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RESEARCH ARTICLE | *Neurogastroenterology and Motility*

Associations of gastric volumes, ingestive behavior, calorie and volume intake, and fullness in obesity

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Vijayvargiya P, Chedid V, Wang XJ, Atieh J, Maselli D, Burton DD, Clark MM, Acosta A, Camilleri M. Associations of gastric volumes, ingestive behavior, calorie and volume intake, and fullness in obesity. *Am J Physiol Gastrointest Liver Physiol* 319: G238–G244, 2020. First published July 6, 2020; doi:10.1152/ajpgi.00140.2020.—Whereas gastric emptying significantly predicts calorie intake, the association between gastric capacity and satiation and satiety is unclear. To study the associations between gastric volumes and ingestive behaviors with satiation and satiety in obesity, 62 healthy adult obese patients (57 female) with no eating disorders underwent measurements of satiety, as determined by kilocalories of ingestion at a buffet meal, and satiation by volume to comfortable fullness (VTF) and maximum tolerated volume (MTV), while drinking Ensure (30 mL/min). Fasting and postprandial gastric volumes were measured by validated single-photon emission computed tomography. We also measured eating [Weight Efficacy Life-Style Questionnaire score (WEL)] and exercise behaviors associated with obesity. Spearman correlation-assessed relationships of measured traits and linear regression analysis to identify predictors of satiation or satiety. The participants were aged 38 ± 10.1 yr and the body mass index (BMI) 36.8 ± 4.8 kg/m^2. Fasting gastric volume was significantly correlated with VTF (r_s = 0.3, P = 0.03), but not with MTV or buffet meal kilocalorie ingestion. Regression analysis identified sex (P = 0.02, with males having significantly higher fasting gastric volume) and fasting gastric volume (0.04) as predictors of higher VTF. An increase in fasting gastric volume of 50 mL resulted in a 6-mL increase in VTF. Buffet meal intake was inversely related to the ability to resist the urge to eat; factors associated with ingestive behavior (increase in total WEL score) significantly correlated with satiety and gastric accommodation (P < 0.05). Gastric capacity during fasting is associated with calorie intake to the point of comfortable fullness; factors associated with ingestive behavior are associated with satiety and gastric accommodation.

NEW & NOTEWORTHY Buffet meal intake was inversely related to the ability to resist the urge to overeat. Factors associated with ingestive behavior significantly correlated with satiety and gastric accommodation. Gastric capacity during fasting is associated with calorie intake to the point of comfortable fullness; factors associated with ingestive behavior are associated with satiety and gastric accommodation.

accommodation; appetite; postprandial; reservoir; satiety

INTRODUCTION

Up to 40% of the United States population meets criteria for obesity [body mass index (BMI) >30 kg/m^2]. The balance between calorie intake and energy expenditure determines body weight. Clearly, physiological, social, genetic, and behavioral factors influence obesity. In terms of physiological factors, previous studies have documented a 28-mL greater average fasting volume of the stomach in obesity class II/III (BMI: 35–39.9 kg/m^2 and >40 kg/m^2, respectively) compared with the average fasting gastric volume in normal weight and overweight participants (1). Eating behaviors may also have an impact, as patients with bulimia have enlarged gastric volume (18). In assessing the influence of gastric volume on caloric intake, it is, therefore, necessary to ensure the patient cohort does not include patients with bulimia and, possibly, those with binge-eating disorder. In addition to eating behaviors, gastric motor functions in health and disease, pyloric obstruction (8), as well as hormones influence postprandial symptoms of bloating, fullness, and nausea, and caloric intake. Thus, gastric emptying is a significant predictor of calorie intake (19), and slowing of gastric emptying with the glucagon-like peptide 1 (GLP-1) receptor analog, liraglutide, was associated with lower maximum tolerated volume compared with placebo in a 16-wk, randomized, controlled trial (20). GLP-1 itself enhanced gastric accommodation in healthy controls (13), and this effect is dependent on normal vagal function, as the effect of GLP-1 on gastric accommodation is not observed in patients with diabetic vagal neuropathy (14).

Several studies have assessed the association of other stomach functions with postprandial symptoms using pharmacological perturbations. In a large study of 292 patients with functional dyspepsia, low-dose antidepressants (amitriptyline and escitalopram) reduced aggregate symptoms in response to nutrient challenge (maximum tolerated volume of Ensure during nutrient drink test), and this was associated with increased postprandial gastric accommodation, but not with alteration in gastric emptying (23). In healthy participants, the neurokinin-1 receptor antagonist aprepitant increased fasting and postprandial and accommodation gastric volume, and there was a numerical, but not statistically significant, increase in volume to fullness and maximum tolerated volume by ~200 kcal (21). In a prior study of the association of gastric fasting and accommodation volumes across the spectrum of normal BMI to class II/III obesity (that is BMI >35.0 kg/m^2), there was no significant overall relationship with satiation or satiety (19).

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Overall, the associations between gastric reservoir capacity during fasting and postprandially and satiation and satiety are unclear. However, to assess these associations, it is important to characterize potential confounders related to activities associated with obesity itself, including anxiety and depression, eating behavior and physical activity. Therefore, the aim of this study was to evaluate the associations between fasting and postprandial gastric volume measurements and satiation and satiety in obese, otherwise healthy, participants.

METHODS

Participants

Sixty-two otherwise healthy patients with obesity (BMI >30 kg/m^2) with no evidence of active psychiatric symptoms, eating disorders (specifically, bulimia), or alcohol use disorders were prospectively enrolled as part of ClinicalTrials.gov NCT03523273. Participants did have comorbidities associated with the underlying obesity, and associated medications were allowed as long as they have not been reported to disrupt gastric emptying or accommodation or appetite. The studies reported here constitute the baseline measurements before inclusion in the therapeutic trial comparing effects of liraglutide and placebo on gastric functions, appetite, and weight. The study was approved by Mayo Clinic Institutional Review Board (IRB no. 15-001783), and all patients provided informed consent.

All participants underwent screening visits and baseline measurements of gastrointestinal, behavioral, and psychological factors. Figure 1 provides a study schema. Satiety, satiation, and gastric volume measurements were most commonly completed 14–21 days after baseline. Physiological measurements were completed at a minimum 2 days after baseline questionnaires, and there was at least 1 day between gastric volume with satiety evaluation and satiation testing. There were no changes in clinical status or medications throughout the testing period.

Characterization of Functions Attributable to Gastric Functions or Eating Behaviors

Measurement of satiety. Satiety was measured by kilocalorie ingestion at an ad libitum buffet meal (9) with foods of known nutritional value and information on caloric intake and macronutrient distribution in the chosen foods. Four hours after ingesting 300 mL liquid nutrient as part of the single photon emission computed tomography (SPECT) study, participants were invited to eat, over a 30-min period, a standard ad libitum meal that included (Fig. 1): *1*) vegetable lasagna [Stouffers, Nestle, Solon, OH; nutritional analysis of each 326 g box: 420 kcal, 17 g protein (16% of energy), 38 g carbohydrate (37% of energy), and 22 g fat (47% of energy)]; *2*) vanilla pudding [Hunts, Kraft Foods North America, Tarrytown, NY; nutritional analysis of each 99 g carton: 130 kcal, 1 g protein (3% of energy), 21 g carbohydrate (65% of energy), and 4.5 g fat (32% of energy)]; and *3*) skim milk [nutritional analysis of each 236 mL carton: 90 kcal, 8 g protein (36% of energy), 13 g carbohydrate (64% of energy), and 0 g fat].

The total amount (grams and kilocalories) of food consumed and the kilocalories of each macronutrient at the ad libitum meal were analyzed by using validated software (ProNutra 3.0; Viocare Technologies, Princeton, NJ).

Measurement of satiation. Satiation was determined by volume to comfortable fullness (VTF) and maximum tolerated volume (MTV) while drinking Ensure [(1 kcal/mL, 11% fat, 73% carbohydrate, 16% protein), Abbott Laboratories, Lake Bluff, IL] at a constant rate of 30 mL/min to the MTV (7). This was performed after a minimum 4-h fasting period. Participants recorded their sensations every 5 min using a numerical scale from 0 to 5, with *level 0* being no symptoms, *level 3* corresponding to fullness sensation after a typical meal (VTF), and *level 5* corresponding to the MTV (maximum or unbearable fullness/satiation). Nutrient intake was stopped when subjects reached the score of 5. The nutrient drink volume (and hence calorie intake) needed to achieve maximum satiation was recorded (Fig. 1).

Measurement of gastric volume. Fasting and postprandial gastric volumes were measured by a validated SPECT method (5, 6). We measured gastric volume during fasting and for 15 min after 300 mL of Ensure (316 kcal). The method has been previously validated, and performance, including interindividual and intraindividual coefficients of variation, have been characterized (5, 6). Intravenous injection of ^{99m}Tc sodium pertechnetate, which is taken up by the parietal and nonparietal cells of the gastric mucosa, allows visualization of the stomach wall. There is high intraobserver reproducibility to measure gastric volume with this technique (16).

Characterization of Activities Associated with Obesity

Eating disorders. The Questionnaire on Eating and Weight Patterns-Revised (QEWP-R) (29) was used to screen for bulimia nervosa and binge-eating disorder. Participants with an eating disorder were not enrolled into the study.

Mood: anxiety and depression. Patients were screened for psychiatric dysfunction with the Hospital Anxiety and Depression Scale (HADS) (30). A total score in addition to anxiety and depression subscales were tabulated. If a HADS score >11 was obtained for either the anxiety or depression subscales, the participant was excluded.

Physical activity. The patients' physical activity levels were assessed with the four-item Physical Activity Stages of Change Ques-

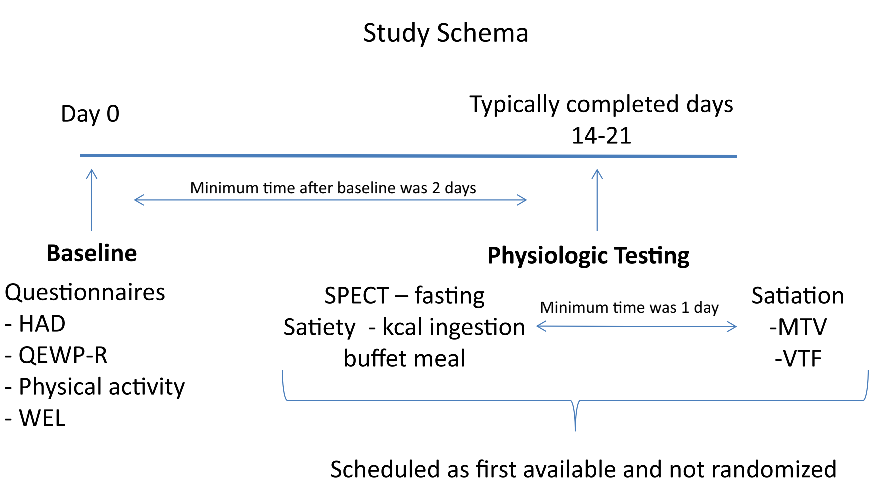

Fig. 1. Study schema. HAD, hospital anxiety and depression score; MTV, maximum tolerated volume; QEWP-R, Questionnaire on Eating and Weight Patterns-5; SPECT, single-photon emission computed tomography; WEL, weight efficacy lifestyle; VTF, volume to fullness.

tionnaire (25). Patients answered four questions: *1*) Are they physically active currently? *2*) Will they increase physical activity in the next 6 mo? *3*) Are they regularly active (defined as at least 30 min at least 5 days/week) currently? and *4*) Have they been regularly active for the past 6 mo?

Physical activity was categorized into precontemplation, contemplation, preparation, action, and maintenance. Analysis of physical activity was based on categorical categories based on the responses to the five questions in the questionnaire: precontemplation denotes no current physical activity and no intention to increase in the next 6 mo; contemplation denotes not currently physically active, but plan to start in the next six months; preparation denotes some physical activity, but not meeting the criteria of 30 min at least 5 days per week; action denotes currently physically active (30 min at least 5 days per week); and maintenance denotes for at least 6 mo has met criteria for structured physical activity (28).

Eating self-efficacy. Patient eating self-efficacy was assessed by the Weight Efficacy Life-Style Questionnaire (WEL) (10), a validated measure of a patient's ability to resist the urge to overeat and as a marker of discipline to initiate and adhere to an eating plan and calorie monitoring (24). It is a 20-question evaluation using a 10-point scale ranging from 0 = not confident to 9 = very confident. In addition to a total score (sum of all question answers), there are five situational factors: negative emotions, availability, social pressure, physical discomfort, and positive activities. Our team has found that the WEL scores improve after weight loss (3) and that having a food addiction is associated with a low WEL score (22). Higher self-efficacy was a predictor of long-term weight loss maintenance in patients with very low calorie diets and weight loss surgery (11, 15). Additionally, improvement in WEL scores was predictive of successful weight maintenance after having bariatric surgery (17).

Statistical Analysis

Data are shown as mean and SDs. Spearman correlation determined the association of gastric fasting and accommodation volumes (postprandial – fasting gastric volume) and measures of satiety and satiation. We used linear regression analysis to identify predictors of higher volume to fullness, maximum tolerated volume, and buffet meal intake.

RESULTS

Demographics, Gastric Volumes, Satiety, and Satiation

The baseline demographics of the 62 study participants (57 female, 5 male) were aged 38 ± 10.1 yr and BMI 36.8 ± 4.8 kg/m^2. Fasting gastric volume was 194 ± 50 mL, postprandial change in gastric volume (or accommodation volume) was 341 ± 86 mL (examples in Fig. 2), satiety based on buffet meal ingestion was 927 ± 324 kcal, satiation from volume to fullness was 686 ± 266 mL, and maximum tolerated volume was 1,157 ± 348 mL (Table 1). There were significant correlations between measurements of satiation (VTF or MTV) and satiety (kilocalorie intake at buffet meal) (Table 2).

Anxiety, Depression, Physical Activity Level, and Eating Behaviors

Table 1 shows all data for psychiatric screening, physical activity, and eating behavior patterns. Not surprisingly, most

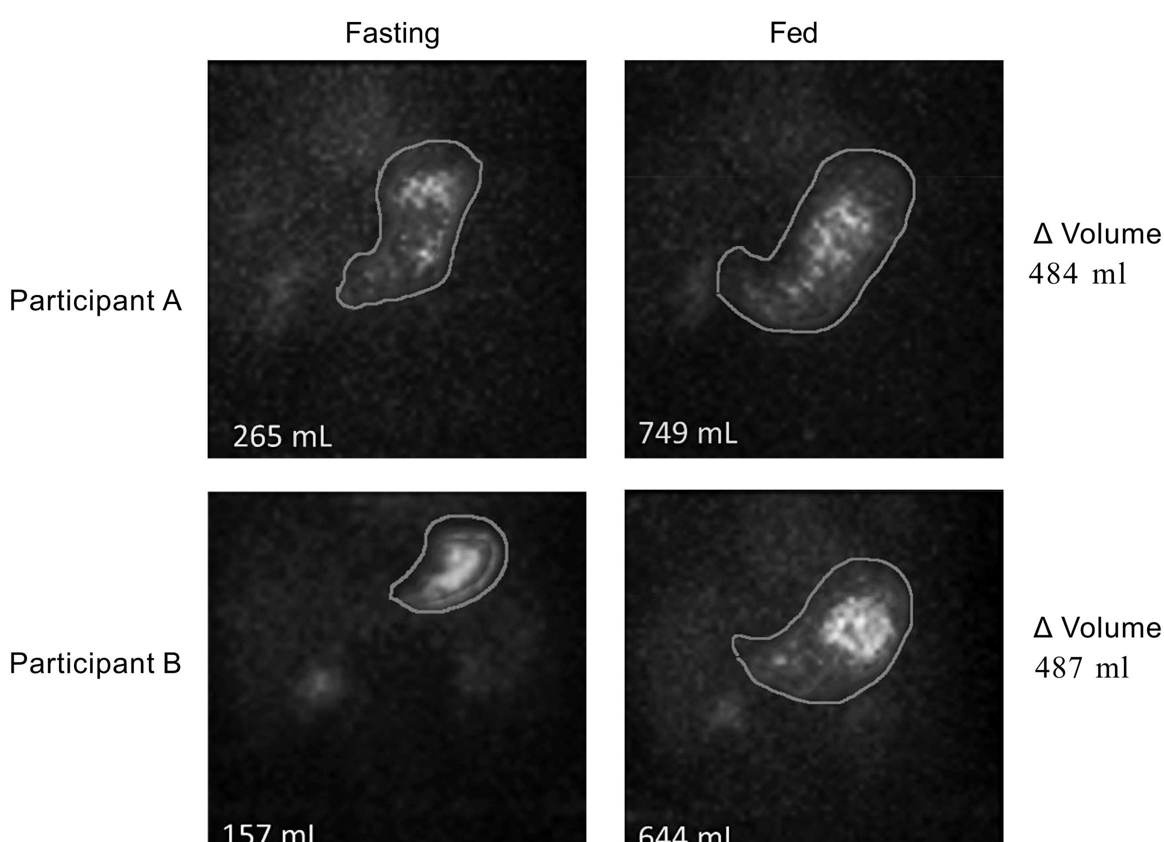

Fig. 2. Examples of fasting and postprandial gastric volumes. Note the differences in fasting gastric volumes in these two individual obese participants, and the almost identical accommodation volumes.

Table 1. *Demographics, markers of satiety and satiation, Hospital Anxiety and Depression Scale scores, physical activity, and Weight Efficacy Life-Style Questionnaire scores*

Parameter	Value
n (F/M)	62 (57/5)
Age, years	38 ± 10.1
BMI, kg/m^2	36.8 ± 4.8
Satiety, satiation, and gastric accommodation	
Satiety	
Buffet meal ingestion, kcal	927 ± 324
Protein (kcal)	206.7 ± 69.1
Fat (kcal)	192 ± 74.4
Carbohydrates (kcal)	528 ± 189
Satiation	
Volume to fullness, mL	686 ± 266
Maximum tolerated volume, mL	1157 ± 348
Fasting gastric volume, mL	194 ± 50
Gastric accommodation (Δ gastric volume), mL	341 ± 86
Anxiety and depression	
Hospital Anxiety and Depression Scale scores	4.5 ± 3.6
Anxiety	3.2 ± 2.8
Depression	1.3 ± 1.3
Physical activity	
Physical activity	
Pre-contemplation, %	5 (3/59)
Contemplation, %	41 (24/59)
Preparation, %	14 (8/59)
Action, %	14 (8/59)
Maintenance, %	27 (16/59)
Eating behavior	
WEL questionnaire total scores	124 ± 28.2
WEL negative emotions	23.9 ± 6.2
WEL availability	20.2 ± 7.0
WEL social pressure	23.7 ± 9.2
WEL physical discomfort	28.3 ± 5.5
WEL positive activities	28.1 ± 6.0

Data are expressed as means ± SD. BMI, body mass index; WEL, Weight Efficacy Life-Style Questionnaire.

Table 2. *Relationships between gastric volumes, measures of satiation and satiety, and behaviors associated with obesity based on Spearman correlation*

Satiety	
Buffet meal, kcal	
WEL total	$r_s = -0.26$, $P = 0.045$
WEL social pressure	$r_s = -0.44$, $P < 0.001$
Satiation	
Volume to fullness	
Fasting gastric volume	$r_s = 0.3$, $P = 0.03$
Buffet meal, kcal	$r_s = 0.45$, $P < 0.001$
Maximum tolerated volume	
Buffet meal, kcal	$r_s = 0.6$, $P < 0.001$
Gastric accommodation	
Δ Gastric volume	
Physical activity stage	$r_s = 0.31$, $P = 0.018$
WEL total	$r_s = 0.31$, $P = 0.02$
WEL negative emotions	$r_s = 0.3$, $P = 0.034$
WEL availability	$r_s = 0.3$, $P = 0.04$
WEL social pressure	$r_s = 0.3$, $P = 0.04$
WEL positive activities	$r_s = 0.3$, $P = 0.04$

WEL, Weight Efficacy Life-Style questionnaire. r_s, Spearman correlation. $n = 62$ participants (57 female).

participants were in the early stages of change of physical activity, with only 41% in either the "action" or "maintenance" stages of change. Satiety was inversely correlated with resisting the urge to eat, indicating that the less control participants had on managing their urge to eat (based on total WEL score), the greater the caloric consumption at the buffet meal (Table 2).

Relationships Between Gastric Volumes and Measures of Satiation and Satiety

Spearman correlation demonstrated no significant correlation between gastric accommodation and measures of satiety and satiation ($P > 0.05$). Satiation was directly correlated with fasting gastric volume (Fig. 3) and buffet meal caloric intake (Table 2). However, physical activity stage and eating self-efficacy demonstrated a significant correlation. A higher WEL score (indicating greater control of resisting the urge to eat) was positively associated with greater gastric accommodation. Additionally, those at a higher stage of change for physical activity were associated with greater gastric accommodation.

Predictors of Measures of Satiation and Satiety

Linear regression analysis showed that carbohydrate intake at the buffet meal (which measures satiety) was significant predictor of maximum tolerated volume, unlike the other macronutrients (protein and fat). For every 100-kcal increase in carbohydrate intake, there was an increase in maximum tolerated volume of 114 mL.

Total WEL score was a significant predictor of gastric accommodation. For every 30-point increase in total WEL score, there was a 30-mL increase in gastric accommodation, indicating that greater control on the urge to eat resulted in greater change in gastric accommodation volume. Sex ($P = 0.02$) and fasting gastric volume ($P = 0.04$) were predictors of higher volume to fullness on the satiation test. The regression analysis showed that for the entire cohort, an increase in fasting gastric volume of 50 mL would be predicted to be associated with a 67-mL increase in volume to fullness.

The WEL physical discomfort subscale ($P = 0.01$) and sex ($P < 0.001$) were also significant predictors of satiety based on buffet meal caloric intake. Males had significantly higher

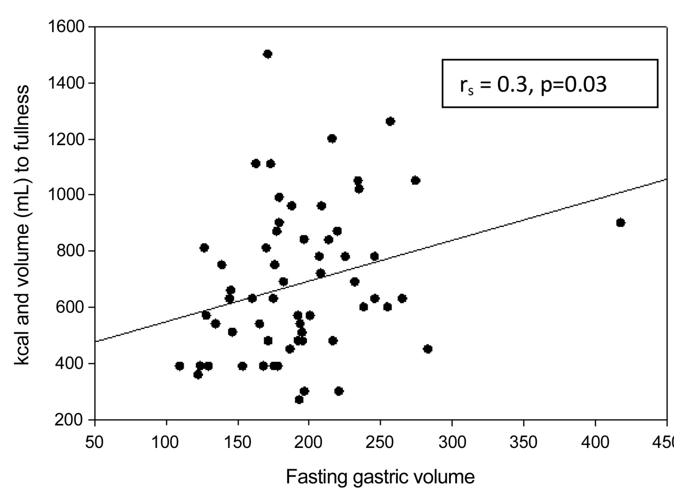

Fig. 3. Spearman correlation (r_s) between fasting gastric volume and volume to fullness based on 62 participants (57 females).

intake at the buffet meal, and a 10-point lower WEL physical discomfort subscale predicts an increase of 157 kcal at the buffet meal.

DISCUSSION

Our study has assessed, in people with obesity, the relationships between gastric motor functions, ingestive behavior, satiation, and satiety measured with standardized laboratory-based tests. First, we have assessed the associations of gastric volumes with indices of satiation and satiety. The study shows that fasting gastric volume is associated with calorie intake to the point of comfortable fullness and maximal satiation (during the nutrient drink test), but not with satiety (measured by total calorie intake at the buffet meal). Increased carbohydrate intake at the buffet meal was significantly correlated with increased maximum tolerated volume of the liquid nutrient drink. In addition, regression analysis identified sex and fasting gastric volume as significant predictors of higher volume to fullness. Thus, an increase in fasting gastric volume of 50 mL was associated with a 67-mL increase in volume to fullness, corresponding to 70 kcal based on the nutrient drink consumed in this study. In terms of clinical significance, obese individuals in the top quartile can ingest at least 70 kcal more per meal to reach comfortable fullness. Over a one-week timeframe, these individuals can consume 1,470 kcal, resulting in a 0.42-lb weight gain per week, if there is not a parallel increase in energy expenditure. Other inferences from these observations are that, for every 20% increase in fasting gastric volume, there is a 10% increase in volume to usual, comfortable fullness after a meal. For patients with the highest fasting gastric volumes exceeding 300 mL, one can expect they will consume an average of 30% more calories per meal. Therefore, fasting gastric volume could be an important determinant of obesity over the long term, just as it has recently been reported that gastric emptying rate is a predictor of weight gain in young adults (26). These observations are hypothesis-generating, and additional evidence is required to prove the association of fasting gastric volume with prospective weight gain.

These observations also suggest that reduction of fasting gastric volume has the potential to reduce calorie intake. While bariatric surgical or endoscopic interventions can clearly reduce the stomach reservoir capacity and this constitutes one of the mechanisms of reduced postprocedure calorie intake, it has been difficult to replicate such effects pharmacologically. Ghrelin is a hormone released predominantly in the stomach during fasting and stimulates increased oral intake. Ghrelin has a molecular composition similar to that of motilin, and it increases gastric emptying when administered at pharmacological doses (reviewed in Ref. 7). Pharmacological doses of ghrelin reduced gastric accommodation in health, but this was not associated with altered satiation (2) and, at the pharmacological doses, ghrelin also enhanced gastric emptying and actually reduced meal-related symptoms (2). Conversely, pharmacological effects of motilin included reduced postprandial proximal gastric volume and increased postprandial symptoms (12).

An infusion of ghrelin to reproduce physiological circulating levels was associated with borderline reduction in fasting gastric volumes (P = 0.056), and postprandial gastric accommodation (P = 0.090), with no significant acceleration of gastric emptying of solid food in healthy, lean, or obese participants (11). These borderline reductions in fasting and postprandial gastric volume were not associated with increased symptoms after a 300-kcal meal (11).

Second, given that fasting and postprandial changes in gastric volume do not correlate with measures of satiety and satiation, we have examined the role of ingestive behavior on satiation, satiety, and gastric functions. In this study, eating behaviors were based on the WEL score, a marker of eating self-efficacy and of the ability to control the urge to eat in various situations. The total WEL score was an inverse predictor of caloric intake at a buffet meal and a direct predictor of gastric accommodation. This means that, with less eating self-efficacy, there was a predicted increase in kilocalorie intake at a buffet meal. However, WEL score had a greater role in buffet meal kilocalorie ingestion (a decrease in 10 points resulted in increase of 157-kcal intake) than the effect or association seen with gastric accommodation volume (an increase of 30 points of WEL score, with modest increase in accommodation of 30 mL). The observed association with higher gastric accommodation with lower WEL is of significant interest, although it is unclear from our study which is the cause and which is the effect. The most simplistic interpretation is that increased food intake results in a larger gastric accommodation and, therefore, it is important to stress that the participants in the study were screened for behaviors, suggestive of bulimia or binge-eating disorder. Geliebter and Hashim (18) had previously shown that the gastric volume was increased in patients with bulimia.

Compared with measurements in 354 healthy volunteers [BMI: 27.7 ± 5.5 (SD) kg/m^2] (6), fasting gastric volumes in healthy participants [239 ± 9 (SD) mL] were numerically similar to those of obese individuals in the current study (194 ± 50 mL). The change in gastric volume (gastric accommodation) in obesity (341 ± 86 mL) was within 1 SD of that of 354 healthy volunteers (517 ± 96 mL) (6). In previous studies of obese individuals with binge- and bulimia-eating patterns, maximum tolerated volumes were measured by filling an intragastric balloon until maximum discomfort was reached. On the basis of the observations evaluated, there was no significant difference in the maximum tolerated volumes in obese patients with binge behavior (mean ~1,050 mL) and in patients with bulimia (mean ~1,200 mL) (18) compared with the obese population in our study (mean 1,157 mL).

Other factors associated with appetite and overall calorie intake include centrally mediated appetite, gastric emptying, or incretins, which are not considered in the current report. There are multiple, centrally acting hormones that influence appetite (such as insulin and leptin) acting through the arcuate nucleus of the hypothalamus to affect anabolic and catabolic pathways (27). A central dampening of this gut-brain axis could influence satiation and satiety. Our prior studies showed that gastric emptying was a known factor significantly associated with satiation and satiety, as measured by the two same methods (19). Postprandial hormone secretion of peptide YY (PYY) and GLP-1 released upon nutrient exposure in the small bowel are known to result in slower gastric emptying and reduced satiety. One possibility is that the decreased peak in postprandial levels of PYY and GLP-1 previously observed in studies of obese individuals are associated with reduced satiety (1, 4).

Limitations of our study include the fact that there was no dynamic measurement (e.g., in response to pharmacological perturbations) of satiety, satiation, and gastric accommodation in obese individuals, which allowed only association analysis. Our future plan is to measure incretin and other hormone changes, satiety, satiation, gastric accommodation, and gastric emptying in a spectrum of patients (lean, overweight, and obese individuals) over a period of time, and to assess the physiological and behavioral traits in association with weight gain and loss to better understand the complex regulation of energy consumption and appetite.

In summary, gastric capacity during fasting is associated with calorie intake to the point of comfortable fullness, and factors involved in ingestive behavior are associated with satiety and gastric accommodation.

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DISCLOSURES

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AUTHOR CONTRIBUTIONS

M.M.C. and M.C. conceived and designed research; D.D.B. performed experiments; P.V., D.D.B., and M.C. analyzed data; P.V. and M.C. interpreted results of experiments; M.C. prepared figures; P.V. and M.C. drafted manuscript; P.V., V.C., X.J.W., J.A., D.M., M.M.C., A.A., and M.C. edited and revised manuscript; P.V., M.M.C., and M.C. approved final version of manuscript.

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