RELATIONSHIP OF APPETITE, OLFACTION AND FOOD REWARD AFTER ROUX-EN-Y GASTRIC BYPASS SURGERY: COULD THIS EXPLAIN WEIGHT REGAIN?

THESIS

By
Jennifer Brown, BSc., RD

Submitted to the Faculty of Graduate and Postdoctoral Studies in Partial Fulfillment of the Requirements for the Degree of Masters of Science

School of Human Kinetics
Faculty of Health Sciences
University of Ottawa

ABSTRACT

Background: Roux-en-y gastric bypass (RYGB) surgery produces significant weight loss, however a number of patients experience some and/or complete recidivism of weight years after surgery. Limited research has investigated why patients are experiencing weight regain after surgical interventions. Our objective was to identify appetite-related measures associated with weight regain after RYGB surgery.
Methods: Using a cross-sectional design, 29 participants (49.6 ± 9.1 years of age; 29-62 months post-RYGB) were divided into three weight categories; (weight maintainers, n = 9; low weight regainers, n = 10; and high weight regainers, n = 10). Appetite, smell function, eating behaviours and food reward were measured in response to a standardized meal.
Results: Weight regain increased significantly in association with time after surgery (r_s = 0.768, p = 0.016). High regainers gained on average 8.6 kg/year, compared to low regainers and maintainers, 3.8 ± 0.9 kg/year and 0.9 ± 0.9 kg/year, respectively (p < 0.001). Dietary restraint (using the Three Factor Eating Questionnaire) was significantly higher in weight maintainers and low regainers compared to high regainers using clinical subscales ($p < 0.05$). Weight regain was associated with higher "liking" of high-fat sweet foods (measured with the Leeds Food Preference Questionnaire) among high weight regainers.
Conclusion: Weight regain after RYGB may be associated with higher preferences for high-fat sweet foods, whereas, higher dietary restraint may be associated with lower wanting of high-fat sweet foods among weight maintainers. Findings provide insight into why some patients after RYGB regain weight, while others maintain their weight. Future research is needed to further explore the relationships between appetite-related factors and weight regain after RYGB employing a longitudinal study design.

Key words: Roux-en-y gastric bypass; weight regain; appetite; olfactory (smell) function; food reward; eating behaviours.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

BMI: Body Mass Index

RYGB: Roux-en-Y Gastric Bypass

EWL: Excess Weight Loss

%EWL: Percentage Excess Weight Loss

EBW: Excess Body Weight

TWL: Total Weight Loss

%TWL: Percentage Total Weight Loss

PYY: Peptide YY

GLP-1: Glucagon-like Protein

VAS: Visual Analog Scale

WMC: The Ottawa Hospital Weight Management Clinic

EDTA: Ethylenediamine Tetraacetic Acid

TFEQ: Three Factor Eating Questionnaire

LFPQ: Leeds Food Preference Questionnaire

SPSRQ: Sensitivity to Punishment and Sensitivity to Reward Questionnaire

ACKNOWLEDGMENTS

I would like express my sincere gratitude and appreciation to all my family, friends, colleagues and patients for making this thesis a reality.

My deepest gratitude to my supervisor, Dr. Eric Doucet, for your enthusiasm, invaluable support and passion for this field; you bring such an empowering vision and interest to the field of physiology and weight regulation. Thank you for being such an inspiration! Special thanks to my co-supervisor and colleague, Dr. Bob Dent for your support and belief in me; you are truly a trail-blazer in the field of weight management and I am proud and honored to have learned so much from you. My sincere gratitude to my committee advisors, Dr. Gary Goldfield and Dr. Denis Prud'homme for your commitment and suggestions throughout this process. As well as everyone at the Behavioural and Metabolic Research Unit (BMRU); thank you Vicki Burns and Luzia J. Hintze for all your assistance and last minute support! Jessica McNeil, my utmost appreciation for all your help with stats and questions in the lab! But I literally, could not have done this without Ann Beninato, my angel and partner-in-crime! Thank you for being such a great nurse, person and friend! (You're a "superstar"!!)

My sincere gratefulness to my colleagues and my manager, Michelle Foulkes, at The Ottawa Hospital Weight Management Clinic. Thank you to everyone that kept me motivated and supported me during my ups and downs.

None of this would have been possible without my participants; thank you a thousand times for your commitment and on-going interests to support my research. I am inspired every day by your relentless pursuit and drive to improve your health and wellbeing. Because of you, my passion for research and searching for answers is possible!

Finally and most important, my family; thank you to my parents, Jim and Barb Brown, your unwavering love and support has been incredible. My sister, Laura Clarke for always being just-a-call away to keep me laughing and smiling; and to my husband, my best-friend and my biggest supporter during these difficult years, Dennis Vowles. You have been my rock, my number-one enthusiast and I could not have done this without you. Thank you for making the sacrifices you've made, supporting our family and always believing in me. I love you….. "It's all about teamwork and compromise"!

CHAPTER 1: INTRODUCTION

Roux-en-Y gastric bypass (RYGB) surgery is considered the gold standard in regards to surgical options for the management of severe obesity (Adams et al., 2012; Buchwald et al., 2004; Colquitt, Clegg, Loveman, Royle, & Sidhu, 2005; Picot, Jones, Colquitt, Loveman, & Clegg, 2012; Sjostrom et al., 2007; Sjostrom et al., 2012; Sugerman, Wolfe, Sica, & Clore, 2003). It has been reported that patients will lose approximately 20-30% of their total body weight (TBW) or 50-80% of their excessive body weight within the first 2 years after surgery (Adams et al., 2012; Buchwald et al., 2004; Christou, Look, & Maclean, 2006; J. Karlsson, Taft, Ryden, Sjostrom, & Sullivan, 2007; Ortega et al., 2012; Pories et al., 1995; Sjostrom et al., 2004; Sjostrom et al., 2012; Sugerman et al., 2003; Wittgrove & Clark, 2000). Excess body weight; also referred to as excess weight loss (EWL) is defined as (weight loss/excess weight), where excess weight refers to pre-surgical weight – ideal body weight using a BMI of 24.9 kg/m^2. Although a number of patients have successful weight loss long term (Buchwald et al., 2004; Sjostrom et al., 2004; Sjostrom et al., 2012), it has been documented that approximately 20-30% of patients will regain weight (Christou et al., 2006; Faria, de Oliveira Kelly, Lins, & Faria, 2010; Freire, Borges, Alvarez-Leite, & Toulson Davisson Correia, 2012; Magro et al., 2008; Meguid, Glade, & Middleton, 2008; Melton, Steele, Schweitzer, Lidor, & Magnuson, 2008; Wittgrove & Clark, 2000). This can have a detrimental effect on the health care system; with the return of co-morbidities requiring long-term treatment and management. Not to mention the devastating impact weight regain can have on the patient; their physical health, mental health and overall quality of life.

There appears to be a gap in the literature as to what drives the positive energy balance in patients who regain weight following RYGB. Some have found an increase in caloric intake (Faria et al., 2010; Freire et al., 2012; Kruseman, Leimgruber, Zumbach, & Golay, 2010; Meguid et al., 2008), derived from eating higher sugar and higher fat foods (Freire et al., 2012; Warde-Kamar, Rogers, Flancbaum, & Laferrere, 2004). Others have speculated changes to the peripheral hormones that are said to be the driving mechanisms for satiety after surgery however amongst the abundance of studies that have tested peripheral hormones up to 4 year post-RYBG (Beckman, Beckman, & Earthman, 2010); no study, to our knowledge has investigated the peripheral hormones in patients that have regained weight as it relates to appetite. This study will investigate appetite measures associated with weight change after RYGB surgery, specifically looking at appetite sensations, smell function, eating behaviours and food reward. This study will also measure peripheral hormones ghrelin, PYY, GLP-1 and leptin, however data presented in this paper will not include the results of peripheral hormone results (results will be presented in a future paper). A secondary aim of this study will also investigate smell performance among these groups and compare appetite (desire to eat, hunger, satiety, prospective food consumption, and food reward) to determine if other factors are contributing to weight regain.

CHAPTER 2: REVIEW OF LITERATURE

Roux-en-Y Gastric Bypass – Mechanism for Weight Loss

Roux-en-Y gastric bypass (RYGB) is a restrictive and malabsorptive procedure which results in a 30 mL gastric pouch that is divided from the stomach. The jejunum is anastomosed to the new pouch allowing a 100 cm Roux limb to bypass the stomach, duodenum and proximal jejunum resulting in the malabsorptive nature of the surgery. The remaining biliopancreatic limb (75 cm) is then anastomosed to the proximal jejunum creating a common channel (figure 1). The mere volume restriction from this procedure results in a negative energy balance, ultimately contributing to the rapid weight loss observed after this surgery. Flauchbaum et al. reported a dramatic decline in caloric intake from 2603±982 kcal preoperatively to 677±204 kcal, 815±196 kcal, 969±241 kcal, 1095±307 kcal, 1259±466 kcal, and 1373±620 kcal at 6 weeks, 3, 6, 12, 18 and 24-months post-operative, respectively (Flancbaum, Choban, Bradley, & Burge, 1997). Similar results have been reported (table 1). This restricted caloric intake and the physical bypassing of the stomach and duodenum results in suboptimal vitamin and mineral absorption as food is not directly exposed to stomach acids or enzymes produced by the liver, pancreas or duodenum.

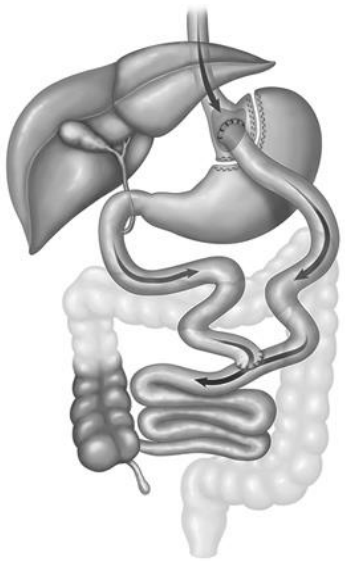

Figure 1. Roux-en-y gastric bypass (RYGB) Surgery

Table 1. Caloric intake before and after RYGB surgery

Study	n	Pre-op	1 month	3 month	6 month	9 month	12 month	18 month	24 month	96 month	120 month
(Bavaresco et al., 2010)	48	2347 ± 1016	773 ± 206	796 ± 306	910 ± 245	963 ± 242	1034 ± 345	-	-	-	-
(Dias et al., 2006)	40	-	-	529 ± 300	710 ± 301	833 ± 407	866 ± 343	-	-	-	-
(Flancbaum et al., 1997)	70	2603 ± 982	-	815 ± 196	969 ± 241	-	1095 ± 307	1259 ± 466	1373 ± 620	-	-
(Kruseman et al., 2010)	141	2355 ± 775	-	-	-	-	1442 ± 340	-	-	1680 ± 506	
(Sjostrom et al., 2004) (reported in Shah, 2006)	34	2882†	-	-	1500†	-	1700†	-	1800†	-	2519†
(Trostler, Mann, Zilberbush, Avinoach, & Charuzi, 1995)	19	5032 ± 708	636 ± 108	496 ± 151	1046 ± 189	1171 ± 279	1374 ± 199	1377 ± 170	-	-	-
(Brolin, Robertson, Kenler, & Cody, 1994)	108	2604 ± 1087	-	-	890 ± 407	-	1116 ± 426	1256 ± 504	1319 ± 912	-	-

Values are the mean ± SEM in kilocalories (kcal), unless specified. † Values are expressed as estimates. n = sample size; - data not available.

Defining Weight Loss after Roux-en-Y Gastric Bypass Surgery

RYGB surgery produces weight loss; however discrepancies within the literature fail to come to a consensus on standardized weight loss success after surgery. The most common method in the literature has been to measure percentage of excess weight loss (%EWL), which has historically been favored by surgeons (Dixon, McPhail, & O'Brien, 2005). Unfortunately, %EWL is dependent on a number of variables that create inconsistencies in the calculation (Montero, Stefanidis, Norton, Gersin, & Kuwada, 2011). In other words, heavier patients have poor %EWL despite having lost more total body weight (Montero et al., 2011; A. van de Laar, de Caluwe, & Dillemans, 2011). This has detrimental impacts on patient expectations and surgical program statistics. There is push to standardize "successful weight loss" with newer evidence to support the use of percentage total weight loss (%TWL), which diminishes variations (Courcoulas et al., 2013; Montero et al., 2011; A. van de Laar, 2012; A. van de Laar et al., 2011; A. W. van de Laar & Acherman, 2013). For the purpose of defining weight loss produced by RYGB, this review will highlight both methods to represent the variability seen in the literature. Multiple studies have characterized successful weight loss as >50% EWL with approximately 50-80% EWL seen within the first 2 years (Buchwald et al., 2004; Christou et al., 2006; Ortega et al., 2012; Pories et al., 1995; Schauer et al., 2003; Schauer, Ikramuddin, Gourash, Ramanathan, & Luketich, 2000; Sjostrom et al., 2012; Sugerman et al., 2003; Wittgrove & Clark, 2000). Buchwald et al. reported 62% EWL in a meta-analysis of 22,094 patients (Buchwald et al., 2004), while the Swedish Obesity Study (SOS), one of the largest multi-centered, prospective, controlled studies, followed over 2000 bariatric surgical patients over 20 years and found RYGB elicits a 23% TWL

after 2 years with weight loss maintained at 18% TWL at 20 years post-surgery (EWL data not available) (Sjostrom et al., 2012). Unfortunately, the 20-year data from the SOS is limited in that the follow-up rate from year 10 to year 20 dropped by 92% leaving only 13 participants of the original cohort. Adams et al. followed 418 RYGB patients for 6 years and reported superior weight loss maintenance with 94% and 76% maintaining at least 20% TWL at year 2 and 6, respectively (Adams et al., 2012). However, this equates to an 18% weight change over the 4 years, suggesting weight regain. In fact, further analysis of this study found that patients in the peak weight loss category (30-45% TWL) decreased by 10% in year 2 to 6. Interestingly, the shift favored the lower weight loss category (10-25% TWL) increasing by 7% from year 2 to 6, supporting the literature that weight regain occurs after 2 years from surgery (Christou, Look, & McLean, 2005; Faria et al., 2010; Freire et al., 2012; Magro et al., 2008; Meguid et al., 2008).

Weight Regain after Roux-en-Y Gastric Bypass Surgery

Despite the long-term success rates associated with weight loss from bariatric surgery, weight regain remains a growing concern. According to Christou et al. (Christou et al., 2006), 20-34% of patients that have RYGB will regain weight after 10 years. A 5-year prospective study on 782 patients found that by 2 years post-operatively, 359 patients (46%) regained a mean weight of 8.8 kg and by 4 years, this increased to 497 patients (63.6%) (Magro et al., 2008). Interestingly, a number of studies found that patients who regained weight were consuming equivalent caloric intake to before surgery or more (Faria et al., 2010; Freire et al., 2012; Meguid et al., 2008). In the literature, caloric intake after surgery varies from 820±130 kcal/day (Trostler et al., 1995) to 1634±526 kcal/day

(Kruseman et al., 2010) in successful weight loss patients after surgery (refer to Table 1). Faria et al. observed patients that had regained weight after RYGB were consuming 1885±412 kcal/day (Faria et al., 2010). While, Kruseman et al. found patients with <50% EWL compared to ≥50% EWL at 8 years post-RYGB consumed 1934±501 kcal and 1634±526 kcal ($p=0.02$), respectively (Kruseman et al., 2010). Similarly, Freire et al. (Freire et al., 2012) concluded that weight regain was associated with excessive caloric intake from sweets and snacks ($p<0.05$) and oils and fatty foods ($p<0.01$) compared to patients that had no weight regain (Freire et al., 2012). Despite the growing evidence that excessive caloric intake results in weight regain, there remains questions surrounding why RYGB patients with poor weight loss are consuming more calories from sweets and fats. One suggestion may be changes in peripheral hormones initially affected by the surgical procedure, which returns to pre-surgical levels years following the surgery, or perhaps food cravings for higher fat and sweet foods are driven by non-homeostatic factors.

Ghrelin

Ghrelin, an orexigenic hormone or appetite-stimulating hormone, secreted in the distal stomach, is known as the "hunger" hormone as it increases before a meal and is suppressed after a meal. Ghrelin is postulated to act as a protective response in relation to energy deprivation in underweight individuals and be suppressed in overweight individuals (Pournaras & Le Roux, 2009; Wren & Bloom, 2007). However, in individuals with obesity, ghrelin is not suppressed with food intake (English, Ghatei, Malik, Bloom, & Wilding, 2002; le Roux et al., 2005), resulting in a continuous "hunger" sensation. In

2002, Cummings et al (Cummings et al., 2002) found plasma ghrelin levels increased in diet-induced weight loss participants, while significantly decreased in RYGB patients, regardless of meal timing or food ingestion. This ground-breaking study led to stronger designed studies reporting similar results (Christou et al., 2005; Engstrom, Ohrvall, Sundbom, Lind, & Karlsson, 2007; Korner et al., 2005; le Roux et al., 2006; le Roux et al., 2007; Lin et al., 2004; Morinigo et al., 2004), in that plasma ghrelin levels decreased following RYGB surgery and remains low after 1 year following surgery (Christou et al., 2005; Cummings et al., 2002; le Roux et al., 2006; Tritos et al., 2003), contributing to the lack of hunger post-surgery. However, contradicting evidence by Morinigo et al. (Morinigo et al., 2004), reported ghrelin levels increased at 52 weeks post RYGB compared to levels measures at 6 weeks post-op. Similarly, Peterli et al. (Peterli et al., 2012) found ghrelin levels returned to preoperative levels after 1 year from surgery, suggesting changes to this orexigenic hormone may not be permanent. Even more controversial is the findings by Dirksen et al. (Dirksen et al., 2013) with regards to reporting higher ghrelin levels in patients that have poor weight loss compared to good weight loss responders after RYGB. Whether ghrelin levels have an effect on weight regain or poor weight loss following RYGB remains unclear, however it continues to be one of the most highly researched and controversial peripheral hormones.

PYY & GLP-1

Peptide YY (PYY) is an anorexigenic hormone secreted in the L-cells of the colon in response to contact with nutrients. PYY secretion slows gastric emptying by reducing the expression of neuropeptide Y (NPY) from the hypothalamus (Batterham et al., 2002).

The degree of PYY secretion is proportionate to the caloric load and composition of the meal (le Roux et al., 2006), raising PYY for 1-2 hours postprandially and increasing satiety levels. A number of studies have looked at PPY in patients with obesity (Sumithran et al., 2011; Wren & Bloom, 2007), and found lower fasting and postprandial levels after diet-induced weight loss, suggesting energy deprivation promotes weight regain as this anorexigenic hormone is unable to sustain satiety after diet-induced weight loss. However, in RYGB patients, there is a general consensus that postprandial PYY levels are elevated compared to lean (Korner et al., 2005; le Roux et al., 2006), normal weight (Morinigo et al., 2008), overweight (Korner et al., 2005; Rodieux, Giusti, D'Alessio, Suter, & Tappy, 2008) and persons with obesity (Korner et al., 2005; le Roux et al., 2006; Morinigo et al., 2006). Interestingly, PYY levels appear to increase as early as 2 days post-surgery, irrelevant to weight loss (le Roux et al., 2007) and remains elevated up to 3 years post op (Borg et al., 2006; Korner et al., 2005; le Roux et al., 2006; le Roux et al., 2007; Morinigo et al., 2008; Reinehr et al., 2007; Rodieux et al., 2008). Korner et al. (Korner et al., 2005) assessed RYGB patients 3 years after surgery and found weight maintenance was related to early and exaggerated PYY response to nutrients rather than volume restriction. Similarly, Rodieux et al. concluded the same results; reporting that elevated PYY was associated with long-term weight maintenance (Rodieux et al., 2008). Controversially though, animal studies by Meguid et al. (Meguid et al., 2008) found weight regain in RYGB rats, as a consequence of failure to sustain elevated PYY concentrations. Le Roux et al. also found lower PYY levels had a significant correlation ($p < 0.05$) to increased appetite in “poor weight loss” patients (characterized by BMI >30) (le Roux et al., 2007). Whereas, a more recent study

comparing “good” weight loss verses “poor” weight loss responders found no significant difference in PYY levels between these groups, however a number of limitations to this study warrants repeated investigation to determine the outcome of PYY in patients that have regained weight compared to those that have maintained weight.

Similar to PYY, glucagon-like-peptide-1 (GLP-1) is secreted from the L-cells of the ileum and colon in response to food intake (Cummings & Overduin, 2007; Murphy & Bloom, 2006; Vincent & le Roux, 2008a, 2008b; Wren & Bloom, 2007). After RYGB, GLP-1 assists with decreasing gastric emptying after meal ingestion (Frezza, Wachtel, & Chiriva-Internati, 2007; le Roux & Bloom, 2005; Vincent & le Roux, 2008a) and appears to play a driving role behind increased satiety levels (De Silva et al., 2011; Naslund et al., 1999). Peterili et al (Peterli et al., 2012) recently published results of a prospective, randomized 1-year trial looking at the outcomes of peripheral hormones after RYGB; GLP-1 levels were lower prior to surgery and had markedly increased at 1 week, 3 months and 1 year post-operatively. Interestingly, two studies compared RYGB patients with good weight loss (characterized by BMI <30; or excess body mass index lost (EBL) >60%) to those with poor weight loss (BMI >30; EBL <50%) and found higher levels of GLP-1 in the “good” weight loss group (Dirksen et al., 2013; le Roux et al., 2007). Additionally, there was a correlation in appetite and lower GLP-1 levels in the poor weight loss groups (Dirksen et al., 2013; le Roux et al., 2007), suggesting that appetite returns when GLP-1 levels are inhibited. Unfortunately, there is limited research to conclude that return of appetite is dependent on GLP-1 after RYGB, rather, it is likely multifaceted and remains an area of further investigation.

Leptin

Leptin is a peptide, found primarily in adiposity cells, but also abundant in the hypothalamus, pituitary, gastric epithelium, and in reproductive organs (Budak et al., 2006). It is an indicator of fat mass and acts as a homeostatic regulator between energy expenditure and food intake. During weight loss or food restriction, leptin decreases in proportion to body fat (Gale, Castracane, & Mantzoros, 2004; Molina et al., 2003), signaling energy depletion to the brain initiating the need to feed and restore adiposity. Sumithran et al (Sumithran et al., 2011) found multiple circulating hormones associated with poor weight maintenance long term in a diet-induced weight loss study. They found leptin levels proportional to weight loss; as weight decreased in the early diet phase, leptin levels fell concurrently. After the diet phase (at 1 year follow-up), weight regain was noted with similar response to rising leptin levels. However, after RYGB, it is thought that decreased appetite and elevated anorexigenic hormones contribute to weight loss, yet leptin has not been conclusively found to be lower after RYGB (Laferrere et al., 2007; Meier & Gressner, 2004; Molina et al., 2003) and appears to be more related to body fat (Lee et al., 2011; Swarbrick et al., 2008), changes in body weight (Swarbrick et al., 2008), and body mass index (Korner et al., 2005; Lee et al., 2011; Molina et al., 2003). Korner et al. (Korner et al., 2005) found leptin to be highly correlated ($r=0.68$, $p<0.001$) to BMI with similar leptin concentrations between lean controls and post-RYGB patients, despite the fact that the post-RYGB patients had a BMI of 32.8±1.6, compared to lean controls, 21.6±0.7. Given this difference in BMI between the groups, it would be expected that leptin levels would be higher in the post-RYGB group compared to the lean controls as BMI remained in an "obese" classification. However, this was not

the case, raising suspicion to other peripheral hormones to have a more essential role. In animal studies, Meguid et al. used a rat-RYGB model to identify physiological mechanisms producing weight regain after RYGB (Meguid et al., 2008). They concluded that RYGB rats unable to sustain weight loss exhibited a lower plasma PYY:leptin ratio, suggesting that elevated PYY concentrations are essentials in preserving weight loss after RYGB. More so, leptin has been found to influence taste (Bohlender, Rauh, Zenk, & Groschl, 2003), smell (Bohlender et al., 2003; Julliard et al., 2007) and reward pathways (Fulton, Woodside, & Shizgal, 2000) that support the role of hedonic influences on appetite. Cameron et al. (J. D. Cameron, Goldfield, & Doucet, 2012) was one of the first studies to show a link between smell performance and changes in food palatability among participants in an acute energy deprivation among diet-induced weight loss participants. However, it remains unclear if patients with or without poor weight loss after RYGB would display similar results with regards to peripheral hormone levels, appetite and smell performance.

Appetite Changes after Weight Loss

Food intake is complex and not solely derived from hypothalamic regulation. Motivation, reward, learned behaviours, habits, social and environmental influences, availability of food and external sensory cues such as visual, smell and taste of food all impact the hedonics of food consumption (Bohlender et al., 2003; Cornier, 2011; Farooqi et al., 2007; Julliard et al., 2007; Rosenbaum, Sy, Pavlovich, Leibel, & Hirsch, 2008; Thirlby, Bahiraei, Randall, & Drewnoski, 2006; Watts, 2000). Epstein et al. (Epstein, Leddy, Temple, & Faith, 2007) reported that food deprivation increases energy intake and

motivates people to eat (Epstein, Truesdale, Wojcik, Paluch, & Raynor, 2003; Raynor & Epstein, 2003), similarly, growing evidence supports perceived rewarding properties of food after diet-induced weight loss (J. D. Cameron, Goldfield, Cyr, & Doucet, 2008). In fact, studies have found diet-induced weight loss associated with increased appetite (Doucet, St-Pierre, Almeras, & Tremblay, 2003; Gilbert, Drapeau, Astrup, & Tremblay, 2009; Sumithran et al., 2011), increased desire to eat (Cornier, Grunwald, Johnson, & Bessesen, 2004) and higher perspective food consumption (PFC) (Drapeau et al., 2007), which is the opposite effect reported after RYGB surgery (Ochner, Kwok, et al., 2011; Schultes, Ernst, Wilms, Thurnheer, & Hallschmid, 2010; Jennifer Ullrich, Ernst, Wilms, Thurnheer, & Schultes). Schultes et al. (Schultes et al., 2010) found a decreased drive for food, specifically, lower intake of palatable foods (i.e. chocolate, cake, candy), lower hunger ratings, and decreased food intake in RYGB patients when compared to non-surgical patients with obesity. Ochner et al. published data on changes in neural activation and desire to eat following RYGB and found a decreased preference for energy-dense foods, decreased energy intake and decreased desire to eat (Ochner, Gibson, Shanik, Goel, & Geliebter, 2011; Ochner, Kwok, et al., 2011). Interestingly though, Le Roux (le Roux et al., 2007) and Dirksen (Dirksen et al., 2013) both found increased appetite and hunger in RYGB patients that had "poor" weight loss compared to "good" weight loss, suggesting satiety may not be sustainable long-term and increases in hunger may possibly be changed by peripheral pathways influencing appetite or vise versa. The premise that diet-induced weight loss influences pathways that regulate appetite, store and utilize energy and ultimately predispose the dieter to weight regain

(Reed, Chaput, Tremblay, & Doucet, 2013), is fascinating as this could also occur in patients after RYGB, especially those with poor weight loss or weight regain.

Eating behaviours

The Eating Inventory (EI) or originally named the Three Factor Eating Questionnaire (TFEQ) (Stunkard & Messick, 1985) has been widely used in obesity research; both in behavioural weight loss studies (Bond, Phelan, Leahey, Hill, & Wing, 2009; Clark, Marcus, Pera, & Niaura, 1994; Foster et al., 1998; F. Karlsson, Modica, & Mooe, 2007; J. Karlsson et al., 2007; Lowe, Doshi, Katterman, & Feig, 2013; McGuire, Wing, Klem, Lang, & Hill, 1999; Niemeier, Phelan, Fava, & Wing, 2007) and surgical studies (Adami, Gandolfo, Dapueto, Jurich, & Scopinaro, 1993; Bond et al., 2009; Livhits et al., 2011; Sarwer et al., 2008; Turkmen, Andreen, & Cengiz, 2014). The TFEQ includes three subscales that measure eating behaviours associated with dietary restraint (cognitive dietary control), disinhibition (susceptibility of loss of control over eating) and hunger (level of perceived hunger). The disinhibition subscale has been associated with weight regain after conventional weight loss treatment (i.e. behavioural weight loss programs), subsequently, higher disinhibition scores have been found as a predictor for future weight regain (Bond et al., 2009; J. Karlsson et al., 2007; McGuire et al., 1999; Niemeier et al., 2007). Similar to bariatric surgical treatment, the TFEQ has been associated with changes to eating behaviours, favouring weight regain (Bond et al., 2009; J. Karlsson et al., 2007; Livhits et al., 2011; Turkmen et al., 2014) and weight loss (Sarwer et al., 2008). Sarwer et al. found that higher dietary restraint scores predicted postoperative weight loss. More so, they found an association between higher dietary restraint scores and lower intake of %

kcal/d from sweets and fat. Very few studies have investigated the eating behaviours of post-RYGB patients experiencing weight regain. Odom et al. (2010) found increased food urges associated with significant weight regain after RYGB (Odom et al., 2010). More so, other studies have reported weight regain associated with loss of control when eating (Freire et al., 2012; Kofman, Lent, & Swencionis, 2010; Konttinen, Haukkala, Sarlio-Lahteenkorva, Silventoinen, & Jousilahti, 2009; Livhits et al., 2011), however no study to our knowledge has investigated eating behaviours, using the TFEQ, among post-RYGB patients specifically with weight regain.

Olfaction (Smell) Function

Emerging evidence supports the role of smell and weight regulation with one of the first studies to link smell performance and energy intake in an energy deprived state (J. Cameron et al.). Previous work by Cameron et al (J. D. Cameron et al., 2012) found a relationship between smell performance and changes in palatability, suggesting not only were participants more likely to rate palatable foods higher in an energy deprived state, but participants with higher body weight displayed greater smell improvements during energy deprivation. Others have identified a correlation between elevated BMI and smell dysfunction (Richardson, Vander Woude, Sudan, Thompson, & Leopold, 2004), finding differences in smell performance between patients with obesity (BMI >45) and patients with normal weight to moderate obesity (BMI <45). Interestingly, Richardson et al. looked at smell dysfunction after RYGB and found no change after 12 months from surgery, suggesting smell dysfunction may play a role in the development of obesity rather than by affected by weight loss (Richardson, Vanderwoude, Sudan, Leopold, &

Thompson, 2012). Similarly, Jurowich et al. found no effect of weight loss on olfactory perception after RYGB surgery (Jurowich et al., 2014). Unfortunately, no research to our knowledge has been conducted investigating smell function in patients with weight regain after RYGB. Findings of this nature may answer questions surrounding smell function after bariatric surgery, as well as the influence of peripheral hormones on smell function and the link between smell and appetite.

Conclusion

Roux-en-Y gastric bypass (RYGB) is the gold standard procedure for bariatric surgery. Chronic disease comorbidities such as diabetes, hypertension and hyperlipidemia are resolved by 84%, 68%, and 97%, respectively following RYGB (Buchwald et al., 2004). It has also been concluded that RYGB is more cost-effective than conventional weight management treatment options (Padwal et al., 2011; Terranova, Busetto, Vestri, & Zappa, 2012), in terms of operational cost-recovery and life expectancy (Peeters et al., 2003).

Despite the positive outcomes associated with weight loss from RYGB, approximately 20-30% of patients will regain some if not all their lost weight (Christou et al., 2006; Faria et al., 2010; Freire et al., 2012; Magro et al., 2008; Meguid et al., 2008), pressuring direct and indirect costs to the Canadian health care system. Not to mention, the negative affects weight regain will have on patient's quality of life (QoL) and possibly exacerbating chronic diseases.

There appears to be multiple reasons for weight regain after surgery and this study will investigate changes in peripheral hormones associated with appetite. Results found in this study will help researchers understand factors that may contribute to weight regain and/or weight maintenance after surgery. These results may provide future insight to prevent weight regain long-term.

CHAPTER 3: RESEARCH QUESTION

OBJECTIVES

The purpose of this study was three-fold. The primary aim of this study was to determine the weight trajectory of RYGB patients after surgery. Specifically comparing results between weight maintainers, low weight regainers and high weight regainers. The secondary aim was to investigate appetite measures associated with weight changes, including satiety quotient (testing desire to eat, hunger, satiety and prospective food consumption), smell function, and eating behaviours among these patient groups. The third aim was to determine if there is a relationship between peripheral hormones; ghrelin, PYY, GLP-1, and leptin in patients who have regained weight compared to patients that have maintained weight after RYGB. However, data presented in this paper will not include peripheral hormone results (results will be presented in a future paper).

HYPOTHESES

It is hypothesized that:

1) The weight trajectory of RYGB patients experiencing weight regain will be higher than those maintaining weight.
2) The length of time from surgery will be higher in regain participants than weight maintainers.
3) Patients that have regained weight will have higher appetite outcomes compared to patients that have maintained weight after bariatric surgery.

4) Smell function will be higher among weight regainers than participants that have maintained weight.
5) Eating behaviours is hypothesized to be different in participants with weight regain compared to maintainers. Specifically, dietary restraint will be favoured among weight maintainers compared to regain participants. Disinhibition and perceived hunger scores will be higher among weight regainers then maintainers.
6) Measures of food reward for liking and wanting of high fat sweet foods will be elevated in weight regainers.

CHAPTER 4: MATERIALS & METHODS

Participants

Twenty-nine participants (3 male; 26 female) aged 49.6 ± 9.1 years were included in the final study after an initial screening process involving a sample of 38 volunteers from The Ottawa Hospital Weight Management Clinic & Bariatric Centre of Excellence (WMC) in Ottawa, Canada. The initial screening process excluded those who were less than 2 years from RYGB surgery, underwent an alternative procedure than the RYGB surgery or did not undergo their RYGB surgery at The Ottawa Hospital. Additional exclusion criteria included current use of meal replacements, admitted to hospital for surgical intervention within 2 months of the testing date, pregnant and/or breastfeeding, impaired nasal breathing or history of sinus surgery, and inability to read, write or speak English. Participants were divided into tertiles (33% and 66%) based on their rate of weight regain, defined as weight regained from nadir to current weight divided by the number of months from nadir to current weight. For simplicity purposes, weight regained (kg) per month was converted into weight regained (kg) per year, resulting in three groups based on tertiles; weight maintainers, low weight regainers and high weight regainers. Rate of weight regain ranged from 0-1.8 kg/year for weight maintainers, 2.9-4.7 kg/year for low weight regainers and 5.0-12.2 kg/year for high regainers. This method was chosen for its clinical relevance as weight regained after RYGB surgery is anticipated to be greater for participants the further post-op they are. Informed written consent was obtained prior to the study and ethics approval was granted from the Ottawa Health Science Research Ethics Board and the University of Ottawa Office of Research

Ethics and Integrity. All research procedures were compliant with the Declaration of Helsinki.

Design and Procedure

A cross-sectional design was used with participants in three weight change groups; weight maintainers, low weight regainers and high weight regainers. All testing occurred in private research rooms in the Behavioural & Metabolic Research Unit (BMRU) at the University of Ottawa. Participants arrived at 0700, 0730 or 0800 after a 12-hour fast and complete a demographic questionnaire followed by having body weight and height recorded. Participants completed a visual analogue scale (VAS) to measure fasting appetite levels, followed by a computer task using the LFPQ (Leeds Food Preference Questionnaire) to measure fasting levels of explicit "liking" and "wanting" for foods. Venous blood was drawn from the antecubital vein of participant's non-dominant arm 5 minutes before and 30, 60, 90, 120, 150 and 180 minutes after a meal. Plasma samples for assay of hormones (ghrelin, PYY, GLP-1 and leptin TBD) were collected in tubes containing ethylenediamine tetraacetic acid (EDTA). Blood samples were immediately centrifuged at ≤1300 rpm at 4°C for 10 minutes, evenly pipetted to 4 aliquot tubes and stored at -80^{0}C until assayed. All blood samples were stored in the BMRU for future analysis and are not reported in this paper. Olfaction (smell) performance was completed 90 minutes after the meal, while eating behaviours using the Three Factor Eating Questionnaire (TFEQ) and Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ) was completed 120 minutes after the meal.

Standardized breakfast

A 300 kcal breakfast consisting of 4 slices (20g) of melba toast®, 1 Tbsp. (15g) natural peanut butter (Kraft®), 100g Vanilla Greek yogurt (Liberte®), 4 slices (50g) of apples and 6 almonds (6g) (providing 45% carbohydrates, 20% protein, and 35% fat) was served to participants approximately 30 minutes after arrival and they had 20 minutes to consume the breakfast. Previous studies have used a similar macronutrient meal distribution (Evans et al., 2012; Faria et al., 2010; Pournaras et al., 2010). Participants completed the VAS for appetite and satiety measures every 60 minutes from completion of the breakfast, food reward measures using the LFPQ were complete 60 minutes after the breakfast, while olfactory measures and eating behaviour measures were completed at 90 and 120 minutes, respectively. The testing ended immediately after completing the 180-minute VAS and blood draw.

Measurements

Demographic information including age, sex, ethnicity and education level was obtained from a written questionnaire. Additional questions related to pre-surgical medical conditions (including diabetes and binge eating disorders) were collected, along with questions affecting study results, including tobacco use and menstrual cycle.

Anthropometrics

Height (HR-100 Height Rod; Tanita Corporation of America Inc. Arlington Heights, IL) and body weight (HR-100; BWB-800AS, Tanita Corporation, Arlington Heights, IL., USA) were measured after a 12 hour overnight fast.

Appetite and Satiety

Appetite and satiety were measured using a semantic differential scale in the form of a computerized visual analog scale (VAS – 100 mm) adapted from Hill, Magson and Blundell (Hill, Magson, & Blundell, 1984). Desire to eat, hunger, satiety and prospective food consumption (PFC) were rated using the following questions: 1) "How strong is your desire to eat?" (Very week – Very strong); 2) "How hungry do you feel?" (Not hungry at all – As hungry as I have ever felt); 3) "How full do you feel?" (Not full at all – Very full), and 4) "How much food do you think you could eat?" (Nothing at all – A large amount). Participants completed the VAS at baseline (30 minutes before a meal) and at 60, 120, and 180 minutes after a meal. Participants could not compare to previous ratings and could not communicate with others regarding the VAS task. The satiety efficiency was assessed by the "Satiety Quotient" (SQ) method adapted from Green et al. (Green, Delargy, Joanes, & Blundell, 1997), which represents changes in hunger ratings in mm/100 kcal of food consumed.

Food Reward – Leeds Food Preference Questionnaire (LFPQ)

The Leeds Food Preference Questionnaire (LFPQ) measures liking and wanting for food and has been widely used in other studies (J. D. Cameron, Goldfield, Finlayson, Blundell, & Doucet, 2014; Finlayson, Arlotti, Dalton, King, & Blundell, 2011; Griffioen-Roose, Finlayson, Mars, Blundell, & de Graaf, 2010). Participants are asked to assess food choices and personal ratings of various food items that subjectively measures their "liking" and "wanting" for photographic food stimuli varying in taste (sweet or savory) and fat content (high fat or low fat). To measure explicit liking, participants are shown

images of foods and asked to rate "How pleasant would it be to taste some of this food now?" while explicit wanting asked "How much do you want some of this food now?" Data was collected from a 100-mm VAS related to each image and averaged for each food type (HFSW, high fat sweet; HFSA, high fat savory; LFSW, low fat sweet; LFSA, low fat savory) while reaction times were measured (in milliseconds) to indicate participants' motivation (wanting) for food preferences. Implicit wanting was measured by asking "which food do you most want to eat now?" using a force-choice method of two images and paired against each food image over ninety-six trials. This LFPQ is described in more detail elsewhere (Finlayson et al., 2011).

Three Factor Eating Questionnaire (TFEQ)

The Three Factor Eating Questionnaire (TFEQ) or alternatively called the Eating Inventory (EI) is a 51 item self-administered questionnaire that determines a subject's individual eating habits (Stunkard & Messick, 1985). This instrument measures cognitive restraint (21 questions) which measures dietary self-regulation; disinhibition (16 questions) which assesses loss of control over eating and susceptibility to hunger (14 questions), which describes subjective feelings of hunger and cravings.

Sensitivity to Punishment and Sensitive to Reward Questionnaire (SPSRQ)

The Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ) is a 48 yes–no response item questionnaire which incorporates two scales: sensitivity to punishment (24 items) and sensitivity to reward (24 items) (Torrubia, Avila, Molto, & Caseras, 2001). The scale items reflect both the anticipation of reward (*e.g.* Does the

good prospect of obtaining money motivate you strongly to do some things?) and pleasure experienced from rewarding activities (*e.g.* Does your attention easily stray from your work in the presence of an attractive stranger?).

Olfactory Performance

Olfactory (smell) performance was assessed by using Sniffin' Sticks® (Burghart Instruments, Wedel, Germany), a 3-test battery of odorized pens (Haehner et al., 2009; Hummel, Kobal, Gudziol, & Mackay-Sim, 2007; Hummel, Sekinger, Wolf, Pauli, & Kobal, 1997). Participants were required to complete 3 different odor tests, which included an odor threshold test, an odor discrimination test and an odor identification test (Hummel et al., 1997). The olfactory threshold test consisted of a set of 3 capsules, two contained an odorless solvent (propylene glycol) and the other pen contained a concentrated level of beta-phenylethyl alcohol in a single-staircase procedure. Participants were instructed to identify the pen containing the concentrated odor (beta-phenylethyl alcohol), if correctly identified (twice in a row), the concentration was increased and decreased if incorrectly identified. As for the odor discrimination test, a set of 3 capsules were subsequently presented to participants and instructed to discriminate the different odor between 16 triplets of odors (2 odors being identical and 1 being different). Lastly, the odor identification test consists of 16 odor pens and a booklet with multiple-choice answers on each page (one page is associated with one odor capsule). Participants are required to identify the correct odor released by the capsule, based on the multiple-choice answers that are provided to them. Examples of some of the odors presented to the participant were rose, lemon, banana, and fish.

Statistical Analysis

Data is expressed as mean ± standard deviation unless otherwise specified. All continuous and categorical variables were assessed for distributional assumptions according to statistical test used and parametric and non-parametric statistical tests were used when appropriate. Weight change outcomes were based on the rate of weight regained, as defined by kilograms gained from nadir to current weight divided by the number of month from nadir to testing date. Data was then categorized into tertiary percentiles as 33rd percentile and 66th percentile to illustrate equal groups and minimize overlapping weight ranges that could manipulate outcomes. The three categories will be henceforth referred to as weight maintainers, low weight regainers and high weight regainers. To examine weight trajectories between the weight change groups; a repeated measures analysis of variance (ANOVA) was conducted and a Bonferroni post-hoc test was utilized for significant differences between time points. To evaluate appetite changes before and after the standardized breakfast, a two-way repeated measures ANOVA was utilized for time (0, 60, 120, 180 minutes) and groups (maintainers, low regainers and high regainers). A two-way ANOVA was used to measure the appetite sensation (AS) using the satiety quotient (Green et al., 1997). Satiety quotient (SQ) was standardized for equal comparisons on a 0-100% scale to correct for participants unable to consume the entire test meal. SQ was calculated with this equation:

$$[SQ] = \frac{(\text{fasting AS} - \text{mean 60 minute post-meal AS})}{\text{Energy content of test meal (kcal)}} \times 100$$

A Kruskal-Wallis ANOVA was conducted to determine differences in olfactory measures between weight change groups. Correlations using Spearman's coefficient were utilized for olfactory measures and weight trajectory outcomes (i.e. TWL, BMI, months post-op, etc.). Eating behaviour measures (TFEQ and SPSRQ) were analyzed by a two-way ANOVA and Pearson's correlation between other parametric variables. All food reward measures (explicit liking; wanting and implicit wanting) were assessed with a Kruskal-Wallis ANOVA for food type delta scores while time effects (fasting vs fed) were evaluated using a Wilcoxon-rank-order test. Spearman correlations were used to assess the linear relationship of food reward measures to the study's other measures for the entire cohort and between groups. A p-value of ≤ 0.05 was determined statistically significant. Data was analyzed using IBM SPSS Statistics for Windows, version 22.0 (Armonk, NY: IBM Corp).

CHAPTER 5: RESULTS

Participants' Characteristics

In accordance with the statistical procedure used to divide groups, 9 maintained weight (7 women and 2 men, 49.6 ± 10.9 years of age, 44.1 ± 8.2 months from surgery), 10 regained a low amount of weight (10 women, 50.0 ± 6.7 years of age, 45.2 ± 8.5 months from surgery) and 10 regained a high amount of weight (9 women and 1 men, 49.1 ± 10.2 years of age, 41.5 ± 10.5 months from surgery). Sex distribution did not differ between the groups (p = 0.295). Eighty-three percent of the participants were Caucasian and 41.4%completed post-secondary education. Descriptive statistics for the participants were normally distributed and are summarized in Table 2.

Table 2. Participants' Characteristics

		Groups		
	Total n = 29	Maintained Weight n = 9	Low Regain n = 10	High Regain n = 10
Age (y)	49.6 ± 9.1	49.6 ± 10.9	50.0 ± 6.7	49.1 ± 10.2
Sex (male/female)	3/26	2/7	0/10	1/9
Post menopause n (%)	10 (34.5)	2 (22.2)	4 (40)	4 (40)
Ethnicity n (%)				
African	1 (3.5)	0 (0)	1 (10)	0 (0)
Arabian	1 (3.5)	0 (0)	1 (10)	0 (0)
Asian	1 (3.5)	0 (0)	0 (0)	1 (10)
Caucasian	24 (82.8)	8 (88.9)	7 (70)	9 (90)
Latino	1 (3.5)	1 (11.1)	0 (0)	0 (0)
Multiracial	1 (3.5)	0 (0)	1 (10)	0 (0)
Education n (%)				
Some High School	1 (3.4)	0 (0)	0 (0)	1 (10)
High School Diploma	5 (17.2)	1 (11.1)	2 (20)	2 (20)
Some Post-Secondary	5 (17.2)	2 (22.2)	1 (10)	2 (20)
Completed Post-Secondary	12 (41.4)	3 (33.3)	4 (40)	5 (50)
Graduate Studies	6 (20.7)	3 (33.3)	3 (30)	0 (0)

Data reported as mean ± SD

Weight Trajectory Outcomes

Participants' changes in body weight are presented in Table 3. Weight before surgery was not different for the weight maintenance and low/high regain groups (p = 0.22), as was the number of month to nadir body weight (21.9 ± 15.2, 13.0 ± 4.2 and 19.3 ± 10.5, respectively, p = 0.20). There was no significant difference for weight loss at nadir (44.5 ± 11.3 kg vs. 46.5 ± 12.5 kg vs. 54.1 ± 12.4 kg; p = 0.21, respectively). As designed, there was a significant difference in weight gained between the weight maintenance and low/high regain groups with 2.2 ± 2.5 kg, 10.0 ± 3.4 kg and 15.0 ± 6.3 kg, respectively (p < 0.001). High weight regain participants gained on average 8.6 kg/year (p <0.001), compared to low weight regain participants and weight maintenance participants at 3.8 ± 0.9 kg/year and 0.9 ± 0.9 kg/year, respectively. The weight maintenance group maintained 1.8 ± 1.8 % Total Weight Loss (TWL) from nadir to current weight (34.7 ± 6.9% to 32.9 ± 6.7%, respectively), whereas the low and high regain groups regained 8.6 ± 3.0% and 11.3 ± 4.9%, respectively, from nadir to current weight (38.7 ± 7.3% to 30.1 ± 8.1% and 40.3 ± 8.4 % to 29.0 ± 8.9% TWL, respectively, p < 0.001). A strong positive correlation using Spearman's rank-order correlation was found between weight regained after surgery and how long it took to regain the weight in the weight maintenance group, r_s = 0.768, p = 0.016. Similar correlations were found in the low regain group, r_s = 0.669, p = 0.035 but not in the high regain group, r_s = 0.626, p = 0.053. No correlation was found between the amount of weight lost and how long it took to lose, r = -0.206, p = 0.284, even when correlations were run within each group. A two-way repeated measures ANOVA was conducted to determine whether there was a statistically significant difference in weight change from pre-surgery and current weight (date of testing). There

were no outliers and data was normally distributed at each time point, as assessed by boxplot and Shapiro-Wilk test (p <0.05). The assumption of sphericity was violated, as assessed by Mauchly's test of spherecity, $x^2(2) = 29.9$, p <0.0001. Weight change was significantly different over time, $F(1.178, 30.616) = 341.72$, p <0.001, $\Pi^2 = 1.0$, with weight decreasing from pre-surgery (127.2 ± 19.0 kg) to nadir weight (78.9 ± 14.0 kg), then increasing from nadir to current weight (88.0 ± 15.0 kg). Post-hoc analysis with a Bonferroni adjustment revealed that weight change was statistically significantly decreased from pre-surgery to nadir weight (M = 48.4 kg, 95% CI [42.6 to 54.1], p <0.001) and pre-surgery to current weight (M = 39.3 kg, 95% CI [33.1 to 45.5], p <0.001) and increased significantly from nadir to current weight (M = -9.1 kg, 95% CI [-11.1 to -7.0], p <0.001) (Figure 2). It should be noted that despite a significant amount of weight regained from nadir (28.6 ± 10.9%), the high regain group remained 39.1 ± 13.8 kg (29.0 ± 8.9% TWL) below their pre-surgical weight.

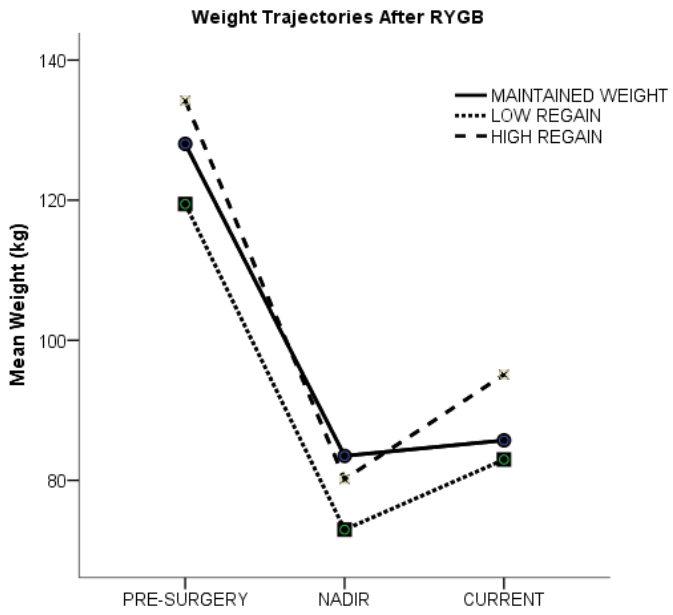

Figure 2. *Participants weight change trajectories for weight maintainers (n=9), low regainers (n=10) and high regainers (n=10) from pre-surgical weight to nadir and current weights.*

Table 3. Participant's change in body weight

		Group		
	Total *n* = 29	Weight Maintenance *n* = 9	Low Regain *n* = 10	High Regain *n* = 10
Pre-surgical weight (kg)	127.2 ± 19.0	128.0 ± 22.9	119 ± 19.5	134.2 ± 12.3
Pre-surgical BMI (kg/m^2)	46.9 ± 5.7	47.1 ± 7.8	46.3 ± 6.3	47.2 ± 2.7
Nadir post-surgical weight (kg)	78.9 ± 14.7	83.5 ± 16.8	73.0 ± 12.7	80.2 ± 13.8
TWL at nadir weight (kg)	48.5 ± 12.4	44.5 ±11.3	46.5 ± 12.5	54.1 ± 12.4
Months to nadir	17.9 ± 11.0	21.9 ± 15.2	13.0 ± 4.2	19.3 ± 10.5
Current weight (kg)	88.0 ± 15.0	85.7 ± 16.1	83.0 ± 13.6	95.1 ± 14.0
Current BMI (kg/m^2)	32.4 ± 4.7	31.5 ± 5.4	32.3 ± 4.9	33.4 ± 3.9
TWL at current weight (kg)	39.2 ± 12.7	42.3 ± 11.7	36.5 ± 13.2	39.1 ± 13.8
Months to current weight	43.6 ± 8.9	44.1 ± 8.2	45.2 ± 8.5	41.5 ± 10.5
Rate of weight loss per month (kg)	3.4 ± 1.6	2.6 ± 1.1	3.8 ± 1.2	3.6 ± 2.2
Weight gained (kg)	9.3 ± 6.7*	2.2 ± 2.5[a,b]	10.0 ± 3.4[a,c]	15.0 ± 6.3[b,c]
Months from nadir to current weight	25.7 ± 11.5	22.2 ± 14.4	32.2 ± 9.6	22.2 ± 8.0
Rate of weight regained (kg/yr)	4.6 ± 3.9**	0.9 ± 0.9[a,b]	3.8 ± 0.9[a,c]	8.6 ± 3.6[b,c]
Percentage weight regained (%)	19.4 ± 12.9*	5.4 ± 5.1[a,b]	23.0 ± 8.4[a]	28.6 ± 10.9[b]
Percentage TWL at nadir weight (%)	38.0 ± 7.7	34.7 ± 6.9	38.7 ± 7.3	40.3 ± 8.4
Percentage TWL at current weight (%)	30.6 ± 7.9	32.9 ± 6.7	30.1 ± 8.1	29.0 ± 8.9
Percentage EWL at nadir weight (%)	83.4 ± 18.0	77.3 ± 19.7	86.6 ± 17.9	85.7 ± 17.0
Percentage EWL at current weight (%)	67.1 ± 18.2	72.9 ± 18.2	67.3 ± 18.8	61.7 ± 17.9

TWL = Total weight loss; EWL = Excess weight loss. Data reported as mean ± SD

*Denotes significance at $p<0.05$ by post hoc Tukey test

**Denotes significance at $p<0.001$ by post hoc Games-Howell (non-parametric)

[a] Significant difference between weight maintenance and low regain group

[b] Significant difference between weight maintenance and high regain group

[c] Significant difference between low regain group and high regain group

Appetite Results

A two-way repeated measured analysis of variance (ANOVA) was conducted to evaluate appetite (desire to eat, hunger, fullness and prospective food consumption) at 60, 120 and 180 minutes after a meal. The results of the ANOVA indicated a significant time effect, Wilks' Lambda = 0.26, $F(3, 24) = 22.33$, $p < 0.001$, $\eta^2 = 0.74$. However, no group differences were noted (Figure 3).

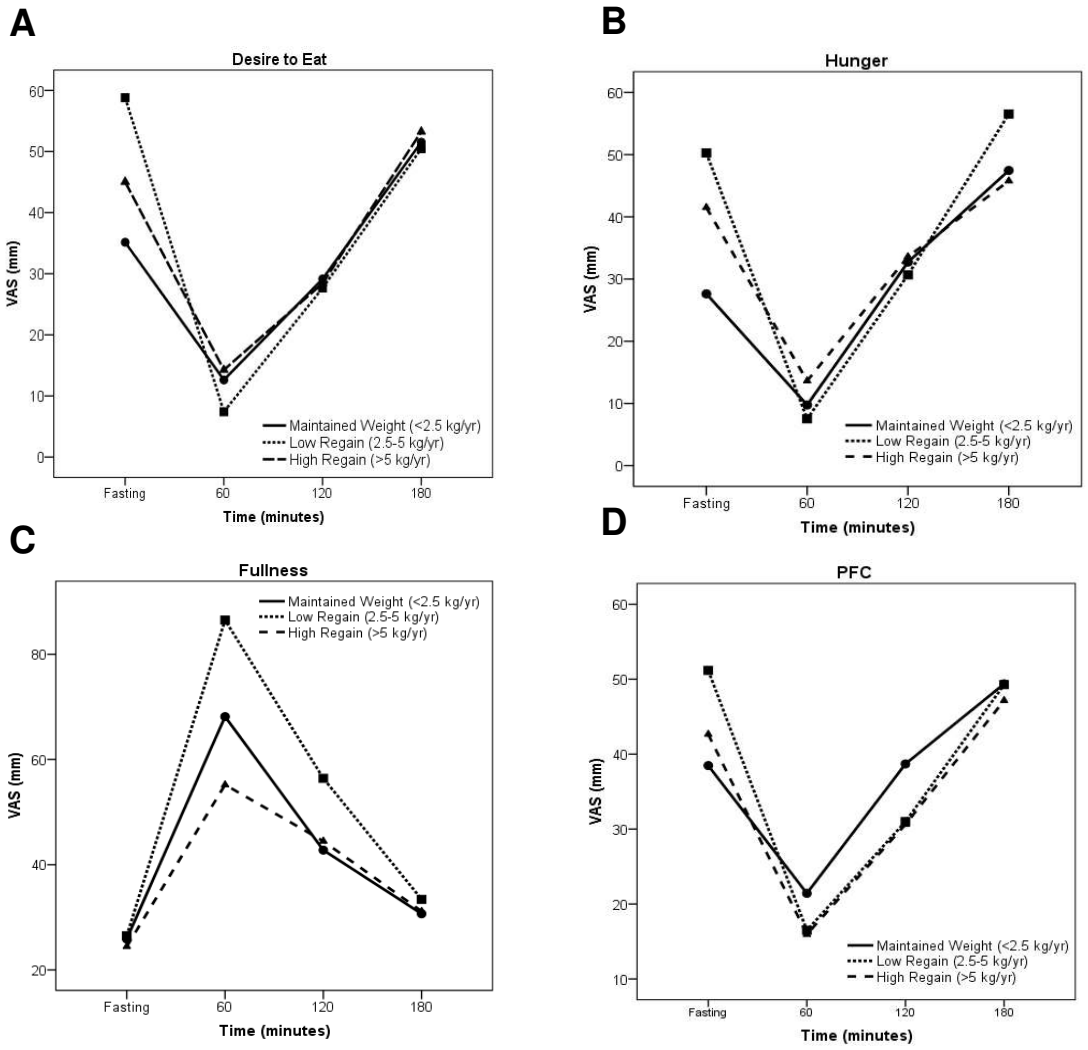

Figure 3. *Appetite scores reported as mean (± SD) for (A) desire to eat, (B) hunger, (C) fullness, and (D) perceived food consumption in participants with maintained weight (n=10) verses low regain (n=9) and high regain (n=10).*

Satiety Quotient

The relationships between appetite sensations (satiety quotient) and weight variables were evaluated for data pooled of weight maintenance, low regain and high regain groups as well for these groups separately. After correcting for genuinely unusual outliers, appetite measures were normally distributed, regardless of outliers in the dataset, as assessed by Shapiro-Wilk test (p >0.05), therefore the outliers remained in the analyses. Leven's test for homogeneity of variance confirmed homogeneity for all appetite measures (p >0.05). Lower hunger levels were observed in the weight maintainers (12.9 ± 8.6 mm/100 kcal) compared to low and high regainers (27.3 ± 14.9 and 20.3 ± 18.2, respectively), but the differences between these groups were not statistically significant, $F(2, 26) = 2.285$, $p = 0.122$. No correlations were found between appetite sensation measures and weight regain in the whole group or within each subgroup.

Smell Function

The results of the threshold, identification, discrimination and TDI scores are presented in Table 4. A Kruskal-Wallis H test was conducted to determine if there were differences in olfactory measures between groups that differed in weight change after RYGB surgery. Threshold scores increased from weight maintainers (*Mdn* = 8.5) to low regainers (*Mdn* = 8.9) to high regainers (Mdn = *10.1*), but these differences were not statistically significant, $x^2(2) = 1.016$, $p = 0.602$. Similar results were found for discrimination and identification scores. Comparisons between the weight maintainers and regain groups are summarized in Figure 4. A positive relationship was observed between pre-surgical BMI and threshold measures, $r_s = 0.705$, p <0.05, as well as pre-surgical BMI and TDI scores,

r_s = 0.693, p <0.05, among the high regain group using Spearman's rank-order correlation.

Table 4. Smell Function Tests

	Total $n = 29$	Group		
		Weight Maintenance $n = 9$	Low Regain $n = 10$	High Regain $n = 10$
Threshold	9.5 ± 3.0	8.6 ± 2.6	9.5 ± 2.6	10.4 ± 3.8
Discrimination	12.7 ± 1.8	13.2 ± 1.3	12.2 ± 2.3	12.8 ± 1.7
Identification	13.0 ± 1.7	13.3 ± 1.7	13.1 ± 1.5	12.5 ± 1.9
TDI Score	35.3 ± 4.3	35.4 ± 4.2	34.8 ± 4.6	35.7 ± 4.5

Data reported as mean ± SD

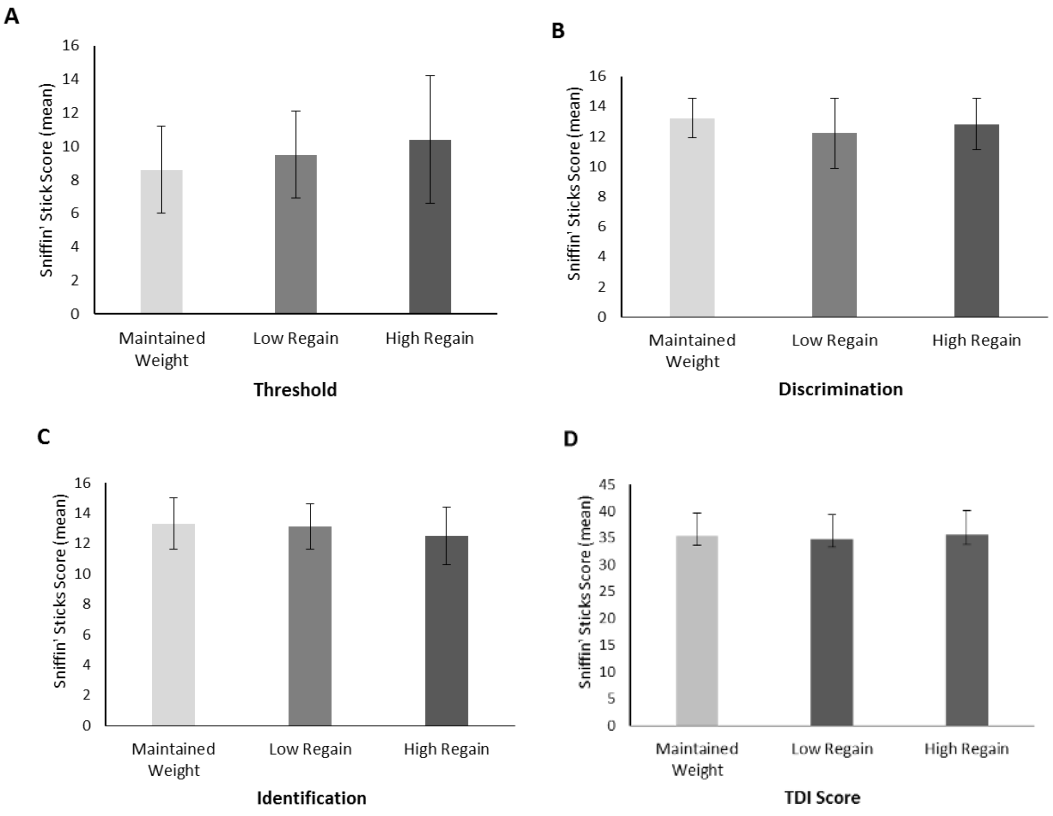

Figure 4. *Sniffin' Stick scores reported as mean (± SD) for (A) threshold, (B) discrimination, (C) identification, and (D) TDI score for olfactory performance in participants with maintained weight (n=9) verses low weight regained (n=10) and high weight regain (n=10).*

Three Factor Eating Questionnaire

A two-way ANOVA was conducted to determine if there were differences in eating behaviours, (using the Three Factor Eating Questionnaire) measured by dietary restraint, disinhibition (the vulnerability to lose-control when eating) and susceptibility to hunger between weight change groups after RYGB surgery. There were no outliers, as assessed by boxplot; data was normally distributed for all variables, except susceptibility to hunger in the low regain group (p = 0.02). Data was transformed by squaring data points (moderately positively skewed data) and was found to be normally distributed (p = 0.053). Data is presented as mean ± SD (Table 5) Eating behaviours subtests were not statistically significant between groups for dietary restraint (p = 0.365), disinhibition (p = 0.242) and susceptibility to hunger (p = 0.669). Each weight group (maintainers and low/high regainers) illustrated clinically significant results in each of the subtests (dietary restraint, disinhibition and susceptibility to hunger). Statistical significance was found between the weight maintainers (11.0 ± 3.5) and low regainers (12.4 ± 4.3) compared to the clinical comparison cutoffs for dietary restraint (p = 0.032 and p = 0.011, respectively) (Figure 5).

Table 5. Three Factor Eating Questionnaire & Sensitivity to Reward and Sensitivity to Punishment Questionnaire

TFEQ & SPSRQ	Group			
	Weight Maintenance	Low Regain	High Regain	p-value
Dietary Restraint (≥ 8)	11.0 ± 3.5	12.4 ± 4.3	9.9 ± 3.7	0.365
Disinhibition (≥ 6)	6.7 ± 2.8	6.1 ± 2.1	8.4 ± 4.0	0.242
Susceptibility to Hunger (≥ 5)	7.0 ± 3.8	5.6 ± 2.9	6.5 ± 3.6	0.669
Sensitivity to Reward	7.7 ± 3.7	9.4 ± 2.9	8.7 ± 3.9	0.566
Sensitivity to Punishment	13.2 ± 8.8	12.3 ± 4.3	13.5 ± 4.9	0.904

Data reported as mean ± SD. Weight maintenance (n = 9); Low regainers (n = 10); High regainers (n = 10)

Figure 5. Eating behavior scores for dietary restraint, disinhibition and susceptibility to hunger between weight groups and clinical comparison cutoffs. * $p < 0.05$

Sensitivity to Punishment and Sensitivity to Reward

Sensitivity to reward subscale found lower mean scores among weight maintainers (7.7 ± 3.7), compared to low and high regain groups (9.4 ± 2.8 and 8.7 ± 3.9, respectively), however the differences between these groups were not statistically significant (p = 0.566). Pearson's correlation to examine the relationship between the amount of weight lost since surgery and sensitivity to reward was positive among weight maintainers (r = 0.786, p <0.05) and the high regain group (r = 0.818, p <0.05), suggesting that participants that lost more weight, had higher sensitivity for reward (Figure 6). There was no correlation between weight regained from nadir and sensitivity to reward.

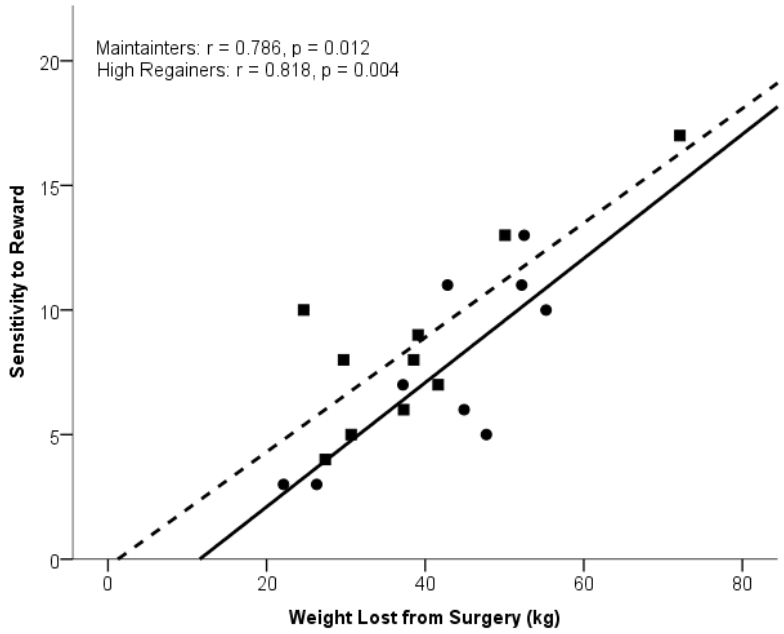

Figure 6. *Positive correlation between weight lost since surgery and sensitivity to reward scores* ● *weight maintainers (straight line) and* ■ *high weight regainers (broken line).*

Food Reward

Explicit Liking

Ratings of explicit liking for food were higher for all weight categories (maintainers, low and high regainers) in the fasting compared to fed state, z = -3.298, p = 0.001 (Figure 7). There was a statistically significant effect of time between fasting and fed states for low and high regainers for taste (sweet and savory) and fat content (high fat and low fat) (Table 6). Using a Wilcoxon rank-order test, a statistically significant time effect was found between fasting (*Mdn* = 39.5) and fed (*Mdn* = 23.9) states for HFSW foods among high regainers (z = -2.192, p = 0.028). Furthermore, a positive correlation was found between weight regained and explicit liking for HFSW foods, r_s = 0.754, p = 0.012. Interestingly, participants that lost more weight in the high regain group, showed a positive correlation with savory tastes, regardless of fat content – high or low (r_s = 0.745,

p = 0.013 and r_s = 0.721, p = 0.019, respectively). When compare to other dependent variables, a positive correlation was found between olfactory subscale, threshold and explicit liking for HFSW (r_s = 0.434, p = 0.019) and LFSA foods (r_s = 0420, p = 0.023). More specifically, participants in the weight maintenance group with higher smell threshold scores positively correlated with higher explicit liking for both types of savory foods (HFSA, r_s = 0.714, p = 0.031 and LFSA, r_s = 0.765, p = 0.016), despite elevated dietary restraint scores (11.0 ± 3.5).

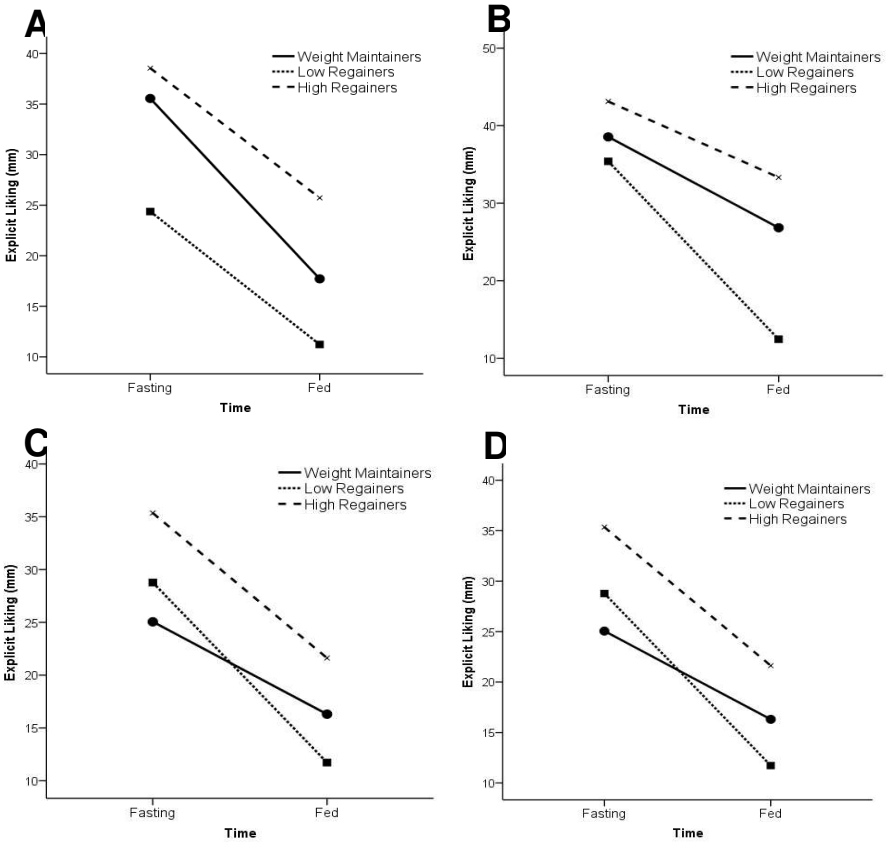

Figure 7. *Explicit liking for food categories (A) HFSW, high fat sweet; (B) HFSA, high fat savory; (C) LFSW, low fat sweet; (D) LFSA, low fat savory among weight maintainers (n=9), low weight regainers(n=10) and high weight regainers (n=10).*

Table 6. Explicit Liking (mm) for food categories

	Fasting				Fed			
	HFSW	HFSA	LFSW	LFSA	HFSW	HFSA	LFSW	LFSA
Weight Maintainers	35.6 ± 22.1	38.6 ± 21.6	25.1 ± 13.2	22.2 ± 14.1	17.7 ± 15.8	26.8 ± 14.5	16.3 ± 14.2	21.9 ± 29.0
Low Regainers	24.4 ± 23.2	35.4 ± 13.8	28.8 ± 9.5	28.9 ± 21.9	11.2 ± 16.3	12.5 ± 21.4*	11.7 ± 9.8*	12.4 ± 19.0*
High Regainers	38.6 ± 15.4	43.1 ± 19.1	35.4 ± 16.5	37.2 ± 25.9	25.7 ± 22.8*	33.3 ± 23.4	21.6 ± 15.9**	25.1 ± 20.6
Total (n=29)	32.7 ± 20.7	39.0 ± 18.0	29.9 ± 13.6	29.6 ± 21.5	18.2 ± 19.0*	24.1 ± 21.5*	16.6 ± 13.7**	25.1 ± 20.6*

Data reported as mean ± SD; Wilcoxon rank-order test, * $p < 0.05$; ** $p < 0.001$
HFSW: high-fat sweet; LFSW: low-fat sweet; HFSA: high-fat savory; LFSA: low-fat savory
Weight maintenance (n=9); Low regainers (n=10); High regainers (n=10).

Explicit Wanting

Explicit wanting for food was greater in a fasting state compared to a fed state for all weight categories (maintainers, low and high regainers), z = -3.622, p <0.0001 (Table 7). Among weight maintainers, food reward measures for explicit wanting revealed a decreasing trend between fasting (*Mdn* = 42.5) and fed (*Mdn* = 4.8) states for HFSW foods, z = -2.371, p = 0.018. Whereas, low and high regainers indicated a lower wanting for LFSW foods in the fasting state (*Mdn* = 25.8 and 26.9, respectively) compared to the fed state (*Mdn* = 15.4 and 17.8, respectively), with a significance of z = -2.701, p = 0.007 for both low and high regain groups. Furthermore, among high regainers, a strong interaction between food type and month post-op revealed lower explicit wanting for savory foods, more so for HFSA, r_s = -0.815, p = 0.004 then LFSA, r_s = -0.610, p = 0.061. In a fed state, there is a positive relationship between total weight lost since surgery (TWL) and explicit wanting for HFSA foods among high weight regainers, r_s = 0.709, p = 0.022.

Implicit Wanting

There was no effect of time between fasting or fed states for any food type. Among low regainers, the more weight they lost, the lower their implicit wanting for HFSW foods, r_s = -0.661, p = 0.038. In a fed state, however, participants that regained more weight and were further post-op in the low regainer group, displayed higher wanting for LFSW foods, r_s = 0.685, p = 0.029 and r_s = 0.705, p = 0.023, respectively. Interestingly, the higher the dietary restraint, as measured by the TFEQ, the lower their implicit motivation for wanting HFSW foods, r_s = -0.405, p = 0.029, which could partly explain those with lower weight regain.

Table 7. Explicit Wanting (mm) for food categories

	Fasting				Fed			
	HFSW	HFSA	LFSW	LFSA	HFSW	HFSA	LFSW	LFSA
Weight Maintainers	34.2 ± 21.7	39.2 ± 24.5	23.0 ± 12.1	26.4 ± 16.0	11.7 ± 13.5*	20.9 ± 18.5	10.6 ± 10.5	22.7 ± 29.9
Low Regainers	25.0 ± 24.8	34.5 ± 12.6	29.0 ± 8.5	26.1 ± 21.7	11.0 ± 15.6*	12.6 ± 20.3*	12.9 ± 10.6*	11.7 ± 19.3*
High Regainers	36.8 ± 13.9	43.9 ± 20.1	34.5 ± 16.5	39.3 ± 27.9	25.6 ± 22.6	28.1 ± 23.4*	17.3 ± 14.1*	20.2 ± 19.3
Total (n=29)	31.9 ± 20.6	39.2 ± 19.2	29.0 ± 13.2	30.8 ± 22.6	16.2 ± 18.5**	20.5 ± 21.2**	13.7 ± 11.8**	18.0 ± 22.7*

Data reported as mean ± SD; Wilcoxon rank-order test, * $p < 0.05$; ** $p < 0.001$
HFSW: high-fat sweet; LFSW: low-fat sweet; HFSA: high-fat savory; LFSA: low-fat savory
Weight maintenance (n=9); Low regainers (n=10); High regainers (n=10).

CHAPTER 6: DISCUSSION

Roux-en-y gastric bypass (RYGB) surgery results in significant weight loss and improvements in health conditions, produces significant weight loss and is considered the gold standard for the management of severe obesity, however a number of patients experience some and/or complete recidivism of weight years after surgery. Limited research has investigated why patients are experiencing weight regain after surgical interventions. In a clinical setting, it is often noted that patients >2 years from RYGB experiencing weight regain report intense cravings for high fat and sweet foods. Hunger and increased appetite is also reported by patients, contributing to the challenges of maintaining weight and ultimately, maintaining health. We therefore aimed to investigate appetite measures associated with weight change after RYGB surgery, specifically looking at appetite sensations, smell performance, eating behaviours and food reward. We demonstrated that weight regain increased significantly in association with time after surgery and that weight increased significantly from nadir to current weight regardless of group. We observed a significant time effect for appetite measures (desire to eat, hunger, fullness and PFC) before and after food ingestion, however we found no evidence to support higher appetite measures among weight regainers. Our data did not support the idea that smell performance would be different in weight regainers than maintainers and we were unable to demonstrate any group differences for eating behaviours, similar to dietary restraint, disinhibition or susceptibility to hunger. We were able to find statistical significance for dietary restraint among weight maintainers and low regainers and found an association between high dietary restraint and low wanting of high-fat sweet foods.

Finally, weight regain was associated with higher liking of high fat-sweet foods, particularly in high weight regainers.

Weight Trajectory

Our study revealed that weight trajectories are changed remarkably after RYGB surgery, with decreasing trends from pre-surgery to nadir weight and increasing from nadir and current weight. According to the Swedish Obesity Study (SOS), one of the largest longitudinal studies on bariatric surgical patients, it is expected that patients will regain at least 10% of total weight lost (TWL) over 10 years from surgery (J. Karlsson et al., 2007). Our study looked at patients that were 29-62 months (2.4-5.1 years) post-op with a mean weight regain of 12% (using TWL), which is similar to other studies (J. Karlsson et al., 2007; Livhits et al., 2011; Odom et al., 2010). However, like the SOS and most other studies, very little is known about the population of bariatric patients that experience weight regain. One reason for this is the indecisiveness among the research community as there is no universal definition for weight regain after bariatric surgery. In fact, over eight methods have been reported in the literature to define weight regain. Excess weight loss (EWL) <50% is the most frequently defined method, according to a recent systematic review by Mann, et al. (2014) (Mann, Jakes, Hayden, & Barth, 2014). Total weight loss (TWL), percentage weight loss (%WL), excess weight loss (EWL), excess body mass index loss (EBMIL), BMI>35 kg/m2, kg gained from nadir, adjusted weight loss (AWL), rate or weight regain and percentage regained, etc. are all definitions reported in the literature. Given the abundance of definitions, it is often difficult to objectively evaluate a patients' post-operative weight outcomes, and even more challenging for researchers to

conduct studies on weight recidivism or weight trajectories when there is no standardized definition.

Recently, Belle et al. (2013) recommended standardized reporting for weight loss outcomes using percent weight loss (%WL) or commonly reported as total weight loss (TWL). Yanos (2014) used %TWL to measure weight changes in their cohort, defining weight regain as >20% regained from nadir to current weight (Yanos, Saules, Schuh, & Sogg, 2014). Similarly, other studies used >15% regained using %WL (Livhits et al., 2011; Odom et al., 2010) and an analysis of the SOS used %WL to report changes in body weight (J. Karlsson et al., 2007). Interestingly, Karlsson et al. (2007) separated surgical patients into categories of higher weight loss participants defined as ≥10% (percent change in body weight) and lower weight loss participants or <10% change in body weight and found over the ten year follow-up, lower weight loss participants regained a significant amount of weight compared to higher weight loss participants (2.8% weight loss vs 22.1% weight loss, respectively) (J. Karlsson et al., 2007). The LABS consortium published weight change trajectories on RYGB patients 3-yrs post-surgery and also found variability in weight change among participants, identifying 5 weight change trajectory groups, all demonstrating some form of weight regain. The report found that all 5 groups lost approximately 20-30% total weight (TWL) within the first 6 months after surgery (Courcoulas et al., 2013). One group began to steadily regain weight, while the other 4 groups reach nadir weight loss around year 1 or 2 and gradually increased weight by 2-8% at year three. These studies found discrepancies among participants losing and gaining weight and therefore used categories to represent weight

trajectories. Similar to our study, where participants were categorized as weight maintainers, low regainers or high regainers, weight regain appears to have difference trajectories within the groups.

Very few studies have taken into account the time (in months or years) it took to regain the weight, which should be an important factor when determining how much weight is lost or gained. For example, our study had participants ranging from 29 - 60 months post-op and 2.6-16.0 kg regained, with a positive correlation between the amount of weight regained after surgery and the length in time post-op. To compare weight trajectories within a cohort, the population should be standardized into the rate of regain, taking into account the time it took to regain the weight. In our study, weight regain was measured in kilograms regained from nadir to current weight divided by the number of months from nadir to current weight. For simplicity purposes, weight regained (kg) per month was converted into weight regained (kg) per year then split into three groups (tertiles). Similar to previous studies mentioned (Courcoulas et al., 2013; J. Karlsson et al., 2007; Tamboli et al., 2014), weight regain among RYGB patients appears to have different trajectories with some patients regaining at a higher rate and others maintaining weight. We feel confident that these methods have a greater impact on clinical relevance than other weight loss methods (i.e. %EWL or %EBMIL), given the variability in baseline values, such as height and chosen ideal body weight method (Belle et al., 2013; Karmali, Birch, & Sharma, 2009; Mann et al., 2014; Montero et al., 2011; A. van de Laar et al., 2011).

Appetite changes

In a weight loss state, it has been shown that measures of appetite (desire to eat, hunger and prospective food consumption) are heightened and measures of satiety (fullness) are depressed (Cornier, 2011; Cornier et al., 2004; Doucet et al., 2003; Drapeau et al., 2007; Gilbert et al., 2009). These factors contribute to weight regain, hence the number of studies that have shown less than 10% of participants are able to maintain weight loss for more than 5 years in conventional weight loss programs (Anderson, Konz, Frederich, & Wood, 2001; Byrne, Cooper, & Fairburn, 2004; Cornier, 2011; Phelan, Wing, Loria, Kim, & Lewis, 2010; Wadden, 1993; Wadden & Frey, 1997). Interestingly, in bariatric surgical patients, results are inconclusive. Bryant (2013) found decreased desire to eat and hunger score and increased fullness in a sample of twelve 1-year post-RYGB participants (Bryant et al., 2013). Conversely, Christou (2005) found no differences in appetite or satiety among patients with failed vs successful weight loss (Christou et al., 2005). Similarly, Dirkson et al. (2013) reported that hunger levels did not decrease after a meal in participants with poor weight loss or a control group compared to good weight loss responders (p = 0.006) (A. W. van de Laar & Acherman, 2013). Our findings were consistent with this as we did not observe any statistical significant differences for appetite (desire to eat, hunger, fullness and prospective food consumption) between the weight change groups or when comparing the highest tertile (high regainers) to the lowest tertile (weight maintainers). However, in conventional weight loss methods (i.e. through diet and/or exercise), increased appetite is associated with body weight loss (Cornier et al., 2004; Doucet et al., 2000; Drapeau et al., 2007; Schwartz, Woods, Porte, Seeley, & Baskin, 2000) and changes in leptin (Crujeiras et al., 2010; Doucet et al., 2000; Heini et

al., 1998; Rosenbaum et al., 2008). In surgical interventions, weight loss is proportional to leptin levels (Molina et al., 2003; Swarbrick et al., 2008). More so, reduced appetite after RYGB surgery appears to be related to elevated post-prandial PYY and GLP-1 and has been associated with sustained weight loss after surgery (Beckman et al., 2010; Korner et al., 2005; le Roux et al., 2006; Morinigo et al., 2008), however some research is indicating weight regain or poor weight loss may be associated with lower levels of PYY and GLP-1, increasing appetite (le Roux et al., 2007) or increases in leptin (Meguid et al., 2008). Although we did not report any significant findings in our study related to appetite, plasma samples were collected for future assay peripheral markers of appetite in our study (not tested at current date). Therefore further research is needed to investigate the relationship of peripheral hormones and appetite signals in RYGB patients post-surgery.

Smell Function

To our knowledge, the present study is the first to investigate olfactory function using the Sniffin' Sticks equipment in patients experiencing weight regain. There were no statistical significant findings for smell measures between groups, however when compared to other study measures, higher olfactory threshold scores were associated with liking of both high fat and low fat savory foods among weight maintainers and preferred liking for high fat sweet foods among high regainers. Limited research has investigated smell function in bariatric surgical patients, let alone, participants experiencing weight regain. Jurowich et al. (2014) concluded weight loss from surgical intervention did not influence olfactory perception in RYGB patients at 24 months post-op (as measured by

the Sniffin' Sticks) (Jurowich et al., 2014). Our results are comparable with the exception that we found higher mean threshold scores in high weight regainers (10.4 ± 3.8) compared to Jurowich et al. (2014) mean threshold score of 7.8 ± 1.4 (24 weeks post-RYGB), which is more comparable to our weight maintainer group (8.6 ± 2.6). In a recent study by Graham, Murty and Bowrey (2014), changes in smell were reported by 44%, 40%, 67%, and 22% of their sample at <12, 12-23, 24-35 and >36 months post-op, respectively (Graham, Murty, & Bowrey, 2014). Very few studies have looked at smell after bariatric surgery (Jurowich et al., 2014; Richardson et al., 2012), yet there is evidence to support that olfactory function is associated with increased palatability ratings and greater smell improvements in higher body weight participants during energy deprivation as a result of conventional weight loss (J. D. Cameron et al., 2012; Rolls, 2007). It has also been suggested that odor identification is closely related to memory (Stevenson, 2010), learned behaviours (Stevenson, 2010) and increased leptin levels (Morrison, 2009; Trellakis et al., 2011), hence the need to further investigate the effect of olfactory function and peripheral hormones in patients experiencing weight regain after RYGB surgery.

Eating Behaviours

Limited research has been conducted on the rationale behind those susceptible to weight regain while others maintain weight after bariatric surgery, however growing evidence supports adherence-related behaviours (Bastos, Barbosa, Soriano, dos Santos, & Vasconcelos, 2013; Karmali et al., 2013), pathological patterns of eating (Sarwer, Dilks, & West-Smith, 2011; Sarwer et al., 2008) and loss of control over food urges (Colles,

Dixon, & O'Brien, 2008; Konttinen et al., 2009; Odom et al., 2010) as possible explanations for weight regain. It has been well documented that patients prone to weight regain have lower dietary restraint (Klesges, Isbell, & Klesges, 1992; Persson, Welsh, Jonides, & Reuter-Lorenz, 2007; Sarwer et al., 2011), higher disinhibition (Bond et al., 2009; Epstein, Lin, Carr, & Fletcher, 2012; Livhits et al., 2011; McGuire et al., 1999; Niemeier et al., 2007) and perceived hunger (Marcus, Wing, & Lamparski, 1985; Sarwer et al., 2011), using the Eating Inventory, also known as the Three Factor Eating Questionnaire (TFEQ) (Belle et al., 2013). Our study was unable to statistically demonstrate any group differences for eating behaviours, such as dietary restraint, disinhibition or susceptibility to hunger, however we were able to find clinical statistical significance for dietary restraint among weight maintainers and low regainers and found an association between high dietary restraint and food reward measures (lower wanting of high-fat sweet foods).

Bond et al. (2009) examined eating behaviours (using the EI/TFEQ) in surgical and non-surgical participants from the National Weight Control Registry (NWCR) and found that higher levels of disinhibition predicted weight regained in both groups (Bond et al., 2009). Another study found similar results with higher levels of disinhibition associated with weight regain after RYGB (Livhits et al., 2011), which is observed in our study with higher levels of disinhibition among high regainers but no statistical significance was found between groups. Sarwer et al. (2008) found higher levels of cognitive or dietary restraint among patients experiencing greater weight loss postoperatively (p = 0.003) (Sarwer et al., 2008). More so, they found weight regain associated with low dietary

adherence over time. Interestingly, Sarwer (2008) also found a negative correlation between preoperative dietary restraint and % kcal/d from sweets ($r = -0.30$, $p = 0.003$) and % kcal/d from fat ($r = -0.21$, $p = 0.01$), which would suggest healthier eating behaviours preoperatively among those with higher dietary restraint. Conversely, our study found lower dietary restraint among patients experiencing weight regain, and although not investigated in our study, it could be suggested that weight regainers have diets higher in sweets and fat, as reported by other authors (Faria et al., 2010; Freire et al., 2012). Clinically, this has importance as post-operative patients reporting increased cravings for sweets and fats may have different dietary restraint scores, as seen in our study, proposing the administration of the EI/TFEQ into clinical practice to help identify patients at risk for possible weight regain.

Food Reward

Conventional weight loss (i.e. diet/exercise-induced weight loss) appears to cause a reverse effect on appetite opposed to bariatric surgery; as weight loss decreases, hunger increases. This counter-regulatory reaction has been well documented in weight loss or energy deprived studies (Berthoud, Lenard, & Shin, 2011; J. D. Cameron et al., 2014; Sumithran et al., 2011; Sumithran & Proietto, 2013), however growing evidence is finding RYGB surgery reduces this hunger response (Berthoud, Zheng, & Shin, 2012; Ernst, Thurnheer, Wilms, & Schultes, 2009), suggesting changes in homeostatic and non-homeostatic mechanisms. In fact, studies looking at the hedonic value of food or "liking vs wanting" of food are finding a transfer in food choices after RYGB (Leahey et al., 2012; Miras & le Roux, 2010; Ochner et al., 2012; J. Ullrich, Ernst, Wilms, Thurnheer, &

Schultes, 2013) with preferences towards lower calorie foods (Miras & le Roux, 2010; Ochner et al., 2012; J. Ullrich et al., 2013), specifically lower fat and lower sugar (Miras & le Roux, 2010; J. Ullrich et al., 2013). This shift towards healthier food choices could be in response to dietary and behavioural counselling before and after surgery, however, what is not well known, is what happens to hedonic values of food when RYGB patients regain weight? Munzberg et al. (2015) recently summarized the role of appetite and weight regulation after bariatric surgery and also concluded a gap in this area of food hedonic and weight regain after bariatric surgery (Munzberg, Laque, Yu, Rezai-Zadeh, & Berthoud, 2015). A number of authors have documented increased calories from high fat and high sugar foods among RYGB regainers (Bond et al., 2009; Brolin et al., 1994; Freire et al., 2012), however to our knowledge, our study is the first to investigate food hedonics using the LFPQ in bariatric surgical patients. We found that higher weight regainers preferred high-fat sweet foods and had higher explicit liking for taste (sweet and savory) and fat content (high fat and low fat) compared to weight maintainers. While dietary restraint was associated with wanting less high-fat sweet foods among weight maintainers and low regainers. These are interesting findings as it may explain how some RYGB patients are able to maintain their weight while others overconsume, returning to higher fat, higher sugar foods and eventually regain weight.

Several limitations are present in this study. The sample size was small and a cross-sectional design was chosen, therefore, generalization to all RYGB patients is not possible. This study shows associations between appetite-related measures and weight outcomes, however these do not pose a causality relationship. As previously mentioned,

weight regain is not defined in the literature, resulting in various interpretations and possible inaccurate comparisons. We did not control for psychological diagnoses, such as depression, anxiety, binge eating disorder or other mental health disorders, although, questions related binge eating disorder was collected, no clinical diagnostic testing was administered. Lastly, we did not include a control group, which may have influenced differences between the post-surgical weight groups and non-surgical controls.

In conclusion, the results of this study suggest that patients experiencing weight regain after RYGB surgery are exhibiting high liking for high-fat sweet foods, whereas weight maintainers have depressed wanting for high-fat sweet foods and appears to be associated with higher dietary restraint. Further investigation is necessary to determine the true relationship between smell function, appetite and peripheral hormones in patients experiencing weight regain after RYGB surgery.

CHAPTER 7: GENERAL DISCUSSION & FUTURE PERSPECTIVES

In reflection, there are a number of recommendations to improve the design and analysis of this study, however being that this study is quite novel, there are also a number of strengths. As mentioned previously, defining weight regain or determining successful weight trajectories was difficult as there is no standardized method in the literature. Researchers also fail to reflect on the clinical relevance of reporting weight change after bariatric surgery as some weight regain is inevitable as a normal biological outcome. In fact, it has been reported that the population will gain at least 1 kg/year, according to large population studies (Anderson et al., 2001; Chaput et al., 2009; Fine et al., 1999; Whitlock et al., 2009) and patients with obesity and/or a history of weight cycling will regain more weight as a compensation response to large energy imbalances (Fine et al., 1999; Sorensen, Rissanen, Korkeila, & Kaprio, 2005; Wing & Phelan, 2005). Instead, researchers should report weight regain at a percentage of weight from their nadir weight to current and include the number of months or years it took to regain the weight. This is considered a strength in our study, as weight regained was not categorized solely by a percentage of weight regained but by considering how long it took to regain the weight. Further standardized definitions need to be advocated in research and clinical practice, not just for the clinicians but for patient-expectations as well.

Future studies following similar objectives should include a larger sample size and a control group. Power calculations conducted prior to our data collection found a sample of 28 participants would suffice, however our study resulted in a sample of 29 participants, split into three groups. Results and statistical interpretation may be

inaccurate and would have been ideal if each group included 29 participants (for a total of 87 participants). Our study failed to provide a large enough gap between the weight maintenance group and weight regain groups, as a result, three groups emerged with possible overlapping weights. Future research should recruit participants with a much higher rate of regain and compare only high regainers to maintainers or a control group. More so, this study failed to include a control group, which would have provided much needed comparisons between the weight regainers and non-surgical patients with obesity. As reported in our study, food behaviours favouring higher-fat sweet foods appears to be higher among weight regainers; a control group would have proved a good comparison for food reward behaviours and appetite measures.

Additionally, our study applied a cross-sectional design without pre-surgical data except for body weight and BMI. A prospective study collecting appetite measures before and after surgery long-term would be recommended for complete overview of weight relapse after obesity surgery. Nadir weight was self-reported by participants and confirmed by chart review, however not all participants attended clinical appointments or may not have attended a clinical appointment during their nadir weight. This study failed to measure how long participants were able to maintain nadir weight, more so, adherence to follow-up was not measured and is considered a predictor for weight regain (Freire et al., 2012; Harper, Madan, Ternovits, & Tichansky, 2007; Magro et al., 2008; McGuire et al., 1999), hence, future research should consider these limitations.

Despite the number of limitations and general recommendations, this study does provide novel insight to appetite-measures among weight changes after RYGB surgery. This study is the first, to our knowledge, to investigate smell function using the Sniffin' Sticks among surgical patients with weight regain. Food reward using the Leeds Food Preference Questionnaire (LFPQ) is also a novel measurement in post-RYGB patients, as well as comparing these appetite measures among weight change groups and peripheral hormones. Although, this study failed to present the data analysis of the peripheral hormones, blood samples were completed and will be analyzed at a later date. This will also be a novel contribution of our study, as no study has investigated appetite-related measures, including peripheral hormones specifically among weight regain participants after RYGB surgery. Our findings, along with future analysis of hormone levels may provide substantial evidence for why patients may be experiencing weight regain after a surgical intervention. Furthermore, future research is needed in this area looking at longitudinal studies and evidentially knowledge translation for clinical distribution and counselling.

REFERENCES:

Adami, G. F., Gandolfo, P., Dapueto, R., Jurich, D., & Scopinaro, N. (1993). Eating behavior following biliopancreatic diversion for obesity: study with a three-factor eating questionnaire. [Comparative Study]. *Int J Eat Disord, 14*(1), 81-86.

Adams, T. D., Davidson, L. E., Litwin, S. E., Kolotkin, R. L., LaMonte, M. J., Pendleton, R. C., . . . Hunt, S. C. (2012). Health benefits of gastric bypass surgery after 6 years. [Research Support, N.I.H., Extramural]. *JAMA, 308*(11), 1122-1131. doi: 10.1001/2012.jama.11164

Anderson, J. W., Konz, E. C., Frederich, R. C., & Wood, C. L. (2001). Long-term weight-loss maintenance: a meta-analysis of US studies. [Meta-Analysis Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, Non-P.H.S.]. *Am J Clin Nutr, 74*(5), 579-584.

Bastos, E. C., Barbosa, E. M., Soriano, G. M., dos Santos, E. A., & Vasconcelos, S. M. (2013). Determinants of weight regain after bariatric surgery. *Arq Bras Cir Dig, 26 Suppl 1*, 26-32.

Batterham, R. L., Cowley, M. A., Small, C. J., Herzog, H., Cohen, M. A., Dakin, C. L., . . . Bloom, S. R. (2002). Gut hormone PYY(3-36) physiologically inhibits food intake. *Nature, 418*(6898), 650-654. doi: 10.1038/nature02666

Bavaresco, M., Paganini, S., Lima, T. P., Salgado, W., Jr., Ceneviva, R., Dos Santos, J. E., & Nonino-Borges, C. B. (2010). Nutritional course of patients submitted to bariatric surgery. *Obes Surg, 20*(6), 716-721. doi: 10.1007/s11695-008-9721-6

Beckman, L. M., Beckman, T. R., & Earthman, C. P. (2010). Changes in gastrointestinal hormones and leptin after Roux-en-Y gastric bypass procedure: a review. [Review]. *J Am Diet Assoc, 110*(4), 571-584.

Belle, S. H., Berk, P. D., Courcoulas, A. P., Engel, S., Flum, D. R., Gourash, W. (2013). Reporting weight change: standardized reporting accounting for baseline weight. [Research Support, N.I.H., Extramural]. *Surg Obes Relat Dis, 9*(5), 782-789. doi: 10.1016/j.soard.2012.11.006

Berthoud, H. R., Lenard, N. R., & Shin, A. C. (2011). Food reward, hyperphagia, and obesity. [Research Support, N.I.H., Extramural

Review]. *Am J Physiol Regul Integr Comp Physiol, 300*(6), R1266-1277. doi: 10.1152/ajpregu.00028.2011

Berthoud, H. R., Zheng, H., & Shin, A. C. (2012). Food reward in the obese and after weight loss induced by calorie restriction and bariatric surgery. *Ann N Y Acad Sci, 1264*(1), 36-48. doi: 10.1111/j.1749-6632.2012.06573.x

Bohlender, J., Rauh, M., Zenk, J., & Groschl, M. (2003). Differential distribution and expression of leptin and the functional leptin receptor in major salivary glands of humans. *J Endocrinol, 178*(2), 217-223.

Bond, D. S., Phelan, S., Leahey, T. M., Hill, J. O., & Wing, R. R. (2009). Weight-loss maintenance in successful weight losers: surgical vs non-surgical methods. [Comparative Study

Research Support, N.I.H., Extramural]. *Int J Obes (Lond), 33*(1), 173-180. doi: 10.1038/ijo.2008.256

Borg, C. M., le Roux, C. W., Ghatei, M. A., Bloom, S. R., Patel, A. G., & Aylwin, S. J. (2006). Progressive rise in gut hormone levels after Roux-en-Y gastric bypass

suggests gut adaptation and explains altered satiety. *Br J Surg, 93*(2), 210-215. doi: 10.1002/bjs.5227

Brolin, R. E., Robertson, L. B., Kenler, H. A., & Cody, R. P. (1994). Weight loss and dietary intake after vertical banded gastroplasty and Roux-en-Y gastric bypass. [Clinical Trial]. *Ann Surg, 220*(6), 782-790.

Bryant, E. J., King, N. A., Falken, Y., Hellstrom, P. M., Holst, J. J., Blundell, J. E., & Naslund, E. (2013). Relationships among tonic and episodic aspects of motivation to eat, gut peptides, and weight before and after bariatric surgery. [Research Support, Non-U.S. Gov't]. *Surg Obes Relat Dis, 9*(5), 802-808. doi: 10.1016/j.soard.2012.09.011

Buchwald, H., Avidor, Y., Braunwald, E., Jensen, M. D., Pories, W., Fahrbach, K., & Schoelles, K. (2004). Bariatric surgery: a systematic review and meta-analysis. [Meta-Analysis Research Support, Non-U.S. Gov't Review]. *JAMA, 292*(14), 1724-1737. doi: 10.1001/jama.292.14.1724

Budak, E., Fernandez Sanchez, M., Bellver, J., Cervero, A., Simon, C., & Pellicer, A. (2006). Interactions of the hormones leptin, ghrelin, adiponectin, resistin, and PYY3-36 with the reproductive system. [Review]. *Fertil Steril, 85*(6), 1563-1581. doi: 10.1016/j.fertnstert.2005.09.065

Byrne, S. M., Cooper, Z., & Fairburn, C. G. (2004). Psychological predictors of weight regain in obesity. [Research Support, Non-U.S. Gov't]. *Behav Res Ther, 42*(11), 1341-1356. doi: 10.1016/j.brat.2003.09.004

Cameron, J., Riou, M. E., Goldfield, G. S., Finlayson, G., Blundell, J. E., & Doucet, E. *Deprivation by diet alone or by aerobic exercise alone: how modality of a acute intervention can differently impact olfaction, food reward, and ad libitum feeding, and appetite hormones.* . Unpublished manuscript.

Cameron, J. D., Goldfield, G. S., Cyr, M. J., & Doucet, E. (2008). The effects of prolonged caloric restriction leading to weight-loss on food hedonics and reinforcement. [Research Support, Non-U.S. Gov't]. *Physiol Behav, 94*(3), 474-480. doi: 10.1016/j.physbeh.2008.02.014

Cameron, J. D., Goldfield, G. S., & Doucet, E. (2012). Fasting for 24 h improves nasal chemosensory performance and food palatability in a related manner. [Randomized Controlled Trial

Research Support, Non-U.S. Gov't]. *Appetite, 58*(3), 978-981. doi: 10.1016/j.appet.2012.02.050

Cameron, J. D., Goldfield, G. S., Finlayson, G., Blundell, J. E., & Doucet, E. (2014). Fasting for 24 hours heightens reward from food and food-related cues. [Randomized Controlled Trial

Research Support, Non-U.S. Gov't]. *PLoS One, 9*(1), e85970. doi: 10.1371/journal.pone.0085970

Chaput, J. P., Leblanc, C., Perusse, L., Despres, J. P., Bouchard, C., & Tremblay, A. (2009). Risk factors for adult overweight and obesity in the Quebec Family Study: have we been barking up the wrong tree? [Research Support, Non-U.S. Gov't]. *Obesity (Silver Spring), 17*(10), 1964-1970. doi: 10.1038/oby.2009.116

Christou, N. V., Look, D., & Maclean, L. D. (2006). Weight gain after short- and long-limb gastric bypass in patients followed for longer than 10 years. [Research

Support, Non-U.S. Gov't]. *Ann Surg, 244*(5), 734-740. doi: 10.1097/01.sla.0000217592.04061.d5

Christou, N. V., Look, D., & McLean, A. P. (2005). Pre- and post-prandial plasma ghrelin levels do not correlate with satiety or failure to achieve a successful outcome after Roux-en-Y gastric bypass. [Comparative Study]. *Obes Surg, 15*(7), 1017-1023. doi: 10.1381/0960892054621071

Clark, M. M., Marcus, B. H., Pera, V., & Niaura, R. S. (1994). Changes in eating inventory scores following obesity treatment. *Int J Eat Disord, 15*(4), 401-405.

Colles, S. L., Dixon, J. B., & O'Brien, P. E. (2008). Grazing and loss of control related to eating: two high-risk factors following bariatric surgery. [Clinical Trial

Research Support, Non-U.S. Gov't]. *Obesity (Silver Spring), 16*(3), 615-622. doi: 10.1038/oby.2007.101

Colquitt, J., Clegg, A., Loveman, E., Royle, P., & Sidhu, M. K. (2005). Surgery for morbid obesity. [Review]. *Cochrane Database Syst Rev*(4), CD003641. doi: 10.1002/14651858.CD003641.pub2

Cornier, M. A. (2011). Is your brain to blame for weight regain? [Research Support, N.I.H., Extramural Review]. *Physiol Behav, 104*(4), 608-612. doi: 10.1016/j.physbeh.2011.04.003

Cornier, M. A., Grunwald, G. K., Johnson, S. L., & Bessesen, D. H. (2004). Effects of short-term overfeeding on hunger, satiety, and energy intake in thin and reduced-obese individuals. [Research Support, U.S. Gov't, P.H.S.]. *Appetite, 43*(3), 253-259. doi: 10.1016/j.appet.2004.06.003

Courcoulas, A. P., Christian, N. J., Belle, S. H., Berk, P. D., Flum, D. R., Garcia, L. Longitudinal Assessment of Bariatric Surgery, C. (2013). Weight change and health outcomes at 3 years after bariatric surgery among individuals with severe obesity. [Multicenter Study Observational Study Research Support, N.I.H., Extramural]. *JAMA, 310*(22), 2416-2425. doi: 10.1001/jama.2013.280928

Crujeiras, A. B., Goyenechea, E., Abete, I., Lage, M., Carreira, M. C., Martinez, J. A., & Casanueva, F. F. (2010). Weight regain after a diet-induced loss is predicted by higher baseline leptin and lower ghrelin plasma levels. [Research Support, Non-U.S. Gov't]. *J Clin Endocrinol Metab, 95*(11), 5037-5044. doi: 10.1210/jc.2009-2566

Cummings, D. E., & Overduin, J. (2007). Gastrointestinal regulation of food intake. [Research Support, N.I.H., Extramural Review]. *J Clin Invest, 117*(1), 13-23. doi: 10.1172/JCI30227

Cummings, D. E., Weigle, D. S., Frayo, R. S., Breen, P. A., Ma, M. K., Dellinger, E. P., & Purnell, J. Q. (2002). Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. [Comparative Study Research Support, Non-U S Gov't Research Support, U S Gov't, Non-P H S Research Support, U S Gov't, P H S]. *N Engl J Med, 346*(21), 1623-1630.

De Silva, A., Salem, V., Long, C. J., Makwana, A., Newbould, R. D., Rabiner, E. A., Dhillo, W. S. (2011). The gut hormones PYY 3-36 and GLP-1 7-36 amide reduce food intake and modulate brain activity in appetite centers in humans. [Randomized Controlled Trial Research Support, Non-U S Gov't]. *Cell Metab, 14*(5), 700-706.

Dias, M. C., Ribeiro, A. G., Scabim, V. M., Faintuch, J., Zilberstein, B., & Gama-Rodrigues, J. J. (2006). Dietary intake of female bariatric patients after anti-obesity gastroplasty. *Clinics (Sao Paulo), 61*(2), 93-98. doi: /S1807-59322006000200002

Dirksen, C., Jorgensen, N. B., Bojsen-Moller, K. N., Kielgast, U., Jacobsen, S. H., Clausen, T. R., . . . Hansen, D. L. (2013). Gut hormones, early dumping and resting energy expenditure in patients with good and poor weight loss response after Roux-en-Y gastric bypass. *Int J Obes (Lond)*. doi: 10.1038/ijo.2013.15

Dixon, J. B., McPhail, T., & O'Brien, P. E. (2005). Minimal reporting requirements for weight loss: current methods not ideal. [Comparative Study]. *Obes Surg, 15*(7), 1034-1039. doi: 10.1381/0960892054621053

Doucet, E., Imbeault, P., St-Pierre, S., Almeras, N., Mauriege, P., Richard, D., & Tremblay, A. (2000). Appetite after weight loss by energy restriction and a low-fat diet-exercise follow-up. [Research Support, Non-U.S. Gov't]. *Int J Obes Relat Metab Disord, 24*(7), 906-914.

Doucet, E., St-Pierre, S., Almeras, N., & Tremblay, A. (2003). Relation between appetite ratings before and after a standard meal and estimates of daily energy intake in obese and reduced obese individuals. [Research Support, Non-U.S. Gov't]. *Appetite, 40*(2), 137-143.

Drapeau, V., King, N., Hetherington, M., Doucet, E., Blundell, J., & Tremblay, A. (2007). Appetite sensations and satiety quotient: predictors of energy intake and weight loss. [Research Support, Non-U.S. Gov't]. *Appetite, 48*(2), 159-166. doi: 10.1016/j.appet.2006.08.002

English, P. J., Ghatei, M. A., Malik, I. A., Bloom, S. R., & Wilding, J. P. (2002). Food fails to suppress ghrelin levels in obese humans. *J Clin Endocrinol Metab, 87*(6), 2984.

Engstrom, B. E., Ohrvall, M., Sundbom, M., Lind, L., & Karlsson, F. A. (2007). Meal suppression of circulating ghrelin is normalized in obese individuals following gastric bypass surgery. *Int J Obes (Lond), 31*(3), 476-480. doi: 10.1038/sj.ijo.0803440

Epstein, L. H., Leddy, J. J., Temple, J. L., & Faith, M. S. (2007). Food reinforcement and eating: a multilevel analysis. [Research Support, N.I.H., Extramural Review]. *Psychol Bull, 133*(5), 884-906. doi: 10.1037/0033-2909.133.5.884

Epstein, L. H., Lin, H., Carr, K. A., & Fletcher, K. D. (2012). Food reinforcement and obesity. Psychological moderators. [Research Support, N.I.H., Extramural]. *Appetite, 58*(1), 157-162. doi: 10.1016/j.appet.2011.09.025

Epstein, L. H., Truesdale, R., Wojcik, A., Paluch, R. A., & Raynor, H. A. (2003). Effects of deprivation on hedonics and reinforcing value of food. [Clinical Trial Randomized Controlled Trial Research Support, U.S. Gov't, P.H.S.]. *Physiol Behav, 78*(2), 221-227.

Ernst, B., Thurnheer, M., Wilms, B., & Schultes, B. (2009). Differential changes in dietary habits after gastric bypass versus gastric banding operations. [Comparative Study Research Support, Non-U.S. Gov't]. *Obes Surg, 19*(3), 274-280. doi: 10.1007/s11695-008-9769-3

Evans, S., Pamuklar, Z., Rosko, J., Mahaney, P., Jiang, N., Park, C., & Torquati, A. (2012). Gastric bypass surgery restores meal stimulation of the anorexigenic gut

hormones glucagon-like peptide-1 and peptide YY independently of caloric restriction. [Research Support, N.I.H., Extramural]. *Surg Endosc, 26*(4), 1086-1094. doi: 10.1007/s00464-011-2004-7

Faria, S. L., de Oliveira Kelly, E., Lins, R. D., & Faria, O. P. (2010). Nutritional management of weight regain after bariatric surgery. *Obes Surg, 20*(2), 135-139. doi: 10.1007/s11695-008-9610-z

Farooqi, I. S., Bullmore, E., Keogh, J., Gillard, J., O'Rahilly, S., & Fletcher, P. C. (2007). Leptin regulates striatal regions and human eating behavior. [Case Reports Clinical Trial Research Support, Non-U.S. Gov't]. *Science, 317*(5843), 1355. doi: 10.1126/science.1144599

Fine, J. T., Colditz, G. A., Coakley, E. H., Moseley, G., Manson, J. E., Willett, W. C., & Kawachi, I. (1999). A prospective study of weight change and health-related quality of life in women. [Research Support, U.S. Gov't, P.H.S.]. *JAMA, 282*(22), 2136-2142.

Finlayson, G., Arlotti, A., Dalton, M., King, N., & Blundell, J. E. (2011). Implicit wanting and explicit liking are markers for trait binge eating. A susceptible phenotype for overeating. [Research Support, Non-U.S. Gov't]. *Appetite, 57*(3), 722-728. doi: 10.1016/j.appet.2011.08.012

Flancbaum, L., Choban, P. S., Bradley, L. R., & Burge, J. C. (1997). Changes in measured resting energy expenditure after Roux-en-Y gastric bypass for clinically severe obesity. *Surgery, 122*(5), 943-949.

Foster, G. D., Wadden, T. A., Swain, R. M., Stunkard, A. J., Platte, P., & Vogt, R. A. (1998). The Eating Inventory in obese women: clinical correlates and relationship to weight loss. [Research Support, U.S. Gov't, P.H.S.]. *Int J Obes Relat Metab Disord, 22*(8), 778-785.

Freire, R. H., Borges, M. C., Alvarez-Leite, J. I., & Toulson Davisson Correia, M. I. (2012). Food quality, physical activity, and nutritional follow-up as determinant of weight regain after Roux-en-Y gastric bypass. [Research Support, Non-U.S. Gov't]. *Nutrition, 28*(1), 53-58. doi: 10.1016/j.nut.2011.01.011

Frezza, E. E., Wachtel, M. S., & Chiriva-Internati, M. (2007). The multiple faces of glucagon-like peptide-1--obesity, appetite, and stress: what is next? A review. [Review]. *Dig Dis Sci, 52*(3), 643-649. doi: 10.1007/s10620-006-9096-2

Fulton, S., Woodside, B., & Shizgal, P. (2000). Modulation of brain reward circuitry by leptin. [Research Support, Non-U.S. Gov't]. *Science, 287*(5450), 125-128.

Gale, S. M., Castracane, V. D., & Mantzoros, C. S. (2004). Energy homeostasis, obesity and eating disorders: recent advances in endocrinology. [Review]. *J Nutr, 134*(2), 295-298.

Gilbert, J. A., Drapeau, V., Astrup, A., & Tremblay, A. (2009). Relationship between diet-induced changes in body fat and appetite sensations in women. *Appetite, 52*(3), 809-812. doi: 10.1016/j.appet.2009.04.003

Graham, L., Murty, G., & Bowrey, D. J. (2014). Taste, smell and appetite change after Roux-en-Y gastric bypass surgery. [Research Support, Non-U.S. Gov't]. *Obes Surg, 24*(9), 1463-1468. doi: 10.1007/s11695-014-1221-2

Green, S. M., Delargy, H. J., Joanes, D., & Blundell, J. E. (1997). A satiety quotient: a formulation to assess the satiating effect of food. [Comparative Study]. *Appetite, 29*(3), 291-304.

Griffioen-Roose, S., Finlayson, G., Mars, M., Blundell, J. E., & de Graaf, C. (2010). Measuring food reward and the transfer effect of sensory specific satiety. [Comparative Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *Appetite, 55*(3), 648-655. doi: 10.1016/j.appet.2010.09.018

Haehner, A., Mayer, A. M., Landis, B. N., Pournaras, I., Lill, K., Gudziol, V., & Hummel, T. (2009). High test-retest reliability of the extended version of the "Sniffin' Sticks" test. [Evaluation Studies Research Support, Non-U.S. Gov't]. *Chem Senses, 34*(8), 705-711. doi: 10.1093/chemse/bjp057

Harper, J., Madan, A. K., Ternovits, C. A., & Tichansky, D. S. (2007). What happens to patients who do not follow-up after bariatric surgery? [Comparative Study]. *Am Surg, 73*(2), 181-184.

Heini, A. F., Lara-Castro, C., Kirk, K. A., Considine, R. V., Caro, J. F., & Weinsier, R. L. (1998). Association of leptin and hunger-satiety ratings in obese women. [Research Support, Non-U.S. Gov't]. *Int J Obes Relat Metab Disord, 22*(11), 1084-1087.

Hill, A. J., Magson, L. D., & Blundell, J. E. (1984). Hunger and palatability: tracking ratings of subjective experience before, during and after the consumption of preferred and less preferred food. *Appetite, 5*(4), 361-371.

Hummel, T., Kobal, G., Gudziol, H., & Mackay-Sim, A. (2007). Normative data for the "Sniffin' Sticks" including tests of odor identification, odor discrimination, and olfactory thresholds: an upgrade based on a group of more than 3,000 subjects. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. *Eur Arch Otorhinolaryngol, 264*(3), 237-243. doi: 10.1007/s00405-006-0173-0

Hummel, T., Sekinger, B., Wolf, S. R., Pauli, E., & Kobal, G. (1997). 'Sniffin' sticks': olfactory performance assessed by the combined testing of odor identification, odor discrimination and olfactory threshold. *Chem Senses, 22*(1), 39-52.

Julliard, A. K., Chaput, M. A., Apelbaum, A., Aime, P., Mahfouz, M., & Duchamp-Viret, P. (2007). Changes in rat olfactory detection performance induced by orexin and leptin mimicking fasting and satiation. [Research Support, Non-U.S. Gov't]. *Behav Brain Res, 183*(2), 123-129. doi: 10.1016/j.bbr.2007.05.033

Jurowich, C. F., Seyfried, F., Miras, A. D., Bueter, M., Deckelmann, J., Fassnacht, M., Thalheimer, A. (2014). Does bariatric surgery change olfactory perception? Results of the early postoperative course. *Int J Colorectal Dis, 29*(2), 253-260. doi: 10.1007/s00384-013-1795-5

Karlsson, F., Modica, A., & Mooe, T. (2007). Dynamics of platelet activation in diabetic and non-diabetic subjects during the course of an acute myocardial infarction. [Research Support, Non-U.S. Gov't]. *Thromb Res, 121*(2), 269-273. doi: 10.1016/j.thromres.2007.04.011

Karlsson, J., Taft, C., Ryden, A., Sjostrom, L., & Sullivan, M. (2007). Ten-year trends in health-related quality of life after surgical and conventional treatment for severe obesity: the SOS intervention study. [Research Support, Non-U.S. Gov't]. *Int J Obes (Lond), 31*(8), 1248-1261. doi: 10.1038/sj.ijo.0803573

Karmali, S., Birch, D. W., & Sharma, A. M. (2009). Is it time to abandon excess weight loss in reporting surgical weight loss? [Review]. *Surg Obes Relat Dis, 5*(4), 503-506. doi: 10.1016/j.soard.2009.04.014

Karmali, S., Brar, B., Shi, X., Sharma, A. M., de Gara, C., & Birch, D. W. (2013). Weight recidivism post-bariatric surgery: a systematic review. [Review]. *Obes Surg, 23*(11), 1922-1933. doi: 10.1007/s11695-013-1070-4

Klesges, R. C., Isbell, T. R., & Klesges, L. M. (1992). Relationship between dietary restraint, energy intake, physical activity, and body weight: a prospective analysis. [Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.]. *J Abnorm Psychol, 101*(4), 668-674.

Kofman, M. D., Lent, M. R., & Swencionis, C. (2010). Maladaptive eating patterns, quality of life, and weight outcomes following gastric bypass: results of an Internet survey. *Obesity (Silver Spring), 18*(10), 1938-1943. doi: 10.1038/oby.2010.27

Konttinen, H., Haukkala, A., Sarlio-Lahteenkorva, S., Silventoinen, K., & Jousilahti, P. (2009). Eating styles, self-control and obesity indicators. The moderating role of obesity status and dieting history on restrained eating. [Research Support, Non-U.S. Gov't]. *Appetite, 53*(1), 131-134. doi: 10.1016/j.appet.2009.05.001

Korner, J., Bessler, M., Cirilo, L. J., Conwell, I. M., Daud, A., Restuccia, N. L., & Wardlaw, S. L. (2005). Effects of Roux-en-Y gastric bypass surgery on fasting and postprandial concentrations of plasma ghrelin, peptide YY, and insulin. [Research Support, U.S. Gov't, P.H.S.]. *J Clin Endocrinol Metab, 90*(1), 359-365. doi: 10.1210/jc.2004-1076

Kruseman, M., Leimgruber, A., Zumbach, F., & Golay, A. (2010). Dietary, weight, and psychological changes among patients with obesity, 8 years after gastric bypass. *J Am Diet Assoc, 110*(4), 527-534. doi: 10.1016/j.jada.2009.12.028

Laferrere, B., Heshka, S., Wang, K., Khan, Y., McGinty, J., Teixeira, J., Olivan, B. (2007). Incretin levels and effect are markedly enhanced 1 month after Roux-en-Y gastric bypass surgery in obese patients with type 2 diabetes. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. *Diabetes Care, 30*(7), 1709-1716. doi: 10.2337/dc06-1549

le Roux, C. W., Aylwin, S. J., Batterham, R. L., Borg, C. M., Coyle, F., Prasad, V., Bloom, S. R. (2006). Gut hormone profiles following bariatric surgery favor an anorectic state, facilitate weight loss, and improve metabolic parameters. *Ann Surg, 243*(1), 108-114. doi: 00000658-200601000-00017 [pii]

le Roux, C. W., & Bloom, S. R. (2005). Peptide YY, appetite and food intake. [Review]. *Proc Nutr Soc, 64*(2), 213-216.

le Roux, C. W., Neary, N. M., Halsey, T. J., Small, C. J., Martinez-Isla, A. M., Ghatei, M. A., . . . Bloom, S. R. (2005). Ghrelin does not stimulate food intake in patients with surgical procedures involving vagotomy. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *J Clin Endocrinol Metab, 90*(8), 4521-4524. doi: 10.1210/jc.2004-2537

le Roux, C. W., Welbourn, R., Werling, M., Osborne, A., Kokkinos, A., Laurenius, A., . . . Olbers, T. (2007). Gut hormones as mediators of appetite and weight loss after Roux-en-Y gastric bypass. [Clinical Trial Research Support, Non-U.S. Gov't]. *Ann Surg, 246*(5), 780-785. doi: 10.1097/SLA.0b013e3180caa3e3

Leahey, T. M., Bond, D. S., Raynor, H., Roye, D., Vithiananthan, S., Ryder, B. A., Wing, R. R. (2012). Effects of bariatric surgery on food cravings: do food cravings and

the consumption of craved foods "normalize" after surgery? *Surg Obes Relat Dis, 8*(1), 84-91. doi: 10.1016/j.soard.2011.07.016

Lee, W. J., Chen, C. Y., Chong, K., Lee, Y. C., Chen, S. C., & Lee, S. D. (2011). Changes in postprandial gut hormones after metabolic surgery: a comparison of gastric bypass and sleeve gastrectomy. [Multicenter Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *Surg Obes Relat Dis, 7*(6), 683-690. doi: 10.1016/j.soard.2011.07.009

Lin, E., Gletsu, N., Fugate, K., McClusky, D., Gu, L. H., Zhu, J. L., Smith, C. D. (2004). The effects of gastric surgery on systemic ghrelin levels in the morbidly obese. [Research Support, U.S. Gov't, P.H.S.]. *Arch Surg, 139*(7), 780-784. doi: 10.1001/archsurg.139.7.780

Livhits, M., Mercado, C., Yermilov, I., Parikh, J. A., Dutson, E., Mehran, A., . . . Gibbons, M. M. (2011). Patient behaviors associated with weight regain after laparoscopic gastric bypass. *Obes Res Clin Pract, 5*(3), e169-266. doi: 10.1016/j.orcp.2011.03.004

Lowe, M. R., Doshi, S. D., Katterman, S. N., & Feig, E. H. (2013). Dieting and restrained eating as prospective predictors of weight gain. [Review]. *Front Psychol, 4*, 577. doi: 10.3389/fpsyg.2013.00577

Magro, D. O., Geloneze, B., Delfini, R., Pareja, B. C., Callejas, F., & Pareja, J. C. (2008). Long-term weight regain after gastric bypass: a 5-year prospective study. *Obes Surg, 18*(6), 648-651. doi: 10.1007/s11695-007-9265-1

Mann, J. P., Jakes, A. D., Hayden, J. D., & Barth, J. H. (2014). Systematic Review of Definitions of Failure in Revisional Bariatric Surgery. *Obes Surg*. doi: 10.1007/s11695-014-1541-2

Marcus, M. D., Wing, R. R., & Lamparski, D. M. (1985). Binge eating and dietary restraint in obese patients. *Addict Behav, 10*(2), 163-168.

McGuire, M. T., Wing, R. R., Klem, M. L., Lang, W., & Hill, J. O. (1999). What predicts weight regain in a group of successful weight losers? [Comparative Study Research Support, Non-U.S. Gov't]. *J Consult Clin Psychol, 67*(2), 177-185.

Meguid, M. M., Glade, M. J., & Middleton, F. A. (2008). Weight regain after Roux-en-Y: a significant 20% complication related to PYY. *Nutrition, 24*(9), 832-842. doi: S0899-9007(08)00300-6 [pii] 10.1016/j.nut.2008.06.027

Meier, U., & Gressner, A. M. (2004). Endocrine regulation of energy metabolism: review of pathobiochemical and clinical chemical aspects of leptin, ghrelin, adiponectin, and resistin. [Review]. C*lin Chem, 50(*9), 1511-1525. doi: 10.1373/clinchem.2004.032482

Melton, G. B., Steele, K. E., Schweitzer, M. A., Lidor, A. O., & Magnuson, T. H. (2008). Suboptimal weight loss after gastric bypass surgery: correlation of demographics, comorbidities, and insurance status with outcomes. J *Gastrointest Surg, 12(*2), 250-255. doi: 10.1007/s11605-007-0427-1

Miras, A. D., & le Roux, C. W. (2010). Bariatric surgery and taste: novel mechanisms of weight loss. [Review]. C*urr Opin Gastroenterol, 26(*2), 140-145. doi: 10.1097/MOG.0b013e328333e94a

Molina, A., Vendrell, J., Gutierrez, C., Simon, I., Masdevall, C., Soler, J., & Gomez, J. M. (2003). Insulin resistance, leptin and TNF-alpha system in morbidly obese

women after gastric bypass. [Research Support, Non-U.S. Gov't]. O*bes Surg, 13(*4), 615-621. doi: 10.1381/096089203322190844

Montero, P. N., Stefanidis, D., Norton, H. J., Gersin, K., & Kuwada, T. (2011). Reported excess weight loss after bariatric surgery could vary significantly depending on calculation method: a plea for standardization. S*urg Obes Relat Dis, 7(*4), 531-534. doi: 10.1016/j.soard.2010.09.025

Morinigo, R., Casamitjana, R., Moize, V., Lacy, A. M., Delgado, S., Gomis, R., & Vidal, J. (2004). Short-term effects of gastric bypass surgery on circulating ghrelin levels. [Research Support, Non-U.S. Gov't]. O*bes Res, 12(*7), 1108-1116. doi: 10.1038/oby.2004.139

Morinigo, R., Moize, V., Musri, M., Lacy, A. M., Navarro, S., Marin, J. L., Vidal, J. (2006). Glucagon-like peptide-1, peptide YY, hunger, and satiety after gastric bypass surgery in morbidly obese subjects. [Research Support, Non-U.S. Gov't]. J *Clin Endocrinol Metab, 91(*5), 1735-1740. doi: 10.1210/jc.2005-0904

Morinigo, R., Vidal, J., Lacy, A. M., Delgado, S., Casamitjana, R., & Gomis, R. (2008). Circulating peptide YY, weight loss, and glucose homeostasis after gastric bypass surgery in morbidly obese subjects. [Comparative Study Research Support, Non-U.S. Gov't]. A*nn Surg, 247(*2), 270-275. doi: 10.1097/SLA.0b013e31815f6e77

Morrison, C. D. (2009). Leptin signaling in brain: A link between nutrition and cognition? [Review]. B*iochim Biophys Acta, 1792(*5), 401-408. doi: 10.1016/j.bbadis.2008.12.004

Munzberg, H., Laque, A., Yu, S., Rezai-Zadeh, K., & Berthoud, H. R. (2015). Appetite and body weight regulation after bariatric surgery. O*bes Rev, 16 Suppl 1,* 77-90. doi: 10.1111/obr.12258

Murphy, K. G., & Bloom, S. R. (2006). Gut hormones and the regulation of energy homeostasis. [Research Support, Non-U.S. Gov't Review]. N*ature, 444(*7121), 854-859. doi: 10.1038/nature05484

Naslund, E., Barkeling, B., King, N., Gutniak, M., Blundell, J. E., Holst, J. J., Hellstrom, P. M. (1999). Energy intake and appetite are suppressed by glucagon-like peptide-1 (GLP-1) in obese men. [Clinical Trial Randomized Controlled Trial Research Support, Non-U.S. Gov't]. I*nt J Obes Relat Metab Disord, 23(*3), 304-311.

Niemeier, H. M., Phelan, S., Fava, J. L., & Wing, R. R. (2007). Internal disinhibition predicts weight regain following weight loss and weight loss maintenance. [Research Support, N.I.H., Extramural]. O*besity (Silver Spring), 15(*10), 2485-2494. doi: 10.1038/oby.2007.295

Ochner, C. N., Gibson, C., Shanik, M., Goel, V., & Geliebter, A. (2011). Changes in neurohormonal gut peptides following bariatric surgery. [Review]. I*nt J Obes (Lond), 35(*2), 153-166. doi: 10.1038/ijo.2010.132

Ochner, C. N., Kwok, Y., Conceicao, E., Pantazatos, S. P., Puma, L. M., Carnell, S., Geliebter, A. (2011). Selective reduction in neural responses to high calorie foods following gastric bypass surgery. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. A*nn Surg, 253(*3), 502-507. doi: 10.1097/SLA.0b013e318203a289

Ochner, C. N., Stice, E., Hutchins, E., Afifi, L., Geliebter, A., Hirsch, J., & Teixeira, J. (2012). Relation between changes in neural responsivity and reductions in desire to eat high-calorie foods following gastric bypass surgery. [Research Support,

N.I.H., Extramural]. N*euroscience, 209,* 128-135. doi: 10.1016/j.neuroscience.2012.02.030
Odom, J., Zalesin, K. C., Washington, T. L., Miller, W. W., Hakmeh, B., Zaremba, D. L., . . . McCullough, P. A. (2010). Behavioral predictors of weight regain after bariatric surgery. O*bes Surg, 20(*3), 349-356. doi: 10.1007/s11695-009-9895-6
Ortega, E., Morinigo, R., Flores, L., Moize, V., Rios, M., Lacy, A. M., & Vidal, J. (2012). Predictive factors of excess body weight loss 1 year after laparoscopic bariatric surgery. S*urg Endosc, 26(*6), 1744-1750. doi: 10.1007/s00464-011-2104-4
Padwal, R., Klarenbach, S., Wiebe, N., Hazel, M., Birch, D., Karmali, S., Tonelli, M. (2011). Bariatric surgery: a systematic review of the clinical and economic evidence. [Research Support, Non-U.S. Gov't Review]. J *Gen Intern Med, 26(*10), 1183-1194. doi: 10.1007/s11606-011-1721-x
Peeters, A., Barendregt, J. J., Willekens, F., Mackenbach, J. P., Al Mamun, A., Bonneux, L., . . . Demography Compression of Morbidity Research, G. (2003). Obesity in adulthood and its consequences for life expectancy: a life-table analysis. [Research Support, Non-U.S. Gov't]. A*nn Intern Med, 138(*1), 24-32.
Persson, J., Welsh, K. M., Jonides, J., & Reuter-Lorenz, P. A. (2007). Cognitive fatigue of executive processes: interaction between interference resolution tasks. [Research Support, N.I.H., Extramural]. N*europsychologia, 45(*7), 1571-1579. doi: 10.1016/j.neuropsychologia.2006.12.007
Peterli, R., Steinert, R. E., Woelnerhanssen, B., Peters, T., Christoffel-Courtin, C., Gass, M., . . . Beglinger, C. (2012). Metabolic and hormonal changes after laparoscopic Roux-en-Y gastric bypass and sleeve gastrectomy: a randomized, prospective trial. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. O*bes Surg, 22(*5), 740-748. doi: 10.1007/s11695-012-0622-3
Phelan, S., Wing, R. R., Loria, C. M., Kim, Y., & Lewis, C. E. (2010). Prevalence and predictors of weight-loss maintenance in a biracial cohort: results from the coronary artery risk development in young adults study. [Multicenter Study Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. A*m J Prev Med, 39(*6), 546-554. doi: 10.1016/j.amepre.2010.08.008
Picot, J., Jones, J., Colquitt, J. L., Loveman, E., & Clegg, A. J. (2012). Weight loss surgery for mild to moderate obesity: a systematic review and economic evaluation. O*bes Surg, 22(*9), 1496-1506. doi: 10.1007/s11695-012-0679-z
Pories, W. J., Swanson, M. S., MacDonald, K. G., Long, S. B., Morris, P. G., Brown, B. M., . . . et al. (1995). Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. [Clinical Trial]. A*nn Surg, 222(*3), 339-350; discussion 350-332.
Pournaras, D. J., & Le Roux, C. W. (2009). The effect of bariatric surgery on gut hormones that alter appetite. [Review]. D*iabetes Metab, 35(*6 Pt 2), 508-512.
Pournaras, D. J., Osborne, A., Hawkins, S. C., Mahon, D., Ghatei, M. A., Bloom, S. R., . . . le Roux, C. W. (2010). The gut hormone response following Roux-en-Y gastric bypass: cross-sectional and prospective study. O*bes Surg, 20(*1), 56-60. doi: 10.1007/s11695-009-9989-1
Raynor, H. A., & Epstein, L. H. (2003). The relative-reinforcing value of food under differing levels of food deprivation and restriction. [Clinical Trial Randomized Controlled Trial]. A*ppetite, 40(*1), 15-24.

Reed, J. L., Chaput, J. P., Tremblay, A., & Doucet, E. (2013). The maintenance of energy balance is compromised after weight loss. [Research Support, Non-U.S. Gov't]. C*an J Diabetes, 37(*2), 121-127. doi: 10.1016/j.jcjd.2013.03.022

Reinehr, T., Roth, C. L., Schernthaner, G. H., Kopp, H. P., Kriwanek, S., & Schernthaner, G. (2007). Peptide YY and glucagon-like peptide-1 in morbidly obese patients before and after surgically induced weight loss. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. O*bes Surg, 17(*12), 1571-1577. doi: 10.1007/s11695-007-9323-8

Richardson, B. E., Vander Woude, E. A., Sudan, R., Thompson, J. S., & Leopold, D. A. (2004). Altered olfactory acuity in the morbidly obese. O*bes Surg, 14(*7), 967-969. doi: 10.1381/0960892041719617

Richardson, B. E., Vanderwoude, E. A., Sudan, R., Leopold, D. A., & Thompson, J. S. (2012). Gastric bypass does not influence olfactory function in obese patients. O*bes Surg, 22(*2), 283-286. doi: 10.1007/s11695-011-0487-x

Rodieux, F., Giusti, V., D'Alessio, D. A., Suter, M., & Tappy, L. (2008). Effects of gastric bypass and gastric banding on glucose kinetics and gut hormone release. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. O*besity (Silver Spring), 16(*2), 298-305. doi: 10.1038/oby.2007.83

Rolls, E. T. (2007). Sensory processing in the brain related to the control of food intake. [Lectures Research Support, Non-U.S. Gov't]. P*roc Nutr Soc, 66(*1), 96-112. doi: 10.1017/S0029665107005332

Rosenbaum, M., Sy, M., Pavlovich, K., Leibel, R. L., & Hirsch, J. (2008). Leptin reverses weight loss-induced changes in regional neural activity responses to visual food stimuli. [Randomized Controlled Trial Research Support, N.I.H., Extramural]. J *Clin Invest, 118(*7), 2583-2591. doi: 10.1172/JCI35055

Sarwer, D. B., Dilks, R. J., & West-Smith, L. (2011). Dietary intake and eating behavior after bariatric surgery: threats to weight loss maintenance and strategies for success. [Research Support, N.I.H., Extramural Review]. S*urg Obes Relat Dis, 7(*5), 644-651. doi: 10.1016/j.soard.2011.06.016

Sarwer, D. B., Wadden, T. A., Moore, R. H., Baker, A. W., Gibbons, L. M., Raper, S. E., & Williams, N. N. (2008). Preoperative eating behavior, postoperative dietary adherence, and weight loss after gastric bypass surgery. [Comparative Study Research Support, N.I.H., Extramural]. S*urg Obes Relat Dis, 4(*5), 640-646. doi: 10.1016/j.soard.2008.04.013

Schauer, P. R., Burguera, B., Ikramuddin, S., Cottam, D., Gourash, W., Hamad, G., Kelley, D. (2003). Effect of laparoscopic Roux-en Y gastric bypass on type 2 diabetes mellitus. A*nn Surg, 238(*4), 467-484; discussion 484-465. doi: 10.1097/01.sla.0000089851.41115.1b

Schauer, P. R., Ikramuddin, S., Gourash, W., Ramanathan, R., & Luketich, J. (2000). Outcomes after laparoscopic Roux-en-Y gastric bypass for morbid obesity. A*nn Surg, 232(*4), 515-529.

Schultes, B., Ernst, B., Wilms, B., Thurnheer, M., & Hallschmid, M. (2010). Hedonic hunger is increased in severely obese patients and is reduced after gastric bypass surgery. A*m J Clin Nutr, 92(*2), 277-283. doi: ajcn.2009.29007 [pii] 10.3945/ajcn.2009.29007

Schwartz, M. W., Woods, S. C., Porte, D., Jr., Seeley, R. J., & Baskin, D. G. (2000). Central nervous system control of food intake. [Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, Non-P.H.S Research Support, U.S. Gov't, P.H.S. Review]. Na*ture, 404(6*778), 661-671. doi: 10.1038/35007534

Sjostrom, L., Lindroos, A. K., Peltonen, M., Torgerson, J., Bouchard, C., Carlsson, B. Swedish Obese Subjects Study Scientific (2004). Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. [Clinical Trial Comparative Study Controlled Clinical Trial Research Support, Non-U.S. Gov't]. N *Engl J Med, 351(2*6), 2683-2693. doi: 10.1056/NEJMoa035622

Sjostrom, L., Narbro, K., Sjostrom, C. D., Karason, K., Larsson, B., Wedel, H. Swedish Obese Subjects. (2007). Effects of bariatric surgery on mortality in Swedish obese subjects. [Research Support, Non-U.S. Gov't]. N *Engl J Med, 357(8*), 741-752. doi: 10.1056/NEJMoa066254

Sjostrom, L., Peltonen, M., Jacobson, P., Sjostrom, C. D., Karason, K., Wedel, H., Carlsson, L. M. (2012). Bariatric surgery and long-term cardiovascular events. [Research Support, Non-U.S. Gov't]. JA*MA, 307(1*), 56-65. doi: 10.1001/jama.2011.1914

Sorensen, T. I., Rissanen, A., Korkeila, M., & Kaprio, J. (2005). Intention to lose weight, weight changes, and 18-y mortality in overweight individuals without co-morbidities. [Comparative Study Research Support, Non-U.S. Gov't Twin Study]. PL*oS Med, 2(6*), e171. doi: 10.1371/journal.pmed.0020171

Stevenson, R. J. (2010). An initial evaluation of the functions of human olfaction. [Review]. Ch*em Senses, 35(1*), 3-20. doi: 10.1093/chemse/bjp083

Stunkard, A. J., & Messick, S. (1985). The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. [Research Support, U.S. Gov't, P.H.S.]. J *Psychosom Res, 29(1*), 71-83.

Sugerman, H. J., Wolfe, L. G., Sica, D. A., & Clore, J. N. (2003). Diabetes and hypertension in severe obesity and effects of gastric bypass-induced weight loss. An*n Surg, 237(6*), 751-756; discussion 757-758. doi: 10.1097/01.SLA.0000071560.76194.11

Sumithran, P., Prendergast, L. A., Delbridge, E., Purcell, K., Shulkes, A., Kriketos, A., & Proietto, J. (2011). Long-term persistence of hormonal adaptations to weight loss. [Clinical Trial Research Support, Non-U.S. Gov't]. N *Engl J Med, 365(1*7), 1597-1604. doi: 10.1056/NEJMoa1105816

Sumithran, P., & Proietto, J. (2013). The defence of body weight: a physiological basis for weight regain after weight loss. [Review]. Cl*in Sci (Lond), 124(4*), 231-241. doi: 10.1042/CS20120223

Swarbrick, M. M., Stanhope, K. L., Austrheim-Smith, I. T., Van Loan, M. D., Ali, M. R., Wolfe, B. M., & Havel, P. J. (2008). Longitudinal changes in pancreatic and adipocyte hormones following Roux-en-Y gastric bypass surgery. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. Di*abetologia, 51(1*0), 1901-1911. doi: 10.1007/s00125-008-1118-5

Tamboli, R. A., Breitman, I., Marks-Shulman, P. A., Jabbour, K., Melvin, W., Williams, B., Abumrad, N. N. (2014). Early weight regain after gastric bypass does not affect insulin sensitivity but is associated with elevated ghrelin. [Research

Support, N.I.H., Extramural]. Ob*esity (Silver Spring), 22(7*), 1617-1622. doi: 10.1002/oby.20776

Terranova, L., Busetto, L., Vestri, A., & Zappa, M. A. (2012). Bariatric surgery: cost-effectiveness and budget impact. [Review]. Ob*es Surg, 22(4*), 646-653. doi: 10.1007/s11695-012-0608-1

Thirlby, R. C., Bahiraei, F., Randall, J., & Drewnoski, A. (2006). Effect of Roux-en-Y gastric bypass on satiety and food likes: the role of genetics. J *Gastrointest Surg, 10(2*), 270-277. doi: 10.1016/j.gassur.2005.06.012

Torrubia, R., Avila, C., Molto, J., & Caseras, X. (2001). The Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ) as a measure of Gray's anxiety and impulsivity dimensions. P*ersonality and Individual Differences, 31(6*), 837-862.

Trellakis, S., Tagay, S., Fischer, C., Rydleuskaya, A., Scherag, A., Bruderek, K., Brandau, S. (2011). Ghrelin, leptin and adiponectin as possible predictors of the hedonic value of odors. [Research Support, Non-U.S. Gov't]. Re*gul Pept, 167(1*), 112-117. doi: 10.1016/j.regpep.2010.12.005

Tritos, N. A., Mun, E., Bertkau, A., Grayson, R., Maratos-Flier, E., & Goldfine, A. (2003). Serum ghrelin levels in response to glucose load in obese subjects post-gastric bypass surgery. [Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.]. Ob*es Res, 11(8*), 919-924. doi: 10.1038/oby.2003.126

Trostler, N., Mann, A., Zilberbush, N., Avinoach, E., & Charuzi, I. I. (1995). Weight Loss and Food Intake 18 Months following Vertical Banded Gastroplasty or Gastric Bypass for Severe Obesity. Ob*es Surg, 5(1*), 39-51. doi: 10.1381/096089295765558141

Turkmen, S., Andreen, L., & Cengiz, Y. (2014). Effects of Roux-en-Y gastric bypass surgery on eating behaviour and allopregnanolone levels in obese women with polycystic ovary syndrome. Gy*necol Endocrinol,* 1-5. doi: 10.3109/09513590.2014.994600

Ullrich, J., Ernst, B., Wilms, B., Thurnheer, M., & Schultes, B. Roux-en Y Gastric Bypass Surgery Reduces Hedonic Hunger and Improves Dietary Habits in Severely Obese Subjects. Ob*esity Surgery,* 1-6. doi: 10.1007/s11695-012-0754-5

Ullrich, J., Ernst, B., Wilms, B., Thurnheer, M., & Schultes, B. (2013). Roux-en Y gastric bypass surgery reduces hedonic hunger and improves dietary habits in severely obese subjects. [Research Support, Non-U.S. Gov't]. Ob*es Surg, 23(1*), 50-55. doi: 10.1007/s11695-012-0754-5

van de Laar, A. (2012). Bariatric Outcomes Longitudinal Database (BOLD) suggests excess weight loss and excess BMI loss to be inappropriate outcome measures, demonstrating better alternatives. Ob*es Surg, 22(12*), 1843-1847. doi: 10.1007/s11695-012-0736-7

van de Laar, A., de Caluwe, L., & Dillemans, B. (2011). Relative outcome measures for bariatric surgery. Evidence against excess weight loss and excess body mass index loss from a series of laparoscopic Roux-en-Y gastric bypass patients. Ob*es Surg, 21(6*), 763-767. doi: 10.1007/s11695-010-0347-0

van de Laar, A. W., & Acherman, Y. I. (2013). Weight Loss Percentile Charts of Large Representative Series: a Benchmark Defining Sufficient Weight Loss Challenging

Current Criteria for Success of Bariatric Surgery. Ob*es Surg.* doi: 10.1007/s11695-013-1130-9

Vincent, R. P., & le Roux, C. W. (2008a). Changes in gut hormones after bariatric surgery. [Review]. Cl*in Endocrinol (Oxf), 69(2*), 173-179. doi: 10.1111/j.1365-2265.2007.03164.x

Vincent, R. P., & le Roux, C. W. (2008b). The satiety hormone peptide YY as a regulator of appetite. [Review]. J *Clin Pathol, 61(5*), 548-552. doi: 10.1136/jcp.2007.048488

Wadden, T. A. (1993). Treatment of obesity by moderate and severe caloric restriction. Results of clinical research trials. [Research Support, U.S. Gov't, P.H.S. Review]. An*n Intern Med, 119(7* Pt 2), 688-693.

Wadden, T. A., & Frey, D. L. (1997). A multicenter evaluation of a proprietary weight loss program for the treatment of marked obesity: a five-year follow-up. [Clinical Trial Multicenter Study Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S.]. In*t J Eat Disord, 22(2*), 203-212.

Warde-Kamar, J., Rogers, M., Flancbaum, L., & Laferrere, B. (2004). Calorie intake and meal patterns up to 4 years after Roux-en-Y gastric bypass surgery. Ob*es Surg, 14(8*), 1070-1079. doi: 10.1381/0960892041975668

Watts, A. G. (2000). Understanding the neural control of ingestive behaviors: helping to separate cause from effect with dehydration-associated anorexia. [Research Support, U.S. Gov't, P.H.S. Review]. Ho*rm Behav, 37(4*), 261-283. doi: 10.1006/hbeh.2000.1581

Whitlock, G., Lewington, S., Sherliker, P., Clarke, R., Emberson, J., Halsey, J., Peto, R. (2009). Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. La*ncet, 373(9*669), 1083-1096. doi: 10.1016/S0140-6736(09)60318-4

Wing, R. R., & Phelan, S. (2005). Long-term weight loss maintenance. [Research Support, N.I.H., Extramural Research Support, U.S. Gov't, P.H.S. Review]. Am *J Clin Nutr, 82(1* Suppl), 222S-225S.

Wittgrove, A. C., & Clark, G. W. (2000). Laparoscopic gastric bypass, Roux-en-Y- 500 patients: technique and results, with 3-60 month follow-up. Ob*es Surg, 10(3*), 233-239. doi: 10.1381/096089200321643511

Wren, A. M., & Bloom, S. R. (2007). Gut hormones and appetite control. [Review]. Ga*stroenterology, 132(6*), 2116-2130. doi: 10.1053/j.gastro.2007.03.048

Yanos, B. R., Saules, K. K., Schuh, L. M., & Sogg, S. (2014). Predictors of Lowest Weight and Long-Term Weight Regain Among Roux-en-Y Gastric Bypass Patients. Ob*es Surg.* doi: 10.1007/s11695-014-1536-z

APPENDIX 1:

ETHICS APPROVAL NOTICE (UNIVERSITY OF OTTAWA)

File Number: H10-14-04 **Date (mm/dd/yyyy):** 10/03/2014

Université d'Ottawa University of Ottawa
Bureau d'éthique et d'intégrité de la recherche Office of Research Ethics and Integrity

Ethics Approval Notice

Health Sciences and Science REB

Principal Investigator / Supervisor / Co-investigator(s) / Student(s)

First Name	Last Name	Affiliation	Role
Robert	Dent	Medicine / Medicine	Principal Investigator
Eric	Doucet	Health Sciences / Human Kinetics	Co-investigator
Jeff	Kilbreath	Health Sciences / Nursing	Co-investigator
Jennifer	Brown	Health Sciences / Human Kinetics	Student Researcher

File Number: H10-14-04

Type of Project: Professor

Title: Relationship of appetite, olfaction and gut hormones after Roux-en-Y gastric bypass surgery: Could this explain weight regain?

Approval Date (mm/dd/yyyy)	Expiry Date (mm/dd/yyyy)	Approval Type
10/03/2014	04/01/2015	Ia

(Ia: Approval, Ib: Approval for initial stage only)

Special Conditions / Comments:
N/A

550, rue Cumberland, pièce 154 550 Cumberland Street, room 154
Ottawa (Ontario) K1N 6N5 Canada Ottawa, Ontario K1N 6N5 Canada
(613) 562-5387 • Téléc./Fax (613) 562-5338
www.recherche.uottawa.ca/deontologie/ www.research.uottawa.ca/ethics/

File Number: H10-14-04 **Date (mm/dd/yyyy):** 10/03/2014

Université d'Ottawa University of Ottawa
Bureau d'éthique et d'intégrité de la recherche Office of Research Ethics and Integrity

This is to confirm that the University of Ottawa Research Ethics Board identified above, which operates in accordance with the Tri-Council Policy Statement (2010) and other applicable laws and regulations in Ontario, has examined and approved the ethics application for the above named research project. Ethics approval is valid for the period indicated above and subject to the conditions listed in the section entitled "Special Conditions / Comments".

During the course of the project, the protocol may not be modified without prior written approval from the REB except when necessary to remove participants from immediate endangerment or when the modification(s) pertain to only administrative or logistical components of the project (e.g., change of telephone number). Investigators must also promptly alert the REB of any changes which increase the risk to participant(s), any changes which considerably affect the conduct of the project, all unanticipated and harmful events that occur, and new information that may negatively affect the conduct of the project and safety of the participant(s). Modifications to the project, including consent and recruitment documentation, should be submitted to the Ethics Office for approval using the "Modification to research project" form available at: http://www.research.uottawa.ca/ethics/forms.html.

Please submit an annual report to the Ethics Office four weeks before the above-referenced expiry date to request a renewal of this ethics approval. To close the file, a final report must be submitted. These documents can be found at: http://www.research.uottawa.ca/ethics/forms.html.

If you have any questions, please do not hesitate to contact the Ethics Office at extension 5387 or by e-mail at: ethics@uOttawa.ca.

Signature:

Catherine Paquet
Director
For Daniel Lagarec, Chair of the Health Sciences and Sciences REB

Université d'Ottawa University of Ottawa
Bureau d'éthique et d'intégrité de la recherche Office of Research Ethics and Integrity

July 14th, 2014

Robert Dent
Endocrinologist
Weight Management Clinic
The Ottawa Hospital
bdent@ottawahospital.on.ca

Jennifer Brown
Master's Student
School of Human Kinetics
University of Ottawa
jebrown@toh.on.ca

Co-investigators: Eric Doucet, University of Ottawa
Jeff Kilbreath, The Ottawa Hospital

Re: U of O Ethics file no. A07-14-01 – "Relationship of appetite, olfaction and gut hormones after Roux-en-Y gastric bypass surgery: Could this explain weight regain?"

Dear Dr. Dent, Ms. Brown, Professor Doucet and Dr. Kilbreath,

Thank you for the protocol documents and Certificate of Approval from the OHSN-REB (REB # 20140097-01H) for your project named above.

This is to confirm that, in accordance with the agreement between the University of Ottawa and OHSN-REB, the University of Ottawa has authorized this board to act as Board of Record for the review and oversight of research involving human participants conducted at or through the hospital.

We remind you of your obligation to:

- Follow all procedures of the OHSN-REB including reporting and renewal procedures;
- Submit to the authority of the OHSN-REB and that you are subject to OHSN-REB requirements, including, without limitation, the requirement to modify or stop the research on demand of the OHSN-REB.

If you have any questions, please contact our ethics office at 562-5387.

Sincerely yours,

Catherine Paquet
Director
Office of Research Ethics and Integrity

550, rue Cumberland 550 Cumberland Street
Ottawa (Ontario) K1N 6N5 Canada Ottawa, Ontario K1N 6N5 Canada

(613) 562-5387 • Téléc./Fax (613) 562-5338
http://www.recherche.uottawa.ca/deontologie/
http://www.research.uottawa.ca/ethics/

APPENDIX 2:

OTTAWA HEALTH SCIENCE NETWORK RESEARCH ETHICS BOARD

Ottawa Hospital Research Institute
Institut de recherche de l'Hôpital d'Ottawa

uOttawa

UNIVERSITY OF OTTAWA HEART INSTITUTE
INSTITUT DE CARDIOLOGIE DE L'UNIVERSITÉ D'OTTAWA

***Ottawa Health Science Network Research Ethics Board/* Réseau des sciences de la santé d'Ottawa Conseil d'éthique de la recherche**

Civic Box 411 725 Parkdale Avenue, Ottawa, Ontario K1Y 4E9 613-798-5555 ext. 14902 Fax : 613-761-4311
http://www.ohri.ca/ohsn-reb

September 26, 2014

Dr. Robert Dent
Weight Management Clinic
Third Floor, Grimes Lodge
Ottawa Hospital - Civic Campus
1053 Carling Ave.
Ottawa, Ontario K1Y 4E9

Dear Dr. Dent:

Re: Protocol # 20140097-01H Relationship of appetite, olfaction and gut hormones after Roux-en-Y gastric bypass surgery: Could this explain weight regain?

I am pleased to inform you that the following documentation is approved:

- Protocol Amendment Report, dated August 12, 2014
- Revised Protocol, version 2, dated August 12, 2014
- Revised Olfactory Performance Test, version 2, dated August 12, 2014
- Revised Participant Informed Consent Form, version 2, dated August 12, 2014
- New Case Report Forms #3, 4 & 5, version dated August 12, 2014
- New Participant Characteristics Questionnaire, version 1, dated August 12, 2014
- New Three-Factor Eating Questionnaire, version 1, dated August 12, 2014
- New Sensitivity to Punishment/Reward Questionnaire, version 1, dated August 12, 2014

Approval is conditional upon receipt of the approval letter from the University of Ottawa Office of Research Ethics & Integrity.

Ethical approval remains in effect until April 01, 2015.

OHSN-REB complies with the membership requirements and operates in compliance with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans; the International Conference on Harmonization - Good Clinical Practice: Consolidated Guideline; and the provisions of the Personal Health Information Protection Act 2004.

Yours sincerely,

Raphael Saginur, M.D.
Chairman
Ottawa Health Science Network Research Ethics Board

Ottawa Hospital Research Institute
Institut de recherche de l'Hôpital d'Ottawa

uOttawa

UNIVERSITY OF OTTAWA HEART INSTITUTE
INSTITUT DE CARDIOLOGIE DE L'UNIVERSITÉ D'OTTAWA

***Ottawa Health Science Network Research Ethics Board/* Réseau des sciences de la san d'Ottawa Conseil d'éthique de la recherche**

Civic Box 411 725 Parkdale Avenue, Ottawa, Ontario K1Y 4E9 613-798-5555 ext. 14902 Fax : 613-761-4311
http://www.ohri.ca/ohsn-reb

April 02, 2014

Dr. Robert Dent
Weight Management Clinic
Third Floor, Grimes Lodge
Ottawa Hospital - Civic Campus
1053 Carling Ave.
Ottawa, Ontario K1Y 4E9

Dear Dr. Dent:

Re: Protocol #	**20140097-01H**	**Relationship of appetite, olfaction and gut hormones after Roux-en-Y gastric bypass surgery: Could this explain weight regain?**
Protocol approval valid until -		**April 01, 2015**

I am pleased to inform you that this protocol underwent delegated review by the Ottawa Health Science Network Research Ethics Board (OHSN-REB) and is approved for the recruitment of English speaking participants only. No changes, amendments or addenda may be made to the protocol or the consent form without the OHSN-REB's review and approval.

Approval is for the following:
- Protocol, version 1, dated January 30, 2014
- English Recruitment Letter, version 1, dated March 27, 2014
- English Screening Script, version 1, dated March 27, 2014
- English Poster, version 1, dated March 27, 2014
- English Informed Consent Recruitment Letter, version 1, dated March 27, 2014
- English Participant Informed Consent Form, version 1, dated March 27, 2014
- English Screening Questionnaire, version 1, dated March 27, 2014
- English Olfactory Performance Test, version 1, dated March 27, 2014

The REB no longer requires a 'valid until' date at the bottom of all approved informed consent forms. The consent form currently approved for use by the REB is listed above.

If the study is to continue beyond the expiry date noted above, a Renewal Form should be submitted to the REB approximately six weeks prior to the current expiry date. If the study has been completed by this date, a Termination Report should be submitted.

The Ottawa Health Science Network Research Ethics Board (OHSN-REB) was created by the merger of both the Ottawa Hospital Research Ethics Board (OHREB) and the Human Research Ethics Board (HREB) for meetings held at the University of Ottawa Heart Institute.

OHSN-REB complies with the membership requirements and operates in compliance with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans; the International Conference on Harmonization - Good Clinical Practice: Consolidated Guideline and the provisions of the Personal Health Information Protection Act 2004.

Yours sincerely,

Francine F-A. Sarazin, Ph.D., C.Psych
Vice Chairperson
Ottawa Health Science Network Research Ethics Board
/HM

APPENDIX 3:

PARTICIPANT INFORMED CONSENT FORM

PARTICIPANT INFORMED CONSENT FORM

Title of Study: Relationship of Appetite, Olfaction and Gut Hormones after Roux-en-Y Gastric Bypass Surgery: Could this Explain Weight Regain?

Local Site Principal Investigator (PI):
Dr. Robert Dent (The Ottawa Hospital Weight Management Clinic) 613-798-5555 ext. 19647
Co-investigators: Dr. Eric Doucet (University of Ottawa) 613-562-5800 ext. 4271
Jennifer Brown (The Ottawa Hospital & uOttawa) 613-798-5555 ext. 10532

Participation in this study is voluntary. Please read this Participant Informed Consent Form carefully before you decide if you would like to participate. Ask the study doctor and study team as many questions as you like. We encourage you to discuss your options with family, friends or your healthcare team.

Why am I being given this form?

You are being asked to participate in this research study because you have had Roux-en-Y gastric bypass (RYGB) surgery within the last two years or you are a patient at The Ottawa Hospital Weight Management Clinic & Bariatric Centre of Excellence (WMC) with no previous bariatric surgery (either waiting for surgery or in a medical program at WMC).

Why is this study being done?

There appears to be a gap in the literature as to what causes some people to regain weight following RYGB. Weight regain can have a devastating impact on a person's physical health, mental health and overall quality of life, but it also negatively affects the body with the return of diabetes, high blood pressure and obesity – all diseases that require long-term treatment and management, which cost the health care system millions of dollars.

There appears to be multiple reasons for weight regain after surgery. Some research has found an increase in caloric intake from eating higher sugar and higher fat foods. Others have found changes to the peripheral hormones (Ghrelin, PYY, GLP-1 and leptin). These hormones are said to be the driving forces for fullness and lack of hunger after surgery. However, no study, to our knowledge has tested the peripheral hormones in people who have regained weight compared to those who have maintained weight after RYGB. Additionally, there is limited research on the impact of smell or appetite after RYGB surgery. Results found in this study will help researchers understand factors that may contribute to weight regain and/or weight maintenance after surgery. These results may provide future insight to prevent weight regain long-term.

The purpose of this study is to determine if there are factors that contribute to weight regain after Roux-en-Y gastric bypass (RYGB). The study will test peripheral hormones; ghrelin, PYY, GLP-1 and leptin in people who have regained weight compared to those who have maintained their weight after RYGB. A second purpose of this study is to test smell performance among these groups and compare appetite to determine if other factors are contributing to weight regain.

We estimate that 90 participants will be enrolled in the study from The Ottawa Hospital Weight Management Clinic & Bariatric Centre of Excellence (WMC). All study related activities will take place at the Behavioural & Metabolic Research Unit (BMRU) located at 200 Lees Avenue, Block E.

How is the study designed?

This study will be a cross-sectional design, which means a total of 90 participants will be recruited for 3 groups with 30 participants in each group. Everyone in all 3 groups will participate in the same tests. The researchers will compare the results between the groups to understand factors that might contribute to weight regain.
One group will be called (R) for weight regain. Participants in the R-group will be more than 2 years after RYGB surgery and have regained over 10% of their lowest weight lost since surgery. Another group will be called (M) for weight maintenance. Participants in the M-group will be more than 2 years after RYGB surgery and have maintained weight (0-5% of their lowest weight lost since surgery).
Lastly, the third group will be called (C) for control group. Participants in the C-group have not had bariatric surgery and are patients of the WMC. All participants in these groups will need to meet study criteria to take part.
Main outcomes of interest are the relationships between hormones (PYY, GLP-1, ghrelin and leptin), appetite and smell function. These outcomes will be tested between the weight regain (R) group, the weight maintenance (M) group and compared to a control group (C). All three groups will follow the design illustrated in figure 1.

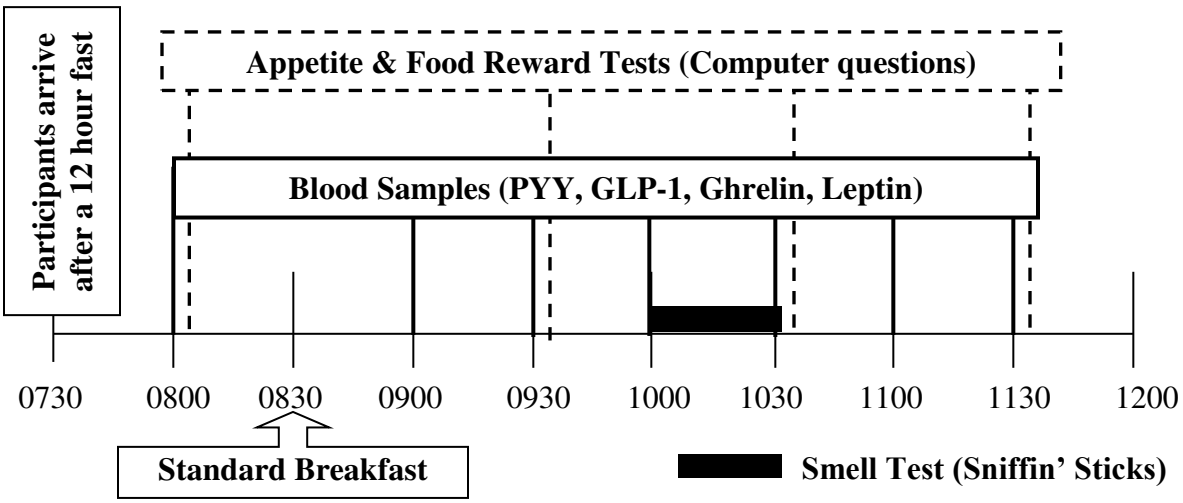

Figure 1. Study design

What is expected of me?

The first study visit will be a screening visit. You will be asked to complete a questionnaire over the phone or in person which should take approximately 5 minutes of your time. The results of the questions asked at the screening visit will help the study team determine whether you can continue in this study. If you meet the criteria for this study, you will be asked to come into the BMRU at the University of Ottawa – 200 Lee's Avenue for testing. This will take approximately 4.5 hours of your time. Figure 1 and the session content below use an arrival time of 7:30am (0730h) as an example. We can change this arrival time to 7:00am, 7:30am or 8:00am to accommodate your needs. The study coordinator will inform you what time you will need to stop eating at as you will need to be fasting for 12 hours before the study begins.

Session Content:

A. **Arrival at BMRU (0730):** You will arrive at the BMRU at 7:30 am (0730h). You will need to be in a fasting state overnight for 12 hours, which means no food or fluids other than water during this time. You will be accompanied by the study coordinator and a registered nurse into a sterile exam room. Your height and body weight will be taken. The registered nurse will insert a venous catheter in your non-dominant forearm to collect blood samples. This catheter will stay in your forearm for the remainder of the study (approximately 4.5 hours). It will be properly secured to your arm so that you can move around without the needle being tugged or pulled out.

B. **Testing (0730-0820):**

    1. **Blood Tests:** You will have 7 blood samples drawn to test hormones ghrelin, PYY, GLP-1 and leptin. Blood samples will be collected before breakfast and every 30 minutes for 3 hours. Each sample will require approximately 6 ml or less than 1 Tbsp. of blood. After the last blood collection is complete, the registered nurse will remove the venous catheter and provide you with a sterile bandage.

    2. **Participant Characteristic Questionnaire:** You will be asked to complete a questionnaire about your age, sex, menstrual status, history of diabetes. This is complete with a pen and paper and should take 5 minutes to complete.

    3. **Appetite Ratings:** Appetite will be measured every hour from before breakfast to 3 hours after breakfast. This will be done on a computer. You will be asked to click the mouse along a line that asks you the following questions: 1) "How strong is your desire to eat?" (Very week – Very strong); 2) "How hungry do you feel?" (Not hungry at all – As hungry as I have ever felt); 3) "How full do you feel?" (Not full at all – Very full), and 4) "How much food do you think you could eat?" (Nothing at all – A large amount).

    4. **Food Reward Ratings:** You will be asked to do a computer task to assess food choices and personal ratings of various food items. You will sit in

front of a computer with a mouse and mouse pad. A series of food pictures will be shown to you and you will need to answer some questions about these foods. All answers are recorded by selecting and clicking with the mouse.

C. **Standardized Breakfast (0830):** You will be required to eat 4 slices of Melba Toast®), 1 Tbsp. natural peanut butter (Kraft®), 100g Vanilla Greek yogurt (Liberte®), 4 slices of apples, and 6 almonds. You will have 20 minutes to consume the entire breakfast.

D. **Testing (0900-1130):**

1. **Blood Tests:** Every 30 minutes after meal: 0900; 0930; 1000; 1030; 1100; 1130
2. **Appetite Ratings:** Every 60 minutes after meal for 3 hours: 0930; 1030; 1130
3. **Smell Test:** Only once after breakfast at 0930; you will be required to complete 3 smell tests; an odor threshold test, an odor discrimination test and an odor identification test. These tests will be assessed using Sniffin' Sticks (Burghart Instruments, Wedel, Germany), a 3-test battery of odorized pens. For the odor threshold test, you will be asked to smell a set of 3 pens and identify which of the 3 pens presents an odor. As for the odor discrimination test, you must identify which of the 3 pens presents a different smell. Finally, for the odor identification test, you will be required to identify the correct odor released by the pen. This test uses multiple choice answers that are provided in a booklet (one page is linked with one odor pen). Examples of some of the odors which will be presented to you are rose, marker, banana, and grass. This test may take 20-45 minutes to complete.
4. **Food Reward Ratings:** Questionnaires at 10:30. You will be asked to complete two questionnaires that measure food reward. These can be completed with a pen and paper or completed on the computer. This test may take up to 30 minutes to complete.

E. **End of Session (1130-1200):** The registered nurse will remove the venous catheter from your forearm and provide you with a sterile bandage. Study results cannot be shared with you until after the study is fully completed (approximately 3 months). You will be invited to schedule another appointment to review your personal results in person or over the phone (if you are interested).

How long will I be involved in the study?

The entire study will last approximately 3 months. Your participation in the study will last approximately 4.5 hours. Over this time, you will be required to visit the BMRU once for the testing session of this study and possibly one visit in-person at the WMC for the screening questionnaire. However, this screening questionnaire may be conducted over the telephone instead, limiting your visits to one.

Your participation in the study may be stopped for any of the following reasons:

- The study doctor feels it is in your best interest.
- You need medical treatment that would interfere with the study.
- You do not follow the study staff's instructions.

What are the potential risks I may experience?

Blood Sample Risks

You may experience some temporary discomfort when the blood sample is taken. There is a small risk of bruising, infection or swelling at the site where the needle is inserted, and some people may feel faint or dizzy.

Overnight Fast Risks

An overnight fast (12 hours) may present some feelings of lightheadedness and mild discomfort, possibly nausea. It must be noted that each person responds differently to a fasting state.

Breakfast Risks

The standard breakfast used in this study has no foreseeable harm. Some people may experience nausea and/or discomfort when consuming a meal after having RYGB. You are reminded to follow post-RYGB diet habits; chew slowly, avoid large bites, avoid fluids within 30 minutes before and after solid meals.

Is there a concern with pregnancy or breastfeeding?

The results from the smell tests may not be accurate in women that are pregnant and/or breastfeeding. Similarly, the hormones (ghrelin, PYY, GLP-1 and leptin) may also have incorrect results in women that are pregnant and/or breastfeeding. For this reason, women that are pregnant or breastfeeding are excluded from this study. In the event of pregnancy, or suspected pregnancy before the study, you must tell your study doctor immediately. The study procedures may be stopped in order to avoid unknown risks to you or the fetus.

Can I expect to benefit from participating in this research study?

Your participation may allow the researchers to better understand what factors may be contributing to weight regain and/or weight maintenance after surgery and provide future insight to prevent weight regain long-term. You may also benefit from your personal results of the gut hormone tests, smell performance and appetite function, as this may help you to improve your dietary habits and lifestyle.

Do I have to participate? What alternatives do I have?

You can choose not to participate in this study. If you choose not to participate, there are no consequences to your care in the WMC. Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now, and then change your mind later without affecting the medical care, education, or other services to which you are entitled or are presently receiving at this institution.

If I agree now, can I change my mind and withdraw later?

You may withdraw from the study at any time without any impact on your current or future care at this institution. If you withdraw your consent, the study team will no longer collect your personal health information for research purposes, unless it is needed for review of safety.

What compensation will I receive if I am injured or become ill in this study?

In the event of a study-related injury or illness, you will be provided with appropriate medical treatment and care. You are not waiving any of your legal rights by agreeing to participate in this study. The study doctor and The Ottawa Hospital still have their legal and professional responsibilities.

Will I be paid for my participation or will there be any additional costs to me?

You will not be paid for participating in this study. The study tests (blood samples, appetite, food reward and smell tests) will be provided to you free of charge as long as you are taking part in the study. You will be provided with a parking pass for all study visits.

How is my personal information being protected?

- All personal health information (PHI) and your personal identifying information (PII), such as your name, address, date of birth, etc. will be kept confidential.
- Release of your PHI/PII information will only be allowed if it is legally required.
- As a participant, you will be assigned a coded study number that will be used throughout the study on all your study records.
- Documents or samples leaving the University of Ottawa will only contain the coded study number.
- Blood samples will be stored in a secured container within a locked freezer in a password protected lab within the Behavioural and Metabolic Research Unit (BMRU) of the University of Ottawa – 200 Lees Avenue, Block E. Blood samples will be kept in this research unit's laboratory's freezer. The research unit has 3 levels of locked doors; (1) the research lab in the Block E of 200 Lees Avenue; (2) each lab room; and (3) the freezer, where blood samples are stored. Blood samples will be identified by a coded study number which will not be traceable other than by the principal investigator and study coordinator(s).
- The Master List will be stored securely in the WMC in a locked file in a locked office. Study data will be stored on a secure hospital server on a password-protected computer and accessible by Dr. Dent and the study coordinator. No study data will be stored on any portable devices, laptops, USB keys, DVD's or CD's.

- A Master List provides the link between your identifying information and the coded study number. This list will only be available to Dr. Dent and his staff and will not leave the Weight Management Clinic (WMC).
- For audit purposes only, your original medical records may be reviewed under the supervision of Dr. Dent's staff by representatives from:
    - the Weight Management Clinic, Jennifer Brown and Jeff Kilbreath
    - the Ottawa Health Science Network Research Ethics Board (OHSN-REB)
    - the University of Ottawa Office of Research Ethics & Integrity, and
    - the University of Ottawa, Dr. Eric Doucet.
- You will not be identified in any publications or presentations resulting from this study.

Research records will be kept for 10 years, as required by the OHSN-REB. At the end of the storage time, all paper records will be shredded and all electronic records will be securely deleted.

Do the investigators have any conflicts of interest?

There are no conflicts of interest to declare related to this study. However, study coordinator, Jennifer Brown is receiving funding in-kind from the Ottawa Hospital to include this study as her Master's degree with the University of Ottawa. You may request any details about this arrangement from Jeff Kilbreath, Weight Management Clinic, via telephone number 613-798-5555 ext. 13953.

What are my responsibilities as a study participant?

It is important to remember the following things during this study:

- Ask your study coordinator, Jennifer Brown, if you have any questions or concerns.
- Tell your study coordinator, Jennifer Brown, if anything about your health has changed.
- Remember the following responsibilities:
    - You should not eat for 12 hours before your visit.
    - You can drink only water before your visit.
    - You should not take vitamin and mineral supplements before your visit.
    - You will be committing about 4.5 hours of your time to this study.
- Call the study doctor if you experience any side effects, even if you are unsure whether it has anything to do with this study.

Will I be informed about any new information that might affect my decision to continue participating?

You will be told in a timely fashion of any new findings during the study that could affect your willingness to continue in the study. You may be asked to sign a new consent form.

Who do I contact if I have any further questions?

If you have any questions about this study, or if you feel that you have experienced a study-related injury or illness, please contact Dr. Robert Dent at 613-761-5101.

The Ottawa Health Science Network Research Ethics Board (OHSN-REB) and the University of Ottawa Office of Research Ethics & Integrity has reviewed this protocol. The Board considers the ethical aspects of all research studies involving human participants at the Ottawa Hospital. If you have any questions about your rights as a study participant, you may contact the OHSN-RED Chairperson at 613-798-5555, extension 16719 or the University of Ottawa ethics office at 613-562-5387.

Consent to Participate in Research

- I understand that I am being asked to participate in a research study about weight regain after Roux-en-Y gastric bypass (RYGB), specifically to find out if hormones (ghrelin, PYY, GLP-1 and leptin), smell performance and appetite are different in patients that have experienced weight regain after RYGB compared to patients that have maintained weight.
- This study was explained to me by _____.
- I have read, or have had read to me, each page of this Participant Informed Consent Form.
- All of my questions have been answered to my satisfaction.
- If I decide later that I would like to withdraw my participation and/or consent from the study, I can do so at any time.
- I voluntarily agree to participate in this study.
- I will be given a copy of this signed Participant Informed Consent Form.

_____ _____ _____

Participant's Printed Name Participant's Signature Date

Investigator or Delegate Statement

I have carefully explained the study to the study participant. To the best of my knowledge, the participant understands the nature, demands, risks and benefits involved in taking part in this study.

_____ _____ _____

Investigator/Delegate's Printed Name Investigator/Delegate's Signature Date

Assistance Declaration

Was the participant assisted during the consent process? ❑ Yes ❑ No

❑ The consent form was read to the participant/substitute decision-maker, and the person signing below attests that the study was accurately explained to, and apparently understood by, and consent was freely given by the participant/substitute decision-maker.

❑ The person signing below acted as a translator for the participant/substitute decision-maker during the consent process. He/she attests that they have accurately translated the information for the participant/substitute decision-maker, and believe that the participant/substitute decision-maker has understood the information translated.

_____ _____ _____

Name of Person Assisting (Print) Signature Date

APPENDIX 4:

THREE FACTOR EATING QUESTIONNAIRE

Three-Factor Eating Questionnaire (TFEQ) CFR 07

Participant ID# ☐☐☐ **Date of Birth:** ☐☐☐☐ ☐☐
Year *month*

THREE-FACTOR EATING QUESTIONNAIRE
(Stunkard et Messick, 1984)

This questionnaire contains a certain number of proposition statements.

If you **agree** with the statement or if you feel like it can be applied to you, check the **TRUE** box corresponding to that statement.

If you **disagree** with the statement or if you feel like it does not apply to you, check the **FALSE** box corresponding to that statement.

Part 1

		TRUE	FALSE
1.	When I smell a sizzling steak or see a juicy piece of meat, I find it difficult to keep from eating, even if I have just finished a meal.	☐	☐
2.	I usually eat too much at social occasions, like parties and picnics.	☐	☐
3.	I am actually so hungry that I eat more than 3 times per day.	☐	☐
4.	When I have eaten my quota of calories, I am usually good about not eating any more.	☐	☐
5.	Dieting is so hard for me because I just get too hungry.	☐	☐
6.	I deliberately take small helpings as a means of controlling my weight.	☐	☐
7.	Sometimes things just taste so good that I keep on eating even when I am no longer hungry.	☐	☐
8.	Since I am often hungry, I sometimes wish that while I am eating, an expert would tell me that I had enough or that I can have something more to eat.	☐	☐
9.	When I feel anxious, I find myself eating.	☐	☐
10.	Life is too short to worry about dieting.	☐	☐
11.	Since my weight goes up and down, I have gone on reducing diets more than once.	☐	☐
12.	I often feel so hungry that I just have to eat something.	☐	☐
13.	When I am with someone who is overeating, I usually overeat too.	☐	☐
14.	I have a pretty good idea of the number of calories in common food.	☐	☐

Turn page over

Part 1 Continued

		TRUE	FALSE
15.	Sometimes when I start eating, I just can't seem to stop.	☐	☐
16.	It is not difficult for me to leave something on my plate.	☐	☐
17.	At certain times of the day, I get hungry because I have gotten used to eating then.	☐	☐
18.	While on a diet, if I eat food that is not allowed, I consciously eat less for a period of time to make up for it.	☐	☐
19.	Being with someone who is eating often makes me hungry enough to eat also.	☐	☐
20.	When I feel "blue", I often overeat.	☐	☐
21.	I enjoy eating too much to spoil it by counting calories or watching my weight.	☐	☐
22.	When I see a real delicacy, I often get so hungry that I have to eat right away.	☐	☐
23.	I often stop eating when I am not really full as a conscious means of limiting the amount that I eat.	☐	☐
24.	I get so hungry that my stomach often seems like a bottomless pit.	☐	☐
25.	My weight has hardly changed at all in the last 10 years.	☐	☐
26.	I am always hungry so it is hard for me to stop eating before I finish the food on my plate.	☐	☐
27.	When I feel lonely, I console myself by eating.	☐	☐
28.	I consciously hold back at meals in order not to gain weight.	☐	☐
29.	I sometimes get very hungry late in the evening or at night.	☐	☐
30.	I eat anything I want, anytime I want.	☐	☐
31.	Without even thinking about it, I take a long time to eat.	☐	☐
32.	I count calories as a conscious means of controlling weight.	☐	☐
33.	I do not eat some foods because they make me fat.	☐	☐
34.	I am always hungry enough to eat at any time.	☐	☐
35.	I pay a great deal of attention to changes in my figure.	☐	☐
36.	While on a diet, if I eat a food that is not allowed, I often then splurge and eat other high calorie foods.	☐	☐

Turn page over

PART 2

Please answer the following questions by CIRCLING the word that best agrees to you.

37.	How often are you dieting in a conscious effort to control your weight?	**Rarely**	**Some times**	**Usually**	**Always**
38.	Would a weight fluctuation of 5lbs (2 kgs) affect the way you live your life?	**Not at all**	**Slightly**	**Moderately**	**Very much**
39.	How often do you feel hungry?	**Only at mealtimes**	**Sometimes between meals**	**Often between meals**	**Almost always**
40.	Do your feelings of guilt about overeating help you control your food intake?	**Never**	**Rarely**	**Often**	**Always**
41.	How difficult would it be for you to stop eating halfway through dinner and not eat for the next 4 hours?	**Easy**	**Slightly difficult**	**Moderately difficult**	**Very difficult**
42.	How conscious are you of what you are eating?	**Not at all**	**Slightly**	**Moderately**	**Extremely**
43.	How frequently do you avoid "stocking up" on tempting foods?	**Almost never**	**Seldom**	**Usually**	**Almost always**
44.	How likely are you to shop for low calorie foods?	**Unlikely**	**Slightly unlikely**	**Moderately likely**	**Very likely**
45.	Do you eat sensibly in front of others and splurge alone?	**Never**	**Rarely**	**Often**	**Always**
46.	How likely are you to consciously eat slowly in order to cut down on how much you eat?	**Unlikely**	**Slightly unlikely**	**Moderately likely**	**Very likely**
47.	How frequently do you skip dessert because you are no longer hungry?	**Almost never**	**Seldom**	**At least once per week**	**Almost every day**
48.	How likely are you to consciously eat less than you want?	**Unlikely**	**Slightly unlikely**	**Moderately likely**	**Very likely**
49.	Do you go on eating binges though you are not hungry?	**Never**	**Rarely**	**Sometimes**	**At least once per week**

Turn page over

Part 2 Continued

50.	On a scale of 1 to 5, where 0 (zero) means no restraint in eating (eating whatever you want, whenever you want it) and, 5 means total restraint (constantly limiting food intake and never "giving in"), What number would you give yourself? (circle your answer)

0	Eat whatever you want, whenever you want it
1	Usually eat whatever you want, whenever you want it
2	Often eat whatever you want, whenever you want it
3	Often limit food intake, but often "give in"
4	Usually limit food intake, rarely "give in"
5	Constantly limiting food intake, never "giving in"

51. To what extent does this statement describe your eating behaviour?

"I start dieting in the morning, but because of many different things that happen during the day, by evening I have given up and eat what I want, promising myself to start dieting again tomorrow"

Not like me	**Little like me**	**Pretty good description of me**	**Describes me perfectly**

Thank you.

APPENDIX 5:

SENSITIVITY TO PUNISHMENT & REWARD QUESTIONNAIRE

Sensitivity to Punishment and Sensitivity to Reward (SPSRQ) CFR 08

Participant ID# ☐☐☐ **Date of Birth:** ☐☐☐☐ ☐☐
Year *month*

	Please check the box YES or NO for each question.	**YES**	**NO**
1.	Do you often refrain from doing something because you are afraid of it being illegal?	☐	☐
2.	Does the good prospect of obtaining money motivate you strongly to do some things?	☐	☐
3.	Do you prefer not to ask for something when you are not sure you will obtain it?	☐	☐
4.	Are you frequently encouraged to act by the possibility of being valued in your work, in your studies, with your friends or with your family?	☐	☐
5.	Are you often afraid of new or unexpected situations?	☐	☐
6.	Do you often meet people that you find physically attractive?	☐	☐
7.	Is it difficult for you to telephone someone you do not know?	☐	☐
8.	Do you like to take some drugs because of the pleasure you get from them?	☐	☐
9.	Do you often renounce your rights when you know you can avoid a quarrel with a person or an organization?	☐	☐
10.	Do you often do things to be praised?	☐	☐
11.	As a child were you troubled by punishments at home or in school?	☐	☐
12.	Do you like being the center of attention at a party or social meeting?	☐	☐
13.	In tasks that you are not prepared for, do you attach great importance to the possibility of failure?	☐	☐
14.	Do you spend a lot of your time on obtaining a good image?	☐	☐
15.	Are you easily discouraged in difficult situations?	☐	☐
16.	Do you need people to show their affection for you all the time?	☐	☐
17.	Are you a shy person?	☐	☐
18.	When you are in a group, do you try to make your opinions the most intelligent or the funniest?	☐	☐
19.	Whenever possible, do you avoid demonstrating your skills for fear of being embarrassed?	☐	☐
20.	Do you often take the opportunity to pick up people you find attractive?	☐	☐
21.	When you are with a group, do you have difficulties selecting a good topic to talk about?	☐	☐
22.	As a child, did you do a lot of things to get people's approval?	☐	☐

Turn page over

Continued		YES	NO
23.	Is it often difficult for you to fall asleep when you think about things you have done or must do?	☐	☐
24.	Does the possibility of social advancement, move you to action, even if this involves not playing fair?	☐	☐
25.	Do you think a lot before complaining in a restaurant if your meal is not well prepared?	☐	☐
26.	Do you generally give your preference to those activities that imply an immediate gain?	☐	☐
27.	Would you be bothered if you had to return to a store when you noticed you were given the wrong change?	☐	☐
28.	Do you often have trouble resisting the temptation of forbidden things?	☐	☐
29.	Whenever you can, do you avoid going to unknown places?	☐	☐
30.	Do you like to compete and do everything you can to win?	☐	☐
31.	Are you often worried by things that you said or did?	☐	☐
32.	Is it easy for you to associate tastes and smells to very pleasant events?	☐	☐
33.	Would it be difficult for you to ask your boss for a raise (salary increase)?	☐	☐
34.	Are there a large number of objects or sensations that remind you of pleasant events?	☐	☐
35.	Do you generally avoid speaking in public?	☐	☐
36.	When you start to play with a slot machine, is it often difficult for you to stop?	☐	☐
37.	Do you, on a regular basis, think that you could do more things if it was not for your insecurity or fear?	☐	☐
38.	Do you sometimes do things for quick gains?	☐	☐
39.	Comparing yourself to people you know, are you afraid of many things?	☐	☐
40.	Does your attention easily stray from your work in the presence of an attractive stranger?	☐	☐
41.	Do you often find yourself worrying about things to the extent that performance in intellectual abilities is impaired?	☐	☐
42.	Are you interested in money to the point of being able to do risky jobs?	☐	☐
43.	Do you often refrain from doing something you like in order not to be rejected or disapproved of by others?	☐	☐
44.	Do you like to put competitive ingredients in all of your activities?	☐	☐
45.	Generally, do you pay more attention to threats than to pleasant events?	☐	☐
46.	Would you like to be a socially powerful person?	☐	☐
47.	Do you often refrain from doing something because of your fear of being embarrassed?	☐	☐
48.	Do you like displaying your physical abilities even though this may involve danger?	☐	☐

Thank you.