REVIEW

Intense sweeteners, energy intake and the control of body weight

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Replacing sugar with low-calorie sweeteners is a common strategy for facilitating weight control. By providing sweet taste without calories, intense sweeteners help lower energy density of beverages and some foods. Reduced dietary energy density should result in lower energy intakes – but are the energy reduction goals, in fact, achieved? The uncoupling of sweetness and energy, afforded by intense sweeteners, has been the focus of numerous studies over the past two decades. There are recurring arguments that intense sweeteners increase appetite for sweet foods, promote overeating, and may even lead to weight gain. Does reducing energy density of sweet beverages and foods have a measurable impact on appetite and energy intakes, as examined both in short-term studies and over a longer period? Can reductions in dietary energy density achieved with intense sweeteners really affect body weight control? This paper reviews evidence from laboratory, clinical and epidemiological studies in the context of current research on energy density, satiety and the control of food intake.


Keywords: intense sweeteners; energy density; hunger; satiety; satiation; weight control

Introduction

Throughout human history, sweet taste has been associated with dietary energy and therefore food reward (US Department of Health, 1977). Infants like intensely sweet solutions (Maller and Desor, 1973), whereas young children prefer foods that are both familiar and sweet (Birch, 1987; Gibson and Wardle, 2003). A powerful stimulant of food consumption, sweetness, is often used to introduce new foods into the children’s diet (US Department of Health, 1977). Children learn to accept novel tastes and flavors when they are associated with energy-dense nutrients, such as sugar or fat (Johnson et al., 1991; Birch, 1992).

The innate mechanisms of sweetness acceptance appear to involve a variety of central mechanisms, among them are dopamine, serotonin and the endogenous opioid peptides (Drewnowski et al., 1995; Levine et al., 2003; Schwartz, 2006). Whereas human physiology remains the same, human exposure to dietary sugars has changed dramatically over the past several hundred years (Mintz, 1985). Not only has sugar content of the diet increased, but much of the sugar is consumed in liquid form (Bray et al., 2004). Current research on sugars and body weight has focused on the interactions of physiological systems with sugar content of the food supply (Elliott et al., 2002; Bray et al., 2004; Gross et al., 2004; Isganaitis and Lustig, 2005).

Sweet-tasting foods with high-energy density are said to disrupt appetite regulation and overwhelm the body’s regulatory mechanisms (Erlanson-Albertsson, 2005). Energy-dense diets cause insulin and leptin resistance in the central nervous system (CNS) (Schwartz, 2006) and blunt responses to physiological signals of satiety (Erlanson-Albertsson, 2005). Diet-induced CNS insulin resistance is the suggested reason why pleasure response to energy-dense foods does not diminish even in the face of caloric repletion (Lustig, 2001; Isganaitis and Lustig, 2005). Sweetness may also affect cortisol reactivity and compensate for feelings of stress (Epel et al., 2001). Studies in mice suggest that leptin modulates sweet taste responsiveness (Ninomyia et al., 2002), with further implications for fatness and energy intakes.

Soft drinks are a major source of sugar energy in the American diet (Bray et al., 2004). The consumption of caloric beverages is rising in France (Volatier and Verger, 1999) as well as worldwide. If a sustained innate desire for sweet taste

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Received 25 October 2006; accepted 4 December 2006; published online 7 February 2007
plays a causal role in the development of obesity (Schiffman et al., 2000), then intense sweeteners may provide a viable prevention strategy, since they deliver sweet taste without sugar calories (Bellisle and Perez, 1994; Renwick, 1994; Drewnowski, 1999). Five intense sweeteners are now approved by the US Food and Drug Administration: acesulfame-K, aspartame, neotame, saccharin and sucralose. The European Union also approves the use of cyclamates (European Parliament, 1994; European Parliament, 2004). Because their sweetening power is several hundred times that of sugar, the contribution of intense sweeteners to energy intakes is negligible (see Table 1).

One obvious question is whether the brain responds in the same fashion to caloric sugars and to intense sweeteners. Studies based on magnetic resonance imaging suggest that it may not (Smeets et al., 2005). Whereas the ingestion of a glucose solution by human volunteers led to a prolonged decrease in activity in the upper hypothalamus, no such effect was observed with an equally sweet aspartame solution or with plain water (Smeets et al., 2005). Unlike glucose and maltodextrin, aspartame solutions failed to trigger an insulin response (Smeets et al., 2005). The evidence would suggest that the sweet taste of aspartame does not trigger sugar-like responses in two important organs, the brain and the pancreas.

The second question is whether the differences between sugars and intense sweeteners are reflected in human dietary behavior, as monitored in experimental studies. The scientific literature on the topic of sweetness, satiety and energy intakes is split (Almiron-Roig et al., 2003; Drewnowski and Bellisle, 2007). On the one hand, the so-called ‘sweet tooth’ mechanism implies that sugar sweetness, when accompanied by calories, overwhelms the body’s physiological satiety mechanisms, leading to a loss of control over appetite and overeating (Rodin, 1975; Blundell et al., 1994; Blundell and Green, 1996). The competing view is that sweetness, when not accompanied by calories, results in ambiguous psychobiological signals that confuse the body’s regulatory mechanisms, leading to a loss of control over appetite and overeating (Blundell et al., 1988; Davidson and Swithers, 2004). As a result, caloric sugars and intense sweeteners alike have been blamed for the obesity epidemic (Bray et al., 2004; Davidson and Swithers, 2004).

Adding to the confusion is the fact that sugars are increasingly being consumed as caloric beverages, that is, in liquid form (Bray et al., 2004). There is a persistent notion that liquids, as compared to solids, fail to trigger physiological satiety mechanisms, leading to a loss of control over appetite and overeating (Almiron-Roig and Drewnowski, 2003; Almiron-Roig et al., 2003). At the same time, other studies suggest that solid energy-dense foods cause CNS insulin resistance (Isganaitis and Lustig, 2005); fail to trigger satiety mechanisms, and also lead to overeating. As a result, solid fast foods (Isganaitis and Lustig, 2005; Prentice and Jebb, 2003) and liquid, energy-dilute beverages (Bray et al., 2004) have been blamed, separately and together, for the obesity epidemic.

This paper reviews evidence from laboratory, clinical and epidemiological studies on sugars and sweeteners in the context of current research on energy density and satiety. The two standard approaches to reducing energy density of the diet are reducing fat content and increasing the consumption of vegetables and fruits (Rolls et al., 2005). The present question is whether reducing energy density of sweet beverages and foods through the introduction of intense sweeteners is another useful option for the control of body weight.

### Sugars, intense sweeteners and energy density of foods

Energy density (cal/g) of foods is an important determinant of energy intake in a meal (Bell et al., 1998; Drewnowski, 1998a; Stubbs et al., 2000) or over the course of a day (de Castro, 2004). By substituting for sugar (4 kcal/g), intense sweeteners lower the energy density of beverages and foods. However, this reduction is far greater for caloric beverages than it is for many solid foods (see Table 2). When sugar is the main source of energy, as in soft drinks, intense sweeteners help to bring energy density of beverages from 0.44 kcal/g to close to 0. In contrast, sugar is only one component of medium energy density foods such as yogurt, ice cream or frozen desserts (0.5–2.5 kcal/g), with the remaining calories derived from protein or fat (Drewnowski, 2003). Here, intense sweeteners may lead only to a minor reduction in energy density, especially if gels, fibers, maltodextrins, or even fat are used to make up the missing bulk. In high-energy density foods such as ready-to-eat cereals or chocolate (2.5–6 kcal/g), replacing sugar with intense sweeteners leads to relatively minor reductions in energy density relative to the original product (Ireland-Ripert et al., 1997). As not all intense sweeteners are heat stable, their application to low-sugar versions of cooked goods (such as bakery products) remains limited.

When the two versions of a food do not differ in energy density, their impact on hunger, satiety and energy intakes would be expected to be the same. Replacing sugar with intense sweeteners allows a meaningful reduction in the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Sweetening power of various substances (as compared to that of sucrose)</th>
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</thead>
<tbody>
<tr>
<td>Sweetener</td>
<td>Sweetening power</td>
</tr>
<tr>
<td>Sucrose</td>
<td>1</td>
</tr>
<tr>
<td>Acesulfame-K</td>
<td>100–200</td>
</tr>
<tr>
<td>Aspartame</td>
<td>100–200</td>
</tr>
<tr>
<td>Cyclamates</td>
<td>25–30</td>
</tr>
<tr>
<td>Saccharin</td>
<td>300–400</td>
</tr>
<tr>
<td>Sucralose</td>
<td>600</td>
</tr>
<tr>
<td>Thaumatinne</td>
<td>2500</td>
</tr>
<tr>
<td>Neotame</td>
<td>7000–13000</td>
</tr>
</tbody>
</table>
energy density of beverages; the reduction is smaller for semi-liquid food products, and can be very small for solid foods. The impact of intense sweeteners on energy intakes may, therefore, largely depend on the energy density of the tested food. Table 3 (Blundell and Hill, 1986; Rogers et al., 1988; Anderson et al., 1989; Birch et al., 1989; Rolls et al., 1989, 1990; DiSogra et al., 1990; Rodin, 1990; Mattes, 1990a; Tordoff and Allewa, 1990a; Black et al., 1991, 1993; Canty and Chan, 1991; Drewnowski et al., 1994a, b; Lavin et al., 1997; Beridot-Therond et al., 1998; King et al., 1999; Melanson et al., 1999a; Wilson, 2000; Van Wymelbeke et al., 2004) shows that past studies on sugars, intense sweeteners and satiety have been based on both liquid and solid stimuli of different levels of energy density. Those included aqueous solutions (Blundell and Hill, 1986), soft drinks (Canty and Chan, 1991; Almiron-Roig and Drewnowski, 2003), fruit drinks (Anderson et al., 1989; Birch et al., 1989; Canty and Chan, 1991; Beridot-Therond et al., 1998; King et al., 1999; Van Wymelbeke et al., 2004), fruit juices (Almiron-Roig and Drewnowski, 2003), milk (Wilson, 2000), yogurts (Blundell and Green, 1996), soft creamy white cheese (Drewnowski et al., 1994a, b), puddings (Rolls et al., 1989) and cereal (Mattes, 1990a). As a result, the impact of intense sweeteners on satiety may have been crossed with product consistency (liquid versus solid) or sugar type (sucrose or HFCS), not to mention energy density and preload volume (Almiron-Roig et al., 2003).

### Experimental designs

Most studies on sugars, sweeteners and satiety have made use of the standard preload paradigm (Rogers and Blundell, 1989, 1993; Drewnowski, 1998b). Generally, this takes the form of presenting study subjects with a preload beverage, meal or snack of varying energy, volume, energy density or nutrient composition (Walike et al., 1969; Drewnowski, 1998b). Typically, preload volume is adjusted by the addition of water preload and energy is adjusted by the addition of non-caloric components (intense sweeteners or fat replacements), whereas preload nutrient composition is determined by the proportions of fat, carbohydrate, protein or fiber (Drewnowski, 1998b). The general assumption is that energy ingested in the form of preload will lead to adjustments in energy intakes later on.

In studies of sweetness and satiety, there is a need to distinguish between the addition and the substitution conditions (Blundell and King, 1996). The addition of an intense sweetener to a plain stimulus adds sweetness, however, the energy value remains constant. By contrast, the substitution of an intense sweetener for sucrose maintains sweetness but reduces energy content by a variable amount (see Table 2). Whereas some early studies examined the impact of substituting aspartame for sucrose (Anderson et al., 1989; Rolls et al., 1990), fewer used a plain water control (Blundell et al., 1988; Black et al., 1991). Other studies used a variety of solid and liquid preloads that were either plain, sweetened with sucrose, aspartame or supplemented with maltodextrin or starch (Rogers and Blundell, 1989; Mattes, 1990a; Drewnowski et al., 1994b).

The dependent measures typically take one of two forms. First, motivational ratings of hunger, satiety, desire to eat and thirst are collected at variable intervals (20–30 min) for up to a few hours after the preload (Kissileff et al., 1984; Almiron-Roig and Drewnowski, 2003). Second, the amount of energy consumed at a subsequent test meal is the principal measure of energy adjustment following preload ingestion. There are some questions whether motivational ratings alone are a good predictor of energy intakes at the next meal (Mattes, 1990b; Mattes et al., 2005). Although some early studies used motivational ratings as proxy measures of ingestion, it is a good practice to use both (Almiron-Roig et al., 2003). In general, taste preferences for sweet solutions, once thought to be an index of satiety

### Table 2: Comparison of sugar-reduced and regular foods and drinks

<table>
<thead>
<tr>
<th>Type of food or drink</th>
<th>Regular</th>
<th>Sugar-reduced or sugar-free</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CHO content (per 100 g)</td>
<td>Energy content (kcal per 100 g)</td>
</tr>
<tr>
<td>Cola drinks</td>
<td>10.2</td>
<td>40</td>
</tr>
<tr>
<td>Fruit drinks</td>
<td>14</td>
<td>56</td>
</tr>
<tr>
<td>Cocoa</td>
<td>10.9</td>
<td>50</td>
</tr>
<tr>
<td>Hard candies</td>
<td>100</td>
<td>375</td>
</tr>
<tr>
<td>Drinking yogurt</td>
<td>12.8</td>
<td>72</td>
</tr>
<tr>
<td>Yogurt nonfat</td>
<td>13.8</td>
<td>75</td>
</tr>
<tr>
<td>Fruit Pie</td>
<td>33.6</td>
<td>237</td>
</tr>
<tr>
<td>Gelatin</td>
<td>13.6</td>
<td>57</td>
</tr>
<tr>
<td>Pudding</td>
<td>21.2</td>
<td>131</td>
</tr>
<tr>
<td>RTE cereal</td>
<td>90</td>
<td>360</td>
</tr>
<tr>
<td>Muesli</td>
<td>68</td>
<td>380</td>
</tr>
<tr>
<td>Cookies</td>
<td>33</td>
<td>445</td>
</tr>
<tr>
<td>Chocolate syrup</td>
<td>61</td>
<td>261</td>
</tr>
<tr>
<td>Chocolate</td>
<td>59</td>
<td>513</td>
</tr>
<tr>
<td>Chewing gum</td>
<td>120</td>
<td>500</td>
</tr>
</tbody>
</table>

European Journal of Clinical Nutrition
(Blundell and Hill, 1986) are not a good predictor of actual food consumption (Lucas and Bellisle, 1987; Perez et al., 1994).

In classic preload protocols, the time interval to the next meal can vary between 0 and 150 min. When the study focuses on satiation, the beverage preload is presented with the meal (DellaValle et al., 2005). Energy and at times nutrient intakes at the test meal are the sole dependent variables. Those studies generally do not track the evolution of hunger and satiety profiles with time.

When the focus of the study is on satiety, the meal is presented 60–150 min following the consumption of the preload. However, the longer the postingestive window, the greater the risk that the hunger curves for the low- and the high-energy preloads will eventually converge (Drewnowski et al., 1994a, b). As a result, the likelihood of finding energy compensation will be reduced. Energy intakes may also be affected by the palatability of the test meal (Yeomans, 1996; Yeomans et al., 2001; Almiron-Roig and Drewnowski, 2003).

### Table 3: The impact of intense sweetener aspartame on hunger and energy intakes compared to the control conditions

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Dose (mg)</th>
<th>Volume (ml)</th>
<th>Vehicle</th>
<th>Control condition(s)</th>
<th>Delay (min)</th>
<th>Meal</th>
<th>Hunger</th>
<th>Consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blundell and Hill (1986)</td>
<td>95</td>
<td>162</td>
<td>200</td>
<td>Water</td>
<td>Water</td>
<td>—</td>
<td>Lunch</td>
<td>Increased</td>
<td>—</td>
</tr>
<tr>
<td>Rogers et al. (1988)</td>
<td>8M, 4F</td>
<td>162</td>
<td>200</td>
<td>Water</td>
<td>Water</td>
<td>60</td>
<td>Lunch</td>
<td>Higher</td>
<td>No effect</td>
</tr>
<tr>
<td>Birch et al. (1989)</td>
<td>24 (4–5 years)</td>
<td>140</td>
<td>205</td>
<td>Fruit drink</td>
<td>Water</td>
<td>0–60</td>
<td>Snacks</td>
<td>No effect</td>
<td>No effect</td>
</tr>
<tr>
<td>Rodin (1990)</td>
<td>24</td>
<td>250</td>
<td>500</td>
<td>Water</td>
<td>Water</td>
<td>38</td>
<td>Lunch</td>
<td>—</td>
<td>No effect</td>
</tr>
<tr>
<td>Rolls et al. (1990)</td>
<td>42M</td>
<td>110</td>
<td>240</td>
<td>Lemonade</td>
<td>Glucose</td>
<td>0, 30, 60</td>
<td>Lunch</td>
<td>Decreased</td>
<td>No effect</td>
</tr>
<tr>
<td>Black et al. (1991)</td>
<td>20 M</td>
<td>160</td>
<td>280</td>
<td>Soft drink</td>
<td>Water</td>
<td>60</td>
<td>Lunch</td>
<td>No effect</td>
<td>No effect</td>
</tr>
<tr>
<td>Candy and Chan (1991)</td>
<td>2M, 18F</td>
<td>112</td>
<td>200</td>
<td>Fruit drink</td>
<td>Water</td>
<td>60</td>
<td>Lunch</td>
<td>No effect</td>
<td>No effect</td>
</tr>
<tr>
<td>Black et al. (1993)</td>
<td>18M</td>
<td>340</td>
<td>280</td>
<td>Capsule</td>
<td>Sucrose</td>
<td>65</td>
<td>Lunch</td>
<td>No effect</td>
<td>No effect</td>
</tr>
<tr>
<td>DiSogra et al. (1990)</td>
<td>6M, 6F</td>
<td>234</td>
<td>—</td>
<td>Capsules</td>
<td>Water</td>
<td>60</td>
<td>Lunch</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Tordoff and Alleva (1990a)</td>
<td>10M, 5F</td>
<td>235</td>
<td>470</td>
<td>Capsules</td>
<td>Water</td>
<td>60</td>
<td>Lunch</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Anderson et al. (1989)</td>
<td>0.05–1%</td>
<td>300</td>
<td>211–391</td>
<td>Chewing gum</td>
<td>Plain gum</td>
<td>90</td>
<td>Lunch</td>
<td>No effect</td>
<td>No effect</td>
</tr>
<tr>
<td>Rolls et al. (1989)</td>
<td>12M, 12F</td>
<td>0.16% by weight</td>
<td>70g</td>
<td>Cereal</td>
<td>Sucrose</td>
<td>180</td>
<td>Lunch</td>
<td>Decreased</td>
<td>No effect</td>
</tr>
<tr>
<td>Drewnowski et al. (1994b)</td>
<td>12M, 12F</td>
<td>500</td>
<td>500</td>
<td>Soft white cheese</td>
<td>Plain Sucrose</td>
<td>6.5h</td>
<td>Lunch</td>
<td>Decreased</td>
<td>No effect</td>
</tr>
<tr>
<td>Drewnowski et al. (1994b)</td>
<td>24F</td>
<td>500</td>
<td>500</td>
<td>Soft white cheese</td>
<td>Plain Sucrose</td>
<td>3h</td>
<td>Dinner</td>
<td>Decreased</td>
<td>No effect</td>
</tr>
<tr>
<td>Lavin et al. (1997)</td>
<td>14F</td>
<td>330</td>
<td>—</td>
<td>Lemonade</td>
<td>Water</td>
<td>15h</td>
<td>Dinner</td>
<td>Decreased</td>
<td>No effect</td>
</tr>
<tr>
<td>Beridot-Therond et al. (1998)</td>
<td>12M, 12F</td>
<td>50 mg/l</td>
<td>Ad lib</td>
<td>Fruit drink</td>
<td>Water</td>
<td>6.5h</td>
<td>Dinner</td>
<td>Decreased</td>
<td>No effect</td>
</tr>
<tr>
<td>Melanson et al. (1999b)</td>
<td>10M</td>
<td>~ 100</td>
<td>350</td>
<td>Lemon Water</td>
<td>Carbohydrate Fat</td>
<td>Variable</td>
<td>Lunch</td>
<td>—</td>
<td>No effect</td>
</tr>
<tr>
<td>King et al. (1999)</td>
<td>16M</td>
<td>Not reported</td>
<td>790</td>
<td>Fruit drink</td>
<td>Water</td>
<td>~ 15</td>
<td>Lunch</td>
<td>No effect</td>
<td>Increased</td>
</tr>
<tr>
<td>Wilson (2000)</td>
<td>13S (2–5 years)</td>
<td>Not reported</td>
<td>Ad lib</td>
<td>Milk</td>
<td>Sucrose</td>
<td>0</td>
<td>Lunch</td>
<td>No effect</td>
<td>Increased</td>
</tr>
<tr>
<td>Van Wykembeke et al. (2004)</td>
<td>12M, 12F</td>
<td>40</td>
<td>2000</td>
<td>Fruit drink</td>
<td>Sucrose milk</td>
<td>Variable</td>
<td>Lunch</td>
<td>No effect</td>
<td>No effect</td>
</tr>
</tbody>
</table>

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Typically, the interval to the test meal is determined by the experimenters. The amount consumed is allowed to vary as study participants are encouraged to eat *ad lib*. The amount consumed, taking plate waste into account, as well as nutrient composition of the selected meal are then the chief dependent variables. Only a few studies have measured water consumption at the test meal (Almiron-Roig *et al.*, 2004; Tsuchiya *et al.*, 2006). Interestingly, even though satiety is formally defined as the time interval to the next meal, virtually no studies have selected to use this interval as the key dependent variable. Only Louis-Sylvestre (*Himaya et al.*, 1997) used the meal demand paradigm to measure the impact of preloads on satiety. Those data were later linked to the participants' ghrelin levels, providing a valuable link between data from the behavioral preload paradigm and plasma levels of hunger and satiety hormones (Cummings *et al.*, 2004).

**Intense sweeteners and the preload paradigm**

Studies outlined in Table 3 measured motivational ratings, energy intakes or both. Studies that focused on hunger and satiety were designed to address two specific questions. The first question was whether foods and beverages containing intense sweeteners can provide the same degree of satisfaction as the full-calorie sugar-sweetened products. In one study, there were no differences in hunger ratings at 0, 30 and 60 min following the consumption of aspartame- or sucrose-sweetened lemonade (5 vs 166 kcal) (Rolls *et al.*, 1989). In another study, adults who consumed a high- or a low-calorie pudding or a gelatin dessert (mean energy difference, 206 kcal) had similar ratings of hunger and desire to eat even at 120 min postingestion (Rolls *et al.*, 1989).

It now appears that calories are not detected within the first few minutes postingestion. The chief cue for satiety in short-term laboratory studies is preload volume. In one study (Black *et al.*, 1991), the desire to eat was reduced more effectively by 560 ml as opposed to 280 ml of energy-free carbonated mineral water. Although water volume may have resulted in heightened satiety immediately postingestion, that sensation dissipated shortly afterwards. Studies that failed to demonstrate differences in satiety between caloric and non-caloric preloads may have been underpowered; may have used a large preload volume, or may not have been conducted for long enough.

The second question had to do with the so-called sweetener ‘paradox’, as described in a letter to *The Lancet* (Blundell and Hill, 1986) Blundell and Hill reported that prior ingestion of a sweet aspartame solution suppressed taste preferences for sucrose, but failed to reduce the motivation to eat. The implication was that intense sweeteners produced conflicting signals regarding appetite regulation, leading potentially to eating disorders. The sweetener controversy was re-ignited by a recent brief report (Davidson and Swithers, 2004) that the ability of 10 rat pups to adjust caloric intake was disrupted by prior exposure to solutions containing glucose and 0.3% saccharin.

However, as documented in Table 3, the sweetener ‘paradox’ was not replicated in later studies. Studies using soda, flavored water or lemonade as vehicle failed to show that aspartame stimulated appetite relative to the unsweetened vehicle or water (Birch *et al.*, 1988; Rodin, 1990; Rolls *et al.*, 1990; Black *et al.*, 1991; Canty and Chan, 1991). No stimulation of appetite was observed following the consumption of intense sweeteners in such foods as cereal, gelatin dessert or creamy dessert-type white cheese. Black *et al.* (1993) found no difference in satiety profiles following the ingestion of 560 ml of an aspartame-sweetened soft drink compared to 560 ml plain water but a transient increase in the desire to eat in the aspartame condition using 280 ml (but not 560 ml) preload volume. Food intakes in either condition were not affected.

When it comes to energy compensation, the failure to compensate for the missing calories in the aspartame condition is good news. The failure to compensate means that diet soft drinks can lead to net energy savings at the end of the day and perhaps in the long term. Table 3 shows that most studies that have measured food intakes following the ingestion of aspartame-sweetened preloads, as compared to sucrose, reported no significant effects. For example, the consumption of soft drinks sweetened with aspartame or sucrose (3 vs 90 kcal) failed to affect subsequent energy consumption of soft drinks sweetened with aspartame or sucrose (3 vs 90 kcal) failed to affect subsequent energy intake was disrupted by prior exposure to solutions containing glucose and 0.3% saccharin.

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output, regardless of the energy content of one individual food or beverage.

The notion of energy homeostasis is at the heart of the preload paradigm in that energy compensation is often the expected result. Expert opinion once held that intense sweeteners would fail to reduce energy intakes, because homeostatic mechanisms would act to restore the usual levels of consumption (Booth, 1987; Louis-Sylvestre, 1987; Louis-Sylvestre et al., 1989). Expert opinion still holds that energy homeostasis is capable of adjusting intakes downward following the ingestion of sugar energy in solid – but seemingly not in liquid – form (DiMeglio and Mattes, 2000). The present demonstration that energy compensation in studies of sugars and satiety is weak, regardless of study design, raises a number of issues about the continuing usefulness of the preload paradigm.

**Energy homeostasis and caloric compensation**

The human body compensates for energy deficits far more readily than to an energy excess (Mattes et al., 1988; Blundell and King, 1996). Upward energy adjustment was found in growing children, adolescents and young males but was more elusive among mature adults. Birch and DeGeyer (1986) observed perfect energy compensation among 2 to 5-year olds: the children ate more after an aspartame-sweetened preload than after a sugar-containing preload. However, older children (9–10-year old) did not compensate for sucrose energy and consumed more energy in the sucrose than in the aspartame preload condition (Anderson et al., 1989). Healthy adults housed for 14 days in a hospital ward managed to maintain a constant level of energy intake when provided with diets of different nutrient composition (Foltin et al., 1990). In contrast, downward compensation following excess energy consumption proved much more difficult to demonstrate in the laboratory, and was rarely accurate or complete (Mattes et al., 1988; Levitsky et al., 2005).

One current view (DiMeglio and Mattes, 2000) is that humans are unable to compensate for excess calories from beverages. Repeated ingestion of sweetened caloric beverages (1000 ml/day) failed to induce downward energy adjustment even after 1 month exposure (Van Wyk and Beke, 2004). However, as documented in a recent review (Almiron-Roig et al., 2003), the degree of energy compensation following preload ingestion was influenced by many factors, including subject characteristics, preload volume and the time lag between the preload and the next meal. Whether the preload was liquid or solid seemed immaterial. For example, the ingestion of an energy-dense solid food, potato chips (Rolls et al., 2004) failed to induce downward energy adjustment later on. In another study, isoenenergetic amounts of cola and cookies led to identical hunger and satiety profiles and comparable energy intakes at the next meal (Almiron-Roig et al., 2004). It would appear that human ability to compensate for previously ingested calories is poor, regard-

less of the physical form of the food product. If this is true, if the energy homeostatic mechanisms are even slightly imprecise (Levitsky et al., 2005), then replacing sugars by intense sweeteners may lead to an overall reduction in energy intakes in the long term.

**Clinical studies of intense sweeteners and body weight**

Long-term studies comparing the impact of sugars and intense sweeteners on energy intakes are extremely limited (Table 4) (Porikos et al., 1977; Kanders et al., 1988; Tordoff and Alleva, 1990b; Blackburn et al., 1997; Raben et al., 2002). One early study conducted in a metabolic ward over 24 days (Porikos et al., 1982) showed that male subjects increased their energy intakes, compensating for some (40%) of the missing sucrose energy. In another study (Tordoff and Alleva, 1990b), daily consumption of 113.5 g diet soda over 21 days suppressed the discretionary consumption of regular soda, leading to reduced energy intakes. In a recent clinical study (Raben et al., 2002), supplying a control group of overweight adults with diet sodas for a period of 10 weeks led to an (unexplained) net reduction in food consumption.

Longer term studies on the impact of aspartame on weight loss (Kanders et al., 1988) were inconclusive. In a pilot study (Kanders et al., 1988), 46 obese women lost slightly more weight (7.4 kg as compared to 5.8 kg) in the aspartame condition; however, a small group of male subjects (n = 11) showed the opposite trend. At the 1-year follow-up, sustained weight loss was associated with physical activity levels, aspartame use and reduced preferences for sweets.

In a later study (Blackburn et al., 1997), 163 obese women were placed on a 1500 kcal/day diet. One group was specifically encouraged to use aspartame-sweetened foods and beverages during the active weight loss phase (16 weeks), a 1-year maintenance program, and a 2-year follow-up period; the other group was asked to abstain. Although the initial weight loss (10% of initial body weight) was comparable for the two groups, the aspartame group showed better weight maintenance, regaining only 2.6% of initial body weight after 71 weeks and 4.6% after 175 weeks. In contrast, the abstainers regained 5.4 and 9.4%, respectively.

**The use of intense sweeteners in the free-living populations**

Epidemiological studies of intense sweetener use tend to be cross-sectional in nature. As a result, it is impossible to draw any causal links between sweeteners use and dietary habits or sweetener use and body weight. One study of 195 men and women (Chen and Parham, 1991) showed that 31% of men and 61% of the women consumed both intense sweeteners and sugar containing foods. There was no evidence that use of intense sweeteners was associated with a significant
Intense sweeteners, energy intake and the control of body weight
F Bellisle and A Drewnowski

Table 4 Long-term studies of the impact of intense sweetener aspartame on body weight

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Design</th>
<th>Period</th>
<th>Weight loss diet</th>
<th>Products</th>
<th>Body weight loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tordoff and Alleva (1990b)</td>
<td>21M,9F Normal wt.</td>
<td>Xover</td>
<td>3 × 3 weeks</td>
<td>No</td>
<td>Soda, 1150 g reg. or diet</td>
<td>0.5 kg loss M, F</td>
</tr>
<tr>
<td>Kanders et al. (1988)</td>
<td>13M,46F Obese</td>
<td>2arm</td>
<td>12 weeks</td>
<td>Yes</td>
<td>Aspartame vs not</td>
<td>All lost, non-Asp F lost least</td>
</tr>
<tr>
<td>Blackburn et al. (1997)</td>
<td>163F Obese</td>
<td>2arm</td>
<td>19 weeks + 1 year</td>
<td>Yes</td>
<td>Aspartame vs not</td>
<td>Both lost ∼10%, Asp regained less</td>
</tr>
<tr>
<td>Raben et al. (2002)</td>
<td>6M,35F</td>
<td>2arm</td>
<td>10 weeks</td>
<td>No</td>
<td>Sucrose vs Aspartame</td>
<td>Aspartame lost, sucrose gained</td>
</tr>
<tr>
<td>Porikos et al. (1977)</td>
<td>Overwt.</td>
<td>Xover</td>
<td>3 × 6 × 6 days</td>
<td>No</td>
<td>Sucrose vs Aspartame</td>
<td>No change</td>
</tr>
</tbody>
</table>

Asp = Aspartame.

reduction in sugar intake. On the other hand, Bellisle et al. (2001) found, in a cohort of 4278 French adults, aged 45–60 years, that about 30% of women and 22% of men were at least occasional users of intense sweeteners. As expected, higher body mass index (BMI) values and higher waist/hip ratios were associated with more frequent use, suggesting that overweight persons were using intense sweeteners as a strategy for weight control. Users had lower energy intakes (significant difference in men only) and consumed less carbohydrate than did nonusers. In a Spanish study of 2450 persons (Serra-Majem et al., 1996), about 18% of the population used cyclamate. Within the user group, higher BMI was associated with less frequent use. There is a dearth of longitudinal studies on the dynamics of weight control.

The Gold Standard: the randomized controlled trials (RCTs)

The above-cited literature covers many aspects of the broad research domain of intense sweeteners and their effects on appetite, intake and body weight control. They provide very diverse and complementary pieces of information on a very complex subject. A recent meta-analysis (De La Hunty et al., 2006) considered only those RCTs that did measure energy intake for at least 24 h and/or measured weight changes. The RCT is considered the best experimental design, but in many circumstances it is difficult to implement, especially when dealing with human subjects who have established habits and preferences and will not easily be randomized. For example, it may be difficult to prevent sweetener use over a long period of time in a participant who has been randomized to a no sweetener group.

Out of dozens of works dealing with intense sweeteners’ role in human nutrition, the meta-analysis addressed 15 RCTs with 24-h intake data (Porikos et al., 1977, 1982; Tordoff and Alleva, 1990b; Kanders et al., 1990; Naismith and Rhodes, 1995; Blackburn et al., 1997; Gatenby et al., 1997; Lavin et al., 1997; Reid and Hammersley, 1998; Raben et al., 2002; Van Wymelbeke et al., 2004) and nine RCTs with body weight data (Porikos et al., 1977, 1982; Tordoff and Alleva, 1990b; Kanders et al., 1990; Naismith and Rhodes, 1995; Blackburn et al., 1997; Gatenby et al., 1997; Lavin et al., 1997; Reid and Hammersley, 1998; Raben et al., 2002). These RCTs showed considerable variations in their design, study population, duration and type of control. In addition, certain studies compared dietary conditions that did not only differ by the presence or absence of intense sweeteners. For example the Foltin et al. (1988, 1992) studies did not focus specifically on intense sweeteners but compared diets varying in fat as well as carbohydrate contents, thereby making it impossible to single out the contribution of sweeteners in the reported effects. The meta-analysis revealed significant reduction in energy intakes when aspartame was used, compared with all types of control except when aspartame was compared with non-sucrose controls such as water. The mean reduction was about 10% of total energy intake.

The meta-analysis also included consideration of potential upward compensation for the missing energy. Such compensation was around 32%, but varied widely as a function of numerous factors, among which the size of the energy deficit, the type of food or drink manipulated and the timescale. The four studies that only manipulated soft drinks sugar content suggested a compensation of about 15.5%. Since sugar consumption is not thought to be under physiological control (Berthoud and Seeley, 1999), there is no theoretical reason to expect that any compensation for missing sugar energy – if it occurs – will be selectively directed at sweet foods. Replacing sugar with intense sweeteners should, therefore, help reduce sugar intakes. The authors of the meta-analysis calculated that a conservative figure for the energy deficit in aspartame users would predict a weight loss of about 0.2 kg/week.

The nine studies of aspartame use including body weight data suggested a significant weight reduction of the order of 0.2 s.d. for an average diet duration of 12 weeks. For a 75-kg person, this would represent a weight loss of around 0.2 kg/week. According to de la De La Hunty et al. (2006), the close agreement between the predicted and the observed weight loss suggests that the 0.2 kg/week estimated is robust and applicable to a variety of aspartame-containing foods.
Final considerations

Sugars in the food supply account for a growing proportion of energy intakes in the US (Elliott et al., 2002). Intense sweeteners coexist in the marketplace with sugar-sweetened beverages and foods (Harnack et al., 1999; Saris, 2003). The availability of low-calorie beverages has not reduced consumption of sugar-containing drinks: quite surprisingly, their levels of intake have grown in parallel over the last decades in the United States of America (Saris, 2003).

The present review of clinical and laboratory studies on sweeteners and satiety suggests that the human ability for exact energy homeostasis is limited (Jordan, 1969; Mattes et al., 1988; Blundell and King, 1996). The success of diet beverages and foods depends on imprecise systems of control and the absence of powerful compensatory mechanisms. The results of many studies are, in fact, compatible with such a notion. Diet beverages have the advantage of reducing energy density of the product down to zero, something that is not easily achieved with solid or semi-solid foods. As a result, diet beverages might represent the optimal use of intense sweeteners in the context of a weight control strategy. Although they have been shown to be associated with some modest weight loss in RCTs (De La Hunty et al., 2006), intense sweeteners are not appetite suppressants. Their ultimate effects will depend on their integration within a reduced energy diet.

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