Invited commentary

Glucose utilization dynamics and food intake

In 1955, Jean Mayer postulated that short-term articulation of energy intake with energy needs is under glucostatic control (Mayer, 1955). Since that time, by combining behavioural and metabolic data, a strong and causal relationship has been demonstrated between declines in blood glucose concentration and spontaneous meal onset. These declines are thought to be the signals of a shortage in immediately available glucose and, therefore, a shortage in glucose utilization detected by central specialized neurons. Thus, it is suggested that after an eating episode the delay of occurrence of the drop in glucose availability is dependent on the rate of utilization of the available carbohydrates. The role of glucose in control of food intake is therefore thought to be dynamic: it is a satiety factor and an initiation signal.

Currently, as in the study from Melanson *et al.* (1999*a*), interesting new methods are being used. A sensitive way to evaluate the satiety power is to determine the onset latency of the next meal when freely requested by subjects deprived of time cues. Together with food intake measurements, hunger or fullness or other subjective ratings, metabolic and hormonal data are collected. A precise follow-up of the metabolic and/or hormonal profiles is determined via continuous blood withdrawal associated with either continuous blood glucose determination (Melanson *et al.* 1999*b*) or collection of blood samples in tubes at different rates, i.e. /min (Abdallah *et al.* 1997), /5 min (Marmonier *et al.* 1999) and so on. These methods are useful as they provide strong but indirect arguments about the role of nutrients, particularly glucose utilization. More direct evidence is given by the determination of metabolite oxidation via respiratory gas exchange data.

The study from Melanson *et al.* (1999*a*) in this issue of the *British Journal of Nutrition* first corroborates the synchronization between hunger and declines in blood glucose. The authors also show that the influence of high-fat, high-carbohydrate and aspartame drinks on intermeal interval is related to the duration of blood glucose responses and, therefore, also to glucose utilization.

At each point of the intermeal interval, the amount of available glucose is a function of the rate of glucose absorption, a function of the additional glucose provided by gluconeogenesis and also a function of the rate of glucose utilization (oxidation and storage). This last factor is largely dependent on insulin secretion. Insulin controls the rate of free fatty acid oxidation via its effect on lipogenesis and lipolysis and, therefore, the rate of glucose oxidation (Randle *et al.* 1964; Ferranini *et al.* 1983). Thus, the satiety power of a food is likely to be dependent on the absolute and relative amounts of the three macronutrients via their effects on the insulin profile throughout the intermeal interval.

Results of a number of studies are consistent with this view, although some authors only recorded metabolic data while others provided only food intake measurements. The effects of meals with various carbohydrate and fat contents on the postprandial profile of plasma concentrations of substrates and insulin have been studied, for example by Collier & O'Dea (1983), Collier *et al.* (1984) and Cunningham & Read (1989). In other studies, metabolite oxidation (Flatt *et al.* 1985; Surina *et al.* 1993) or RQ (Gomez *et al.* 1972; Griffiths *et al.* 1994) have been monitored along with the postprandial plasma variables. Careful examination of the results obtained in these two sets of studies, show their complete agreement with the general considerations mentioned previously. Less carbohydrate and more fat in the meal favours lipid oxidation. Fat added to a non-fat meal is partly oxidized and can spare some carbohydrate, while fat added to a fat-containing meal is likely to have a minimal additional effect on the carbohydrate saving.

The satiety effect of such manipulations (Rolls *et al.* 1991; Cotton *et al.* 1994, 1996), evaluated either by hunger ratings or by measurement of intake in a subsequent meal, confirms that fat has a satiety effect in as much as it saves glucose, i.e. to the extent that insulin concentration does not inhibit lipid oxidation. In a study by Himaya *et al.* (1997) food intake data, together with metabolic and hormonal data, were collected: they revealed that when 40 g fat (1588 kJ) was added to a high-carbohydrate meal (2139 kJ) satiety duration was prolonged by approximately 38 min. The difference in the latency of the dinner request is explained by a 10 g glucose saving which corresponds with a 4–5 g fat oxidation. As shown by the free fatty acid profile, this increase in fat oxidation occurred in the last part of the intermeal interval when insulin levels were low.

In the study by Melanson *et al.* (1999*a*) no data are provided on insulin levels but the duration of glucose responses is most probably related to the induced insulin secretion. As pointed out by the authors, this is strongly suggested by the negative correlation between blood glucose responses and sweetness perception.

How are the rate of absorption, the rate of glucose disposal and the decline in blood glucose related? Stricker & McCann (1985) reported that, in the rat, after an initial bolus, gastric loads of concentrated glucose solutions emptied at a relatively constant rate (126–188 J/min) approximately equal to the BMR. The gastric emptying rate of normal-sized chow meals offered to rats after a minimal food deprivation was also found to be approximately 188 J/min and constant for most of the emptying

period (Newman & Booth, 1981) with, however, a slowing near the end. Two other important results were also highlighted by this study. First, it was shown that absorption rate equalled the just preceding gastric emptying rate, suggesting that the final slowing leads to a fall in metabolite absorption. Second, a circadian variation in gastric emptying was noted. The faster gastric emptying at night coincides with (and is not caused by) higher food intake and a higher metabolic rate. Reviewing arguments from the literature data on the relationship between these three factors, Newman & Booth (1981) concluded that gastric emptying is not driven by food intake but that rapid gastric emptying and insulin hyperresponsiveness are primary causal factors for the frequent meals and net storage at night in the rat.

In man it has also been shown that ordinary meals of normal size are emptied in a similar manner: a brief initial rapid phase, a long period of constant rate and a final slowing (Malagelada, 1977). Recent results (Carbonnel *et al.* 1994) have shown that two isoenergetic normal liquid–solid meals differing in volume and density emptied at a stable and identical rate of about 8374 J/min, approximately equal to BMR.

The main feature is that at rest and during the major part of emptying, stomach emptying rate seems to correspond roughly to the metabolic rate but slows down near the end of emptying.

Interestingly, McHugh & Moran (1985) found that delivery of energy directly to the intestines decreased food intake and slowed gastric emptying. In contrast, in rats (Stricker & McCann, 1985) as well as in man (Schvarcz *et al.* 1993), insulin produced a marked increase in gastric emptying. Gastric emptying rate was studied in patients with type I diabetes mellitus submitted to an insulin–glucose clamp. Insulin-induced hypoglycaemia significantly increased the emptying rate compared with euglycaemia. By contrast, a glucagon infusion was shown to induce a marked slowing in gastric emptying (Jonderko *et al.* 1989).

Certainly gastric emptying is not driven by food intake and there are arguments, some of which have already been mentioned, suggesting that gastric emptying is controlled by nutrient disposal. A specific role of glucose availability is strongly suggested by the study of the effect of the insulin–glucose clamp, and supported by the results obtained in diabetic rats. Thus, the stomach could be seen as a reservoir from which nutrients are first, during a short phase, pushed but then pulled out as a function of glucose disposal, with a final slowing which could cause the preprandial fall in blood glucose levels. Further studies similar to the ingenious one from Melanson *et al.* (1999*a*) will be required to substantiate the role of glucose disposal in 'the short term articulation of energy intake with energy needs'. A continuous follow-up of other variables such as respiratory gas exchanges, but also free fatty acid levels and particularly insulin on account of its key role, seems absolutely necessary.

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