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Preliminary Examination of Insulin and Amylin Levels in Women with Purging Disorder

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Abstract

Objective—This preliminary study explored whether differences in meal-stimulated insulin or amylin release are linked to altered ingestive behaviors in individuals with bulimia nervosa (BN) or purging disorder (PD).

Method—Women with BN (n=15), PD (n=16), or no eating disorder (n=18) underwent structured clinical interviews and assessments of gut hormone and subjective responses to a fixed test meal. Multilevel model analyses were used to explore whether gut hormone responses contribute to subjective responses to the test meal and whether these associations differed by group.

Results—Insulin and amylin levels significantly increased following the test meal. Women with PD showed greater insulin release compared to those with BN, but not controls. Multilevel models support significant group X insulin interactions predicting subjective ratings of nausea and urge to vomit, with a stronger association between higher insulin responses and higher nausea and urge to vomit in women with PD and BN. Amylin responses did not differ by group.

Conclusion—Increased sensitivity to the effects of insulin on nausea and urge to vomit may be linked to purging in both PD and BN. Differences in postprandial insulin levels may be linked to purging behavior in the absence versus presence of binge eating.

Keywords

purging disorder; bulimia nervosa; self-induced vomiting; amylin; insulin

Introduction

Bulimia nervosa (BN) and purging disorder (PD) both involve purging (e.g., self-induced vomiting) following the consumption of food. In BN, purging occurs after binge-eating episodes, defined in the DSM-5 by an objectively large amount of food consumed in a short time period accompanied by a loss of control. Individuals with BN experience reduced feelings of fullness following a meal, suggesting that impairments in satiation may contribute to the propensity to consume large quantities of food during binges.^{1–4} In contrast, PD is characterized by excessive fullness, nausea, urge to vomit, and purging after

the consumption of normal quantities of food.^{3–6} Mounting evidence supports that dysfunction in the neuroendocrine systems that control food intake may influence development and maintenance of eating disorders. Several independent examinations have revealed reductions in meal-stimulated release of gut hormones specifically implicated in satiation (i.e., CCK and GLP-1) in individuals with BN^{1,4,7,8}, whereas excessive postprandial release of a satiety peptide, PYY, has been found in individuals with PD compared to BN and controls.⁶ Understanding the factors uniquely linked to binge eating or purging behavior may provide new therapeutic targets to improve outcomes for individuals with eating disorders.

This preliminary study sought to explore whether differences in meal-stimulated insulin or amylin release are linked to altered ingestive behaviors in individuals with BN or PD. Insulin and amylin are peptide hormones co-secreted from pancreatic β -cells following nutrient ingestion.⁹ Insulin is best known for its role in maintaining glucose homeostasis, but behavioral data from animal models and humans suggest that both insulin and amylin promote fullness and reduce the rewarding value of food, making them interesting candidates for further investigation in the context of disordered eating.^{10–14} Amylin also delays gastric emptying, which may underlie the excessive postprandial fullness, nausea, and gastrointestinal distress reported by individuals with PD.^{3,4,6,15} Here, we measured plasma insulin and amylin levels following a meal in women with PD, BN, or controls. We also explored how gut hormone responses contribute to subjective responses to the test meal and whether these associations differed by group. These represent secondary assays of existing samples and exploratory hypotheses were: postprandial insulin or amylin responses are disrupted in BN and PD and may account for altered subjective responses to food intake following a meal compared to controls.

Methods

Participants

Women (n=49) who participated in a larger series of studies provided back-up samples for comparison of meal-related plasma insulin and amylin levels among PD, BN and controls.^{3,6} While original study aims did not include analyses of insulin and amylin, consent forms covered broad aims of examining hormones associated with ingestive behavior to account for new findings that emerged following study initiation. All participants provided written informed consent prior to participation, according our IRB-approved protocol.

BN participants (n=15, mean age 21.3 ± 0.39 years, mean body mass index (BMI) 22.96 ± 0.29 kg/m²), met DSM-5 criteria for BN.¹⁶ PD participants (n=16, mean age 20.87 ± 0.57 years, mean BMI 23.06 ± 0.24 kg/m²) met research criteria for PD.¹⁷ BN and PD participants could not have a lifetime history of anorexia nervosa, and PD participants could not have a lifetime history of BN, BED, or recurrent objective binge episodes. Control participants (n=18, mean age 21.17 ± 0.21 years, mean BMI 23.04 ± 0.18 kg/m²) had no lifetime history of an eating disorder and did not diet for weight loss. Participants were free of medical conditions that could influence weight or appetite, were medication-free except for oral contraceptives, and were asked to abstain from alcohol or other drugs or medications for 72 h prior to the visits in which blood samples were taken.

Procedures

Clinical interviews were conducted to confirm eligibility using the Eating Disorders Examination and Structured Clinical Interview for DSM-IV Axis I Disorders^{18,19} adapted for proposed DSM-5 criteria during a first visit. Samples for hormone analyses were obtained on a subsequent visit, which began between 7:30 and 8:00 AM after an overnight fast. Following placebo administration in a double-blind, cross-over design, an indwelling intravenous catheter was placed in participants' arms. Two baseline blood samples were collected, after which participants consumed a fixed meal of 900 kCal of Ensure Plus (609 mL) over 5 min. Postprandial blood draws occurred 10, 20, 30, 50, 90, and 120 min after the meal ended. After each blood sample, participants completed 100 mm visual analog scales (VAS) to obtain subjective reports of hunger, fullness, nausea, stomachache, urge to binge, and urge to vomit.

Gut Hormone Analyses

Samples were collected into chilled EDTA-treated tubes with 150 µL aprotinin (Sigma #A6279) per 3 mL of blood. Samples were immediately centrifuged at 4°C, after which 50 µL 1.0 N HCl was added to 1 mL of plasma. Plasma was stored at -80°C until assayed. Given the time over which insulin and amylin are released and peak following nutrient ingestion, samples taken at baseline, 30, 50, and 90 min post-meal were assayed for current aims.⁹

Insulin and amylin levels were determined using commercially available enzyme-linked immunoabsorbant assay kits (Catalog #: EZHA52-K and EZHI14K; MilliporeSigma, Burlington, MA). Samples were run in duplicate and batched such that each assay contained balanced representation of diagnostic groups. The detection limits for insulin and amylin were 1 uU/mL and 0.7 pM, respectively. The average intra-assay coefficient of variation (CV %) was 3.95% for insulin and 4.95% for amylin, representing good reliability.

Data Analyses

Multilevel model analyses were used to examine change over time in repeated measures collected before and after the test meal (level 1) and between-subject predictors of change (level 2). Insulin and amylin values were positively skewed and transformed prior to analyses. Time and time-squared were linear and quadratic predictors, respectively, of within-person changes in hormone levels, and time was included as a random effect in models with an unstructured covariance matrix. Diagnostic group was a between-subjects predictor of hormone levels. The group X time and group X time-squared interactions tested whether groups differed on meal-related changes in variables. The assay in which samples were run was included as a covariate to control for interassay variability. Bayesian Information Criteria (BIC) were used to identify the best-fitting model. Primary analyses focused on whether meal-related changes in hormone levels varied by diagnostic group. Secondary analyses explored whether hormone responses were associated with subjective responses to the test meal, and whether these associations differed by group. Analyses were conducted in IBM SPSS 24. Given the exploratory and preliminary nature of analyses, $p < 0.05$ was used.

Results

Insulin

A model including main effects of time, time-squared, group, and covariate of assay demonstrated that time, time-squared, and group were significant predictors of meal-related insulin responses. Insulin increased over time [estimate(SE)=0.233(0.015), $t(157.74)=15.65$, $p<0.001$], and rate of change in insulin decreased over time [estimate(SE)=-0.002(0.0002), $t(136.97)=-13.02$, $p<0.001$], consistent with the effects of food intake on insulin release (Fig. 1). There was no significant main effect of group [$F(2,155.15)=2.34$, $p=0.10$], and assay was not a significant predictor of insulin [$F(5,154.71)=0.66$, $p=0.66$]. The best-fitting model (BIC=915.40 vs. BIC=930.67) included a significant group X time interaction [$F(2,180.26)=3.46$, $p=0.03$] and a nonsignificant group X time-squared effect [$F(2,139.37)=2.27$, $p=0.11$]. *Post-hoc* comparisons demonstrated that PD participants showed significantly greater postprandial increases in insulin compared to BN participants [estimate(SE)=0.07(0.03), $t(180.47)=2.61$, $p=0.01$], but not controls ($p=0.31$).

Given the group effect on postprandial insulin response, we explored the combined influences of group and insulin on subjective test meal responses. For fullness, a model including the main effects of time, time-squared, insulin, group, and group X insulin interaction supported significant effects for time, time-squared, and insulin. Subjective feelings of fullness increased after the test meal [estimate(SE)=1.38(0.20), $t(183.80)=6.85$, $p<0.001$], and then gradually decreased with time [estimate(SE)=-0.01(0.002), $t(172.81)=-5.87$, $p<0.001$]. Insulin levels were significantly and positively associated with fullness [$F(1,187.03)=6.65$, $p=0.01$]. The association between insulin and fullness did not differ by group [$F(2,186.06)=0.95$, $p=0.39$].

For urge to vomit, a model including the main effects of time, time-squared, insulin, group, and group X insulin interaction supported significant effects for time, time-squared, insulin, and group X insulin. Urge to vomit increased after the test meal [estimate(SE)=0.44(0.19), $t(182.2)=2.33$, $p=0.02$], and then gradually decreased [estimate(SE)=-0.004(0.001), $t(166.13)=-2.34$, $p=0.02$]. Insulin was significantly and positively associated with urge to vomit [estimate(SE)=2.46(0.85), $t(176.59)=2.89$, $p<0.01$]. A significant group X insulin interaction [$F(2,179.76)=10.58$, $p<0.001$] predicted urge to vomit. *Post-hoc* comparisons demonstrated that compared to controls, both PD [estimate(SE)=4.13(0.95), $t(180.93)=4.34$, $p<0.001$] and BN participants [estimate(SE)=3.69(1.02), $t(182.50)=3.60$, $p<0.001$] demonstrated a stronger association between higher insulin levels and greater urge to vomit but did not differ from each other ($p=0.65$).

For analyses of nausea, a model including the main effects of time, time-squared, insulin, group, and group X insulin interaction supported significant effects for time-squared, insulin, and group X insulin. Compared to controls, participants with PD and BN demonstrated greater associations between insulin and nausea [PD: estimate(SE)=3.35(0.78), $t(182.14)=4.27$, $p<0.001$] [BN: estimate(SE)=2.39(0.85), $t(183.70)=2.824$, $p=0.005$] but did not differ from each other ($p=0.23$).

No significant effects or interactions were found for analyses of stomachache.

Amylin

A model including main effects of time, time-squared, group, and covariate of assay demonstrated that time, time-squared, and assay were significant predictors of meal-related amylin responses. Amylin levels increased over time [estimate(SE)=0.03(0.004), $t(196)=6.01$, $p<0.001$], and rate of growth decreased as a quadratic effect of time [estimate(SE)=-0.0002(0.00004), $t(196)=-5.38$, $p<0.001$] (Fig. 2). Assay was a significant predictor of amylin levels [$F(7,196)=8.07$, $p<0.001$]. There was no significant main effect of group [$F(2,196)=2.30$, $p=0.10$]. Adding the interactions of group X time and group X time-squared to the model worsened model fit (BIC=469.83 vs. BIC=459.85, respectively). There were no significant interaction effects for group X time [$F(2,196)=0.59$, $p=0.55$] or group X time squared [$F(2,196)=0.15$, $p=0.86$]. Thus, groups did not differ significantly on amylin response, and no further analyses were conducted with amylin.

Discussion

Our preliminary analyses support increased insulin responses differentiate women with PD from those with BN. Differences in food intake between BN and PD may reflect differences in what is required to stimulate comparable physiologic responses to food. Follow-up analyses indicated that insulin was positively associated with subjective ratings of nausea and urge to vomit, and these associations were stronger in individuals with BN or PD than controls. Thus, in PD, greater sensitivity to insulin's effects on meal-related nausea and urge to vomit coupled with elevated insulin release compared to BN may contribute to purging behavior after the consumption of normal amounts of food. Future replication of this preliminary study using larger samples is warranted. Further studies will be necessary to determine whether the link between insulin and urge to vomit is causal. Investigating blood glucose would determine whether altered insulin levels contribute to changes in glucose homeostasis in PD.

Results from prior studies of insulin in BN are mixed and largely suggest that insulin may not be a major influence on the pathophysiology of BN.^{8,20-22} Our results also found no significant difference in insulin release between BN and control participants but did suggest greater sensitivity to the effects of insulin in both BN and PD. Data from prior studies could be re-analyzed to determine whether greater sensitivity to the effects of insulin on subjective responses replicate in other samples of BN participants.

This study has several strengths and limitations to acknowledge. To our knowledge, this is the first investigation of insulin and amylin levels in PD, contributing to a growing body of work on the physiology associated with PD. Furthermore, comparisons between individuals with BN and PD enable more targeted investigation of the physiologic factors specifically linked to binge eating versus purging behavior. Reliance on back-up samples produced a relatively small sample for these analyses, but study participants were well-matched on age and BMI, reducing the likelihood that these factors confounded our findings. Because this study utilized a cross-sectional design, we cannot draw temporal or causal inferences.

This preliminary study suggests that elevated sensitivity to insulin's effects on subjective experiences may be linked to purging behavior and that differences in postprandial insulin

release may be linked to differences in the amount of food that precedes purging in PD versus BN. These findings provide new insight into the physiology involved in PD, and further examination of the role of insulin in PD in a larger sample is warranted.

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Figure 1.

Plasma insulin concentrations in women with purging disorder, bulimia nervosa, and healthy controls in response to a test meal. Pre- and post-meal plasma insulin concentrations are greater in women with PD as compared to BN participants ($p=0.01$) but not controls. Data are mean $\pm$ SEM. $n=18$ controls, $n=16$ PD, $n=15$ BN.

Figure 2.

Plasma amylin concentrations in women with purging disorder, bulimia nervosa, and healthy controls in response to a test meal. Meal-related plasma amylin concentrations do not differ by group. Data are mean $\pm$ SEM. $n=18$ controls, $n=16$ PD, $n=15$ BN.