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Food preferences and underlying mechanisms after bariatric surgery

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Bariatric surgery leads to significant long-term weight loss, particularly Roux-en-Y gastric bypass (RYGB). The mechanisms underlying weight loss have not been fully uncovered. The aim of this review is to explore the changes in food preferences, as a novel mechanism contributing to weight loss, and also focus on the underlying processes modulating eating behaviour after bariatric surgery. Patients after gastric bypass are less hungry and prefer healthier food options. They develop an increased acuity to sweet taste, which is perceived as more intense. The appeal of sweet fatty food decreases, with functional MRI studies showing a corresponding reduction in activation of the brain reward centres to high-energy food cues. Patients experiencing post-ingestive symptoms with sweet and fatty food develop conditioned aversive behaviours towards the triggers. Gut hormones are elevated in RYGB and have the potential to influence the taste system and food hedonics. Current evidence supports a beneficial switch in food preferences after RYGB. Changes within the sensory and reward domain of taste and the development of post-ingestive symptoms appear to be implicated. Gut hormones may be the mediators of these alterations and therefore exploiting this property might prove beneficial for designing future obesity treatment.

Food preferences: Bariatric surgery: Taste

Obesity is a growing epidemic affecting nearly 500 million adults globally[1]. Bariatric surgery is currently the most effective treatment for obesity. The most commonly performed procedures are Roux-en-Y gastric bypass (RYGB), adjustable gastric band (BAND) and vertical sleeve gastrectomy and normally lead to between 20 and 35% loss in body weight[2]. RYGB is considered as the gold standard surgical treatment for obesity and offers sustained weight loss for at least 20 years, as well as marked improvement in cardiovascular risk factors and mortality[3,4]. In contrast, weight loss though lifestyle modification is usually modest and un-sustainable. Even the best available anti-obesity pharmacotherapy only allows a fraction of the weight loss caused by bariatric surgery and is usually plagued with side effects, which have led to the withdrawal of at least two anti-obesity agents over recent years. The success of bariatric surgery clearly stems beyond purely restrictive and malabsorptive mechanisms; however, the mechanisms implicated for long-term weight loss are not fully understood.

Proposed mechanisms include elevation of gut hormones and their effect on the appetite centres of the brain, increased energy expenditure, alteration in the gut microbiota and bile acids levels and composition, changes in vagal nerve signalling and shifts in food preferences, particularly with patients post RYGB[5–7]. Patients post RYGB prefer low-sugar low-fat food and report finding food less enjoyable. These changes in food perception and preferences have been strongly attributed to changes in taste processes and food reward. This is a novel concept, but there is an increased research interest looking for possible mechanisms at play. Elucidating the physiological processes underpinning the changes in the perception of food and hence eating

Abbreviations: BAND, adjustable gastric band, fMRI, functional MRI; GLP-1, glucagon-like peptide-1; RYGB, Roux-en-Y gastric bypass.

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behaviour in patients after bariatric surgery is crucial. This knowledge could potentially translate to the development of more efficient obesity-targeted drugs. The purpose of this review is to explore the changes in food preferences and eating behaviour after bariatric surgery and present the evidence implicating physiological changes in taste, food reward and post-ingestion effects as possible causative factors.

Changes in food preferences and eating behaviour after bariatric surgery

Patients after bariatric surgery report feeling less hungry, reach satiety earlier and prefer different classes of food[8,9]. The first study to objectively investigate the eating behaviour of patients post-bariatric surgery was conducted by Halmi *et al*. The findings from the study showed a reduction in total energy intake and a selective reduction in high-fat and high-carbohydrate intake after surgery[10]. The majority of subsequent studies demonstrated a reduction in total energy consumed after surgery although changes within the macronutrient compositionvaried[11–16]. For example, Coughlin *et al.* found a reduction of energy intake by more than one-third, predominantly due to a reduction in fat consumption, in patients 12 months post RYGB surgery[13]. Kruseman *et al.* provided the longest prospective study of eighty patients, 8 years after RYGB and demonstrated an increase in percentage of protein, a reduction in fat but no change in carbohydrate intake compared with baseline[11], whereas Brolin *et al.* found a significant increase in the contribution of carbohydrates but reduction in fat at 36 months in patients post RYGB[17].

Other studies focused on the consumption of sweet and fatty foods as well as fruit and vegetables in patients undergoing RYGB or BAND. RYGB surgery leads to superior weight loss and it has been suggested that divergence in food preferences may play a role. Some studies reported a reduction in the consumption of sweet food post RYGB compared with both pre-operatively and post BAND. For example Kenler *et al.* performed a 2-year study in patients before and after RYGB and horizontal banded gastrectomy. This group found a reduction of 14–21% in the consumption of sweet and dairy items in the RYGB group, but this was unchanged in the gastrectomy group[18]. Similar results were replicated by Olbers *et al.* who found a lower contribution of sweet and fatty food towards total energy intake in a RYGB group compared with a vertical banded gastroplasty group 6 years post-operatively[19]. Additionally, the same group later reported an increase in both the frequency of meals and mean eating rate in patients post RYGB[20]. Other studies reported that patients post RYGB exhibited less interest in sweet food, finding it less enjoyable and even unpleasant or intolerable in some more extreme cases[15,21,22]. The authors suggested dumping syndrome to be a possible cause. The data for fruit and vegetable consumption after bariatric surgery are inconsistent. Ernst *et al.* reported enhanced intake of vegetables and reduced intake of fatty sweets post RYGB but a reduction in fruit consumption following BAND[23]. This is in agreement with Olbers *et al.* who showed that a superior representation of fruit and vegetables in the diet of patients post RYGB compared with vertical banded gastroplasty[19]. However, others have found no change in the consumption of vegetables with the overall contribution towards energy intake remaining quite low at 5–10%[10,15].

Animal data are consistent with the findings from human studies. Rats after RYGB ate less high-fat high-sugar food compared with sham but more chow, demonstrating a shift in food preferences[21,24,25]. However, conflicting results from animal studies are available for food preferences after vertical sleeve gastrectomy. One study found a reduction in fat intake and a preference towards lower energy-dense food whereas another demonstrated no difference in food preferences in rats compared with pre-operatively[22,26].

Although there are some patterns emerging, there are considerable inconsistencies between human studies and the reasons are varied. Firstly, the methodologies employed in the studies assessing food intake and preference consist of food diaries, questionnaires, interviews and dietary recall. Although they are practical and inexpensive to use, these tools are prone to weaknesses. They provide subjective information which relies on accurate reporting from patients. Verbal report of human eating behaviour does not always reflect actual behaviour and this can be particularly problematic in the context of the stigma associated with obesity[27]. Perhaps, a more objective way to directly assess food intake and preferences is to use a standardised clinical setting where the subject is presented with a variety of food options in a buffet style or performs behavioural tasks. Secondly, factors related to the surgery such as differences in surgical techniques used, time from surgery and type of dietary advice and support provided can all contribute to the inconsistencies. Thirdly, patients' factors such as gender, BMI and stage of menstrual cycle may also contribute to conflicting results, as for example, there is evidence to show that food intake is significantly increased in the luteal phase compared with the follicular phase in menstruating women, due to fluctuating levels of oestrogens and serotonin[28].

In summary, the emerging eating behaviour patterns are that of a lower consumption and preference for sweet and fatty foods after RYGB compared with pre-operatively as well as compared with BAND. Limited data are however available for changes in food preferences after vertical sleeve gastrectomy. As a result, RYGB is now recognised as a procedure able to shape eating behaviour and perception of food towards weight loss. Changes in taste and post-ingestive effects have been heavily implicated.

Taste and bariatric surgery

An important factor governing human eating behaviour is taste. When food comes into contact with taste buds, a series of neural pathways are activated which help to identify food, decide how much to eat and how much we enjoy it and finally prepare for digestion. These

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processes can be categorised into three major domains: (1) sensory domain which deals with the identification and discrimination of the stimulus, e.g. does this cake taste sweet and if so how sweet is it? (2) hedonic domain which refers to the motivational reward driving ingestion of a stimulus, e.g. how much do I want this cake and how much do I like it when I eat it? (3) physiological domain which leads to the triggering of pathways to help with digestion and maintain homeostasis, e.g. salivation and cephalic insulin release following ingestion[29,30]. Bariatric surgery, RYGB in particular, can potentially influence any of the three taste domains in such a way to direct the food preferences and eating behaviour of patients towards long-term weight loss. It is useful to have a basic understanding of the gustatory pathway to appreciate the impact of bariatric surgery on taste.

The gustatory pathway

Taste receptors are located on the tongue and palate and innervated by branches from the facial, glossopharyngeal and vagal nerves. Once activated, signals are transmitted along the nucleus of the solitary tract to the thalamus and finally to the primary taste cortex which comprises the insula and frontal operculum. The primary taste cortex contains taste neurons coding for different taste modalities such as sweet, salt, bitter, sour and umami. However, they do not convey the reward value of taste. Instead the insula projects to the secondary taste cortex, the orbitofrontal cortex, where taste reward is encoded. Further inputs from the olfactory and visual pathways converge and integrate with taste signals within the orbitofrontal cortex and contribute to the concept of flavour as well as the reward aspect of food. The orbitofrontal cortex has further projections to the striatum, cingulate cortex and medial prefrontal cortex enabling appropriate behavioural responses to a given stimulus. Connections with the lateral hypothalamus drive autonomic responses but are also key to the process of sensory-specific satiety, i.e. the selective reduction in the appeal of a specific food in a satiated state[31].

Sensory domain of taste and bariatric surgery

The first study of the effects of RYGB on taste acuity was performed by Scruggs *et al.* using the Henkin forced choice three choice drop stimulus before and after RYGB in women. This technique involves placing drops of water or tastant on the tongue of the volunteer. The lowest concentration at which the volunteer is able to detect a difference between the tastant and water represents the detection threshold[32]. This group found a non-significant trend towards a reduction in the detection threshold of sweet and salty[33]. However, Burge *et al.* reported a lower recognition threshold of sweet in patients as early as 6 weeks post RYGB, but not after energy restriction-induced weight loss. This translated to increased taste acuity resulting in a more intense perception of sweet to which patients adjusted their eating behaviour[34]. In our own unit, we used the method of constant stimuli where increasing concentration of sweet solutions, interspersed with water, were presented in a random fashion to patients post RYGB and normal weight controls. We found a significant increase in sweet taste acuity after surgery[21]. Contrary to our findings, Pepino *et al.* found no change in detection thresholds for sweet, salty or savoury in patients after RYGB and BAND compared with pre-operatively as well as within groups. It must be noted that the authors used a different technique to ours, to assess taste thresholds and administered a standard energy-deficient diet to both groups to achieve a matched weight loss of 20%. Also, after surgery, the RYGB group was switched to a regular diet sooner than what is commonly practiced in most bariatric centres. However, a comparable reduction in preference for sweet and high-energy food in both groups was shown. On this basis, the authors argued that mechanisms other than taste sensitivity account for the shift in food preferences after bariatric surgery, and suggested that weight loss and energetic restriction *per se* may have a causative role[35]. The discrepancy between the earlier study results may amount to differences in the methodologies employed to measure taste thresholds, variation in the diet composition of subjects at the time of testing, time from surgery and sex differences. On balance, some of the evidence points towards an enhancement in the detection and intensity of sweet after RYGB surgery, hence changing the palatability of food. Conversely, it is not clear whether lower taste thresholds actually translate to a modification of eating behaviour in the 'real-world', where supra-threshold taste concentrations reign.

Reward domain of taste and bariatric surgery

The reward domain of taste conveys information related to the appeal of food and directs appropriate eating behaviour. As previously described, taste together with input from the olfactory and visual pathways, merge within the orbitofrontal cortex to encode the reward value of a food stimulus. The orbitofrontal cortex further communicates with other limbic structures such as the ventral tegmental area, nucleus accumbens, amygdala, hippocampus and ventral striatum with dopamine acting as the primary neurotransmitter. Food reward can be divided into appetitive (i.e. wanting) which reflects the effort a subject is ready to put in for the pursuit of a desired food item and consummatory (i.e. liking) which reflects the pleasure derived upon ingestion of the food. To study food reward in humans, neuroimaging in the form of functional (f)MRI and positron emission tomography scans are commonly used, especially in research. fMRI provides both structural and functional information of brain activation by measuring blood–oxygen-level-dependent responses to food cues, usually delivered as a visual, gustatory, olfactory or auditory stimulus. Positron emission tomography, however, relies on the quantitative uptake of a radio-labelled substrate by their specific tissue receptors; for example, there is

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increased ^{18}F-fluorodeoxyglucose (radio-labelled glucose) uptake by activated brain tissues. Another behavioural method used to study appetitive food reward is the progressive ratio task. In this experiment, the subject has to work for a rewarding stimulus; for example, this could involve clicking a computer mouse a number of times. The response requirement increases progressively until the subject stops working for the reward; this is known as the breakpoint. This technique has been used successfully in animal and some human studies. It is however more challenging to study the consummatory reward objectively in human subjects. Nevertheless, some studies have used both fMRI and the Visual Analogue Scale technique to explore this domain, although limited data is available regarding patients after bariatric surgery. The effects of bariatric surgery on both appetitive and consummatory reward are discussed below.

Positron emission tomography studies and food reward

Following food intake, there is a reported increase in dopaminergic neurotransmission within the dorsal striatum, and this appears to correlate with subjective ratings of derived pleasure in human subjects[36]. In obesity, reduced dopamine receptor availability within the striatum has been reported[37]. So far, only a handful of positron emission tomography studies have investigated the effects of bariatric surgery on brain responses and the findings are discordant. Dunn *et al.* used ^{18}F-fallypride tracer to bind to dopamine receptors and found a reduction in the availability of dopamine D_2 receptors within the areas of the brain influencing eating behaviour, in patients post RYGB[38]. The authors speculate this equates to higher free circulating dopamine levels. In contrast, Steele *et al.* used ^{11}C-raclopride as a tracer and produced opposite findings[39]. The results should be interpreted with caution as both studies were of small size, lack a control group for weight loss and each consisted of a set of cohorts with different characteristics.

Functional MRI studies and food reward

In obesity, both appetitive and consummatory responses to food stimuli, especially high-energy food, show a higher activation of the reward areas on fMRI, compared with normal weight individuals in the majority, but not all published studies[40,41]. There is evidence to suggest that weight loss through energy restriction promotes activation of the reward areas to food stimuli compared with baseline weight[42,43]. This potentially contributes to the high relapse rate of dietary-induced weight loss regimens. In fact, Bruce *et al.* compared brain responses to visual food cues in patients after BAND and following a behavioural weight loss programme. The authors found that at similar weight loss, there was greater activation in the medial prefrontal cortex, an area involved in the motivational processing of food cues, within the non-surgical group, i.e. they perceive the food cues as more rewarding[44]. The same group's earlier work showed that patients at 3 months post BAND have reduced activation in the brain regions involved with motivation and reward but increased activity in areas representing cognitive restraint, to food pictures compared with pre-operatively[45]. This is consistent with findings of a reduction in motivation scores for eating palatable foods, using the Power of Food Scale questionnaires, in patients post BAND *v.* obese controls[46]. Ochner *et al.* carried out a series of fMRI studies in patients post RYGB. The authors first showed that not only was there a reduction in activation within the mesolimbic reward areas to visual and auditory food cues 1 month after surgery compared with pre-operatively, but there was also a selective reduction for high- *v.* low-energy food[47]. In a second study, both fMRI and rating scales were used to investigate the appetitive and consummatory responses to high- *v.* low-energy food in fourteen patients undergoing RYGB. Again, a higher reduction in neural activity in the reward areas after surgery was observed and this correlated with a reduction in the 'wanting' but not 'liking' of high-energy over low-energy food[48]. Reduction in appetitive responses after RYGB to high-fat high-sugar food, has also been found using the progressive ratio task. Subjects tend to work less hard and show less motivation to obtain a sweet and fatty reward (candy) after RYGB[49].

In summary, there is consistent evidence that RYGB reduces the appeal of high-energy food and some data suggesting that BAND decreases the reward value of food. However, RYGB causes more weight loss than BAND, suggesting that all bariatric procedures may not exert the same effects on brain activation. Indeed, Scholtz *et al.* compared the two surgical procedures and found that RYGB caused a greater reduction in the activation of brain reward areas to high-energy food pictures compared with BAND. Furthermore, high-energy food pictures were rated as 'less appealing' and ingestion of ice-cream as 'less pleasant to eat' in the RYGB group[50]. RYGB appears to be far superior in modulating brain activity. In fact, several fMRI studies carried out at least 6 months after RYGB, report a restoration in patterns of brain activation to food or glucose stimuli, similar to those observed in normal weight individuals[51,52]. It is worth noting that patients who are less successful at losing weight after RYGB have been shown to have a lower increase in activation of the areas involved in restraint and inhibition but no significant change in the limbic reward areas compared with their more successful weight loss counterparts[53].

Physiological domain of taste and post-ingestive effects of bariatric surgery

Upon ingestion of food, there is a cascade of physiological responses induced to mainly facilitate digestion. These responses may differ between individuals; for example, obese individuals salivate more and are slower to habituate to sweet food compared with lean individuals[54,55]. Post-bariatric surgery, patients may experience unpleasant physiological responses to food ingestion. Food,

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typically consisting of refined carbohydrates and fat are the main triggers and patients often report a conscious avoidance of the food triggers through a learned process. Post-ingestive responses to sugary and fatty food may consist of nausea, vomiting, flushing, bloating, abdominal pain, fainting and even hypoglycaemia and are generally classified as early and late dumping syndrome. The mechanism is poorly understood although it is believed to result from the expedited transit and delivery of highly osmotic food to the gut in RYGB. This may be secondary to rapid gastric emptying and to bypassing the proximal part of the small bowel. Indeed, dumping syndrome has been associated primarily with RYGB, where prevalence rates of up to 70% has been quoted but not with BAND[56]. Similarly, it has also been described in patients after gastrectomy. It is hypothesised that post RYGB, patients modify their eating behaviour in response to the post-ingestive symptoms and eventually formulate conditioned aversions to sweet fatty food. Animal studies using taste and malaise-inducing aversion paradigms to maize and peanut oil following RYGB and vertical sleeve gastrectomy, appear to support this theory[22,25]

Potential mediators

Another physiological consequence of RYGB but not BAND, is enhanced nutrient sensing by the L cells of the distal ileum, promoting the exaggerated release of the gut hormones, glucagon-like peptide-1 (GLP-1), peptide YY and oxyntomodulin in response to a meal[6,57]. However, ghrelin levels have been found to be reduced or increased post RYGB and therefore its impact on food preferences is largely unknown[58,59]. The elevated gut hormones GLP-1, peptide YY and oxyntomodulin, have been hailed as likely mediators of the beneficial effects of RYGB on appetite, taste functions and food preferences. There is a body of evidence to support the gut hormones hypothesis[57,60,61]. GLP-1, peptide YY and oxyntomodulin are anorexic hormones and have been shown to reduce hunger, promote satiety and reduce food intake when given peripherally in human subjects or centrally in rodents[62–66]. In addition, the role of gut hormones on the brain reward centres was clearly demonstrated in an elegantly designed fMRI study by De Silva *et al.* Their study findings showed that co-administration of GLP-1 and peptide YY in lean individuals resulted in an additive reduction in activation of the reward areas (orbitofrontal cortex, amygdala, caudate, insula, nucleus accumbens and putamen) to food pictures, compared with saline infusion. This translated to reduced *ad libitum* food intake with the fMRI changes observed on the hormone infusion comparable with those seen after a meal, i.e. consistent with a satiated state[67]. Furthermore GLP-1 receptors have been located both in the brain as well as in taste bud cells, suggesting GLP-1 has the potential to modulate the taste pathway at the sensory level and the reward system centrally[68,69]. Contrary to the 'gut hormones theory', Ochner *et al.* argued they found no significant difference in brain activity to visual and auditory food cues on fMRI between the fasted (state of low basal gut hormones levels) and fed state (state of elevated postprandial gut hormones levels) in their cohort and therefore cast doubt over the role of elevated gut hormones as observed in RYGB, in modulating food reward[70]. But the cohort size was small and the authors failed to measure actual levels of gut hormones, which is a limitation of this study.

Conclusion

Patients after RYGB eat less, feel less hungry, prefer healthier food options, derive less pleasure and are less preoccupied with food. These changes may account for its superior efficacy on weight loss compared with other procedures. The evidence supports changes within the sensory and hedonic domains of the taste pathway as well as conditioned food aversion following post-ingestive symptoms, to explain the switch in food preferences after RYGB surgery. The limited available data suggest that these effects are sustained for several years in patients after RYGB[17,25,71]. Additional long-term studies are therefore needed to confirm the durability of these effects on eating behaviour and weight.

The exaggerated release of gut hormones post RYGB has been implicated as a potential mediator of the observed changes in food preferences and weight loss. Their anorexigenic properties are already being exploited to treat obesity and gut hormones analogues are showing great promise[72–75], for example, Liraglutide 3 mg, a GLP-1 agonist, has recently been approved as an anti-obesity drug in the USA and Europe. Perhaps the key to a 'medical bypass' relies on successfully mimicking the hormonal milieu of RYGB with the additive or even synergistic effects of combination gut hormones.

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Conflicts of Interest

None.

Authorship

P. B. wrote the manuscript. A. D. M. reviewed and revised the manuscript.

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