# Gastric bypass surgery alters food preferences through changes in the perception of taste

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## Practice Points

- Roux-en-Y gastric bypass (RYGB) modifies eating behavior. It decreases appetite and calorie intake, decreases emotional eating and decreases the consumption of fat and sweet foods.
- RYGB modifies taste perception. It decreases the detection threshold for sweet taste, decreases the appetitive behavior (wanting) for high-calorie foods and decreases the preferences for high concentrations of sucrose and fat.
- Potential causes for RYGB-induced changes in taste perception include that RYGB-induced gut hormone changes are known to impact taste perception, RYGB-induced negative post-ingestive effects may induce conditioned taste aversion and RYGB-induced gut nutrient changes may be involved in taste perception changes.

**SUMMARY** Roux-en-Y gastric bypass is one of the most effective treatments for morbid obesity as it results in long-term weight loss and significant remission of obesity-related comorbidities. Although it is successful in causing weight loss, the underlying mechanisms are not completely understood. A significant decrease in calorie intake related to a shift in food preferences towards lower-calorie-dense foods has been observed after the surgery. This modification in ingestive behavior occurs through changes in the sensory and reward domain of taste. Potential mediators of these taste modifications are the exaggerated levels of gut hormones or altered gut nutrient sensing. Understanding the molecular mechanisms involved in the Roux-en-Y gastric bypass-induced taste/food preference modifications would be crucial for the development of 'knifeless' treatments.

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Obesity is a leading cause of death [101]. The comorbidities of obesity include cardiovascular disease, Type 2 diabetes mellitus, cancer, nonalcoholic fatty liver disease, arthritis and infertility, among others [1–6]. Roux-en-Y gastric bypass (RYGB) is one of the most effective treatments for morbid obesity [7], resulting in long-term weight loss maintenance, significant remission of obesity-related comorbidities [8–10] and decreased overall mortality [10].

RYGB results in five main anatomical changes:

- Reduction of the stomach size (15–30 ml), leaving a large stoma to allow food rapid passage between the esophagus and midgut;
- Food bypassing the stomach and the first part of the proximal small bowel;
- Altered bile flow through the same proximal small bowel;
- Anastomosis of the midgut to the stomach, allowing earlier contact of food with the distal small bowel;
- Disruption of vagal fibers across the stomach, while leaving the main branches of the vagus intact.

Although the RYGB procedure is successful in causing weight loss, the relevant mechanisms are not completely understood. Even though the procedure was originally designed to cause restriction, the flow of food is accelerated from the esophagus to the midgut through the large gastro-jejunostomy [11]. Calorie malabsorption does not play a physiologically significant role as fecal fat and calorie loss is minimal, while many patients actually report constipation after RYGB [11,12]. Significant increase in energy expenditure have been reported after RYGB in animals [6,13–15] and in one study in humans [16] but this change may be triggered by changes in body composition. However, one study has shown that diet-induced thermogenesis of multiple meals results in an overall increase in 24-h energy expenditure compared with a group of patients that lost the same amount of weight with a vertical-banded gastroplasty [16]. Significant decrease in calorie intake has also been reported after the surgery in humans [17,18]. The decrease in total calorie intake is related to reductions in hunger, increases in satiety, changes in meal patterns, in addition to a shift in food preferences towards lower-calorie-dense foods [18–22].

Here, we review the changes in eating behavior after RYGB, and focus on potential mechanisms underlying this shift, including changes in quantitative taste identification and taste ingestive motivation (reward). Finally, we explore potential mediators underlying this mechanism, such as gut hormones or nutrient sensing.

## Impact of gastric bypass surgery on eating behavior & food choices

### Caloric intake, meal patterns & emotional aspects of eating

RYGB decreases appetite and calorie intake by 13–50% [17,19,23–26]. This decrease in calorie intake varies depending on the time after surgery, with the nadir at 6 months (~50%) which then recovers progressively to a stable value of an approximately 13% deficit 4–6 years after the surgery [17]. 10 years after RYGB, patients eat approximately 87% of calories eaten by a control weight-matched group [17]. Patients [20,27,28] and animals [29] also eat smaller but more frequent meals and snacks have been reported to account for 37% of daily intake 18 months after the surgery in humans [28]. Eating rate decreases to 65 and 72% of the preoperative value at 1 and 2 years after RYGB, respectively [20].

RYGB affects psychological aspects of eating behavior by decreasing hunger and disinhibition scores, as measured by the Three-factor Eating Questionnaire [20,30]. RYGB also increases cognitive restraint scores [20,30] but this effect remains temporary and returns to preoperative levels after 1–2 years [20]. RYGB affects emotional eating by decreasing binge eating [30].

### Food intake & selection

Mathes and Spector [31] reviewed all the studies examining the effect of RYGB on macronutrient diet composition by the use of food dietary recall and diet record methods [19,23–26,32,33]. They calculated and reported the change in percentage calories from fat, carbohydrates and protein from 1–36 months, and even up to 11 years after surgery, and concluded that while there is a trend for RYGB to reduce the proportion of calories consumed from fat and carbohydrates, more robust and long-term behavioral data are needed to confirm these findings. Indeed, all these studies were carried out in humans and we cannot exclude the possibility that RYGB

induced a change in macronutrient diet composition as a result of nutritional counseling given after the surgery or by the underreporting and intra-/inter-individual variability of the dietary recall and diet record methods [34]. However, in animal studies that are not influenced by social desirability or nutritional counseling, RYGB appears to strongly decrease the intake of calories derived from high-fat diet and to increase the proportion of calories from low-fat foods [13,21,29]. RYGB seems to decrease the consumption of sweet snack foods, desserts and beverages [19,23,25,26,35], although results are not always consistent. There is no clear effect of RYGB on the consumption of fruits and vegetables as the results are contradictory [26,33,35,36]. It is difficult to conclude whether the changes in food intake observed after RYGB are due to the surgery or related to the weight loss after surgery. A similar amount of weight loss induced by gastric banding and RYGB was shown to not induce the same decrease in sweet intake [35], but the debate is still controversial and further studies should be carried out to assess the direct causality between RYGB and changes in food selection.

In summary, there are some inconsistencies in the results that make it difficult to get a clear picture of the effect of RYGB on food selection. However, RYGB appears to decrease the consumption of fat and sweet foods. Nutritional counseling, variability in eating habits, differences in the type of patients recruited (e.g., BMI and gender), the surgery procedures (size of gastric pouch, distal vs proximal), the times after the surgery (from 1 month to 11 years) and indirect methodologies used to measure eating behavior may account for these inconsistencies.

## Taste changes after RYGB

Taste refers, in the strict sense of the word, to the perceived gustatory sensation resulting from the contact between a sapid stimulus and taste bud receptors [37]. Gustatory sensation is categorized into five basic tastes: sweet, bitter, sour, salty and umami. Increasing evidence supports the existence of a taste of fat [38]. Taste is however generally confused with olfactory and somatosensory sensations and it is commonly used to refer to the result of three sensations experienced when introducing a stimulus in the mouth: gustatory (five basic tastes), olfactory (retro-nasal aroma perception) and trigeminal (temperature, texture, astringency, pain and spicy/hot) [37]. These sensations are difficult to dissociate as they are all integrated in the CNS into a global sensory image of the food and perceived according to three dimensions: the nature of the sensation (qualitative dimension), the intensity of the sensation (quantitative dimension) and the reward induced by the sensation (hedonic dimension) [39].

According to Spector, taste function has three main utilities in ingestive behavior [40]:

- Stimulus identification, which refers to sensory processes that discriminate the quality and intensity of an ingested stimulus;
- Ingestive motivation, which refers to cognitive and emotional processes that leads to the decision to either ingest or reject the food stimulus;
- Digestive preparation, which refers to physiological responses triggered by specific taste stimuli that aid in digestion and assimilation of food.

We have considered the mechanistic role of each of these domains in contributing to the shift in food preference after RYGB. Here we report the effect of RYGB on the first two domains (sensory and reward), because to our knowledge, no reports are available on the effect of RYGB on the taste digestive preparation (physiological domain).

### Modification of the sensory domain of taste following RYGB

When asking patients whether their taste perception has changed after RYGB, 82% of them reported a change in the taste of food or beverages after surgery [41]. This level of self-reported taste changes is important, but the question asked does not allow the nature of these taste changes to be described (i.e., sensory or hedonic domain of taste perception). No studies have yet reported any effect of RYGB on qualitative taste identification that is, gustatory distortion perception (parageusia). However, a few studies have reported changes in the gustatory intensity perception after the surgery, although results are not consistent. Two studies reported an increase in sweet taste sensitivity [42] and in sweet but not bitter taste recognition ability [43] in humans. Another study reported a trend toward a better ability to detect and recognize salty and sweet tastes after RYGB and a significant change in bitter and acid recognition ability

in humans [44]. RYGB thus seems to increase sensitivity to sweet taste around the detection threshold concentration range, but the results are unclear for bitter, acid and salty perception. It is, however, not known whether the sweet taste intensity perception of foods/drinks (far above-threshold concentrations) is perceived more strongly after RYGB. The impact of RYGB has not yet been studied for umami and fatty tastes. As regards to olfactory perception, only one study has reported that RYGB does not alter smell identification [45].

### ■ Modification of the reward domain of taste following RYGB

Although strongly related to the homeostatic control of food intake, ingestive motivation is driven by sensory, cognitive and emotional hedonic motivational processing [46]. In the following paragraphs, the effect of RYGB on taste ingestive motivation will be approached through the three closely related, but dissociable, components of the psychological reward concept defined by Berridge (i.e., appetitive behavior, consummatory behavior and reinforcement, which at times are colloquially referred to as 'liking, wanting and learning') [47].

Appetitive behavior is the process that brings animals/humans to the food stimulus [48] and can be measured by the progressive ratio task that assesses how hard a subject will work to get a specific food [40]. Visual analog scales (VAS) can also assess the desire/wanting to eat a specific food in humans. A few studies assessed the effect of RYGB on appetitive behavior in humans and results seem consistent towards a decrease in the appetitive behavior for high-calorie foods (sweet/fat) after surgery. Indeed using VAS, RYGB induces a selective decrease in the desire to eat high-calorie foods, but not low-calorie foods, in obese women [49]. This decrease has been shown to be associated with significant reductions in reward-related and inhibitory mesolimbic neural responsivity to high-calorie food pictures using brain functional neuroimaging techniques (functional MRI) [49]. Using the Power of Food Scale questionnaire (measuring the motivation to highly palatable foods), RYGB leads to a reduction of the hedonic drive to consume foods that would have been rated as palatable presurgery [50]. A decrease in the reward value for sweet and fat stimuli, but not for vegetables, after RYGB has also been shown using the progressive ratio task in humans [51]. In this study, the reduction of breakpoint ('reward') correlated with the decrease in BMI after surgery.

Consummatory behavior is the hedonic response elicited by contact of the food stimulus with taste receptors [48]. It can be measured directly by taste reactivity test that assess oromotor and somatic responses induced by food stimulus when introduced into the oral cavity [31] or indirectly by VAS that assesses the pleasure elicited by the taste of food stimulus in humans. Two studies reported on the effect of RYGB on consummatory behavior in humans. Using VAS, a decrease in liking for the tasting of high-fat potato chips was observed in obese patients after RYGB [18]. Hedonic perception of sucrose solution with different concentrations (on the just-about-right scale) was however not altered after RYGB [42]. One study in animals using a taste reactivity test has shown that rats exhibited more positive orofacial responses to low concentrations of sucrose but fewer to high concentrations after RYGB surgery [52]. However, although protocols used in animals (e.g., common intake tests such as one or two-bottles test), are not able to strictly dissociate appetitive and consummatory behavior, the literature seems to indicate a decrease in preference for high concentrations of sucrose [42,52–54] and lipids [21,29,52]. Interestingly, RYGB in lean rats does not modify preferences response for sucrose [54]. One study has, however, shown that RYGB increases the licking of sucrose and the appetitive behavior in rats fed *ad libitum* with a standard chow diet [55]. In this study, the increase of licking for sucrose was observed for all the concentrations indicating that RYGB induced a general increase in licking that is not concentration-dependent.

Taste learning refers to the process that brings animals/humans to develop a preference or aversion for a specific taste in association with positive (nutrient feedback) or negative post-ingestive consequences (visceral discomfort e.g., nausea, vomiting) [56]. In this process, the alteration of reward value of food by visceral response leads to the development of either conditioned taste aversions (CTAs) or conditioned taste preferences, and guides the subject to either avoid or seek that taste in the future, respectively [57]. In the case of RYGB, the physiological/anatomical gut changes induced by the operation may trigger visceral discomfort after the ingestion of specific foods. One of the most common visceral discomforts

reported after RYGB is the 'dumping syndrome' that occurs after ingestion of high glycemic index foods or fats [58,59]. Early dumping usually starts 10–30 min after the ingestion of specific foods and is characterized by diverse symptoms such as sweating, palpitation, dizziness, fatigue, nausea, vomiting, bloating, cramping or diarrhea [58,59]. Although controversial, it may be caused, in part, by rapid arrival of hyperosmolar chyme in the jejunum, leading to fluid shifts from the blood to the intestinal, in addition to increased small bowel distension and contractions. Late dumping generally starts 2 h after the ingestion of specific foods and is characterized by weakness, sweating, dizziness, palpitation and mental confusion [58,59], probably as a result of reactive relative hypoglycemia triggered by high GLP-1 and subsequent insulin secretion [60]. The etiology of dumping syndrome after RYGB is not completely understood and the number of patients developing this syndrome, as well as the frequency of the symptoms, is not known, but approximately 50–75% of patients may experience dumping syndrome after the surgery [28,61,62]. There are no data showing that the decreased intake of sweet or fatty foods after the surgery is directly related to the negative post-ingestive effects of the dumping syndrome, but a CTA for sweet and fatty foods may take place without the patient being aware. Olbers *et al.* described that less than 5% of patients avoid sweet foods 1 year after the surgery [36]. However, the authors reported that almost a third of patients avoid fatty foods after RYGB, due to unpleasant feelings after their ingestion. Regarding animal studies, one has shown that oral gavage with corn oil leads to a modest but significant conditioned taste aversion in rats [63]. Another study has shown that lean rats that have undergone RYGB do not decrease their preferences for sucrose as obese rats do, suggesting that the physiological/anatomical gut changes induced by the operation did not trigger CTA for sucrose [54]. It is, however, not known whether animals experience dumping syndrome after RYGB.

Further studies should be carried out by associating a flavor with sucrose or fat (CS+) and water (CS-) infusions directly into the jejunum to measure the impact of RYGB on CTA in animals and humans.

RYGB seems to modulate the mechanisms of taste identification and the three components of taste reward (i.e., appetitive, consummatory and reinforcement toward less caloric foods). It is difficult to assess how much each of these mechanisms contributes to the overall food choice changes observed after the surgery, but there may be a synergistic effect as they are closely interrelated.

## Eating behavior & taste modification after other bariatric surgery procedures

Several bariatric operations are used to treat obesity and some appear equally efficient to RYGB at achieving long-term weight loss. Comparing the impact of the different surgeries on food preferences and eating behavior can be a helpful approach to understanding the link between the physiological changes induced by the surgeries and the potential mediators involved in the modification of eating behavior. The majority of studies have compared RYGB with vertical- or horizontal-banded gastroplasty, both of which are now obsolete. Unfortunately, few studies have thus far made any comparison between operations that are performed currently, such as sleeve gastroectomy and gastric banding.

Comparison of food intake between adjustable gastric banding (AGB) and RYGB surgeries suggests that AGB does not induce the same decrease in sweet intake that RYGB does [35]. Indeed, a food frequency questionnaire completed by patients after AGB suggests a reduction in fruits and eggs but an increase in chocolate compared with RYGB [35]. Interestingly, only 46% of patients that had AGB reported a change in the taste of foods after the surgery, against 82% for RYGB patients [41]. Comparison of food intake between vertical sleeve gastrectomy (VSG) and RYGB surgeries have never been reported in humans but leads to inconsistencies in animal studies. Indeed, one study has shown that VSG induces the same change in eating behavior as RYGB that is, decrease in fat intake and shift in preferences toward lower caloric foods [64]. This decrease in fat intake after VSG was confirmed by Chambers *et al.* [65]. Another study has, however, shown that VSG surgery does not alter food preferences, while RYGB induces a significant modification [13].

## Potential mediators of taste changes after bypass surgery

### ■ Production of gut hormones

Gastric bypass surgery leads to physiologically important changes in the plasma levels of gut

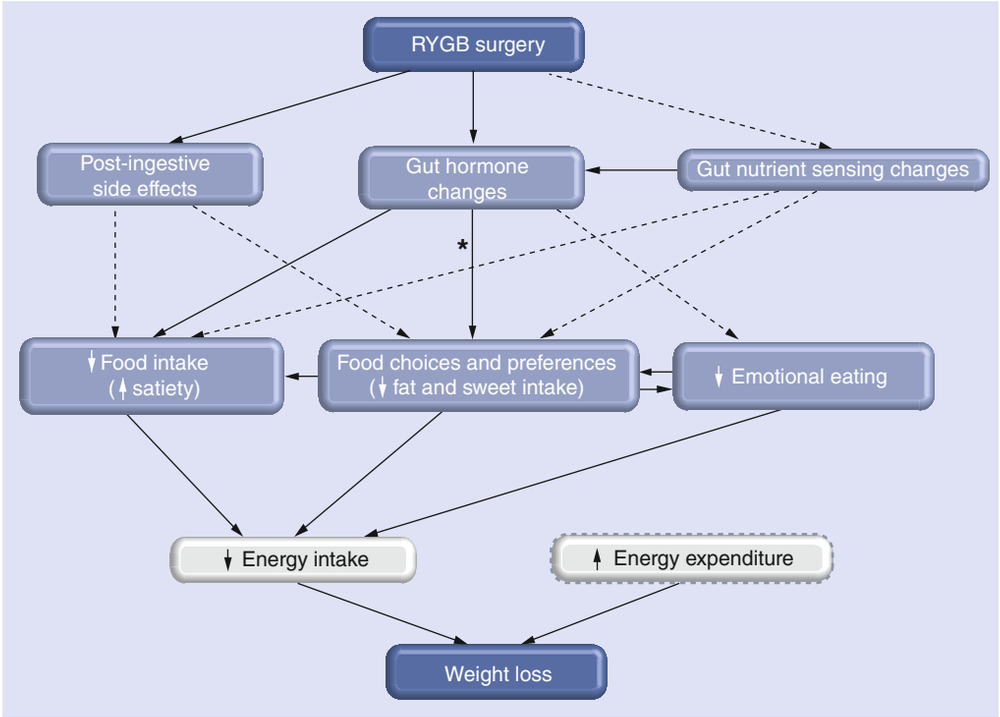


**Figure 1. Potential factors contributing to decreased energy intake and weight loss after Roux-en-Y gastric bypass.** Dotted lines are not-proven cause–consequence relationships and remain to be elucidated. Arrow indicated with an asterisk has been proven in animal studies only. RYGB: Roux-en-Y gastric bypass.

hormones, which is an increase in anorexigenic hormones such as GLP-1, PYY and insulin, as well as attenuated orexigenic ghrelin [63–68]. There is increasing evidence from animal models suggesting that taste perception and food preferences are modulated by hormones participating in the control of energy homeostasis. Indeed, leptin [69] and insulin [70] decrease the gustatory perception of sweetness. GLP-1 receptor-knockout mice have a significant and specific decrease in taste responses to sucralose and sucrose sweeteners suggesting that GLP-1 enhances sweet taste sensitivity [71]. Peripheral ghrelin injection increases the preference and intake for sweet food [72]. In addition, high-fat diet-induced obese rats prefer high sucrose and oily solutions as compared with healthy rats and this preference is reversible when obese rats lose weight after caloric restriction diet but recovered when leptin is administrated to the weight-reduced rats [73]. These taste modulations may be triggered by the presence of gut hormone receptors such as GLP-1R and LEP-R (for leptin) that have been shown to be expressed in taste buds or intragemmal afferent taste nerve fibers in animal models [69,71]. Brain imaging studies using functional MRI suggest that gut hormones can modulate the reward value of food. In healthy subjects, infusion of anorexigenic hormones such as GLP-1 and PYY reduces the neural signal response to visual food cues in brain regions encoding reward value [74], whereas orexigenic ghrelin infusion was shown to increase it [75]. A recent study has also shown that activation of central GLP-1Rs in rats strongly decreased food reward/motivation by interacting with the mesolimbic system [76]. Pharmacological or genetic studies aimed at blocking secretion or action of gut hormones should be carried out to assess whether gut hormones are involved in the taste and food preferences changes induced by RYGB.

## Gut nutrient sensing

Gut nutrient receptors have recently been found to participate in digestive, metabolic and satiating effects that modulate nutrient utilization and appetite [77,78]. They also generate positive feedback signals that can participate in conditioned flavor preferences [77]. This area of research is

relatively new and several studies are aimed at understanding the role of gut nutrient receptors and their mechanisms of action in eating behavior. Given that bariatric surgery increases the concentration and the flow of nutrients into the jejunum, it is possible that these signals activate and modulate gut nutrient sensors and modifies the eating behavior and taste preferences [78].

## Conclusion & future perspective

RYGB modifies food choices toward lower-calorie foods. The underlying mechanisms of this modification involve altered taste sensitivity and reward, resulting in lower energy intake and weight loss. Understanding mechanisms involved in the RYGB-induced taste/preference modifications **(Figure 1)** would be crucial in the management of obesity through the development of 'knifeless' treatments. Notably, combinatorial hormonal therapies should emerge and bring strong hopes in the treatment of overweight and obesity.

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- ▪▪ of considerable interest

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