Reported appetite, taste and smell changes following Roux-en-Y gastric bypass and sleeve gastrectomy: effect of gender, type 2 diabetes and relationship to post-operative weight loss

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Abstract

Reduced energy intake drives weight loss following Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) procedures. Post-operative changes in subjective appetite, taste, and smell and food preferences are reported and suggested to contribute to reduced energy intake. We aimed to investigate the prevalence of these changes following RYGB and SG and to evaluate their relationship with weight loss.

98 patients post-RYGB and 155 post-SG from a single bariatric centre were recruited to a cross-sectional study. Participants completed a questionnaire, previously utilised in post-operative bariatric patients, to assess the prevalence of post-operative food aversions and subjective changes in appetite, taste and smell. Anthropometric data were collected and percentage weight loss (%WL) was calculated. The relationship between food aversions, changes in appetite, taste and smell and %WL was assessed. The influence of time post-surgery, gender and type 2 diabetes (T2D) were evaluated.

Following RYGB and SG the majority of patients reported food aversions (RYGB=62%, SG=59%), appetite changes (RYGB=91%, SG=91%) and taste changes (RYGB=64%, SG=59%). Smell changes were more common post-RYGB than post-SG (RYGB=41%, SG=28%, p=0.039). No temporal effect was observed post-RYGB. In contrast, the prevalence of appetite changes decreased significantly with time following SG.

Post-operative appetite changes associated with and predicted higher %WL post-SG but not post-RYGB. Taste changes associated with and predicted higher %WL following RYGB but not post-SG. There was no gender effect post-RYGB. Post-SG taste changes were less common in males (female=65%, males=40%, p=0.008). T2D status in females did not influence post-operative subjective changes. However, in males with T2D, taste changes were less common post-SG than post-RYGB together with lower %WL (RYGB=27.5±2.7, SG=14.6±2.1, p=0.003). Further research is warranted to define the biology underlying these differences and to individualise treatments.

Keywords: Obesity, Roux-en-Y gastric bypass, sleeve gastrectomy, appetite, taste, smell, food aversions, weight loss.
Introduction

Bariatric surgery is the most effective treatment for patients with severe obesity, leading to sustained weight reduction, improved obesity-associated co-morbidities and decreased mortality (Sjostrom, 2013). The most commonly performed bariatric procedures globally are the Roux-en-Y gastric bypass (RYGB) and the sleeve gastrectomy (SG), accounting for 45% and 37% respectively of operations undertaken in 2013 (Angrisani et al., 2015). Observational studies and a limited number of randomised controlled studies suggest that RYGB and SG produce comparable health improvements in the short-term (Schauer et al., 2014; Sczepaniak, Owens, Shukla, Perlegos, & Garner, 2015). Other procedures, such as the adjustable gastric banding (AGB) are now less commonly performed (Angrisani et al., 2015).

Eating behaviour is a key determinant of the pathogenesis of obesity and weight loss achieved following bariatric surgery (Manning, Pucci, & Batterham, 2015; Scott & Batterham, 2011). An energy intake that consistently exceeds energy expenditure leads to weight gain and eventually obesity (Berthoud, 2011). Obese individuals subjectively rate energy-dense foods as more pleasant compared to lean individuals (Rissanen et al., 2002). In addition, weight gain and obesity have been linked to a reduction in taste sensitivity and smell perception (Miras & le Roux, 2010; Patel, DelGaudio, & Wise, 2015; A. C. Shin, Townsend, Patterson, & Berthoud, 2011). Furthermore, neuroimaging studies have revealed that obese subjects exhibit altered neural responses within reward regions in response to food cues (Atalayer et al., 2014; Rissanen et al., 2002).

The gastrointestinal (GI) tract is established as a key regulator of energy and glucose homeostasis and it is now clear that changes in gut-derived signals as a consequence of altered GI anatomy following bariatric surgery play a key role in driving reduced energy intake and weight loss (Dirksen, Damgaard, et al., 2013; Manning et al., 2015; Scott & Batterham, 2011). Following RYGB and SG patients report reduced hunger in the fasted state, increased post-meal satiety, changes in subjective taste and altered food preferences (Manning et al., 2015; Scott & Batterham, 2011). For example, a recent prospective study of 30 patients undergoing SG reported a 68% decrease in energy intake 6 months post-surgery sustained at 24 months post-surgery. 75% of patients in this study reported reduced preference toward sweet and fatty foods (Coluzzi et al., 2016).

In order to assess changes in subjective taste following bariatric surgery Tichansky et al. developed a questionnaire comprised of 23 questions. They reported that subjective taste changes were more common post-RYGB than following AGB surgery (Tichansky, Boughter, & Madan, 2006). Subsequently, Graham and colleagues used Tichansky’s questionnaire in a cross-sectional study to evaluate taste changes following RYGB in patients who were a median 19 months post-RYGB (Graham, Murty, & Bowrey, 2014). They added 10 additional questions assessing subjective changes in appetite, smell and food aversions. They found that 93% of patients reported a change in appetite, 73% a change in taste, 42% a change in smell and 73% developed food aversions. Additionally, they reported that patients who developed food aversions achieved higher absolute post-operative weight loss and greater reduction in body mass index (BMI) (Graham et al., 2014). Zerrweck et al. using the questionnaire from Graham et al., reported that appetite, taste, smell and food aversions were equally common following RYGB and SG at 10 months post-surgery (Zerrweck et al., 2015). However, it remains unclear...
whether these subjective changes in appetite, taste and smell are a consequence of weight loss per se or if they are mediated by bariatric procedure-dependent physiological changes. The subjective hedonic value of sweet foods has been shown to reduce following RYGB (Ochner et al., 2011; Ochner et al., 2012; Scholtz et al., 2014). This effect was not observed in BMI-matched subjects following AGB, suggesting that post-RYGB hedonic responses to food change independent of weight loss (Scholtz et al., 2014).

The impact of bariatric surgery on objectively assessed olfaction and taste sensitivity is controversial, in part due to methodological issues. There are reports of improved post-operative taste sensitivity for sweet, salty, sour and bitter (Altun et al., 2016; Holinski, Menenakos, Haber, Olze, & Ordemann, 2015), no taste sensitivity changes (Pepino et al., 2014) and improved olfactory sensitivity (Holinski et al., 2015). There is also a suggestion of a difference between RYGB and SG with improved olfactory sensitivity post-SG but not post-RYGB (Jurowich et al., 2014).

Taste and smell perception are complex processes, integrating a range of sensory, cognitive and hormonal signals (Cummings, 2015; Miras & le Roux, 2010). Gender, obesity, presence of T2D and nutritional status (vitamin B12 and zinc levels) have all been reported to impact upon gustatory and olfactory function (Bustos-Saldana et al., 2009; Deglaire et al., 2015; Fabian, Beck, Fejerdy, Hermann, & Fabian, 2015; Hwang, Kang, Seo, Han, & Joo, 2016). The tendency to like fatty and salty tasting foods has been shown to have a linear relationship with increasing BMI in both males and females (A. C. Shin et al., 2011). However, a liking for sweet foods is more commonly reported by obese females compared to obese males (Deglaire et al., 2015) and females outperform males in their ability to detect certain odours (Doty & Cameron, 2009). T2D per se has been linked to impaired taste sensitivity, particularly for sweet stimuli and to impaired olfaction (Bustos-Saldana et al., 2009). Following RYGB, patients with T2D loose significantly less weight compared to patients who do not have T2D (Courcoulas et al., 2015). However, there are no reports comparing the prevalence of changes in subjective appetite, taste or smell following bariatric surgery in people with T2D compared to people without T2D.

Following RYGB and SG, circulating gut hormone levels are markedly altered and these changes are suggested to contribute to post-operative appetite changes (Yousseif et al., 2014). Patients with a poor response to surgery experience increased hunger and reduced satiety levels. In addition, an attenuated gut hormone response is seen in poor weight loss responders compared to good weight loss responders (Dirksen, Jorgensen, et al., 2013; Manning et al., 2015). Interestingly, gut hormones are present in saliva and their cognate receptors are found on taste buds and olfactory neurons (Acosta et al., 2011; Cummings, 2015; Loch, Breer, & Strotmann, 2015; Y. K. Shin et al., 2008). Hence, it is plausible that gut hormones mediate gustatory and olfactory changes following bariatric surgery through weight-independent mechanisms. Of note, RYGB and SG are anatomically very different and differentially impact upon circulating gut hormone levels (le Roux et al., 2007; Yousseif et al., 2014). These differences may in turn result in post-procedural differences in appetite, taste and smell. Whilst the development of food aversions following SG and RYGB has been linked to increased weight loss, it remains to be established whether subjective change in appetite taste or smell associate with weight loss (Graham et al., 2014).
We hypothesized that post-operative subjective changes in appetite, taste and smell would differ between SG and RYGB patients and be influenced by gender and the presence of T2D. In addition that appetite, taste and smell changes would associate with post-operative weight loss. Thus, we aimed to investigate prevalence of appetite, taste, smell changes and food aversions following RYGB and SG and their relationship to post-operative percentage weight loss (%WL). We also aimed to evaluate the influence of gender, T2D and time post-surgery upon these changes.

**Methods**

Patients who attended the University College London Hospitals (UCLH) Bariatric Centre for Weight Management and Metabolic Surgery for follow up appointments after primary RYGB or primary SG were invited to participate. Participation was voluntary and informed consent was obtained in person by a healthcare professional. Ethical approval was obtained from the National Health Service Research Ethics Committee (ID#09/H0715/65) and the study was undertaken in accordance with the Helsinki Declaration. Inclusion criteria were adult patients (18 years or older), following either primary RYGB or SG and proficient in spoken and written English.

Prior to surgery all patients had been assessed by a multidisciplinary team and fulfilled the criteria outlined by the National Institute for Health and Care Excellence (NICE, 2014). In RYGB stomach size is reduced by the creation of a small gastric pouch (~ 20cm³), ingested nutrients pass rapidly from the gastric pouch directly into the mid-jejunum, bypassing the majority of the stomach, the duodenum and the proximal jejunum (Olbers, Lonroth, Fagevik-Olsen, & Lundell, 2003). In SG, 80-90% of the total stomach volume is removed by transecting along the greater curvature of the stomach (Abu-Jaish & Rosenthal, 2010), the remainder of the GI tract is left intact and nutrient follow the normal anatomical route.

Weight was measured using a Walkthrough Platform by a trained health professional. Participants completed a 33-question questionnaire, developed by Tichansky et al., and modified by Graham et al. (Graham et al., 2014; Tichansky et al., 2006) (appendix). Permission to use the questionnaire was obtained (Graham et al., 2014). Clinical data including height and weight on the day of surgery and presence or absence of T2D and exclusion criteria were obtained from the patients’ clinical records. Vitamin B12 and zinc levels were measured by the UCLH Department of Clinical Biochemistry using a competitive immunoassay (Roche) and colorimetric assay (Randox) respectively, as part of routine post-surgical care.

After RYGB or SG surgery, patients are advised to adhere to a soft diet for the first two post-operative weeks, followed by a soft diet with gradual reintroduction of solid food. Patients start eating meals of normal textured food 7 weeks after surgery. Thus, in order to eliminate the effect of early post-operative dietary restriction and allow for their eating behaviour to be established, patients less than 90 days post-surgery were excluded. Patients with factors affecting gustatory (including low zinc and low vitamin B12 levels) or olfactory function or who suffered a severe or debilitating illness, active malignancy and pregnant women were also excluded.
Percentage weight loss (%WL) was calculated by the weight difference between the day of surgery and the day of questionnaire completion and expressed as percentage of the weight on the day of surgery. Data were analysed using GraphPad Prism version 6 and STATA statistical software version 13. Mean and standard error of mean (SEM) were calculated. Continuous data was assessed for normality using D’Angostino and Pearson omnibus normality test. Parametric (t-test or one-way analysis of variance (ANOVA) and non-parametric tests (Mann-Whitney tests)) were used as appropriate. Chi-square tests were used for categorical data. Furthermore, linear regression analyses were performed. Significance was assumed below the 0.05 level.

Results

Patient demographics

253 patients were included in the final analysis, 98 following RYGB and 155 post-SG. 37 patients were excluded from the study due pregnancy (n=8), B12 and/or zinc deficiency (n=4), symptomatic hypoglycaemia (n=3), conversion of SG to RYGB (n=8), active malignancy (n=4), previous cranial radiotherapy (n=1), anosmia (n=2), intolerance to solid foods (n=2), severe illness or reduced mobility (n=4) and inability to read English (n=1). Out of the included patients, 199 (79%) were female and 54 (20%) male. The patient characteristics are presented in Table 1. The RYGB and SG groups had a similar age and BMI but %WL and time post-surgery were significantly greater in the RYGB group.

Table 1: Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Age (years)</th>
<th>BMI (kg/m²)</th>
<th>%WL</th>
<th>Time post-surgery (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RYGB</td>
<td>46.5 ±1.1</td>
<td>44.7 ± 0.7</td>
<td>25.6 ± 0.9</td>
<td>769 ± 53</td>
</tr>
<tr>
<td>n=98 (M=19, F=79)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SG</td>
<td>44.3 ± 1.0</td>
<td>46.1 ± 0.6</td>
<td>21.2 ± 0.8</td>
<td>593 ± 43</td>
</tr>
<tr>
<td>n=155 (M=35, F=120)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p value 0.120 0.260 0.0001 0.001

Mean age, Body Mass Index (BMI), percentage weight loss (%WL) and time post-surgery in patients following Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG)

Subjective changes in appetite, taste and smell post-surgery

The majority of patients reported post-operative change in appetite (Figure 1A, Question 1). Changes in taste and to a lesser extent smell were observed following both RYGB and SG, as were the development of food aversions (Figure 1B, 1C and 1D). While there were no significant differences in appetite, taste and food aversions between the two groups, smell changes were significantly more common following RYGB compared to SG (RYGB=41%, SG=28%, p=0.039).
In view of evidence regarding difference in taste perception between males and females, we examined the influence of gender upon the frequency of reported appetite, taste and smell changes and development of food aversions. No significant differences were found when comparing responses of female and male patients following RYGB (Table 2). However, within the SG group, taste and smell changes were significantly more common in female compared to male patients (Table 2). Furthermore, men post-SG lost significantly less weight compared to men following RYGB (%WL: RYGB=26.7 ± 2.13, SG=18.7 ± 1.7 p=0.004).

(Figure 1 here)

Table 2: Gender differences in the prevalence of subjective appetite, taste, smell changes and food aversions

<table>
<thead>
<tr>
<th></th>
<th>RYGB Group (%) of patients/number reporting post-surgery change</th>
<th>SG Group (%) of patients/number reporting post-surgery change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Females Males p value</td>
<td>Females Males p value</td>
</tr>
<tr>
<td><strong>Appetite changes</strong></td>
<td>92.4% (73) 84.2% (16) 0.370</td>
<td>91.7% (110) 88.6% (31) 0.521</td>
</tr>
<tr>
<td><strong>Taste changes</strong></td>
<td>62.0% (49) 73.7% (14) 0.341</td>
<td>65% (78) 40% (14) 0.008</td>
</tr>
<tr>
<td><strong>Smell changes</strong></td>
<td>41.8% (33) 36.8% (7) 0.695</td>
<td>31.7% (38) 14.3% (5) 0.043</td>
</tr>
<tr>
<td><strong>Food aversions</strong></td>
<td>45.7% (49) 66.7% (12) 0.713</td>
<td>62.3% (76) 45.7% (16) 0.062</td>
</tr>
</tbody>
</table>

Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG)

Influence of time post-surgery upon subjective changes in appetite, taste, smell, food aversions and %WL

In light of the cross-sectional nature of our study, we investigated the effect of time since surgery on patients reporting perceived changes in appetite, taste and smell (Table 3). Following RYGB, no differences were found in the frequency of changes in appetite, taste, smell and food aversions at different time points. In contrast, following SG, the prevalence of subjective appetite changes decreased after 3 years (Table 3). The prevalence of taste and smell changes also reduced with time post-SG but these failed to reach significance. Following RYGB, maximum %WL was achieved at 1-2 years post-surgery and was similar at 2-3 years and 3-5 years post-RYGB (Table 4). Maximum %WL following SG was also observed at 1-2 years post-surgery and was comparable to that seen in the RYGB group. %WL decreased with time post-surgery in the SG group (Table 4). Comparison of 2-5 year %WL between the RYGB and SG groups revealed greater %WL post-RYGB (%WL; RYGB=26.2±1.3, SG=20.8 ±1.9, p=0.023).
Table 3: Effect of time post-surgery on the prevalence of food aversions, subjective changes in appetite, taste and smell changes

<table>
<thead>
<tr>
<th>Time post-surgery</th>
<th>RYGB Group</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Change in appetite</td>
<td>Change in taste</td>
<td>Change in smell</td>
<td>Food aversions</td>
</tr>
<tr>
<td>&lt; 180 days (n=6)</td>
<td>100.0%</td>
<td>50.0%</td>
<td>50.0%</td>
<td>66.7%</td>
</tr>
<tr>
<td>180-364 days (n=24)</td>
<td>83.3%</td>
<td>62.5%</td>
<td>45.8%</td>
<td>54.2%</td>
</tr>
<tr>
<td>p value</td>
<td>0.468</td>
<td>0.458</td>
<td>0.855</td>
<td>0.709</td>
</tr>
<tr>
<td>1-2 years (n=23)</td>
<td>95.7%</td>
<td>73.9%</td>
<td>43.5%</td>
<td>65.2%</td>
</tr>
<tr>
<td>p value</td>
<td>0.267</td>
<td>0.289</td>
<td>0.817</td>
<td>0.528</td>
</tr>
<tr>
<td>2-3 years (n=16)</td>
<td>100%</td>
<td>62.5%</td>
<td>31.3%</td>
<td>62.5%</td>
</tr>
<tr>
<td>p value</td>
<td>0.202</td>
<td>0.795</td>
<td>0.292</td>
<td>0.879</td>
</tr>
<tr>
<td>3-5 years (n=29)</td>
<td>86.2%</td>
<td>62.1%</td>
<td>37.9%</td>
<td>65.5%</td>
</tr>
<tr>
<td>p value</td>
<td>0.306</td>
<td>0.767</td>
<td>0.706</td>
<td>0.665</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time post-surgery</th>
<th>SG Group</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Change in appetite</td>
<td>Change in taste</td>
<td>Change in smell</td>
<td>Aversions</td>
</tr>
<tr>
<td>&lt; 180 days (n=36)</td>
<td>97.2%</td>
<td>75.0%</td>
<td>44.4%</td>
<td>58.5%</td>
</tr>
<tr>
<td>180-364 days (n=41)</td>
<td>100.0%</td>
<td>65.9%</td>
<td>24.4%</td>
<td>68.3%</td>
</tr>
<tr>
<td>p value</td>
<td>0.283</td>
<td>0.321</td>
<td>0.063</td>
<td>0.879</td>
</tr>
<tr>
<td>1-2 years (n=27)</td>
<td>88.9%</td>
<td>48.1%</td>
<td>14.8%</td>
<td>59.3%</td>
</tr>
<tr>
<td>p value</td>
<td>0.072</td>
<td>0.065</td>
<td>0.067</td>
<td>0.485</td>
</tr>
<tr>
<td>2-3 years (n=19)</td>
<td>84.2%</td>
<td>57.9%</td>
<td>21.1%</td>
<td>52.6%</td>
</tr>
<tr>
<td>p value</td>
<td>0.722</td>
<td>0.797</td>
<td>0.499</td>
<td>0.309</td>
</tr>
<tr>
<td>3-5 years (n=32)</td>
<td>78.1%</td>
<td>43.8%</td>
<td>28.1%</td>
<td>43.8%</td>
</tr>
<tr>
<td>p value</td>
<td>0.001</td>
<td>0.110</td>
<td>0.056</td>
<td>0.068</td>
</tr>
</tbody>
</table>

Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG). Fisher’s exact correlation, p values represent comparison of given time interval versus previous data.
Table 4: Weight loss at different time points following RYGB and SG

<table>
<thead>
<tr>
<th>Time post-surgery</th>
<th>%WL in RYGB patients</th>
<th>%WL in SG patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 180 days</td>
<td>18.8 ± 2.2</td>
<td>17.0 ± 1.0</td>
</tr>
<tr>
<td>180-364 days</td>
<td>24.6 ± 1.4</td>
<td>23.1 ± 1.1</td>
</tr>
<tr>
<td>1-2 years</td>
<td>27.4 ± 1.9</td>
<td>26.2 ± 1.9</td>
</tr>
<tr>
<td>2-3 years</td>
<td>26.1 ± 1.9</td>
<td>19.9 ± 3.3</td>
</tr>
<tr>
<td>3-5 years</td>
<td>26.3 ± 1.8</td>
<td>20.3 ± 2.1</td>
</tr>
</tbody>
</table>

Roux-Y gastric bypass (RYGB), sleeve gastrectomy (SG), percentage weight loss (%WL)

Relationship between subjective changes in appetite, taste, smell, food aversion and %WL

We investigated the relationship between post-operative changes in appetite, taste, smell, food aversions and %WL. In the RYGB group there was significant association between a change in taste and higher %WL (27.8 ± 1.0 vs. 23.1 ± 1.6, p=0.036). In the SG group a significantly higher %WL was detected in patients with a change in appetite (21.9 ± 0.8 vs. 13.4 ± 3.1, p=0.006) and food aversions (22.6 ± 1 vs. 19.2 ± 1.3, p=0.032). However, there was no association between subjective taste changes and %WL.

Table 5: %WL in patients with and without subjective changes in appetite, taste, smell and food aversion post-RYGB

<table>
<thead>
<tr>
<th></th>
<th>Appetite</th>
<th>Taste</th>
<th>Smell</th>
<th>Food aversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change</td>
<td>25.8 ± 0.9</td>
<td>27.8 ± 1.0</td>
<td>26.3 ± 1.5</td>
<td>26.5 ± 1.1</td>
</tr>
<tr>
<td></td>
<td>n=89</td>
<td>n=63</td>
<td>n=40</td>
<td>n=61</td>
</tr>
<tr>
<td>No change</td>
<td>23.8 ± 3.2</td>
<td>23.1 ± 1.6</td>
<td>25.2 ± 1.1</td>
<td>24.2 ± 1.2</td>
</tr>
<tr>
<td></td>
<td>n=9</td>
<td>n=35</td>
<td>n=58</td>
<td>n=37</td>
</tr>
<tr>
<td>p value</td>
<td>0.435</td>
<td>0.036</td>
<td>0.595</td>
<td>0.111</td>
</tr>
</tbody>
</table>

Roux-en-Y gastric bypass (RYGB), percentage weight loss (%WL)

Table 6: %WL in patients with and without subjective changes in appetite, taste, smell and food aversion post-SG

<table>
<thead>
<tr>
<th></th>
<th>Appetite</th>
<th>Taste</th>
<th>Smell</th>
<th>Food aversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change</td>
<td>21.9 ± 0.8</td>
<td>21.9 ± 1.0</td>
<td>21.7 ± 1.8</td>
<td>22.6 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>n=141</td>
<td>n=92</td>
<td>n=43</td>
<td>n=92</td>
</tr>
<tr>
<td>No change</td>
<td>13.4 ± 3.1</td>
<td>20.3 ± 1.3</td>
<td>21.1 ± 0.9</td>
<td>19.2 ± 1.3</td>
</tr>
<tr>
<td></td>
<td>n=14</td>
<td>n=63</td>
<td>n=112</td>
<td>n=63</td>
</tr>
<tr>
<td>p value</td>
<td>0.006</td>
<td>0.520</td>
<td>0.772</td>
<td>0.032</td>
</tr>
</tbody>
</table>

Sleeve gastrectomy (SG), percentage weight loss (%WL)

Subjective changes in taste towards sweet and salty foods

Patients were asked if they had experienced a change in their taste towards sweet and salty foods. They were asked separately if they had experienced an increase or decrease in the
taste of sweet or salty tasting foods (Appendix: Questions 9, 10, 12 and 13). 87.8% of RYGB patients responded that their taste for sweet foods had either increased or decreased compared to 65.2% of SG patients (p=0.001). Changes in taste towards salty tasting foods were also significantly more common following RYGB (% of patients reporting change in taste towards salty tasting foods: RYGB =56.1, SG= 40.6%, p=0.020, Figure 2).

Following RYGB, there were no gender differences in subjective taste change towards sweet foods (females 89% and males 84%, p=0.685). However, post-SG a change in taste towards sweet foods, either an increase or decrease, was significantly more common in females compared to males (females 70% and males 45%, p=0.009).

(Figure 2 here)

Influence of T2D

T2D was present in 92 patients (53 RYGB and 39 SG). No differences were seen in the prevalence of subjective change in appetite, taste, smell or food aversion between individuals with and without T2D post-RYGB (appetite change: no T2D=93.3%, T2D=88.7%; taste change: no T2D=73.3%, T2D=56.6%, smell change: no T2D=40%, T2D=41.5%; food aversions: no T2D=62.2%, T2D=62.3%; all p > 0.05) or post-SG (appetite change: no T2D=89.7%, T2D=94.9%; taste change: no T2D=62.1%, T2D=51.3%, smell change: no T2D=26.7%, T2D=30.8%; food aversions: no T2D=62.1%, T2D=51.3%; all p > 0.05). However, within the SG group, taste changes were significantly less common in males with T2D compared to females with T2D (% of patients reporting change in taste: T2D females=61.3%, T2D males=12.5%, p=0.020. Furthermore, taste changes were less common in males with T2D following SG than post-RYGB (change in taste prevalence: T2D men RYGB=69.2%, T2D men SG=12.5%, p=0.024). Moreover, %WL was significantly lower in male T2D patients following SG compared to post-RYGB (%WL: SG=14.6 ± 2.1, RYGB=27.5 ± 2.7, p=0.003).

Table 7: Frequency of reported appetite, taste, smell changes and food aversions by gender in patients with T2D following RYGB and SG.

<table>
<thead>
<tr>
<th></th>
<th>RYGB Females</th>
<th>RYGB Males</th>
<th>p value</th>
<th>SG Females</th>
<th>SG Males</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appetite</td>
<td>87.5%</td>
<td>92.3%</td>
<td>0.370</td>
<td>96.8%</td>
<td>87.5%</td>
<td>0.372</td>
</tr>
<tr>
<td>Taste</td>
<td>52.5%</td>
<td>69.2%</td>
<td>1.0</td>
<td>61.3%</td>
<td>12.5%</td>
<td>0.019</td>
</tr>
<tr>
<td>Smell</td>
<td>42.5%</td>
<td>38.5%</td>
<td>1.0</td>
<td>35.5%</td>
<td>12.5%</td>
<td>0.393</td>
</tr>
<tr>
<td>Food aversions</td>
<td>65.0%</td>
<td>53.4%</td>
<td>0.522</td>
<td>58.1%</td>
<td>25%</td>
<td>0.123</td>
</tr>
</tbody>
</table>

Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG)

Predictors of weight loss

Linear regression analyses were performed in order to correct for characteristics within groups and identify predictors of %WL. The models for RYGB and SG patients are illustrated in Table 8. The basic model (M1) adjusted for gender and days since surgery. Subjective taste changes following surgery were associated with greater %WL post-RYGB, even after adjusting for gender, age, duration since surgery and the presence of T2D. In contrast, post-SG,
subjective taste change was not related to %WL. However, in patients post-SG subjective change in appetite strongly associated with greater %WL after adjusting for gender, age, duration since surgery and T2D, which is not observed in RYGB.

Table 8: Linear regression model testing %WL by appetite, taste, smell and aversions

<table>
<thead>
<tr>
<th>Model</th>
<th>Appetite</th>
<th>Taste</th>
<th>Smell</th>
<th>Aversions</th>
</tr>
</thead>
</table>
| RYGB  
Basic Model (M1) | Coefficient (95% CI) | Coefficient (95% CI) | Coefficient (95% CI) | Coefficient (95% CI) |
|               | 2.4 (-3.5; 8.4) | 4.0 (0.5; 7.5)* | 1.3 (-2.2; 4.9) | 1.1 (-2.6; 4.8) |
| M1 + age      | 2.5 (-3.4; 8.4) | 3.6 (0.7; 7.1)* | 1.1 (-2.4; 4.5) | 0.9 (-2.7; 4.5) |
| M1 + T2D      | 2.3 (-3.7; 8.3) | 3.8 (0.2; 7.4)* | 1.4 (-2.1; 4.9) | 1.3 (-2.4; 4.7) |
| SG  
Basic Model (M1) | 8.1 (2.5; 13.7)** | 0.9 (-2.5; 4.3) | 0.1 (-3.5; 3.7) | 3.1 (-0.1; 6.4) |
| M1 + age      | 8.7 (3.2; 14.1)** | 0.6 (-2.7; 3.9) | 0.4 (-3.2; 3.9) | 2.8 (-0.5; 5.9) |
| M1 + T2D      | 8.9 (3.4; 14.9)** | 0.5 (-2.8; 3.9) | 0.3 (-3.2; 3.8) | 2.8 (-0.4; 6.0) |

* p<0.05, ** p<0.01; Basic model adjusts for gender and days since surgery

Discussion

In this cross-sectional study we examined the prevalence of food aversions and subjective changes in appetite, taste and smell in a cohort of patients 6 months to 5 years following primary RYGB or SG. Our cohort included the largest SG group examined to date with the longest duration post-surgery. Our data show that whilst subjective changes in appetite, taste, smell and food aversions are common following both RYGB and SG they differ in their impact on subjective changes in smell and taste, durability of changes, influence of gender and relationship with %WL.

In the RYGB group the prevalence of changes in appetite, taste, smell and food aversions was similar across all periods examined, with 86% of patients reporting appetite changes and 64% taste changes 3-5 years following RYGB. We observed no influence of gender or T2D status upon changes in appetite, taste or smell. %WL was similar at 1-2, 2-3 and 3-5 years post-surgery. Linear regression analysis showed that subjective taste changes associated with and predicted %WL.

After SG, smell changes were less common than after RYGB, as were also changes in taste towards sweet and salty tasting foods. The prevalence of changes in appetite significantly decreased with time post-surgery; the prevalence of changes in taste, smell and food aversion showed a trend to decrease with time post-surgery. Importantly, following SG the prevalence of changes in taste and smell was lower in males compared to females particularly in male patients with T2D. While %WL was comparable between RYGB and SG during the first post-
operative 2-year period, between 2-5 years %WL was significantly greater in the RYGB group at 2-5 years post-surgery compared to the SG group. Subjective appetite changes associated with and predicted %WL in the SG group.

Gender differences in taste sensitivity have been reported in obesity (Doty & Cameron, 2009; Hwang et al., 2016). Similarly, T2D, which is known to impact upon gut hormone profiles, has also been suggested to affect taste sensitivity, particularly toward sweet tasting foods (Bustos-Saldana et al., 2009). However, until now, no data existed with regards to effects of gender or T2D on appetite, taste or smell in patients following bariatric surgery. While no significant gender differences were seen within our RYGB group, there was a marked gender effect following SG. In particular, following SG the prevalence of taste changes was significantly lower in males with T2D compared to females with T2D. Moreover, the prevalence of taste changes and %WL were significantly lower in males with T2D following SG compared to RYGB. Our findings highlight the need for further research into the underlying physiology of these gender differences.

The role of weight loss in mediating subjective changes in taste and smell remains to be clarified. Interestingly, reduced subjective taste and smell following GI surgery were first reported in normal weight patients as a transient complication following gastrectomy and oesophagectomy for GI malignancies (Harris & Griffin, 2003), suggesting that these changes are not restricted to people with obesity. In our cohort, the prevalence of smell changes was greater in the RYGB group compared to the SG despite comparable %WL during the first two post-operative years, suggesting weight independent processes may be involved. The perception of flavour is thought to be predominantly mediated through smell (Yeomans, 2006), thus our findings of much higher prevalence of taste changes compared to smell changes following RYGB and SG is somewhat surprising. However, recent studies have identified gut hormone receptors on taste buds, gut hormones within saliva and postulated a role for saliva gut hormones in taste modulation (Acosta et al., 2011; Y. K. Shin et al., 2008). Circulating levels of gut hormones, in particular ghrelin, GLP-1 and PYY, change post-operatively (Yousseif et al., 2014). Thus, these changes offer not only a plausible biological explanation for appetite changes post-surgery but also for the higher prevalence of taste compared to smell changes. In addition, the differential gut hormone pattern observed following RYGB and SG may underlie the procedural differences in appetite, taste and smell post-surgery (Cummings, 2015; Fabian et al., 2015). Longitudinal studies examining hormone levels in blood and saliva coupled with subjective and objective assessments of appetite, taste and smell in large cohorts of males and females undergoing RYGB and SG are now needed.

Our study does have limitations. The study was cross-sectional, which resulted in a large variation in time post-surgery. Reported changes in appetite, taste and smell were subjective and no control group was included. In addition, since no data was collected pre-operatively, our data could be subject to recall bias, which is likely to increase with longer duration from surgery. Furthermore, the number of male participants in our study cohort was small. However, this reflects the higher number of females undergoing bariatric surgery in the UK compared to males (Wellbourn R, 2014). Our findings of appetite, taste, smell changes and food aversions include the largest cohort of SG patients to date. Our SG sample size was larger compared to the RYGB group, while the post-RYGB patients had a significantly longer duration since surgery, which reflects the increasing popularity of SG over recent years and the trend
to perform a higher number SG (Angrisani et al., 2015). The higher %WL in the RYGB group is in concordance with previous findings from studies that have compared post-operative outcomes between RYGB and SG (Schauer et al., 2014; Szepaniak et al., 2015). Similarly, weight loss post-RYGB was also higher compared to SG in the study conducted by Zerrweck et al (Zerrweck et al., 2015). The higher percentage of T2D in the RYGB population reflects that RYGB remains the preferred procedure in T2D, given the better T2D outcomes post-RYGB in the literature (Schauer et al., 2014). Graham et al. and Zerrweck et al. reported associations with food aversions and weight loss (Graham et al., 2014; Zerrweck et al., 2015). This effect was observed only following SG in our cohort. However, the wording of the question relating to food aversions did not allow for a clear distinction between true food aversions, and post-ingestive phenomena such as dumping syndrome. This ambiguity needs to be borne in mind when interpreting these results, as food tolerance and GI quality of life may play a role as aversive drivers of eating behaviour (Overs, Freeman, Zarshenas, Walton, & Jorgensen, 2012). Furthermore, feedback from our participants also highlighted the ambiguity of some of the questions, particularly relating to “increase” or “loss” of taste.

Nevertheless, compared to previous studies, our study design has several strengths and provides novel findings. We obtained consent in person and completed data collection in one visit. Our exclusion criteria allowed for elimination of patients with additional factors that could impact on %WL, including low B12 and zinc. Furthermore, in contrast to previous studies we have used %WL as our outcome for weight loss, in order to avoid for confounding outcomes by pre-operative BMI. Our analysis identified procedure dependent differences in appetite, taste, smell changes and their impact upon %WL. In addition, we investigated the effect of gender and found marked gender differences within the SG group that are exacerbated by the presence of T2D. Finally, we performed linear regression analyses and thereby, for the first time, identified appetite and taste changes as predictors of %WL for SG and RYGB respectively.

In conclusion, whilst subjective changes in appetite, taste, smell and food aversions are common following both RYGB and SG, marked differences between them exist in relation to the prevalence of changes in smell, taste, durability of changes, influence of gender and %WL. The presence of gender differences highlights the need to study comparable numbers of males and females. Furthermore, correlating gut hormone profiles with appetite and taste changes, will not only aid to further our understanding of the biological mediators for weight loss post-bariatric surgery allowing for personalised procedure allocation but may also lead to novel therapies, such as taste modulation approaches.

Acknowledgements

We would like to thank all members, past and present, of the University College London Hospitals Bariatric Group and all our patients. This work was supported by the Rosetrees Trust, Stoneygate Trust and the National Institute for Health Research.
Figure Legends

Figure 1: Frequency of reported appetite, taste, smell changes and food aversions following Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG)

A: Appetite changes (Q1) B: Taste changes (Q2) C: Smell changes (Q3) D: Food aversions (Q4)

Figure 2: Change in taste toward sweet and salty foods

Reported frequency of increased and decreased taste toward sweet (A) and salty (B) tasting foods in Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) respectively.
References


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Appendix

Taste and smell questionnaire

Please circle the most appropriate answer or circle the relevant number on the scale (1-10)

Q1. Have you noticed any change in your appetite since your weight loss surgery? 
YES/ NO

Q2. Have you noticed any change in the taste of food or drink since your weight loss surgery? 
YES/ NO

Q3. Have you noticed any change in your sense of smell since your weight loss surgery? 
YES/ NO

Q4. Have you experienced an overall loss of taste since your weight loss surgery? 
YES/ NO

If you answered YES to the above questions please continue. If you answered NO to all of the above questions, do not proceed any further. Please return the questionnaire.

Q5. If you have had a loss of taste, is that loss:

No loss  Partial  Complete

1  2  3  4  5  6  7  8  9  10

Q6. Are there any foods that are repulsive or intolerable to you since your weight loss surgery? 
YES/ NO

If you answered yes then please state what:

Q7. Are there any foods that taste different to you since your weight loss surgery? 
YES/ NO

If yes, please state what food:
Q8. Has your overall taste increased in intensity since your weight loss surgery?
YES/ NO

Q9. Have you experienced an increase in taste for sweet foods?
YES/ NO

Q10. Have you experienced a decrease in taste for sweet foods?
YES/ NO

Q11. If you have had a loss of sweet taste, is that loss:
No loss Partial Complete

Q12. Have you experienced an increase in taste for salty foods?
YES/ NO

Q13. Have you experienced a decrease in taste for salty foods?
YES/ NO

Q14. If you have had a loss of salty taste, is that loss:
No loss Partial Complete

Q15. Have you experienced an increase in taste for sour foods?
YES/ NO
Q16. Have you experienced a decrease in taste for sour foods?

YES/ NO

Q17. If you have had a loss of sour taste, is that loss:

<table>
<thead>
<tr>
<th>No loss</th>
<th>Partial</th>
<th>Complete</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>10</td>
<td></td>
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</tbody>
</table>

Q18. Has this change in taste affected how much you eat?

YES/ NO

Q19. In your opinion, has your change in taste affected your weight loss?

YES/ NO

Q20. Overall, do you feel that your taste has increased or decreased in intensity since your weight loss surgery?

Increased/ Decreased

Q21. In your opinion, does loss of taste lead to better weight loss?

YES/ NO

Q22. Is your postoperative change in taste greater or less than what you expected preoperatively?

Greater/ Less

Q23. How important is taste to the enjoyment of food?

Important/ Not important

Q24. Have you experienced an overall loss in your sense of smell since your weight loss surgery?

YES/ NO
Q25. If you have had a loss of smell, is that loss:

<table>
<thead>
<tr>
<th>No loss</th>
<th>Partial</th>
<th>Complete</th>
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</thead>
<tbody>
<tr>
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<td>10</td>
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</table>

Q26. Are there any foods that smell differently to you since your weight loss surgery?

YES/ NO

If yes, please state what food?

Q27. In your opinion, has your change in smell affected your weight loss?

YES/ NO

Q28. Overall, do you feel that your smell has increased or decreased in intensity since your weight loss surgery?

Increased/ Decreased

Q29. Is your postoperative change in smell greater or less than what you expected preoperatively?

Greater/ Less

Q30. How important is smell to the enjoyment of food?

Important/ Not important

Q31. Do you eat less food because it does not taste or smell good?

YES/ NO

Q32. Do you eat less food because you are simply not hungry?

YES/ NO
Q33. Is your postoperative change in appetite greater or less than what you expected preoperatively?

Greater/ Less