Metabolic Impacts of Food Oral Processing

Oral Processing and Consumer Perception

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CHAPTER 6

Metabolic Impacts of Food Oral Processing

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6.1 A Role for Oral Processing in Metabolism and Health

The important contribution of oral processing to digestion has been known for centuries, dating back to Roman times where it was acknowledged that '*prima digestio fit in ore*' or 'first digestion occurs in the mouth'.[1] Over 100 years ago, Horace Fletcher popularized the phrase 'nature will castigate those that don't masticate', and believed that you could derive an equivalent satisfaction from one-third of the amount of food by simply chewing each mouthful for longer.[2] Despite this conventional wisdom, the mechanisms and metabolic impact of oral processing are often overlooked in food design and in diet and lifestyle interventions that target improved health.

Much of what food does to the body and how the digestive system reacts happens acutely, within the first 30 minutes of the post-prandial period.[3] It is during this period that the extent to which a food is digested, the production

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and release of the nutrient components and associated metabolites, and the partitioning of energy and nutrients into storage or oxidative substrates is decided. Two of the key factors that contribute to the breakdown and release of food components during this key period are individual differences in oral processing behaviour during consumption, and individual differences in the metabolic response during the cephalic, gastric and intestinal phases of digestion.

Everyone is unique in their metabolic response to foods. Even identical twins differ in their metabolic response to exactly the same meal.[4] An individual's genetics explain only a fraction of the inter-individual variability in metabolic response. Results from the PREDICT trial highlight that, beyond meal macronutrients, a wide range of individual factors – including the gut microbiome, meal order, meal timing and meal combinations – have a strong influence on post-prandial glycaemic and triglyceride responses.[3] How and when we eat can have a significant impact on the energy we consume and our bodies' metabolic responses to what we eat.

Over time, extended periods of positive energy balance or hyperglycaemia and elevated plasma HbA1C levels can influence body weight and our predisposition to non-communicable, diet-related chronic diseases such as type 2 diabetes.[5] Avoiding excess calories and hyperglycaemia can be supported by diet and lifestyle.[6] As we will show in this chapter, inter-individual variations in oral processing behaviour also significantly affect post-prandial metabolic responses.[7] Beyond what is in a food, the current chapter focuses on how we eat, and how this influences the way we respond to an ingested food.

6.1.1 What Happens to Food During Mastication? A Primer on Food Oral Processing

Both the physical properties of a food and an individual's oral physiology can influence how a food is orally processed and breaks down in mouth during consumption.[8,9] The teeth, tongue, soft palate and saliva all contribute to the rate and extent of food breakdown (see Chapters 1–4). Oral processing is often discussed as a series of sub-processes or phases, from the first bite to chew down, swallow and final mouth clearance (Figure 6.1).[10–12] A food's initial physical, mechanical and lubrication properties provide feedback to the eater during the first bite stage on the optimum bite size and the mastication required to make the transition from a food to an agglomerated bolus that is safe to swallow.[13] For a food to become safe to swallow, it must achieve a state in which it is sufficiently reduced in size and sufficiently softened and lubricated to prompt a safe-to-swallow response. Oral processing is therefore needed to fragment and lubricate food pieces to facilitate swallowing and the later phases of digestion.[14,15]

Solid foods must be chewed to reduce their bolus particle size and to soften and moisten bolus particles so that a bolus is formed that is smooth and cohesive and therefore suitable for swallowing (Figure 6.1).[16,17] During mastication, the physical and physicochemical characteristics of

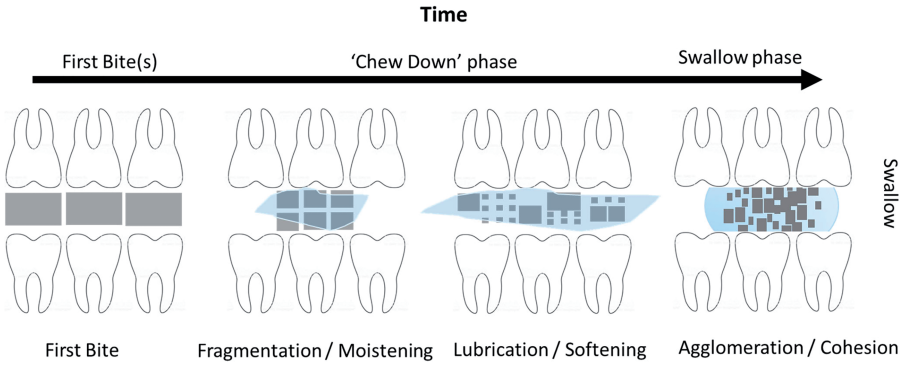

Figure 6.1 The distinct phases of food oral breakdown during mastication, from first bite to swallow.

solid foods change considerably (*e.g.* their mechanical, rheological and tribological properties, structure and texture, particle size, and moisture content).[18]

Many approaches have been used to describe the changes to a food bolus from first bite to swallowing.[16,19,20] The most widely accepted model is the breakdown pathway model, which describes a three-dimensional conceptual framework that summarizes the dynamics of food breakdown based on 'time in mouth' and changes in the 'degree of structure' and 'degree of lubrication'.[12] Foods with distinct mechanical and structural properties follow different breakdown paths. A food bolus must cross a threshold for size, structure and lubrication before prompting the moment of safe swallowing. Swallowing initiation is voluntary and occurs when food particles are sufficiently bound together to form a cohesive bolus.[16] The swallow threshold differs widely across foods, but has been shown to be consistent within individuals for a given food.[21] For the same food, the safe swallow threshold can differ considerably between individuals, so that different individuals are comfortable swallowing food boluses that differ widely in their physicochemical properties.[17,22]

The time taken to prepare a bolus for swallow is an important parameter that dictates the bolus properties at the moment of swallowing and, subsequently, the available time and surface area for food substrates to interact with oral and digestive enzymes. Mastication time depends on each individual's preferred swallow threshold.[23] Food properties (*e.g.* volume, size/shape, mechanical and rheological properties, and moisture content) have a direct effect on oral breakdown characteristics and influence the time required to reach sufficient lubrication for swallowing.[24–26] Habitual mastication processes differ between individuals in characteristics such as bite size, frequency, duration and thoroughness,[27] which can influence sensory perception, and have a cascading effect on bolus properties and metabolism. For example, within healthy populations, individuals differ by a factor of two

in mastication time.[22] As described later, this has significant implications for how the oral phase of digestion moderates an individual's metabolic response to the macronutrients consumed.

In terms of the metabolic impact of oral processing, the comminution phase plays an important part in increasing the available surface area of the food particles for the action of digestive enzymes in the oral, gastric and intestinal phases of digestion. Although initially developed to describe texture perception, the breakdown pathway model can be adapted to include eating rate and describe the textural properties that influence the rate of food intake.[28] Eating at a faster rate is associated with larger bite sizes, a shorter mastication time and fewer chews per bite.[29,30] By contrast, slower eating rates are related to longer mastication times, smaller bite sizes and a higher number of chews per bite. Eating rate is known to influence within-meal energy intake,[31] post-meal satiety[32] and therefore represents a crucial parameter describing oral processing behaviour as it relates to energy balance and metabolic health. The dynamic structural changes a food undergoes during mastication, and the incorporation of saliva and enzymes that influence post-prandial metabolites, can be linked back to differences in eating rate, which can also influence the properties of the bolus at swallow (Figure 6.2). In this regard, the modified breakdown pathway model creates an opportunity to visualize how differences in oral processing behaviour between consumers can contribute to inter-individual variability in sensory perception, energy intake and their metabolic response to different foods.

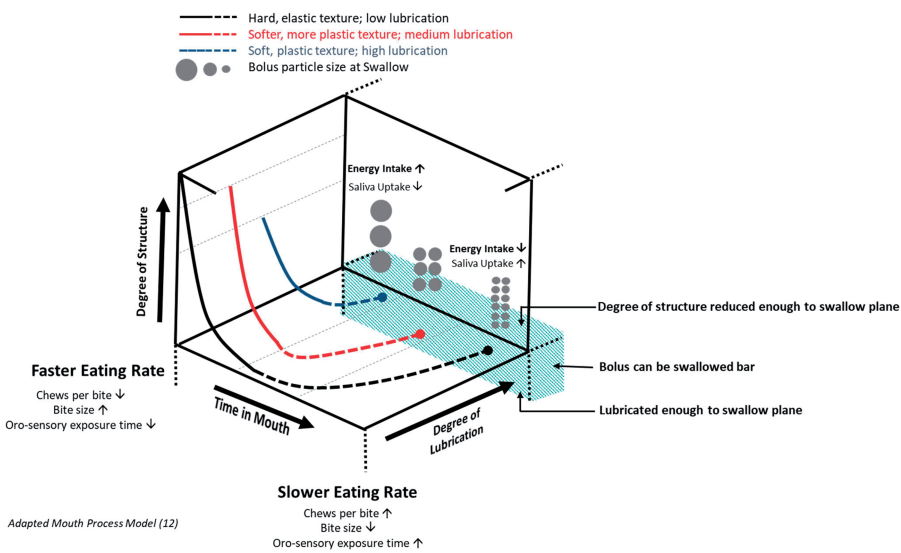

Figure 6.2 Modified breakdown pathway model as it relates to eating rates.

Food oral processing offers an opportunity to moderate metabolic responses to ingested macronutrients by manipulating mastication time, the rate and extent of food breakdown, and the changes in bolus surface area and saliva uptake (and through this the degree of enzyme–substrate interaction) that occur during consumption. Oral processing behaviour varies considerably across different food structures (Figure 6.2) because dynamic changes in hardness and lubrication control mastication time and the extent of bolus breakdown. For example, harder products that have a low moisture content require a greater number of chewing cycles and a longer time in the mouth for sufficient breakdown and saliva incorporation to form a bolus that is safe to swallow.[33] Oral processing behaviour also differs between individuals masticating the same food. For example, the same hard food with a low moisture content requires fewer chewing cycles for individuals with high saliva flow rates to reach the same swallow threshold.[21] In this way, the duration and extent of food breakdown during mastication is informed by a combination of food texture properties and differences in the oral processing behaviour of individual consumers.

6.1.2 Contribution of Oral Processing to Metabolic Variability: Metabo-types

There is substantial inter-individual variation in the metabolic responses to an equivalent nutrient challenge or dietary intervention.[34] Distinct groups of individuals who have the same metabolic response to a nutrient challenge have been described as metabo-types. As with oral processing, inter-individual differences in metabolic responses are influenced by physiological, genetic and/or environmental factors.[35] A metabo-type is usually determined by cluster analysis based on combinations of specific metabolites. Whereas genetics can play a significant part in our metabolic response to food (*i.e.* glucose release), a range of other factors can also affect this response.[36] Longitudinal studies show that specific metabo-types are associated with higher cardio-metabolic risk factors and diet-related disease outcomes.[37] However, less is known about how differences in a person's oral processing behaviour contributes to their distinct metabo-type, or whether eating behaviour phenotypes align with metabo-types.[7,38]

The oral phase of digestion makes a significant contribution to our early metabolic response to ingested nutrients through variability in habitual oral processing behaviour and saliva composition, which have been shown to contribute to inter-individual differences in glycaemic responses[39] and energy intake.[31] Mastication enables complex carbohydrates, proteins and lipids to be broken down into simpler forms to support nutrient release and absorption. A food's physical form and the way it is chewed has a significant effect on the rate and extent of starch digestion and the post-prandial glucose (PPG) response to starchy foods.[8] Bolus properties at swallow can alter digestive kinetics and the post-prandial metabolic or endocrine responses to an

ingested macronutrient.[40] For example, a longer mastication time increases the number of bolus particles and particle surface area, and ruptures cell walls and food structures to release macronutrients.

Oral processing behaviours (*e.g.* the average bite size, chews per bite and eating rate) are strongly influenced by the characteristics of the consumed food. We adapt these oral behaviours to the rheological, mechanical and lubrication properties of the foods we encounter during everyday eating.[28,29,41–43] People vary considerably in their eating style[44] and a wide variability across individuals in the number of masticatory cycles used to prepare a bolus for safe swallow have been reported. For example, the number of chewing cycles required before swallowing ranged from 17 to 110 for peanuts, nine to 65 for carrots and 14 to 44 for Brazil nuts.[21,45] These differences in eating styles are consistent at an individual level[46] and are likely to make a sustained contribution to metabolic variability within a population. In addition to metabolic responses, eating rate also influences energy intake within a meal to satiation, post-meal satiety and circulating levels of several post-prandial neuroendocrine signals of satiety. Despite this, the important role of oral processing in metabolism is often overlooked when exploring metabo-types and approaches to personalized nutrition.

6.1.3 Introduction to the Metabolic Impact of Oral Processing

The impact of inter-individual differences in masticatory behaviour on metabolism and energy intake remains poorly understood. The following sections summarize the knowledge currently available on the impact of oral processing on (1) glycaemic and insulin responses, (2) energy intake, satiety and body weight, and (3) gastric emptying and the thermic effect of food. This chapter does not focus on specific foods or macronutrients, or on differences in oral processing as a function of age, sex or culture, although previous research has clearly demonstrated that these factors can influence oral processing behaviour.[27] Here, we focus on the role of inter-individual differences in oral processing behaviour in moderating metabolic responses and energy intake, and on the wider associations with health.

This chapter explores how oral processing behaviour influences PPG and insulin responses. We summarize the contribution made by oral processing to energy intake, satiety and body weight. We outline the impact of oral processing on gastric emptying and diet-induced thermogenesis (DIT). We provide an overview of potential applications of these findings to the design of foods and eating interventions that can be used to promote healthier diets and food intake behaviour. A better understanding of the metabolic impact of oral processing behaviour for specific consumer groups could assist in steering sensory perception, food choice and eating behaviour to promote healthier metabolic responses.

6.2 Impact of Oral Processing on Glycaemic Responses

6.2.1 Oral Processing and Glycaemia

Prolonged exposure to high PPG concentrations is associated with an increased risk of obesity, cardiovascular disease, metabolic syndrome and type 2 diabetes.[47–51] An individual's efficiency in managing their glucose flux is based on a range of different factors, including their oral physiology, gut microbiome, genetics and habitual patterns of oral processing.[7] The efficacy of dietary interventions aimed at controlling high PPG spikes varies considerably between individuals, with large inter-individual variability in PPG responses observed for identical meals.[52,53]

Although it is widely accepted that diet plays an important part in the glucose response, many other factors beyond food composition can influence blood glucose and insulin secretion in the post-prandial period.[54] Variations in glucose and insulin responses are also influenced by the individual differences that occur during the oral phase of digestion.[55] When individuals consume the same food, they adopt different mastication strategies. Oral processing behaviour, such as the average bite size, chews per bite and saliva uptake, can also influence the oral phase of digestion and could potentially moderate the extent to which a food bolus is deformed, fragmented and lubricated with saliva during mastication.[56] These individual differences in mastication behaviour also affect flavour release and sensory perception and are the result of individual adjustments of food oral processing in response to the structural properties of the food consumed.[57–59] Correct mastication, characterized by thorough chewing for a sufficient time, enhances digestion, improves metabolism and nutrient absorption, and helps to control energy intake and body weight.

6.2.2 Mastication to Moderate PPG in Plasma and the Insulin Response

Many studies have investigated the role of mastication in carbohydrate metabolism, blood glucose levels, and the effect of serum insulin on PPG. Variability in PPG excursions has been attributed to the digestibility and absorption properties of carbohydrate sources and the degree of breakdown and mixing that occur during mastication. Studies consistently find that a longer oral processing time and more thorough mastication result in increased PPG and an augmented plasma insulin response. The impact of oral processing on PPG and insulin can be viewed as an integration of three dynamic elements, including: (1) the time required for oral processing; (2) the bolus particle size and surface area at swallow; and (3) individual differences in saliva production, composition and penetration into the bolus.

One of the first studies to explore the impact of mastication on PPG compared the impact of longer and shorter mastication times across a normal glucose tolerance group and a group predisposed to type 2 diabetes.[60] Thorough mastication (chewing time 30 s) of a meal of hamburger and rice elicited a significantly higher insulinogenic response than usual mastication (chewing time 10 s) for the normal glucose tolerance group, leading to a significantly lower plasma glucose concentration and an increase in the insulin response. However, for the participants predisposed to type 2 diabetes, thorough mastication did not potentiate early-phase insulin secretion and elicited a higher PPG glucose concentration in plasma.[60] The lower glucose and enhanced early-phase insulin secretion of the normal glucose tolerance group was attributed to the extended mastication, which may be a behavioural strategy that promotes the management of PPG by insulin secretion.

The impact of extended mastication on PPG has been confirmed in rodent studies. Repeated oral glucose tolerance tests with rodents fed either a hard or soft chow diet showed that rodents fed a hard chow diet extended their mastication time and had enhanced glucose metabolism with a lower PPG for the same carbohydrate load than rodents fed a soft chow diet. These findings suggest a possible metabolic benefit of extended mastication that could be applied in dietary strategies to reduce the risk of lifestyle-related diseases in humans.[61]

Subsequent studies have investigated the key digestive parameters that inform PPG and the insulin response. A study by Tan *et al.* compared inter-individual differences in oral processing and glucose response across three Asian ethnic groups (Chinese, Malay and Asian Indian).[62] Their results confirmed that longer mastication and chewing times per mouthful were associated with increased PPG concentrations. There was no difference in PPG between the different ethnic groups and the study concluded that eating slowly and for longer, but with fewer chews per mouthful, led to fewer and larger bolus particles and could support better management of PPG. By contrast, eating faster had a consistent effect in reducing PPG, in line with previous findings.[39] Eating quickly is associated with a greater food intake and a reduced PPG response by attenuating the oral phase of digestion.

The number of chews per bite has been shown to be important for glycaemic responses because it can have a direct effect on bolus particle size and surface area.[63] Chewing for longer increases the surface area of bolus particles and reduces their particle size; chewing has been shown to differ widely across different foods.[64] Chewing for 15 *versus* 30 chews per bite significantly reduced the glycaemic response, peak glucose and the overall glycaemic index of a rice meal.[65] An inverse correlation between bolus particle size and glycaemic response was also observed for rice (chewing time between participants ranged from 18 to 27 s), indicating that inter-individual differences in mastication behaviour may cause inter-individual differences in rice starch digestion. However, in the same study, this inverse correlation between bolus particle size and glycaemic response was not observed for spaghetti (chewing time between participants ranged from 17 to 31 s).[66]

In a cross-over trial, the impact of extended mastication on PPG was compared between a group with normal glucose tolerance and a group predisposed to type 2 diabetes.[67] Participants were asked to chew in their normal way for a fixed carbohydrate rice meal that corresponded to an average of 29 chews per bolus, and thereafter to consume the same meal, but chewing 40 times per bolus before swallowing. The results showed that thorough mastication significantly reduced blood PPG levels in the normal glucose tolerance group, but had little effect on the group predisposed to type 2 diabetes. These findings confirm earlier reports[60] of a differential response to mastication among people predisposed to type 2 diabetes.

One mechanism by which mastication can support lower PPG levels is through augmented insulin secretion. When participants were asked to chew 10 or 40 times, the longer mastication significantly increased insulin secretion at 30 minutes, suggesting that mastication itself may improve early-phase insulin secretion.[68] Notably in this study, the effect was only observed for longer mastication in the morning, not in the evening, suggesting a circadian enhancement of this effect. This finding has been replicated across several studies using a similar experimental paradigm in which the plasma concentrations of glucose and insulin were higher following 40 chews/bite than 15 chews/bite.[69] Increased early insulin secretion is associated with better glucose absorption and a reduction in overall PPG in some, although not all, people.[70]

The relationship between extended mastication and a stronger insulin response could be mediated, in part, by sensory signals because a longer chewing time extends the period for taste perception and subsequent insulin release. A recent randomized controlled trial controlled the relative impact of eating rate and oro-sensory exposure time and found >80% higher insulin release in the longer oro-sensory exposure group.[71] Enhancing mastication per bite may improve the early anticipation of digestive and metabolic responses, activating earlier insulin secretion to better regulate glucose excursions, although the findings of acute trials are equivocal and higher insulin levels are not always associated with lower PPG. Encouraging increased chews per bite has been suggested to benefit pre-diabetic patients or those with a family history of type 2 diabetes by offering a protective effect over hyperglycaemia to moderate PPG by augmenting early insulin secretion.[72]

Extending mastication increases oro-sensory exposure time, but also has a significant impact on the bolus properties at the point of swallow, including the particle size and surface area, and saliva uptake. Intuitively, this makes sense, because increased mastication encourages the formation of a larger number of smaller bolus particles (Figure 6.2), such that the total bolus surface area increases significantly. Chewing for longer both stimulates greater saliva secretion and affords a longer period for bolus salivary uptake. Differences in the particle size and total surface area of the bolus at swallow can influence digestive kinetics and post-prandial metabolic and endocrine responses to the ingested nutrients.[73]

Several studies have demonstrated how the structural transformations that occur during extended mastication over a longer oro-sensory time are associated with increased PPG and insulin release. For example, taking more chews per bite results in a higher PPG response by producing significant changes in the size and surface area of bolus particles.[65,74] A comparison of particle size and glucose responses showed a positive relationship between a higher percentage of particles with a diameter <500 μm and higher *in vivo* glycaemic responses after 30 minutes. Evidence from rodent studies showed that long-term feeding on a powdered chow causes hyperglycaemia and was linked with an increased risk of illness.[75] This suggests that the degree of habitual mastication and bolus particles at swallow may influence both the magnitude and pattern of an individual's glycaemic response.[74] Increasing chews per bite has been shown to increase the number of particles formed and to reduce the average particle size.[76,77]

Taken together, the impact of oral processing behaviour on PPG is the culmination of three factors, including a larger surface area of the substrate alongside a greater quantity and uptake of the active enzyme, and an extended period for their interaction. The extent to which oral breakdown can influence PPG is moderated by the food structure. For example, salivary amylase penetration into the bolus has been shown to vary significantly when comparing three breads differing in structure and density. Enzymatic activity was higher in the bolus of industrial bread than in an artisan bread and wholemeal bread, despite the chewing durations being similar between all three breads.[78] This creates the potential to attenuate PPG by creating layers of food structure within products that extend mastication, while also reducing the enzymatic action of amylase on starch.

Mastication can reduce the viscosity of starchy foods through the rapid action of salivary amylase and the rate and extent of starch hydrolysis, although this is dependent on the initial structure of the food.[18] The mixing and interaction of starch and amylase continues as the food bolus is transported through the oesophagus to the stomach *via* peristalsis. As the food arrives in the stomach, it generally has a pH between 5 and 6 before sufficient acid is secreted to decrease the pH to about 3, strongly reducing the enzymatic activity of amylase and ending the oral phase of digestion.[79,80] This process of bolus particle breakdown, amylase mixing and initial starch hydrolysis can take about 30 minutes. Swallowing a starch-based meal without premixing it effectively with saliva leads to a significantly lower glycaemic response.[39] Differences in the extent, efficiency and duration of mastication can directly influence the bolus particle size, total surface area and amylase uptake, and have been shown to influence digestive kinetics within the first 30 minutes post-ingestion across both *in vivo* and *in vitro* studies.[65,81,82]

The majority of studies have primarily focused on the impact of oral processing on acute changes to PPG and insulin (*i.e.* within three hours of a meal), but are these acute differences in glucose response sustained from meal to meal? Are they associated with the longer term health risks associated

with hyperglycaemia? Numerous studies from Japan have shown a positive relationship between a higher self-reported eating rate (SRER) and poorer glucose tolerance and insulin resistance. In a large cross-sectional study, higher masticatory performance and slower eating rate were both associated with a lower incidence of diabetes,[83] whereas a faster SRER was a predictor of impaired glucose tolerance among Japanese men and women.[83,84]

Other studies have shown a significant and progressive increase in homeostatic model assessment of insulin resistance among normal weight participants, suggesting that a faster eating rate is associated with insulin resistance and the risk of type 2 diabetes, independently of the increased risk associated with obesity.[85] Among Japanese men, independent of body mass index (BMI) or the homeostatic model assessment of insulin response, a faster rate of eating was positively associated with higher circulating levels of interleukin (IL-1β and IL-6), a risk indicator for type 2 diabetes.[86] Despite this, other researchers have found no relationship between eating faster and higher plasma levels of HbA1C.[87] A number of large population-based cohorts have also shown significant positive associations between higher eating rates and higher rates of metabolic syndrome in Japan, China and Singapore, suggesting that faster self-reported eating may be a useful behavioural marker for diet-related chronic disease risk.[88–90]

In summary, slower, more thorough mastication is associated with elevated PPG and early insulin secretion. This has been attributed to a larger total bolus surface area, increased saliva uptake, enhanced salivary amylase activity and an extended food substrate–enzyme reaction time. Enhancing mastication improves PPG and insulin responsiveness, but seems to be more effective among people with normal glucose tolerance than people with a predisposition to type 2 diabetes. At the population level, faster eating is often associated with poorer glucose tolerance and insulin responsiveness, and an increased prevalence of metabolic syndrome.

6.2.3 An 'Unavoidable Ingredient': the Role of Saliva in Oral Processing and the PPG Response

Mosca and Chen have described saliva as an "unavoidable ingredient" because no food can ever be consumed without it.[91] Although often overlooked, saliva, discussed extensively in Chapter 1, has a profound impact on the eating experience by moderating the perception of tastes, the retro-nasal release of flavours and dynamic changes in bolus cohesion and texture perception.[92] In this regard, what we perceive during consumption is a food–saliva mixture rather than the food served on our plate.[91] Ninety per cent of saliva is produced by three pairs of salivary glands: the parotid, submandibular and sublingual glands. Saliva is predominantly composed of water (99%), mucins, electrolytes and digestive enzymes, with salivary amylase being the most prevalent. Saliva flow rates vary considerably within a population, but, on average, unstimulated saliva flow rates are about 0.3 mL min^{-1}, such that, on average, 300 mL of saliva are produced in a 24-hour period.[93]

Saliva facilitates the softening of bolus particles, hydrating and lubricating food fragments during mastication, which contributes to the formation of a cohesive bolus.[94] Through this, the rate and extent of saliva uptake can influence the oral sensory exposure time and duration of mastication (Figure 6.1). In addition to supporting food breakdown, salivary enzymes (including amylase, lipases and proteases) interact with their respective substrates to form new compounds that stimulate the endocrine responses associated with the oral phase of digestion. Because the activities of salivary lipases and proteases are very low, they make a negligible contribution to fat and protein digestion. We therefore focus on the role of salivary amylase on the PPG response.

Salivary amylase hydrolyses the alpha bonds of starch and glycogen to release glucose and thus begin the process of starch digestion.[95] Bolus saliva uptake is a product of three independent factors, including: (1) the fracture and absorption properties and initial moisture content of the food being consumed; (2) the saliva flow rate of the eater; and (3) the time the food is held in the mouth during consumption.[96] Saliva flow rates vary considerably between people[97] and those with greater saliva production have been reported to require fewer chew cycles for hard/dry foods than those with lower flow rates, although these effects are modest.[21] More thorough mastication encourages a greater production of saliva[15,56] and has been associated with a greater uptake of saliva by the bolus and higher PPG levels.[62,81]

In addition to differences in saliva flow rates, there are well-studied population-wide variations in the concentration of salivary amylase. Salivary α-amylase is encoded by the AMY1 gene. The concentration of salivary α-amylase is proportional to the number of copies of this gene (also known as the copy number variant or CNV), which has been reported to range from 2 to 17 diploid copies, leading to sizeable differences in amylase activity.[98,99]

As a result of these large variations in salivary amylase activity between individuals, research has focused on whether these can help to explain individual variations in glucose responses and the heterogeneity among carbohydrate metabo-types. One hypothesis is that variations in the AMY1-CNVs reflect genetic adaptations to historical diets during evolution, where α-amylase activity was upregulated in cultures that had a historical reliance on starch-based foods as their main energy source.[100] This would have conferred an adaptive advantage and improved regulation of the dietary glucose flux, reducing the health risks associated with hyperglycaemia.[55] Similarly, humans with higher AMY1-CNVs should also be capable of deriving more energy from the same carbohydrate load. Today, AMY1-CNVs are thought to be higher among populations who were historically farmers rather than hunter–gatherers, where having a high salivary amylase activity would support a lower PPG, early post-prandial insulin release and, through this, lower the risk of insulin resistance.[101] In line with this, there is an association between lower AMY1-CNVs and a higher rate of insulin resistance among asymptomatic Koreans.[102]

A number of studies have explored the relationships between AMY1-CNVs, amylase activity and subsequent PPG and insulin responses. Mandel and Breslin screened participants based on amylase activity and asked them to complete an oral glucose tolerance test. Participants with lower salivary amylase activity had higher post-prandial glycaemic responses and lower insulin, whereas those with higher amylase activity had a lower glycaemic response and higher insulin levels. The conclusion is that early glucose release and absorption among the high amylase group stimulated the early release of insulin and attenuated the subsequent PPG levels.[103]

Subsequent studies have compared glucose tolerance among participants with higher and lower salivary amylase activity and have shown a better glycaemic tolerance for starchy foods with high salivary amylase.[104] In one of the most comprehensive studies, participants with higher AMY1-CNVs/amylase activity digested starchy foods more rapidly, producing a higher overall PPG.[105] Atkinson *et al.* examined the impact of salivary amylase activity levels on the post-prandial glycaemic response after the consumption of six different carbohydrate-based foods and showed that participants with higher amylase activity (higher AMY1-CNVs) had a higher glycaemic response after the consumption of starchy foods, but not sugary foods, suggesting that the higher amylase activity increased rapid enzymatic starch digestion to produce a more rapid release of glucose.[105]

By contrast, other researchers have been unable to replicate these findings using similar approaches and showed no evidence of a role for salivary amylase activity on the glycaemic response. In one study, participants who varied significantly in their AMY1-CNVs received a fixed quantity of starch. Although a higher salivary amylase activity was associated with higher early plasma insulin concentrations and lower glycaemic responses, there was no significant difference from a group with lower salivary amylase activity.[106] Other researchers have not shown any relationship between AMY1-CNVs and PPG, with effects on PPG only seen when pre-selecting participants at the extremes of high or low amylase activity.[62] One possibility is that small differences in salivary α-amylase during mastication make only a modest contribution to overall starch digestion compared with the later major contribution of pancreatic amylase, such that the release of glucose is more extensive during the gastric and intestinal phases of digestion.[107] An individual's AMY1-CNV status is likely to explain some of the variation in the inter-individual response to carbohydrates, but the inability to replicate this in the general population and equivocal findings across several controlled studies suggest that these differences are highly variable and food-specific, and probably make a relatively small contribution to the overall variability in PPG.

At a population level, research has compared associations between AMY1-CNVs and metabolic risk to investigate whether a generally lower ability to metabolize carbohydrates is associated with a higher risk of developing obesity and metabolic syndrome. The results vary widely across studies, with lower AMY1-CNVs associated with a higher BMI in some populations,[108–114] but not others.[99,115] A large retrospective analysis concluded that variability in

AMY1-CNVs should not be considered as an important metabolic biomarker of an individual's response to a clinical dietary intervention.[116] The ambiguous relationship between the AMY1-CNV and metabolic outcomes requires further investigation, with suggestions that the long-term metabolic effect of AMY1-CNVs are less likely to be the result of oral variations in carbohydrate digestion and instead relate to the higher amount of undigested fermentable carbohydrate in the ileum among those people with lower AMY1-CNVs.[117,118] A better understanding of the relative contribution of individual variations in amylase in predicting metabolic health may guide novel approaches to counteract diet-related chronic disease.

Despite extensive research into AMY-1 CNVs, the available evidence suggests that these variations in enzymatic activity are unlikely to significantly affect daily variations in an individual's glycaemic response. At a micro-level, inter-individual differences in salivary amylase activity may only contribute to a variability in glycaemic response at extremes of amylase activity (very high or low AMY1-CNVs). In the general population, inter-individual differences in salivary amylase activity are highly variable and probably make a relatively small contribution to the overall variability in glycaemic responses. In this respect, the predominant contribution of saliva to metabolic responses is probably still at a macro-level, where the secretion of saliva influences the extent of bolus particle lubrication and rate of agglomeration, and through this the oro-sensory exposure time to swallow.

6.3 Food Oral Processing, Energy Balance and Satiety

6.3.1 Eating Rate, Energy Intake Rate and Energy Intake

Weight gain results from the sustained excess consumption of energy above what is required and expended.[119] The continued increase in obesity rates globally has been attributed to the ready availability of inexpensive,[120] highly palatable and easily consumed calories in the modern food environment.[121] The cumulative evidence suggests a meaningful association between eating rate, energy intake and body composition and the associated risk of food-based, non-communicable diseases.[122]

Softly textured foods require minimal oral processing and can be consumed at a high eating rate (g min^{-1}) (Figure 6.2), which limits the opportunity to orally meter intake during consumption. By contrast, eating slowly with extended mastication and/or a small bite size is consistently associated with a reduced energy intake. However, it remains unclear whether the reduction in energy intake is due to the action of mastication itself, the reduction in eating speed, stronger post-meal satiety responses or the properties of the food bolus, which influence gastric emptying.[123] It was first reported over 40 years ago that eating at a faster rate increases food intake.[124] A meta-analysis of 22 controlled feeding trials, in which the rate of eating and *ad libitum* energy intake were measured, confirmed that the overall energy intake

increases when foods are eaten faster. This effect was consistent across a wide range of food stimuli and eating manipulations.[31] A separate systematic review and meta-analysis concluded that eating more slowly has the dual effect of reducing food intake and increasing subjective feelings of satiety post-meal for the same calories.[32]

Evidence from several studies has shown that when mastication cycles to swallow are increased, there is an associated reduction in both the eating rate and the total energy required to reach satiation, with effect sizes varying between 9.5 and 15%.[7,125] Simply instructing participants to increase their mastication cycles from 15 to 35 per bite led to a slower eating rate and a 12% reduction in energy intake.[126] Despite the reductions in intake, there was no significant reduction across studies in subjective appetite at the end of the meal or 60 minutes post-meal. In a systematic review and meta-analysis of the impact of oral processing on energy intake and appetite, parameters such as the number of chews and eating rate appeared to have a marked influence on food intake, but little impact on post-meal appetite ratings.[127]

Meal eating rates have been manipulated using a variety of approaches, from verbal instructions to slow down or increase chewing,[69,126,128,129] to devices to cue a defined eating speed[130–135] and manipulations of food texture and shape.[125,136–142] Devices have been used to alter eating rates by tracking the rate of disappearance of food from a plate and providing verbal feedback using a Mandometer,[143] reducing the bite rate using a wrist-worn bite counter device,[130] or by providing vibro-tactile feedback through an electronic fork used to track wrist movements within a meal.[144,145] In all cases, slower eating was associated with reductions in energy intake. These devices have also been used to retrain consumers to eat at a reduced rate. Encouraging a slower eating rate has also been shown to reduce intake, although several studies have shown that this effect is not always equivalent. For example, slowing their eating rate by asking participants to chew to the pace of a metronome led to a reduction in energy intake for men, but not for women,[135] and eating slowly significantly lowered energy intake among normal weight participants, but not among participants with obesity.[146]

Extensive previous research has shown the effect of increasing food viscosity[147] and hardness on oral processing, eating rate and subsequent energy intake. In one study participants were provided with harder or softer versions of a hamburger meal or a rice meal.[136] Eating a softer meal increased food intake by an average of 13%, which was not compensated for by an increase in food intake at a subsequent meal, producing a reduction of 11% in daily energy intake. Similarly, when texture and energy density or the texture and portion size of a meal are controlled, there is a significant reduction in both eating rate and energy intake for a meal, but no associated reduction in either hedonic appeal or post-meal feelings of satiety.[138]

Even small modifications to the texture of a food can influence eating microstructure and energy intake. When the viscosity of yogurt was decreased by 1.8 times, the spoon size, number of chews per spoon and oral exposure time per spoon decreased, but this did not significantly affect the

eating rate or *ad libitum* intake. A decrease in the particle size of granola added to yogurt significantly increased the number of chews per spoon and decreased the spoon size. Eating rate and *ad libitum* intake increased by 7 and 5% without changing liking.[142] This suggests that the number of granola particles added to the yogurt and not the size of particles *per se* was the driver of changes in oral processing behaviour. These findings suggest that, in addition to the bulk mechanical properties, the number and volume of pieces in a composite food can also drive oral processing behaviour and slow intake.

Further research has demonstrated the impact of food size,[148] shape[149] and bolus lubrication[150] on eating speed and energy intake within a test meal. Compared with instructions or devices to slow the rate of intake, the manipulation of food texture provides the most compelling findings because participants naturally adjust their oral processing behaviour in response to the texture challenge to slow their eating rate. Food texture is also likely to influence bolus disintegration and passage through the stomach, which, in turn, can influence gastric emptying and post-meal satiety. Increasing food hardness or viscosity can directly impact the microstructure of eating, primarily by reducing the average bite or sip size.[139,151–153] Other researchers have shown that smaller bite volumes are chewed more.[154] One of the mechanisms by which larger food portions promote energy consumption is by promoting larger bite sizes,[155] which can speed up and increase intake. A longer chewing time also increases the number of particles, the particle surface area and salivary uptake, and may influence the rate of later bolus transit through the gastrointestinal tract.

In addition to the direct effect of a longer oral processing time on energy intake, slower eating rates and the associated eating microstructures are associated with higher expected satiation[156,157] and may influence energy intake through the selection of smaller portions.[29,41,125] Beliefs about the filling properties of foods are informed by the sensory and texture cues experienced during consumption and the associated post-ingestion reinforcement associated with the post-meal feeling of satiety; these beliefs are accumulated over time and with experience.[125,158] Oral processing behaviour is central to the formation of fullness beliefs, with significant links between the expected and experienced fullness and satiety for a food and the associated bite size, oro-sensory exposure time, chews per bite and eating rate.[156] Thicker textures that require longer oral processing and slower eating rates have been shown to have higher than expected fullness per kcal and can be used to condition higher expected fullness for the same energy content over time.[29,159] Textures that require longer oral processing times to consume are associated with a lower energy intake and stronger filling beliefs, whereas foods that can be consumed more rapidly are associated with greater energy intakes[160] and higher body weights and adiposity.[7] Faster eating rates have been associated with poorer episodic memory[161] and thus favour both a greater food intake within a meal and increased energy consumption in the post-meal period (*i.e.* snacks).[162]

The effect of a faster eating rate on energy intake is further amplified when the food being consumed has a high energy density. Consuming foods with a high energy density quickly has been shown to promote both greater passive over-consumption and weaker post-meal satiety per kcal consumed.[163] Both energy density and eating rate can significantly moderate the flow of calories through our daily diets and contribute to excess energy intakes.[43] The energy intake rate (EIR, kcal min^{-1}) of a food unifies both of these measures to quantify the rate at which calories from different foods are ingested.[29,164]

The impact of higher EIR foods on food intake and body composition was seen in a 28-day in-patient randomized controlled feeding study that sought to explore the impact of food processing on energy consumption.[165] Participants completed two weeks on diets consisting of foods that were higher or lower in their level of processing, and both ultra-processed and unprocessed diets were matched for calories served and balanced for the relative contribution of macronutrients to energy intake. Participants were free to consume meals and snacks *ad libitum* and all food intake was recorded and compared between the two diets. The more processed diet resulted in an EIR (kcal min^{-1}) that was >50% higher than the comparison diet (48 *versus* 31 kcal min^{-1}), resulting in an average increase in the energy consumed per day of >500 kcal and a significant increase in body weight (increased by 0.9 kg) and adiposity. However, the two diets were not matched for texture or oral processing properties and both the eating rate (37 *versus* 30 g min^{-1}) and the EIR (48 *versus* 31 kcal min^{-1}) were significantly higher when the participants consumed the ultra-processed diet.[165] A lack of clear neuroendocrine or metabolic differences between the two diets suggests that the increases in energy intake were more likely to be driven by differences in eating behaviour rather than post-ingestion differences in metabolism between the two diets. There was also notable variability in the inter-individual participant responses to the two diets in terms of energy intake and subsequent in body weight, with seven of the 20 participants having no change in body weight and energy intake differences <500 kcal day^{-1} across the two diets. Differences in individual EIRs varied from 0 to 1500 kcal day^{-1}, leading to body weight differences of 0–5 kg (average 0. 9 kg), suggesting that not all the participants were equally susceptible to the effect of higher EIRs on the ultra-processed diet. The implication is that food texture, energy density and oral processing behaviour can combine to increase the EIR, but this is likely to vary considerably within a population and, in some cases, energy intake or body weight are not affected.

A recent comparison of EIR across unprocessed, processed and ultra-processed foods demonstrated that EIRs vary considerably within each class of processed foods, with both low and high EIR within each category.[43] For those susceptible to increased energy intake from higher EIR foods, these dietary patterns are likely to contribute to the sustained calorie excesses required for weight gain and probably have a role in the aetiology of diet-related chronic diseases.[264] The link between EIRs and increased energy intake therefore presents both a challenge and an opportunity

because, in addition to 'pre-chewing' our food and adding energy, many food processes can add texture to food and could be used to slow down the rate and extent of energy intake through direct action on oral processing behaviour.[43] The texture and oral processing properties of foods are rarely considered when making dietary recommendations to reduce the risk of food-based chronic conditions, such as obesity and/or type 2 diabetes, but they form an important connection between a food's form and nutrient composition and the eating behaviours associated with an increased energy intake.[166]

6.3.2 Chewing and Energy Intake and Satiety

The evidence highlighted here shows that a larger bite size and fewer chews per bite are both consistently associated with a greater energy intake. This suggests that increasing the number of chewing cycles during mastication could reduce energy intake and promote increased feelings of fullness per calorie consumed. It is therefore plausible to consider that the act of chewing, or chewing a non-nutritive material such as no-calorie chewing gum, could support a reduction in energy intake and a greater sustained feeling of post-meal fullness. Research relating chewing gum to energy intake and satiety is limited and complicated by methodological variations between studies.

Hetherington *et al.* explored the impact of chewing gum for up to 45 minutes after lunch and showed about a 10% reduction in later snack intake.[167] Chewing gum was shown to suppress the return of hunger following lunch and reduced cravings for sweet and salty snacks, which suggests that chewing could help to control appetite and reduce later intake.[168] However, other researchers have been unable to show an effect of chewing on appetite ratings, meal patterning and food intake following gum chewing.[169] The secretion of the neuroendocrine hormone glucagon-like peptide 1 (GLP-1) is controlled by the nervous system (*via* motor neuron stimulation), whereas other neurotransmitters are secreted in response to the presence of macronutrients in the intestine (*e.g.* glucose-dependent insulinotropic peptide, GIP). Chewing sugarless gum has been shown to increase satiety with no effect on blood glucose insulin or GIP concentrations, suggesting that the action of chewing itself may be sufficient to stimulate the secretion of GLP-1 by the nervous system and augment insulin secretion in humans.[170] Studies in animal models suggest that chewing may augment satiety through the neural activation of central satiety centres.[171]

The consolidated findings from a meta-analysis of mastication and satiety concluded that chewing significantly reduces self-reported hunger and food intake and could augment the release of satiety hormones post-consumption.[32,127] However, the impact of chewing gum on post-meal satiety is likely to be fairly weak and, given the extended chewing protocols required in several trials (*e.g.* 45 minutes of chewing gum[167]), implementing this as an approach to control energy intake may not be practical or appealing to many people. Although chewing gum may offer an economically

viable form of support to patients with obesity to reduce their feelings of appetite, it is unlikely to have a significant impact on long-term appetite control or energy intake.

In summary, there appears to be a small, and in some cases significant, effect of chewing gum on increased subjective feelings of fullness, although the impact on energy intake is inconsistent and probably negligible. Beyond energy intake, the act of chewing gum is associated with many positive physiological changes, including increased blood flow in the cerebral and orofacial region, which is associated with increased alertness and improved memory.[172] Overall, selecting a diet that requires greater masticatory effort is likely to slow down eating rate and decrease energy intake, offering an increased opportunity to orally meter energy consumption and reduce the risks associated with passive consumption and a gain of body weight over time.

6.3.3 Eating Rate and Body Weight

Many population-based epidemiological studies of diet and body composition collect a measure of the SRER, with the advantage that these studies often profile large populations and have extensive diet and body composition information. SRERs have been shown to reflect experimentally observed eating rates.[173] In a cohort of >1000 Japanese women, those self-reporting a faster eating rate on a five-point Likert scale tended to have a higher BMI, with a mean BMI 2.2 points higher for those reporting 'very fast' eating rates.[174] Further studies show that eating quickly and eating until full were associated with being overweight,[175] which has been confirmed by other cohort studies.[176] A meta-analysis of studies that compared SRER with body weight showed there is a consistent positive relationship between SRER and BMI, although there is a wide variation in the strength of the association across studies.[177]

A recent population-based cross-sectional survey in Singapore found that participants reporting a higher SRER consumed an average 105 kcal day^{-1} more, had an average 5 kg greater body weight and a 1.3 kg m^{-2} higher BMI and larger waist circumference.[90] In this study, a higher SRER was also a significant predictor of higher blood pressure, circulating triglycerides and cholesterol, suggesting that SRER is a self-report measure that provides a robust behavioural marker for energy intake as well as body weight, adiposity and several cardio-metabolic health indicators.[90] In another large prospective Japanese study, eating speed was associated with the incidence of metabolic syndrome and the findings suggested that eating slowly was an important lifestyle factor in preventing disease.[178] Faster eating rates are associated with increased cardio-metabolic risk[179] and increased levels of interleukin-1, which is regarded as a metabolic marker of pre-diabetes.[86] The practice of thorough mastication (up to 30 chews per bite) has been proposed as an effective behavioural approach in clinical settings for curbing obesity,[180] with the Obesity Society in the USA advising patients to 'reduce eating speed to control energy intake'.[181]

The oral processing behaviour associated with faster eating styles has previously been described as obesogenic because it supports greater acute energy intakes and may promote a sustained positive energy balance and prospective weight gain.[30] A faster SRER is associated with a higher BMI[176,179,182] and has been shown to predict prospective increases in body weight among both children[183–188] and adults.[189] Among children, the two-year prospective changes in body weight were higher for children who were observed to eat at faster rates (Berkowitz 2010). Across several studies in the Growing up in Singapore to Healthier Outcomes birth cohort, among a large cohort of 4.5-year-old children, the children who were observed to eat faster consumed significantly more energy. These faster eating rates were stable over time and were associated with higher BMI scores, adiposity estimates and a significantly higher omental adipose volume.[190] In a retrospective trial of Japanese men, a higher SRER was predictive of greater longitudinal increases in body weight over an eight-year period, where faster eaters gained on average 1.9 kg and those reporting slower eating only gained an average of 0.8 kg.[189]

The link between body weight status and a distinct eating style has been explored in observational studies in which eating style was tracked across people from different weight classes. In one such study, 271 participants were tracked during meal consumption and significant differences in bite size were found between participants with a normal, overweight or obese BMI. Between the groups, there was a 0.20 g progressive increase in bite size for each increase in BMI category.[191] In a similar study with Thai participants, a comparison of chewing styles between normal and overweight groups showed that participants classified as overweight chewed less and consumed more calories.[192] Isabel *et al.* showed that people with obesity tend to masticate less and swallow larger bolus particle sizes.[193]

It has been suggested that people with obesity show a distinct and consistent eating style that supports an increased acute energy intake and promotes weight gain over time.[194] However, the results to date have been equivocal and many studies have been unable to show a consistent oral processing pattern by weight status.[195] There is insufficient and inconsistent evidence of a distinct obese eating style within a weight class and some researchers have observed this same faster eating style across normal, overweight and obese ranges.[30,190] The question still remains as to what drives eating rate and why some people consistently eat faster than others. It may be that eating at a faster rate is a behavioural adaptation to differences in body composition and higher energy requirements.

Results from one cross-sectional study in a population-based cohort found that a faster eating rate was positively associated with both fat-free mass and basal metabolic rate, a relationship that remained even when controlling for differences in BMI.[196] Differences in basal metabolic rate explained about 15% of the variation in eating rates, suggesting that faster eating rates may be driven by higher energy requirements and could reflect a behavioural adaptation to higher energy needs. This interesting finding requires further

confirmation because it has wider implications for the potential behavioural adaptations that may occur after significant changes in body weight.

Collectively, these studies highlight that, although faster eating rates tend to be associated with increased prospective weight gain, many studies have been unable to show a consistent oral processing style among those with a higher BMI or obese weight status. Eating faster probably promotes weight gain over time and is not exclusively associated with people in the overweight or obese weight category.

6.3.4 Oral Processing and Satiety

Mounting evidence suggests that eating at a faster rate can reduce the subjective experience of fullness post-meal (satiety) per calorie consumed and is associated with circulating levels of neuroendocrine signals related to the satiety response.[32,127,197] Poorer satiety per calorie consumed results in shorter periods of fullness post-meal and has been linked with a greater calorie intake in the inter-meal period and at the next meal.[198] Conversely, slower eating rates promote greater fullness per calorie consumed and can reduce the tendency to snack between meals.

Increasing the number of mastication cycles for a fixed portion of food has been linked to stronger feelings of fullness post-meal and has been associated with influencing the circulating levels of a wide range of neuroendocrine signals linked with satiety, as summarized in Figure 6.3. For example, Cassady *et al.*

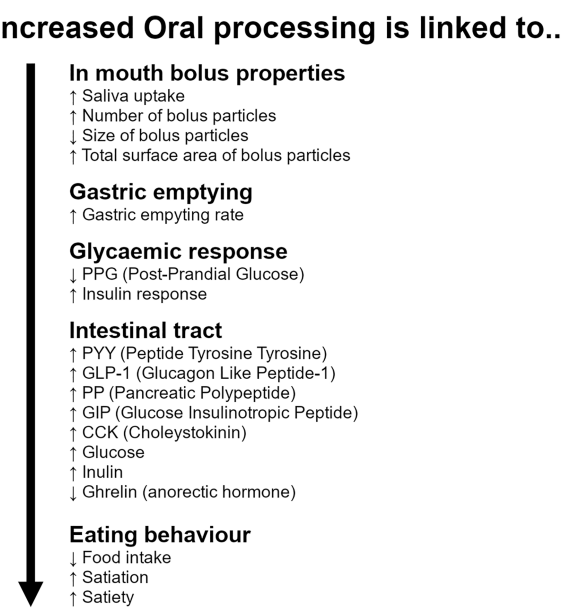

Figure 6.3 Summary of the physiological effects of oral processing behaviour on post-prandial metabolism.

asked participants to chew a portion of almonds for different numbers of chews and showed reduced post-meal hunger, prospective consumption and increased fullness, alongside an increase in post-prandial GLP-1, when increasing the number of chews per mouthful.[199] In a follow-up study using a similar paradigm, fullness was lower and hunger higher for 25 chews than for 10 or 40 chews, which led the authors to suggest that increasing chews pre-bite suppresses hunger.[40] However, the authors note that mastication beyond the point of 'normal chewing' may diminish food palatability and enjoyment, which, in turn, may attenuate hunger ratings.

Using a slow (30-minute) *versus* fast (five-minute) meal consumption paradigm, Kokkinos *et al.* asked participants to consume a fixed portion of ice cream and showed that both peptide tyrosine–tyrosine (PYY) and GLP-1 were higher 30 minutes after meal consumption in the slow-eating condition, but these effects were not consistent across other endocrine signals, with no difference in plasma ghrelin.[200] Eating slowly is therefore likely to increase anorectic (appetite-supressing) hormones and satiety in healthy adults, but may be less effective for orexigenic (appetite-stimulating) hormone production.

In other trials that compared satiety for longer[40] and shorter[15] chewing cycles for a fixed portion meal, it was shown that increasing the number of chews per bite can significantly increase the post-prandial metabolic and endocrine satiety response, producing a stronger feeling of fullness, higher cholecystokinin (CCK) and longer ghrelin suppression. Studies by both Li and Zhu suggest that increasing the number of chewing cycles increased CCK and reduced ghrelin concentrations (trend).[69,129] The Zhu study also found a higher level of GIP in the longer chewing condition. Despite this stronger satiety, food intake at the subsequent test meal did not differ between the different chew conditions.[69] Overall, the findings suggest a stronger subjective feeling of satiety with longer mastication for an equicaloric load, although few studies have shown this to influence later calorie intake on subsequent eating occasions.

Chewing for longer (*e.g.* 30 chews per bite) was shown to increase plasma GLP-1 concentrations, whereas other studies have been unable to replicate the effect of fast or slow ingestion on post-prandial levels of glucose, insulin, GLP-1, GIP, PYY or ghrelin. Hunger was lower and fullness higher when a meal was consumed over 30 minutes rather than five minutes.[201] Despite this, there was no difference in PPG, insulin, PYY, GLP-1 or ghrelin responses. In comparing the responses between healthy participants and patients with type 2 diabetes, eating more slowly did not influence either GLP-a1 or PYY among those with type 2 diabetes, but it did influence them with healthy participants. The authors concluded that eating slowly is likely to influence energy intake among people with overweight or obesity, but is unlikely to significantly influence their post-prandial satiety, glucose or insulin responses. Similar findings have been observed by other researchers who have manipulated eating time (five *versus* 30 minutes), with greater perceived satiety and higher levels of anorexigenic peptides (GLP1 and PYY) observed in the slow-eating condition. As with previous findings among those with type 2

diabetes, it is noteworthy that the GLP-1 and PYY responses were attenuated among participants with obesity.

Differences in the satiety responses were compared among lean and obese participants using a long (40×) *versus* short (15×) chew per bite paradigm. Longer chewing led to a 12% reduction in energy intake from a meal and lower post-prandial ghrelin concentrations, but higher post-prandial GLP-1 concentrations among both lean and obese participants.[129] Importantly, the results showed that the post-prandial ghrelin and GLP-1 responses were blunted among those participants with obesity compared with the lean group, possibly suggesting the limited efficacy of this approach in supporting energy reduction and sustained post-prandial satiety among participants with obesity.

Increased chewing promotes a greater insulin response and findings from a randomized controlled feeding trial suggest that this may be due to increases in the oro-sensory exposure time.[71] Earlier research by Holt *et al.* showed that increased insulin secretion within a meal can also reduce post-meal satiety by suppressing the release of CCK.[202] This highlights the complex and dynamic interplay between the different oral processing behaviours moderated by the central nervous system, and a neuroendocrine system charged with the responsibility of managing the metabolism of the macronutrients consumed in the daily diet. These effects are dynamic from the early to later phases of digestion and influence glucose homeostasis and the satiety response to ingested nutrients. This highlights the interactions of nutrition (meal composition) and behavioural (oral processing) elements of our metabolic responses to food consumption.

Although the effect of eating rate on satiety has been observed across several studies, it is important to note that not all studies have shown similar effects on satiety or neuroendocrine signals.[131] Many studies have shown dissimilar results when comparing faster and slower eating rates for the same neuroendocrine signals. Several studies have manipulated meal duration and mastication per bite in the same way and have been unable to replicate these findings. No significant effect on post-meal satiety or cephalic and intestinal satiety markers in response to an eating rate intervention have been reported. Karl *et al.* manipulated meal rate by asking participants to eat their meal in seven or 28 minutes and found no significant difference in peak fullness, post-meal satiety ratings or significant differences in the measured endocrine mediators of appetite (pancreatic polypeptide (PP), CCK, GLP-1, PYY). Similarly, Lasschuijt *et al.* showed a lack of endocrine changes during the cephalic phase response to large differences in oro-sensory exposure during consumption.[203]

All these trials were acute, accounting for satiety and hormone shifts within two to three hours of the post-prandial period. But what happens if you slow the eating rate for every meal over the longer term: would it be possible to augment the habitual fullness derived per calorie consumed by simply slowing our eating rate? In one 12-month weight loss intervention trial, the intervention group (N = 14) was provided with real-time feedback during meals on their eating rate using a computerized weighing scale feedback system

(Mandometer) and compared with a control group who received standard lifestyle and dietary advice ($N = 13$).[204] Although both groups lost weight, the weight loss was greater among the intervention group who reduced their eating rate. Notably, 12 months after the intervention, the slower eating group had lower concentrations of fasted ghrelin and an improved PYY response compared with those in the standard care group (traditional calorie-restricted weight loss).

These preliminary findings are encouraging and suggest that re-normalizing the eating rate to eat more slowly can stimulate gastrointestinal hormone responses to also re-normalize to the new body weight, creating the possibility that a behavioural adaptation can help sustain physiological changes and support longer term weight maintenance. Previous research has shown that one of the central challenges in maintaining diet-induced weight loss is that satiety hormones continue to circulate at the pre-weight loss body weight, promoting a stronger appetite and encouraging weight regain.[205,206] These results suggest that weight loss achieved by slowing the eating rate to reduce energy intake can also improve circulating levels of appetite hormones, such as ghrelin and PYY, and is therefore more likely to support better long-term maintenance of weight loss than diet-induced weight loss.[204]

6.3.5 Oral Processing and Gastric Emptying

Mastication and bolus texture have been found to affect the stomach emptying rate.[207] The gastric emptying rate and satiety sensation are strongly correlated[208] and have been shown to influence satiety through peripheral neural signals to the brain from stretch receptors in the stomach[209] and by influencing the secretion of neuroendocrine signals based on the rate of elution of digestion products to the duodenum, ileum and large intestine.[210] In addition to satiety, delaying gastric emptying has also been shown to have beneficial effects on the glycaemic response, where a reduced rate was associated with reduced PPG.[211]

The rate of gastric emptying is affected by meal size, energy density, macronutrient composition, physical state (liquid *versus* solid) and by the properties of the chyme in the gastric phase, including density, weight, size, consistency and texture, all of which can influence the rate and extent of food fragmentation in the stomach.[212] Larger food particles that are harder and denser require longer to achieve the necessary size reductions during gastric digestion and therefore have a slower rate of gastric emptying. The macronutrient content of the chyme influences the secretion of neuroendocrine signals, including CCK, that directly influence the rate of gastric emptying in response to fat and protein.[213,214]

The rate of food bolus elution from the stomach can be influenced by the physical properties of the bolus, with liquids having a faster gastric emptying rate than solids (Read & Houghton, 1989). In one study, the consumption of whole apple was compared with the equivalent calories consumed as either apple juice or puree and it was shown that the gastric emptying rate was

slower and satiety was greater for the whole apple, with no significant difference between the juice and puree.[215]

Biphasic meals separate in the stomach into their component physical phases, which empty independently, with the liquid and semi-solid phases emptying more rapidly than the solid phase[216] in a process known as gastric sieving.[217] Studies have shown that eating the same biphasic meal in a blended form can reduce gastric sieving and slow gastric emptying rates compared with the two components separately.[218] Extended mastication increases the rate of gastric emptying by reducing the particle size and increasing the ease with which food particles transit through the antrum. For example, using a similar paradigm to earlier studies on the effect of mastication on satiety, participants were asked to consume a fixed test meal (250 kcal) with shorter (25 chews) or longer (50 chews) oral processing times while their gastric emptying rates were tracked by measuring changes to octanoic acid (^{13}C) in their breath. The results showed that gastric emptying rates were negatively correlated with more extensive mastication, which produced a smaller bolus particle size and required less additional gastric manipulation to pass through the pylorus.[1]

These findings were confirmed in a follow-up trial, which showed that extensive mastication reduced gastric transit times and sped up the rate of gastric emptying.[219] Beyond differences in bolus particle size, other studies have suggested that extended mastication can induce an inhibition of gastric activity and slow the rate of emptying (Figure 6.3). A study by Ohmure *et al.* noted that mastication suppressed gastric motility, which only increased again in the post-mastication phase.[220] This suggests that the act of mastication may in itself promote satiety through delayed gastric emptying. However, follow-up trials that extended mastication (oro-sensory exposure) in combination with modified sham feeding did not show any effect on gastric emptying rates.[221]

In an elegant trial designed to separate the relative contribution of energy density and viscosity to feelings of fullness and gastric emptying rate, the results showed that viscosity was less effective at slowing the gastric emptying rate than energy density, but had a larger effect on subjective feelings of perceived fullness.[222] The study highlighted that the added subjective fullness was a result of the viscosity, which the authors termed 'phantom fullness' because it was unrelated to the energy content of the consumed food. A comparison of biphasic and homogenized equicaloric loads showed that homogenized samples increased the release of fibre and slowed gastric motility and emptying, resulting in significant increases in perceived satiety and fullness and a reduced desire to eat over time.[223] These results were later confirmed using a homogenized meal and drink compared with a meal and drink consumed separately; the mixed condition tended to drain at half the rate of the separate conditions.[217]

This effect of gastric sieving and delayed gastric emptying is thought to be responsible for the unique satiety properties of soup, which is a liquid meal that delays gastric emptying, promotes feelings of post-meal fullness and

supports reductions in daily energy intakes compared with the equivalent energy consumed in other liquid forms.[224] Differences in satiety have even been observed between different types of soups, where smoother, thicker soups provided enhanced satiety and lower glucose responses than thin, 'chunky'-style soups.[225]

Inspired by these studies, several researchers have tried to develop specific food structures that slow the rate of gastric emptying in an effort to promote longer fullness and enhance satiety.[218,226] The addition of soluble fibres such as pectin,[227] guar gum[228,229] or locust bean gum[230,231] reduces the gastric emptying rate and the plasma glucose responses can promote post-meal satiety by increasing gastric viscosity. However, there are many types of fibre that differ in their physicochemical properties and have no effect on gastric emptying or satiety.[232] One challenge is that changes to intra-gastric viscosity need to be fairly large to have an effect on emptying rates and satiety. One study suggested that a 1000-fold increase in viscosity between meals slowed emptying rates by only a factor of 1.3.[233] Similarly, small differences in meal consistency have small effects on the gastric emptying rate – for example, mashed potato emptied at a similar rate to particulate foods such as rice and hamburger meals.[234,235] In this regard, the relatively small differences in food structure and particle size that result from differences in oral processing during the oral phase of breakdown are unlikely to significantly influence gastric emptying rates or perceived satiety, but may have a stronger influence on metabolic responses (such as the PPG or insulin response) as a result of differences in the rate of change of stomach pH and the related penetration of gastric enzymes and acids.

A summary of the physiological effects of oral processing on post-prandial metabolism, gastric emptying and neuroendocrine signalling is shown in Figure 6.3. Increasing stomach viscosity is associated with a reduced gastric emptying rate and stronger feelings of satiety and reduced PPG, yet few studies have demonstrated a clear impact on later food intake. Further studies are needed to comprehensively understand the impact of extended oral processing on gastric emptying rates and satiety to clearly demonstrate whether this can play a meaningful part in the regulation of energy intake.

6.3.6 Oral Processing and DIT

DIT is the increase in energy expenditure associated with the digestion, absorption and storage of foods in the post-prandial period and is typically associated with 10–15% of energy expenditure.[236] The oral phase contributes significantly to an increase in the thermic effect of food intake,[237] where differences in chewing based on food texture can stimulate DIT.[238] This is greatly reduced when the food intake bypasses the oral mouth phase.[236] Chewing is reported to increase DIT by about 20% in cows and can still occur when masticating without an intake of calories.[239] A longer oral processing time has been linked with an increase in DIT, with several studies in rodent and

human models confirming increased energy expenditure, and in some cases reduced energy intake and adiposity. In one study, rodents were fed either a hard or soft chow diet for six months and their energy intake and body composition were compared.[240] Although the daily energy intake did not differ between the hard and soft chow groups, the rodents fed soft chow had a greater weight gain and adiposity by the end of the trial and consistently had a lower body temperature after each meal, suggesting a reduced thermic effect and energy expenditure in this group.

In a similar trial, the consumption of softer pellets by rodents was associated with increased *ad libitum* energy intake and adipose tissue accumulation, but no difference in body weight.[241] This suggests a specific metabolic effect of frequently consuming softer foods that require less mastication, which is consistently seen to contribute to a higher energy intake and greater adiposity, despite an equivalent body weight. Therefore, even when changes to body weight are minimal, there may be an increased risk of diet-related chronic disease associated with the sustained consumption of softer diets (Figure 6.3). Other researchers have extended this further to suggest a possible role for softer food textures in promoting insulin resistance and increased risk of type 2 diabetes in rodent trials.[242,243] Similarly, when rodents were switched from a softer to harder chow diet, it led to a decreased body weight and improved glucose tolerance.[243]

Studies comparing the impact of diet hardness, DIT and body composition are less common in human populations, with only a handful of trials to date. In one cross-sectional comparison, the benefit of increased dietary hardness was assessed among a sample of 454 Japanese women. Body composition was compared between participants with increased dietary hardness and habitual diet and showed that increased dietary hardness was associated with a smaller waist circumference, although not with body weight.[244] In a separate trial, the effect of eating speed (fast/slow) and mastication duration (long/short) were compared for their effects on oxygen uptake (a measure of DIT) and blood flow around the spleen (a measure of post-prandial metabolic activity and DIT).[245] The results showed that increased chewing and longer oro-sensory duration increased both splanchnic blood flow and DIT, suggesting an important role of oral processing in modulating energy expenditure in the post-prandial period.

In the absence of a formal understanding of the specific mechanisms by which the eating rate influences energy intake, and the cascade of post-ingestion effects including glycaemia, satiety and DIT, it is not possible to recommend which element of slower consumption has the single largest effect and would be the best approach for intervention. For example, increasing the mastication per gram of food is collinear with an increase in oro-sensory exposure time,[29] which affects energy intake and DIT, independently of slowing down the eating rate.[123] The advice here would be to increase the number of mastication cycles per bite to lengthen the oro-sensory exposure time to reduce energy intake, promote optimum satiety and increase DIT (Figure 6.4).

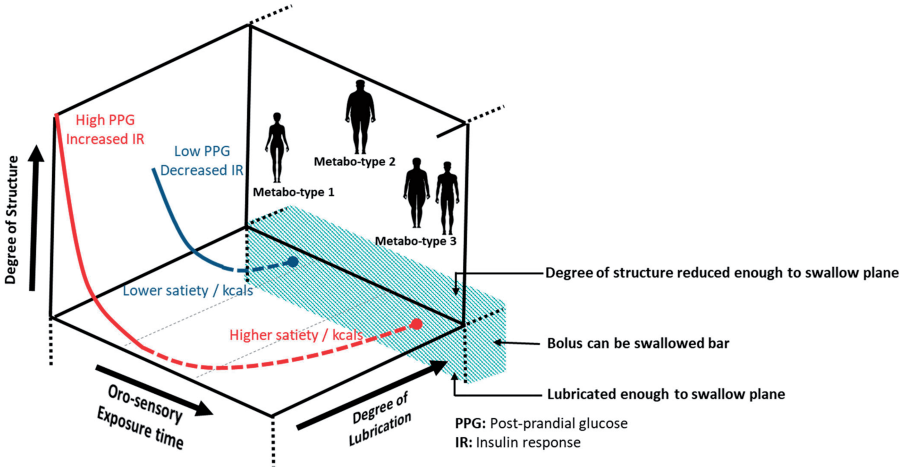

Figure 6.4 Modified breakdown pathway model as it relates to satiety, glucose, insulin and body weight (metabo-types).

Increasing the number of mastication cycles per bite is likely to promote an increase in early glucose release and absorption and to stimulate a higher insulin and lipid response, although it may encourage faster gastric emptying rates. Future food designs should consider optimum textures within the hedonically acceptable range to promote desirable oral processing, while ensuring an appropriate degree of bolus breakdown to enhance metabolism and unlock the nutrient potential of the food consumed and protect against any undesirable metabolic responses. In this regard, the important contribution made by proper mastication to our physiological response to food could provide new opportunities to regulate energy intake and improve healthy nutrient digestion and absorption (Figure 6.4).

6.4 Future Opportunities: Oral Processing to Support Healthy Metabolism

6.4.1 'Eat Yourself Fitter': Food Texture and Oral Processing to Moderate Energy Intake and Glycaemia

This chapter has summarized the current evidence for the impact of oral processing on energy intake, satiety, body weight and metabolic responses to ingested macronutrients. Interventions that target a reduced eating rate to better regulate food intake and body weight have attracted attention for many years as a simple and effective strategy to improve health.[246] There are few formal randomized controlled trials that have tested the long-term efficacy of eating rate interventions on sustained changes to energy intake or body composition. Although a slower eating rate has been shown to

limit weight gain in children and adolescents, the underlying mechanism by which energy intake is reduced remains unclear.[123,204,247] Previous trials have shown clinically significant reductions in BMI based on eating rate interventions that required participants to reduce their rate of food intake to a pre-specified target rate, set using an external device (Mandometer).[247] These reductions in eating rate and body weight were accompanied by a 're-normalization' of satiety hormones post-weight loss,[204] demonstrating the potential long-term efficacy of this approach in supporting sustained reductions in energy intake. These encouraging results have yet to be replicated, and have not been demonstrated using food texture-based dietary interventions to reduce eating rate.

Numerous trials have demonstrated the acute impact of food texture on eating rate and energy intake,[73,122,136] where texture-based reductions in eating rates consistently reduce energy intake to fullness (satiation) by 10–15%.[125] To date, no study has explored whether these changes are sustained in the longer term, or whether texture-based reductions in eating rate could support reductions in body weight. The closest comparison to date has been a two-week, cross-over, in-patient metabolic ward study, which showed that a 50% increase in daily EIR within and across meals sustained an increased energy intake and weight gain; this was reversed when the participants reverted to a lower EIR diet. Both diets were, on average, hedonically equivalent, with the implication being that subtle changes to dietary EIR (kcal min^{-1}) could have a sustained impact on the daily energy intake and body composition.

New approaches have been described to use food structure to reduce eating rates, while also reducing energy density in parallel. For example, combinations of proteins and indigestible polysaccharides can be used to form semi-solid structures that have textural characteristics that maintain sensory appeal and extend oro-sensory exposure time in the mouth.[56] Future studies should examine the effect of these structures and reductions in energy density, and their combination, at the level of the diet and the resultant longitudinal impact this intervention has on energy intake and body weight.

The association between mastication and PPG summarized here highlights the opportunities to apply food texture differences to manipulate mastication and control changes in bolus surface area, saliva uptake and oro-sensory exposure time during the oral phase to moderate PPG and the insulin response. The implication is that extending mastication can support an improved early absorption of glucose, which stimulates greater insulin responsiveness. The preliminary results suggest an opportunity to use food structure and oral processing to improve glucose metabolism and future studies should explore this further, particularly among populations at elevated risk for, or with a family history of, type 2 diabetes.

Further opportunities exist to redesign foods to manipulate their microstructures in such a way that attenuates the starch available for digestive action. For example, adding denatured (unfolded) pea protein to a noodle formulation resulted in reduced starch gelatinization and a subsequent reduction in the *in vitro* glucose response.[248] Adding denatured protein to

the noodle did not significantly influence sensory quality, suggesting that small changes to food microstructure may have a beneficial effect on post-ingestion metabolic responses. In addition to enhancing texture to increase mastication per bite, it is also possible to reduce the carbohydrate available for digestion, in combination with reductions in energy density, to optimize a food's metabolic profile for specific populations. Further research is needed to evaluate unexplored opportunities to use product formulation alongside a reformulation of oral processing behaviour and bolus properties to mitigate the potential negative metabolic aspects of food ingestion.

6.4.2 Food Structure Design to Moderate Oral Processing and Metabolism: The Example of Fat

The natural components in the food matrix can significantly influence the release, transformation and subsequent absorption of some nutrients in the digestive tract.[249] In the same way that bolus particle size and saliva uptake can enhance plasma glucose levels, similar relationships have been observed with food macro- and microstructures for lipids and other nutrients. The food matrix is the largest determinant of the rate of fat digestion and absorption and is important for the modulation of post-prandial triglyceridaemia. For example, research has shown that boluses consisting of a larger number of smaller particles through an extended mastication time can enhance the release of lipids from almonds,[250] although most of the intracellular lipids remained undisturbed in intact cells after mastication.[251] Larger bolus particles resulted in a higher encapsulation of lipids in the cell walls of the nuts, making the fatty acids less bioaccessible and decreasing the post-prandial lipidaemic response. These innate cell wall structures in almonds reduced lipid bioaccessibility, with 89–92% of the lipids retained and excreted.[250]

Similar research with cheese has shown the cheese matrix moderates the release of dairy fat and subsequent post-prandial lipidaemia in healthy people.[252] Consuming an equivalent nutrient load as cheese, rather than as individual nutrients, led to an attenuated lipid response, with significantly lower cholesterol observed when the nutrients were consumed in a cheese matrix.[253] Foods with weaker structures and easier oral processing deform more readily and can be consumed at a faster rate, producing greater post-ingestion spikes in plasma triglycerides, such that for an equivalent fat content there is greater release of lipids from cream cheese (up 44%) than butter (up 24%), both of which are greater than the release from cheddar cheese (up 16%).[254]

When comparing liquid, semi-solid and solid test foods with equivalent nutrients and energy, the solid food showed phase separation during gastric digestion and a lower release of fatty acids during intestinal digestion than both the liquid and semi-solid foods. Solid food produced a lower increase in serum triglycerides than the liquid food, with the added benefit of higher fullness and satisfaction.[254]

Using this knowledge, it is possible to implement structural changes to manipulate the macrostructure of a foods and, through this, influence the oral processing behaviour, bolus surface area and saliva uptake to improve metabolic markers and enhanced satiety for each calorie consumed.[255] For example, when coconut oil was consumed as a liquid or as an oleo-gel (coconut oil solidified with ethyl cellulose), there was a significant reduction in post-prandial triglycerides.[256] Similarly, structuring fat as an oleo-gel can also have beneficial effects on substrate oxidation by reducing post-prandial fat oxidation, which tends to occur when an equivalent amount of fat is consumed as a liquid oil.[257] Structuring fat as an oleo-gel reduces the lipidemic response and could provide additional benefits to PPG and insulin responses and satiety.[258]

It is now possible to apply food design principles to create structures inside foods that are more difficult to break down in the mouth during the oral phase of digestion.[259] Taking inspiration from these natural microstructures creates new opportunities for the design of food structures that encourage extended mastication to enhance digestion while attenuating potential deleterious post-prandial spikes in lipids or other nutrients, or for the targeted downstream delivery of nutrients.[260] Future food design could apply these mimetic design principles to emulate the structural elements of many natural cellular foods to moderate food digestibility and nutrient delivery while maintaining a food's sensory appeal.[261,262] Oral processing behaviour and consequently food intake and possibly metabolism can also be steered by changing the shape and size of foods, which are easily modified by food producers. Future studies are needed to validate this approach and explore the potential to moderate food digestibility and nutrient delivery by modifications to the shape and size of foods.[141,149]

6.5 Conclusions: Opportunities and Challenges in the Application of Oral Processing to Enhance Health

A better understanding of the oral contribution to the variability in metabolic response, or metabo-types, suggests a future role for food oral processing in personalized nutrition to optimize digestion to individual chewing styles. Across all the aspects of metabolism summarized in this chapter, extending mastication and reducing eating speed have been consistently shown to impart benefits, by enhancing glucose absorption or by providing increased satiety and satiation per kcal consumed.

Tailoring a food's texture and breakdown path to the oral behaviour of the individual eater creates new opportunities to adapt food structures, not only for sensory appeal and preferred oral processing style, but also for optimum energy intake and metabolic response to the consumed nutrients. This may include designing structures that extend mastication to enhance early insulin release and improve PPG management within a population at risk of type

2 diabetes. Similarly, it may be possible to add texture to the diets of children who exhibit a heightened propensity to consume their meals quickly and are at an increased risk of weight gain early in life.

Conversely, as oral processing capabilities and saliva flow rates decrease with increasing age, understanding the breakdown path and metabolic consequences of food oral processing for specific textures creates new avenues to use food structures to stimulate mastication and enhance saliva flow, alongside the fracture properties that optimize food appeal and digestion among vulnerable populations of older consumers.[27] Many of the barriers to adequate nutrition among clinical populations or those receiving palliative care are often driven by changes in oral processing abilities that result from the clinical condition or its treatment. A recent review identified a series of orosensory attributes that limit compliance with nutrient supplement intake among patient populations undergoing cancer treatment, highlighting the important role of sensory cues and oral processing alongside nutrient composition.[263]

Historically, food product development has considered the 'eater' and the 'food' separately and attempted to address challenges for each using approaches from distinct disciplines, such as food technology, psychology and human nutrition. Future food design will need to consider both concurrently and to align a food's appeal with an individual's eating behaviour and nutrient needs to optimize their nutrient intake and metabolic response. Future foods will rely on an empirical understanding of how food texture and mechanical breakdown impacts specific oral processing behaviour and the properties of boluses.[28,42] This will inform intelligent food design that improves not only what we eat, but also how we eat.

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