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Sex as an Independent Variable in Satiety

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Background: Satiety is the result of postprandial physiologic events that determine the timing for the next meal by inhibiting the sensation of hunger. It is orchestrated by the brain-gut-axis, with gastric emptying and accommodation being key components of satiety and appetite sensations. Several indices have been used to quantify satiety. Longer time to empty 50% of the stomach content (GET_{1/2}) during a gastric emptying for solid study (GES), and lower SQ for fullness, lower SQ for satisfaction, and higher SQ for hunger after a meal challenge measured by visual analog scales (VAS) are all associated with prolonged satiety and are therefore protective against caloric overconsumption and to the development of obesity. Although obesity prevalence is higher in female compared to male subjects, there is little data on how sex affects biological indices of satiety.

Methods: This retrospective cohort study included patients with overweight and obesity who underwent anthropometric measurements, body composition evaluation, and satiety tests. After an 8-hour overnight fast, patients were provided a radiolabel breakfast (320kcal, 30% fat) to measure GES by scintigraphy over 4 hours and appetite sensations. We measured appetite sensations (hunger, fullness, and satisfaction) with 100-mm VAS every 30 minutes for 4 hours at baseline (before eating breakfast, i.e. VAS_{0'}) and after breakfast (VAS_{30'} to VAS_{240'}). The SQ for each appetite sensation was calculated with the following formula: $(VAS_{0'} - VAS_{30'})/320$. We performed univariate and multiple regression analyses to estimate the contribution

of biological and anthropometric variables to GEt1/2.

Results: We included 743 subjects: 557 females (75%), mean age 40 ± 11 years, mean BMI $33 \pm 8 \text{ kg/m}^2$. Compared to males, female participants had significantly higher BMI and lower height, weight, waist-to-hip ratio (W/H), and percentage lean mass (%LM). Compared to males, female participants had a slower GEt1/2 (123 vs. 98 minutes, $p < 0.0001$), lower SQ for fullness (-15 vs. -12 mm, $p = 0.008$), and lower SQ for satisfaction (-14 vs. -11 mm, $p = 0.01$). Females had higher but not significant SQ for hunger. On univariate analysis, height, BMI, and %LM had a negative but significant correlation with GEt1/2 ($R = -0.3$, $p < 0.0001$; $R = -0.1$, $p = 0.02$; and $R = -0.2$, $p = 0.0003$; respectively). On multiple regression analysis, when taking into consideration age, sex, height, W/H, and %LM, only sex (parameter estimate [PE]=6.8, $p = 0.02$), height (PE=-82, $p = 0.0005$), and W/H (PE=49, $p = 0.004$) were independent predictors of GEt1/2.

Conclusion: This study highlights the sex differences in indices of satiety measured by GEt1/2 with a GES, and by SQ for hunger, fullness, and satisfaction with VAS. Sex is a strong independent predictor of GEt1/2. These observations highlight the importance of considering sex as a variable to understand the pathophysiologic mechanisms involved in obesity's heterogeneity.

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