed 27 September 2012).
3. Wolever TM, Jenkins DJ, Jenkins AL, *et al.* (1991) The glycemic index: methodology and clinical implications. *Am J Clin Nutr* **54**, 846–854.
4. Levitan EB, Westgren CW, Liu S, *et al.* (2007) Reproducibility and validity of dietary glycemic index, dietary glycemic load, and total carbohydrate intake in 141 Swedish men. *Am J Clin Nutr* **85**, 548–553.
5. Brand-Miller J, Hayne S, Petocz P, *et al.* (2003) Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. *Diabetes Care* **26**, 2261–2267.
6. Thomas D & Elliott EJ (2009) Low glycaemic index, or low glycaemic load, diets for diabetes mellitus. *The Cochrane Database of Systematic Reviews*, CD006296.
7. Jenkins DJ, Kendall CW, McKeown-Eyssen G, *et al.* (2008) Effect of a low-glycemic index or a high-cereal fiber diet on type 2 diabetes: a randomized trial. *JAMA* **300**, 2742–2753.
8. Thomas DE, Elliott EJ & Baur L (2007) Low glycaemic index or low glycaemic load diets for overweight and obesity. *The Cochrane Database of Systematic Reviews*, CD005105.
9. Lagerpusch M, Enderle J, Later W, *et al.* (2013) Impact of glycemic index and dietary fibre on insulin sensitivity during the refeeding phase of a weight cycle in young healthy men. *Br J Nutr* **109**, 1606–1616.
10. Syngal S, Coakley EH, Willett WC, *et al.* (1999) Long-term weight patterns and risk for cholecystectomy in women. *Ann Intern Med* **130**, 471–477.
11. Lahti-Koski M, Mannisto S, Pietinen P, *et al.* (2005) Prevalence of weight cycling and its relation to health indicators in Finland. *Obes Res* **13**, 333–341.
12. Tsai CJ, Leitzmann MF, Willett WC, *et al.* (2006) Weight cycling and risk of gallstone disease in men. *Arch Intern Med* **166**, 2369–2374.
13. Albu J & Reed G (1995) Weight cycling: more questions than answers. *Endocr Pract* **1**, 346–352.
14. Wannamethee SG, Shaper AG & Walker M (2002) Weight change, weight fluctuation, and mortality. *Arch Intern Med* **162**, 2575–2580.
15. Salmeron J, Ascherio A, Rimm EB, *et al.* (1997) Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care* **20**, 545–550.
16. Willett W, Manson J & Liu S (2002) Glycemic index, glycemic load, and risk of type 2 diabetes. *Am J Clin Nutr* **76**, 274S–280S.

17. Schulze MB, Liu S, Rimm EB, *et al.* (2004) Glycemic index, glycemic load, and dietary fiber intake and incidence of type 2 diabetes in younger and middle-aged women. *Am J Clin Nutr* **80**, 348–356.
18. Jebb SA, Lovegrove JA, Griffin BA, *et al.* (2010) Effect of changing the amount and type of fat and carbohydrate on insulin sensitivity and cardiovascular risk: the RISCK (Reading, Imperial, Surrey, Cambridge, and Kings) trial. *Am J Clin Nutr* **92**, 748–758.
19. Wolever TM (1990) The glycemic index. *World Rev Nutr Diet* **62**, 120–185.
20. Galgani JE, Moro C & Ravussin E (2008) Metabolic flexibility and insulin resistance. *Am J Physiol Endocrinol Metab* **295**, E1009–E1017.
21. Frost G, Keogh B, Smith D, *et al.* (1996) The effect of low-glycemic carbohydrate on insulin and glucose response *in vivo* and *in vitro* in patients with coronary heart disease. *Metabolism* **45**, 669–672.
22. Frost G, Leeds A, Trew G, *et al.* (1998) Insulin sensitivity in women at risk of coronary heart disease and the effect of a low glycemic diet. *Metabolism* **47**, 1245–1251.
23. Robertson MD, Bickerton AS, Dennis AL, *et al.* (2005) Insulin-sensitizing effects of dietary resistant starch and effects on skeletal muscle and adipose tissue metabolism. *Am J Clin Nutr* **82**, 559–567.
24. Cani PD, Knauf C, Iglesias MA, *et al.* (2006) Improvement of glucose tolerance and hepatic insulin sensitivity by oligofructose requires a functional glucagon-like peptide 1 receptor. *Diabetes* **55**, 1484–1490.
25. Ge H, Li X, Weiszmann J, *et al.* (2008) Activation of G protein-coupled receptor 43 in adipocytes leads to inhibition of lipolysis and suppression of plasma free fatty acids. *Endocrinol* **149**, 4519–4526.

British Journal of Nutrition