Symposium on ‘Nutrition: getting the balance right in 2010’

Session 1: Balancing intake and output: food v. exercise

Why liquid energy results in overconsumption

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Liquids have been shown to have a low satiating efficiency. The may be related to the high rate of consumption for liquids which may be higher than 200 g/min. In a number of studies, we showed that the positive relationship between eating rate and energy intake is mediated by oro-sensory exposure time. Longer sensory exposure times are consistently associated with lower food intakes. This observation maybe linked to the role of cephalic phase responses to foods. Cephalic phase responses are a set of physiological responses, which are conceived to prepare the digestive system for the incoming flow of nutrients after ingestion, with the aim of maintaining homeostasis. Results from various studies suggest that cephalic phase responses are much smaller (absent) for liquids compared to solids. It is hypothesised that the absence of cephalic phase responses to liquid foods may be one of the causes why liquid energies enter the body undetected and lead to weak energy intake compensation. This idea fits with the concept of the taste system as a nutrient-sensing system that informs the brain and the gastro-intestinal system about what is coming into our body. With liquids, this system is bypassed. Slower eating may help the human body to associate the sensory signals from food with their metabolic consequences. Foods that are eaten quickly may impair this association, and may therefore lead to overconsumption of energy, and ultimately to weight gain.

Appetite: Liquid energy: Obesity: Energy intake

In the last few decades it has become clear that the high prevalence of obesity in developing countries is a normal behavioural response to an abnormal obesogenic environment. This obesogenic environment facilitates food (energy) intake and limits energy expenditure. Recent evidence suggests that changes in energy intake are the dominant factors in increasing prevalence of obesity since the 1980s.(1,2). Frequent exposure to food cues, large portion sizes, large available variety, high energy density and high palatability of foods are implicated in this respect(3).

This paper focuses on one additional element of our food supply and our eating environment, i.e. the high eating rate at which we can ingest a vast majority of foods in our current food supply. It is hypothesised that the high eating rate undermines our body’s capacity to regulate energy intake at healthy levels. This may work by impairing the congruent relationship between sensory input and metabolic consequences. The physiological background for this may be that foods that are consumed quickly like liquids do not lead to functional cephalic phase responses (CPR). CPR are the predominantly learned physiological responses to the sensory signals from food. Before focusing on the role of eating rate in the regulation of food intake, we first discuss a simple psycho-biological model of eating behaviour that helps to explain the later reasoning in this paper.

Sensory and metabolic signals involved in eating behaviour

Fig. 1 illustrates how eating behaviour is guided by sensory and metabolic signals. In addition, sensory signals of foods are linked in the brain to the metabolic consequences of eating. These (mostly unconscious) learning processes that take place within the context of our living/eating

Abbreviations: CPR, cephalic phase response; MSF, modified sham feeding.
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environment shape our food pattern. They guide us throughout the day as to what to eat and also what to expect about the consequences of eating and drinking\(^4\). For example, people know what to consume for lunch in order to stay satiated until dinner. People know what to expect from a cup of coffee in the morning or a glass of wine in the evening.

Sensory signals play an important role in food choice; in general, we choose the foods we like, and we avoid the foods we dislike\(^5\). Sensory signals are also involved in the drive for variety in the diet. Repeated exposure to a particular sensory signal (e.g. a meat flavour; a fruit flavour) during a meal leads to a decline in the reward value of that food, and a shift in interest towards other foods. This phenomenon is called sensory-specific satiation and/or satiety, and has been demonstrated in a large number of studies (e.g.\(^6\)-\(^12\)).

Metabolic signals are involved in the regulation of energy intake. Meal initiation is guided by learned associations (time on a clock; a dressed table), which are modulated, for example, by an empty stomach, high ghrelin levels and/or short transient declines in glucose levels in the blood\(^13\)-\(^15\). During eating, hormonal and neural signals from the gastro-intestinal tract to the brain increase our feelings of satiation. Stretch receptors in the stomach and various hormones such as cholecystokinin, glucagon-like peptide-1 and insulin are involved in this process\(^13\)-\(^15\). After the meal we stay satiated for some time depending on the amount and the composition of the foods that we ingest. After a couple of hours the cycle repeats itself. Apart from the short-term regulation of food intake, there is also a longer term regulation of energy balance based on signals coming from the adipose and lean tissue mass\(^13\)-\(^15\). This is, however, outside the scope of this paper.

Various learning processes in food choice and food intake have been well documented. One example of such a learning process is flavour-nutrient learning, which leads to a preference for foods that are high in carbohydrates\(^16\), fat\(^17\),\(^18\) and/or energy density\(^19\). The absence of energy taste conditioning may also explain the low preference for the pure taste vegetables in children and adults\(^20\).

Another example of learning in relation to hunger and satiety is the notion that our meal patterns are highly adjustable to external constraints/environmental circumstances. We usually get hungry just before the regular dinner time, and many people get an appetite for something sweet just before a coffee break. Environmental circumstances provide external cues (e.g. the time on a clock, the emptying of a soup bowl and the smell of food)
related to eating behaviour\(^4\). These patterns and the accompanying anticipatory physiological signals (e.g. ghrelin levels; see e.g. Drazen et al.\(^{15}\)), can be easily changed with varying environmental circumstances. This flexibility and adaptability are reflected in the wide diversity of eating cultures in the world\(^{4,21}\), and also in the continuous change of eating patterns.

**Liquid calories and the regulation of food intake and body weight**

One important difference between our current food supply compared to the food supply of our ancestors is that many processed foods in our current diet can be eaten at a high rate. The Neolithic diet compared to our current diet consisted of a relatively high-protein diet (meat and fish) with many foods with a high-fibre content (fruit, vegetables and root plant foods)\(^{22}\). Meat products and high-fibre products are typically foods that require chewing and are eaten at a relatively low rate. The Neolithic diet did also not contain any liquid calories, except for milk for infants. Infancy is a period of rapid growth of body weight, where body weight at 1 year after birth is usually more than two times the weight at birth\(^{23}\).

Liquids are consumed at much faster rates than solid foods\(^{24}\). This can be seen in Fig. 2, which shows that liquid foods stand out compared to other foods in terms of eating rate. They are consumed at rates higher than 200 g/min, with the exception of soup, which has an eating rate that is comparable to many solid foods (<100 g/min)\(^{24}\).

In this sense, liquid foods can be considered as fast foods, foods that can be eaten quickly. One typical example of the effect of processing food on eating rate is illustrated by a study of Haber et al.\(^{25}\). This showed that it takes about 17 min to consume 500 g apples, whereas 500 g apple juice is consumed in just 1.5 min\(^{25}\). Eating 8368 kJ (2000 kcal), i.e. the average energy requirement for a sedentary woman in the industrialised world, would take more than 2 h for eating apples, whereas for the apple juice the required time would be about 18 min.

From the appetite/satiety literature it has become clear that liquid foods have a lower satiating capacity than solid foods, with the exception of soup. Some early studies have shown that hunger, measured through subjective scales\(^{26}\) is more suppressed after consumption of solid foods compared to an equivalent amount of fruit juices with similar energy and macronutrient content\(^{25,27}\). The results of Hulshof et al.\(^{28}\) reinforced this idea by comparing the effects of hunger on liquid fat preloads with the effects of preloads made solid with gelatin or locust bean gum. The weak effects of liquid calories on energy intake compensation were recently confirmed for liquid and solid proteins, fats and carbohydrates\(^{29,30}\). The exceptional role of soup is illustrated by a study which showed that soups in a variety of forms reduce energy intake at a test meal\(^{31}\). This issue is worked out in the next section on oro-sensory exposure time and satiety.

The low satiating effect of liquids is not only clear from short preload test meal studies but also from longer term intervention studies. For example, a ten-week study showed that the energy from sugar-sweetened beverages added up to the total energy content of a regular diet\(^{32}\). In a four-week cross-over study, fifteen subjects consumed 1-9 MJ of carbohydrates in either a solid or liquid form. The results showed that subjects ate less throughout the remainder of the day when the solid calories were consumed, but subjects did not lower their intake when the
calories were consumed in the form of liquids (33). Body-weight changes varied accordingly; subjects gained weight in the liquid calorie condition, but not in the solid calorie condition. Also with respect to long-term weight change soup is different from caloric beverages. In a one-year weight loss/maintenance study, the provision of two soups led to higher weight loss after one year than providing one soup per day or two snacks (34).

In a recently published long-term (18 months) randomised controlled behavioural trial among 810 subjects, it was shown that a reduction in liquid calorie intake had a stronger effect on weight loss than did a reduction in calorie intake (35). Apparently, people detected the solid calories, but not the liquid calories, even after repeated long-term exposure. The notion that liquid calories are not well detected is in line with the results of a number of large-scale prospective epidemiological studies that show a positive association between sugar-sweetened beverage consumption and weight gain and obesity (36–38).

The role of eating rate and oro-sensory exposure in satiation was recently studied in a series of experiments in which eating rate and oro-sensory exposure were systematically varied. In a first within-subjects cross-over study in a cinema setting 108 subjects consumed ad libitum a liquid (milk) or semi-solid (custard) chocolate dairy product which were equal in palatability, energy density and macro-nutrient composition (42). Subjects consumed the products with a broad straw (1.2 cm diameter) from 1-litre carton boxes which prevented weight cues and visual cues from playing an important role in intake. The ad libitum consumption of the chocolate-flavoured liquid was about 30% higher compared to a similarly flavoured semi-solid. In a subsequent study under laboratory conditions with about fifty subjects, we investigated whether the eating effort and/or eating rate were responsible for the 30% difference in intake. This was done with the help of peristaltic pumps, which eliminated the effort to get the milk/custard into the mouth, and which could be set at standardised rates. Eliminating the effort had little effect on the difference between ad libitum intakes between the liquid and semi-solid (29%). However, when we matched the eating rate for both products, the difference in ad libitum intakes disappeared to a large extent (43) (see Fig. 3).

In a subsequent study, it was shown that changing the oro-sensory exposure of chocolate custard from 3 to 9 s/bite led to a 10% lower ad libitum intake (43). The suppressive effect of oro-sensory exposure time on ad libitum intake was confirmed in another study with orangeade, where we held the eating rate constant (150 g/min) but only varied the relative duration of sensory exposure (long: 30 s/min of consumption; short 15 s/min of consumption) (44). In a later experimental study, harder and softer versions of solid foods were compared with respect to their effect on ad libitum intake (45). Again, foods that were eaten more slowly resulted in lower food and energy intakes (45).

In a recent study, subjects (n 105) were repeatedly (ten times) exposed to liquid and semi-solid yoghurt (drinks) for breakfast. Subjects consumed the breakfast either in a liquid form with a straw (n 35), a liquid form with a spoon (n 35) or in a semi-solid form with a spoon (n 35). Eating rate and energy/food intake were higher in the straw condition compared to the spoon conditions (46). This result suggests, as the results of the other studies, that it is not the texture per se, but that the effect of texture on food intake works through oro-sensory exposure time.

In the studies described, the eating rate was varied within one particular food, and the foods used were mostly liquids and semi-solids. Viskaaal-van Dongen et al. (24) studied the relationship between eating rate and ad libitum food and energy intake across a range of forty-five different food products, representative of the current food supply. One of the most striking results was the magnitude of the differences in eating rate between various foods. Peanuts were consumed at a rate of about 14 g/min, whereas apple juice and diet coke were consumed at rates of more than 600 g/min. In this study, we observed a positive association between eating rate and ad libitum intake in g ($R^2 = 0.37$). With respect to peanuts, it is worth noting that eating rate is not the only factor involved in the satiety process. The texture of the food, the size of the bite, and the time it takes to chew and swallow all play a role in the satiety response.
and smell of food, include a cascade of pre-absorptive physiological responses, which are collectively referred to as CPR\(^{(50,51)}\). CPR are a possible way by which we may explain the different satiating capacities of foods that are eaten quickly and foods that are eaten slowly.

The role of cephalic phase responses in the regulation of food intake

CPR are a set of physiological responses, which are conceived to prepare the digestive system for the incoming flow of nutrients after ingestion, with the aim of maintaining homeostasis\(^{(50)}\). One of the clearest examples is the salivation response after the sight of or the mere thinking about food. The famous Russian scientist Pavlov was one of the first investigators to study this response, showing that dogs started to salivate when they were exposed to meat\(^{(52)}\). CPR are also thought to be learned, implying that they are adjustable to the type and size of the meal that is eaten. The responses are transient and often last for only a few minutes; however, their effects on post-prandial metabolism can be of a longer duration\(^{(53)}\).

The homeostatic function of the CPR is clear from a study which showed that the glucose and insulin responses after an intragastric glucose load were lower when subjects chewed on a peanut butter sandwich compared to a no-chewing control condition\(^{(54)}\). On average plasma glucose levels returned to baseline earlier after oral sensory stimulation (106 min) than when oral stimulation did not occur. The results of this study indicate that the oral sensory stimulation helped in maintaining glucose homeostasis.

Cephalic stimulation works through the mere thought of food, and through the five senses involved in food perception, i.e. the senses of vision, taste, smell, touch and hearing. Cephalic stimulation ultimately activates the vagus nerve, which results in a myriad of autonomic responses such as the release of various physiologically active compounds, including saliva, gastric acid, pancreatic exocrine enzymes, as well as hormones from the endocrine pancreas\(^{(50)}\). Early CPR include saliva and later CPR include gastric acid secretion and the release of pancreatic polypeptide\(^{(50)}\). The pancreatic polypeptide response is usually considered as the biological marker for vagal stimulation\(^{(53)}\). Most CPR are instrumental for digestion such as hydrochloric acid, gastrin and lipase release in the stomach and digestive enzymes from the pancreas and the duodenum. They have little to do with appetite\(^{(51)}\).

The CPR in human subjects is usually assessed through a modified sham-feeding paradigm, where subjects chew on foods and spit the food out at the time where they would normally swallow a food. For a detailed explanation of this methodology, see papers by Teff and co-workers\(^{(54–57)}\) and Robertson and co-workers\(^{(53,58)}\). Recovery rates of the chewed foods should be close to 100\%\(^{(53)}\).

The role of cephalic responses in the regulation of food intake has hardly been studied (for a review see\(^{(51)}\)). There are various possible ways in which CPR may affect appetite. There could be a direct centrally mediated effect on appetite. This direct effect is presumably a learned

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**Fig. 3.** (a) \textit{Ad libitum} intake (g, with standard deviation) and energy intake (kJ) of the liquid, semi-liquid and semi-solid chocolate dairy products in a cinema setting (\(n\ 108\); within subjects). Test products were similar in palatability, energy and macronutrient content, and consumed through a straw from 1-5 litre carton boxes over a period of about 90 min. Intake from the semi-solid was 30\% less than from the liquid test-food. (b) \textit{Ad libitum} intake (g, with standard deviation) and energy intake (kJ) of the liquid and semi-solid chocolate dairy product in a laboratory setting (sensory cabin) (\(n\ 49\); within subjects) within a time frame of about 15 min. In the free eating rate, \textit{different} effort, subjects consumed the products in the same way as in the cinema setting. In the free eating rate, no effort, subjects consumed the product from a tube making use of a peristaltic pump; in this condition subjects could adjust the rate of delivery. In the fixed eating rate, no effort condition, investigators set the rate of delivery of the test-products into the mouth of the subjects. (Source: Zijlstra et al\(^{(42)}\)).

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mentioning that peanuts and other nuts have a high energy density, and therefore they are expected to have a low satiating efficiency. However, they have a high satiating capacity\(^{(47,48)}\) which is attributable to their low consumption rate.

Altogether, these studies show that foods that can be eaten quickly lead to higher food intakes and lower satiating effects. With fast foods, it may be more difficult to learn to associate the sensory signals during eating with the metabolic consequences after eating (see Fig. 1). This idea was recently partly confirmed in a study in which people were capable of adjusting their intake after repeated exposure to high energy dense semi-solids, but not after repeated exposure to high energy dense liquids\(^{(49)}\).

To summarise, the effects of texture on appetite and food intake mainly work through oro-sensory exposure time, and thus oro-sensory stimulation. This finding raises the question: how do these oro-sensory signals exert their effect? The responses to sensory cues, such as the taste
response based on the association between sensory signals and subsequent metabolic consequences. The notion that people can assess expected satiety from various foods immediately, i.e. within a few seconds after the first bite of food is in line with this idea\textsuperscript{(59,60)}. The neuro-biological mechanism behind this effect is not yet clear. The findings of studies showing that tasting and ingesting glucose have an impact on the activity of the hypothalamus within 2 min may be related to this mechanism\textsuperscript{(61,62)}.

CPR may also affect appetite through the release of gastro-intestinal hormones such as insulin, pancreatic polypeptide, leptin and ghrelin\textsuperscript{(51)} In a study where subjects were given a 50 g intra gastric fat load, subjective fullness ratings were increased after 1 h modified sham feeding (MSF) of pizza\textsuperscript{(58)}. In this study, a 25\% suppression in ghrelin concentration was observed after the fat load, which was enhanced further in the MSF condition. The lower ghrelin levels in the MSF condition were accompanied by lower hunger ratings.

In two studies, Smeets and colleagues showed that the 15–20 min oro-sensory stimulation with fat increases satiety and a relative increase in glucose and insulin levels\textsuperscript{(63)}, and may decrease ghrelin levels relative to a water control lunch\textsuperscript{(64)}. Crystall and Teff\textsuperscript{(55)} showed that a 3 min MSF of high-fat cakes led to higher pancreatic polypeptide levels than MSF of non-fat cakes. The 3 min MSF is much shorter than the 15–20 min of Smeets and colleagues\textsuperscript{(63,64)} and the 60 min of Heath et al.\textsuperscript{(58)} Interestingly, the 3 min MSF feeding with high-fat cakes led to a higher intake of high-fat foods.

In one of her first studies on CPR, Teff et al.\textsuperscript{(56)} showed that sweet-tasting liquids are not adequate stimuli for the elicitation of the cephalic phase insulin response. However, in that same study, MSF apple pie did result in changes in glucose and insulin levels. In a very recent study, Teff\textsuperscript{(55)} measured the pancreatic polypeptide response (as a measure of stimulation of the vagal nerve) to liquid stimuli, chewing gum and regular mixed nutrient food that required chewing. This study showed that the liquids and chewing gum were not good elicitors of a CPR. The results from another group\textsuperscript{(65)} showed that consumption of a 2824.2 kJ lunch\textsuperscript{(64)} Crystall and Teff\textsuperscript{(55)} showed that a 3 min MSF of high-fat cakes led to higher pancreatic polypeptide levels than MSF of non-fat cakes. The 3 min MSF is much shorter than the 15–20 min of Smeets and colleagues\textsuperscript{(63,64)} and the 60 min of Heath et al.\textsuperscript{(58)} Interestingly, the 3 min MSF feeding with high-fat cakes led to a higher intake of high-fat foods.

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The role of oro-sensory stimulation in appetite regulation compared to the gastric contribution to satiety was also nicely shown in a series of elegant studies\textsuperscript{(66,67)}. The main characteristic of these studies was the independent manipulation of oral and gastric stimulation. In one of the first studies, it was shown that oral administration of soup produced the greatest suppression of appetite compared to intragastric delivery and intraduodenal delivery of soup\textsuperscript{(66)}. Overt intragastric delivery led to a higher suppression of hunger than covert intragastric delivery\textsuperscript{(66)}. Oral administration also delayed gastric emptying. These findings were later confirmed in other studies with oral and gastric administration of fats and carbohydrates\textsuperscript{(67)} and sucrose v. maltose\textsuperscript{(68)}.

### Discussion

The basic idea of this paper is that liquid foods and foods that can be eaten quickly undermine our body’s capacity to regulate food intake at healthy levels. They do this because they provide insufficient sensory signalling to inform the brain and the gastro-intestinal tract about the inflow of nutrients. Therefore, they have a low-satiating capacity, which in turn may lead to excess energy intake, and ultimately to overweight.

The idea that we can estimate/know the satiating capacity of a familiar food immediately after the first bite\textsuperscript{(59,60)} indicates that sensory signals have acquired meaning in terms of satiety after repeated consumption. Repeated consumption leads to an association between the sensory signals during consumption and the post-ingestive satiety effects, coming from the macronutrients in the food. This idea fits with the concept of the taste system as a nutrient sensing system that informs the brain and the gastrointestinal system about what is coming into our body. With liquids, this system is bypassed.

The transformation in our food supply, especially during the last decades, has gone in the direction of foods that are easy to get and convenient to eat. The convenience to eat may increase with the amount of processing of food. Insight into the effects of processing of foods on the satiating efficiency may be instrumental for the food industry to reverse the direction of food design with respect to eating rate and food intake. A major challenge to the food industry is the design of foods that are pleasant to eat, but at the same time, either provide satiation early enough to prevent overeating and/or provide satiety long and strong enough to postpone the next eating occasion.

The role of the CPR in the explanation of the low satiating capacity of liquids needs further elucidation. There are relatively few data on the relationship between CPR and satiety. The data of Teff\textsuperscript{(55)} and Teff et al.\textsuperscript{(55,56)} of oro-sensory stimulation on insulin and pancreatic polypeptide, the data of Heath et al.\textsuperscript{(58)} and Smeets et al.\textsuperscript{(64)} with respect to ghrelin are in line with the concept that these cephalic phase signals contribute to the satiating effect of foods. The data of Kokkinos et al.\textsuperscript{(65)} indicate that eating slowly leads to higher levels of the satiety hormones glucagon-like peptid e 1 and PYY. However, glucagon-like peptide 1 and PYY have not been implicated in the CPR\textsuperscript{(51)}.

The low satiating capacity of liquid calories has been a controversial issue for some time\textsuperscript{(69,70)}. Almiron-Roig et al.\textsuperscript{(69)} conclude that ‘the evidence that liquids have less impact on satiety than do solid foods remains inconclusive’. Drewnowski and Bellisle\textsuperscript{(70)} conclude that ‘research evidence comparing the short-term satiating power of different types of liquids and solids remains inconclusive’. In the US dietary guidelines of 2010\textsuperscript{(71)}, question 7 in Appendix E-1 Major conclusions with respect to energy balance and weight management, reads, ‘What is the impact of liquid versus solid foods on energy intake and body weight?’. The answer is ‘A limited body of evidence show conflicting results about whether liquid and solid foods differ in their effect on energy intake and body weight except that liquids in the form of soups may lead..."
to decreased energy intake and body weight. This controversy is resolved when we take the eating rate and duration of oro-sensory stimulation into account. Soup is a liquid, but its eating rate is equivalent to a solid food. This is the reason why soup is more satiating than energetic beverages which may be consumed at much higher rates.

The higher satiating effect of soup may be primarily determined by its eating rate comparable to other solid foods. Another issue that may be involved here is the warm temperature at which soup is eaten. A warmer temperature may lead to a stronger sensory response and therefore also a stronger CPR and a higher satiety value. A recent study showed that the cephalic phase insulin response was absent in response to a cold glucose solution, while a room temperature glucose solution did induce these responses. A study in mice found increased gustatory nerve responses with increasing temperature, and a study in human subjects showed reductions in perceived sweetness intensity due to cooling of the tongue. Taken together, these data suggest that chilled energetic beverages might be processed suboptimal, and warm foods like soup may have stronger CPR. Further research on this issue is warranted, also in relation to the widespread consumption of chilled beverages and ice cream.

Coming back to the model presented in Fig. 1, it is clear that sensory signals acquire meaning with respect to liking (hedonic value) and satiation/satiety after repeated exposure to foods. One of the exciting research questions for the near future is where and how the sensory signals during consumption and peripheral signals after ingestion are integrated. Which signals from the gastro-intestinal tract are involved in the process and where do they go to in the brain?

There is an increased need to understand the psychological, neurological and molecular mechanisms through which our current eating environment impairs our control of food intake, and this is the domain of experimental studies. The current state of the art in the field of nutri-genomics, neuro-endocrinology and neuro-imaging techniques may help in unravelling these basic mechanisms. This is an exciting prospect for a growing field that has to deal with an increasing societal problem of obesity.

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