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# Carbohydrate Craving- not everything is sweet

**Yue Ma**[a], **Risheka Ratnasabapathy**[a], and **Dr James Gardiner**[a]

[a]Section of Endocrinology and Investigative Medicine, Department of Medicine, Imperial College London, London, United Kingdom

## Abstract

**Purpose of review—**Cravings for carbohydrates have been known about for hundreds of years but the mechanisms behind it were unclear. This review will highlight recent advances in our knowledge of mechanisms to detect carbohydrates in the diet.

**Recent findings—**Recent work has begun to identify the physiological mechanisms by which carbohydrates and glucose are detected and how this drives their intake. Recently evidence has been found for systems that regulate carbohydrate and glucose intake via taste, hedonic and homeostatic pathways.

**Summary—**Identification of the physiological mechanisms that regulate carbohydrate intake will allow a better understanding of how their intake is regulated and responds to changes in dietary intake. Such an understanding will be key to developing a more rational approach to the development of successful weight loss diets.

### Keywords

Starch; glucose; taste; reward; homeostasis

## Introduction

Energy from food comes in three macronutrient forms: fat, protein, and carbohydrate. Carbohydrates are a major source of energy in the diet and are needed for multiple essential physiological processes. Carbohydrates are divided by their chemical structures which are broadly sugars (monosaccharides and disaccharides), polyols, oligosaccharides (malto-oligosaccharides and non-digestible oligosaccharides) and polysaccharides (starch and non-starch polysaccharides) (Scientific Advisory Committee on Nutrition UK). According to Public Health for England it is recommended that the dietary reference value for total carbohydrate should be 50% of total. The science behind the carbohydrate cravings are not yet fully understood however there are compelling studies looking into changes in neural circuitry, gene expression and central receptor modifications as well as hormonal influences and behavioural changes relating to reward and addiction. Much of the initial work in this field focussed on the effect of sweet taste and ingestion of simple sugars. However this

Correspondence to Dr James Gardiner, 6th Floor Commonwealth Building, Imperial College Hammersmith Campus, Du Cane Road, London, W12 0NN, j.gardiner@imperial.ac.uk, Tel: 0208 383 3942 James Gardiner.

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review aims to detail the most recent evidence for the physiology behind the carbohydrate craving, concentrating on complex carbohydrates and the post-ingestive effects of glucose.

## The Role of Taste

Animals rely on chemoreceptor systems including taste to detect foods containing metabolic fuels such as glucose to meet their physiological needs.

In humans taste is an important factor governing eating behaviour as it contributes to food preference, and it is thought that it modulates appetite and caloric intake [1]. Obese patients report higher enjoyment for sweetness compared with normal weight subjects [2].

Taste in mammals has classically been thought to be limited to sweet, sour, salty, bitter and umami.

Thus much of the work on taste regarding carbohydrate intake has concentrated on simple sugars and sweet taste which is established as a driver of food intake and is activated by a wide range of sweet tastants including sugars and non-nutritive sweeteners.

A polysaccharide taste mechanism was first proposed to exist in rodents more than thirty years ago and a great deal of evidence supports its existence although it still remains controversial [3]. In part this may be due to the inherent difficulty of conducting taste research in species other than humans. Recent research suggests that humans are able to taste carbohydrates in the form of glucose oligomers, via a mechanism independent of the sweet tastes receptors[4]. The participants in the experiment were able to detect the taste of short glucose oligomers between 7-14 monomers but not polymers containing on average 44 monomers. The participants were able to do this in the presence of agents which block both amylase activity and T1R3 a key component of the sweet taste receptor [4]. In addition the participants described the solution as tasting starchy using terms such as bread-like, rice-like and rather than sweet providing further support for a non-sweet based taste pathway.

However the mechanism underlying this ‘carbohydrate’ taste, whether oligomers of other sugars also activate this system and its relative importance in the regulation of carbohydrate intake is currently unclear.

## Post absorptive regulation of carbohydrate intake

While taste is an important driver of carbohydrate intake post absorptive detection and responses to carbohydrate intake are important regulators of its consumption. The importance of this system is highlighted by the finding that mice lacking SGLT1, a sugar transporter and receptor have an intake sweet taste response but lack the intake enhancing effect of gastric infusion of glucose [5]. There are thought to be two main pathways by which glucose enhances its own intake, hedonic or reward effects and homeostatic effects. Although these are considered separately in this review in reality there is considerable overlap between the two pathways and indeed with those of taste so they would act in concert to regulate glucose intake.

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## The hedonic system regulates carbohydrate intake

Much of the ground-breaking work in this area was based upon the interaction between sugar intake and acute changes in hedonic pathways. Some of the more recent work has compared the effects of different sugars or high carbohydrate diets on the reward and hedonic pathways.

In one recent human study, when participants were allowed to eat ad libitum, consumption of high-carbohydrate foods resulted in greater postprandial satiety, greater satiation and lower total daily energy intake compared with the consumption of high-fat foods [6]. Importantly, despite controlling for energy content, weight and palatability, the explicit liking and implicit wanting for high-fat foods were also suppressed to a greater extent following consumption of the high-carbohydrate meal compared to the high fat low carbohydrate meal. However this study did not examine any possible mechanism underlying this finding but suggests that carbohydrates may have a more powerful effect on the hedonic/reward pathways than high fat low carbohydrate foods and thus less is required to sate the reward system. Support for this interpretation has been found in studies in rodents. Intermittent access to an 8% glucose solution resulted in reduced binge drinking compared to intermittent access to 8% fructose on rats. Glucose was also able to abolished cocaine conditioned place preference whereas fructose preserved cocaine conditioned place preference [7]**.** These data were interpreted by the authors to suggest that intake of glucose is more rewarding than that of fructose. Further support for this interpretation comes from another study in mice examining the interaction between sugars and the reward pathway [8]. In a series of experiments examining short-term and long-term preference for fructose, glucose or sucrose compared to non-caloric sweeteners. In short term exposure experiments, the non-caloric sweetener was preferred to all of the sugars. In the long-term exposure test glucose and sucrose were preferred to the non-caloric sweetener but fructose was not. The rewarding effects of the agents were also examined using progressive ratio test. In this paradigm the mice were willing to expend more effort to obtain glucose than any of the other solutions. This result suggests that ingestion of glucose is more rewarding than ingestion of other sugars.

However some of these data could also be interpreted to suggest that intake of glucose is less rewarding that intake of fructose indeed this is the interpretation placed on similar data from a study in human volunteers [9]. In this study healthy volunteers underwent two functional magnetic resonance imaging (fMRI) sessions with ingestion of either fructose or glucose. Ingestion of fructose relative to glucose resulted in greater brain reactivity to palatable food cues in the visual cortex (in whole-brain analysis) and left orbital frontal cortex (in region-of-interest analysis). Fructose ingestion led to greater hunger and desire for food and a greater willingness to give up long-term monetary rewards to obtain immediate high-calorie foods than did glucose ingestion. The authors interpreted these findings to suggest that fructose activates brain regions involved in attention and reward processing to a greater extent than glucose and so and may promote food intake. Which of these two interpretations of the data that glucose activates the reward circuits to a lesser or greater extent than glucose is not yet clear and further work will be required to elucidate this.

## The homeostatic pathway regulates carbohydrate intake

In addition to taste and the hedonic value of food a homeostatic process to control glucose intake has long been proposed. Recent work has focused on trying to identify a hypothalamic mechanism or circuit which could regulate this process. Historically it has been difficult to disentangle the hedonic effects of food from the homeostatic effects entirely especially in studies in rodents and indeed they are unlikely to be separate systems but intimately linked

In a series of elegant experiments, based on gastric infusion of either glucose or sucralose, a non-nutrient sweetener, stimulated by licking of a sucralose solution separate basal ganglia circuitries mediating the hedonic and nutritional actions of sugar were found [10]. Gastric infusion of either glucose or sucralose resulted in increased dopamine in the ventral striatum during sucralose licking. In contrast increased dopamine levels were found in the dorsal striatum during gastric infusion of glucose but not of sucralose. Addition of a bitter taste to the sucralose licking solution inhibited dopamine release in the ventral, but not dorsal, striatum. By contrast gastric infusion of non-metabolizable L-glucose inhibited dopamine release in dorsal, but not ventral, striatum. Optogenetic stimulation of dopamine-excitable cells in the dorsal striatum drove ingestion of bitter tasting sucralose solution in the same fashion as gastric infusion of glucose. In contrast similar stimulation of the ventral striatum did not affect intake of the adulterated solution. This work suggests that the energy content of food can override the hedonic rewarding qualities of the food to drive intake of it. Whether this system is also activated by other energy containing sugars or is specific for glucose is currently unclear and requires further investigation.

One of the major regions of the brain regulating homeostatically driven food intake is the hypothalamus. Several hypothalamic nuclei are involved in the process the best characterised of these is the arcuate nucleus. We have recently reported a mechanism within the arcuate nucleus of rodents which specifically regulates glucose intake and is not responsive to fructose or saccharin [11]. Glucokinase expressed in the arcuate nucleus acts as part of a glucose-sensing system, analogous to that in the β cell, as part of a central macronutrient regulatory system. Increasing glucokinase activity specifically in the arcuate nucleus increased intake of glucose in preference to normal chow in rats. Whilst decreasing glucokinase activity in the arcuate had the opposite effect reducing glucose intake. There is indirect support for this finding since activation of glucokinase expressing cells in the hypothalamus, using selective electromagnetic activation, increased food intake [12].

However arcuate glucokinase is not the sole system regulating homeostatic glucose intake. Recent evidence suggests that ghrelin is an important regulator of glucose intake. Mice with targeted deletion of ghrelin O-acyltransferase, the enzyme responsible for octanylation and thus activation of ghrelin consumed less glucose and maltodextrin than wild type littermates in a two bottle selection test whilst intake of fructose and saccharin was not affected [13]. Conversely administration of acetylated ghrelin to normal mice increased intake of both glucose and maltodextin solution but did not affect intake of either fructose or saccharin. This suggests that ghrelin has an important role on the regulation of glucose intake, however details of the mechanism regulating this are currently lacking. It is possible that ghrelin

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interacts with the glucokinase expressing neurones within the arcuate nucleus to regulate glucose intake currently there is no direct evidence for this however ghrelin receptors are expressed on the appropriate neurones.

## Health effects of dietary carbohydrates

The health effects of consuming a diet rich in carbohydrates is an area of much controversy. This controversy is particularly acute with respect to the role of dietary carbohydrate in the development of obesity or conversely weight loss although a recent meta analysis of studies suggests that low fat and low carbohydrate diets are equally efficient at reducing weight [14].One confounding factor with studies on dietary carbohydrates is the variety of dietary constituents that are classified as carbohydrates. There have been recent efforts to quantify the different classes of carbohydrates within the diet to remove this potentially confounding factor. However this approach has not done much to clarify the situation. One recent study suggests that the quality of the carbohydrate in the diet is a risk factor for the development of type 2 diabetes rather than just the quantity [15] with greater intake of processed starch linked to increased incidence of type 2 diabetes. Although other studies have not supported this finding and indeed found the opposite effect of a low carbohydrate diet [16]. It is possible this difference may be due to the different populations studied or the dietary constituents which replace carbohydrates. Or other characteristics of the study group since it has been suggested that in the obese high carbohydrate diets are a risk factor for the development of diabetes [17]. The evidence for low carbohydrate diets in improving outcomes for patients with diabetes is equally unclear. Although emerging evidence does suggest that the inclusion of complex carbohydrates in the diet rather than fat and glucose may be beneficial [18, 19], although not all recent studies have found this association [20]. Others have found that a low carbohydrate diet may be beneficial to a subset of patients with diabetes who are unable to maintain a calorie restricted diet [21]. Thus the role of dietary carbohydrates in diet and health is still unclear. However this is an area of very active research and undoubtedly more clarity will be provided by more trials.

## Conclusions

The recent identification of a carbohydrate taste mechanism in humans should help resolve some of the controversy about the non-sweet taste of carbohydrates although identification of an underlying mechanism is likely required to do so fully and may allow development of agents which mimic the taste of starch with fewer calories. What is still to be resolved is the health effects of dietary carbohydrate. While there are many studies already on this no clear consensus has so far emerged. This is likely to be due to the confounding factors of different types of carbohydrate in the diet and individual response. Ultimately individual recommendations on diet may be required rather than broad population based recommendations. But such recommendations will require a greater understanding of the interaction between dietary carbohydrate and genetic and other factors.

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**Keypoints**

Carbohydrate taste mechanism independent of sweet taste receptors identified in humans.

Caloric content of glucose activates separate reward pathway to that induced by sweet taste.

Homeostatic pathways regulating glucose intake have been identified