

Pilot Study of Prandial Satiety Peptides in Black and White Women

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Abstract

Objective: Circulating levels of peptide-YY (PYY) have been shown to be diminished in Black individuals compared to their White counterparts. To extend this work, this pilot study examined pre- and post-prandial levels of glucagon-like peptide-1 (GLP-1), cholecystokinin (CCK), pancreatic polypeptide (PP), and gastric inhibitory polypeptide (GIP) measured in 11 women (7 White, 4 Black).

Methods: Before and 30- and 120-minutes after a low-glycemic and a high-glycemic mixed-macronutrient meal, intravenous blood samples were drawn, immediately processed, and stored. Using commercially-available methods, samples were assayed for concentrations of GLP-1, CCK, PP, GIP, and PYY in a multiplex format.

Results: The main effect of race was significant for CCK ($p = 0.03$) and GLP-1 ($p = 0.02$), and the race-by-time interaction was significant for GLP-1 ($p = 0.04$) and GIP ($p = 0.02$). Compared to White women, Black women exhibited significantly lower postprandial CCK, lower GLP-1 at min 30, and higher GIP at min 120. Postprandial PYY ($p = 0.09$) and PP ($p = 0.34$) were numerically but not statistically lower in Black women. The glycemic load effect was non-significant for all outcomes.

Conclusions: Our findings suggest a generalized effect of blunted satiety signaling in Black women. If these preliminary findings are replicated in a larger independent sample, further studies would be warranted to identify underlying biological pathways that may constitute novel therapeutic targets for addressing racial disparities in obesity.

Keywords: Appetite; Hormones; Obesity; Racial Differences; Satiety Response

Introduction

Obesity is a significant public health problem [1] with high economic burden [2]. Future prevention and treatment progress hinges on developing new paradigms and tailored strategies that focus on high risk groups, such as non-Hispanic black/African American (Black) women. Compared to men and non-Hispanic white (White) women, Black women are ~60% more likely to be obese [3] and they suffer greater obesity-related morbidity and mortality [4-6]. Understanding the mechanisms underlying excess obesity risk in Black women is essential to eliminate racial/ethnic disparities in obesity.

Our group [7-10] and others [11,12] have investigated racial differences in satiety signaling as a potential factor contributing to excess obesity in Black women. These studies have consistently showed that peptide-YY (PYY), which affects food intake in humans by directly influencing both the achievement and maintenance of postprandial satiety, is diminished in Blacks compared to Whites.

PYY is one of an extensive family of peptides involved in appetite regulation [13-16]. PYY exerts a satiating effect by inhibiting fluid and electrolyte secretion and slowing intestinal transit so that nutrients are absorbed in the small bowel. PYY secretion is macronutrient-sen-

sitive [17,18] and particularly responsive to linoleic acid and conjugated linoleic acid 9,11 [19]. Other key ‘players’ include cholecystokinin (CCK), glucagon-like peptide-1 (GLP-1), pancreatic polypeptide (PP) and gastric inhibitory polypeptide (GIP), also known as glucose-dependent insulintropic peptide [13-16]. CCK is released from intestinal L cells primarily in response to fatty acids and/or certain amino acids entering the duodenum, especially conjugated linoleic acid isoforms [20]. CCK contributes to postprandial hunger suppression by inhibiting gastric emptying and gastric acid. GLP-1 is nutrient sensitive, inhibits gastric secretion and motility, and primarily exerts a satiating effect by delaying and prolonging carbohydrate absorption. PP, secreted by PP cells in the pancreas mainly in response to protein ingestion, self-regulates pancreatic secretion and contributes to satiety by slowing gastric emptying. GIP is synthesized in intestinal K cells found in the duodenum and jejunum; its primary function is to induce insulin secretion, and in animal studies it has been shown to inhibit gastric motility. These gut peptides and their functional roles in regulating satiety have been extensively reviewed elsewhere [13-16].

Herein, we describe fasting and postprandial levels of CCK, GLP-1, PP, and GIP in 11 women; we hypothesized that levels would be lower in Black compared with White women.

Materials and Methods

Forty adult women completed the study, which is described in detail elsewhere [9]. Eleven of those women constitute the sample for the current report because they had sufficient plasma archive volume for the planned assays. Each woman completed two test meals that were matched for macronutrient composition and standardized to 616.25 kJ but differed in glycemic load (GL). Blood samples were obtained prior to each meal (fasted, time = 0) and 30 and 120 min after the meal, and assayed using commercially-available kits (Millipore) to determine concentrations of PYY₃₋₃₆, GLP-1, PP, and GIP in a multiplex format on a Luminex 100™ (Luminex, Austin, TX). CCK concentration was determined using a double antibody radioimmunoassay kit and protocol including extraction to eliminate non-specific interference from plasma proteins (Alpco Diagnostics, Salem, NH).

Mixed model analyses (Proc Mixed, SAS v. 9.2) were performed to assess the effect of race (Black, White), meal type (high GL, low GL) and time (min 0, 30, 120) on PYY₃₋₃₆, GLP-1, PP, and GIP. A significant number of CCK fasting values fell below the assay lower limit of detection; thus, only two time points (min 30 and min 120) were included in the model. To account for correlation between the repeated observations within participants, an unstructured autoregressive correlation was assumed and was found to fit the observed correlation in the data. BMI was included as a covariate, given its relation with gut peptide levels [13,21-23]. Models initially included all 2- and 3-way interactions after which non-significant factors were eliminated; reported p-values are from the reduced models. P-values less than 0.05 were considered statistically significant.

Results

The groups did not differ in mean age, BMI, fasting insulin or glucose, and insulin sensitivity (Table 1). The participants were age 21 to 50 years with BMI range from 22 to 37 kg/m², and all but one participant were normoglycemic (range: 74 to 132 mg/dL). All results are depicted independent of meal type, which was a non-significant factor for all outcomes.

	White	Black
N	7	4
Age (years)	28.8 (9.3)	32.1 (9.7)
BMI (kg/m ²)	25.5 (5.2)	31.1 (6.9)
Fasting Glucose (mmol/L)	4.4 (0.4)	4.9 (1.1)
Fasting Insulin (pmol/L)	58.7 (53.2)	114.1 (130.7)
Insulin Sensitivity	0.16 (0.02)	0.15 (0.03)

Table 1: Mean (standard deviation) characteristics of the study sample.

Abbreviations: BMI, body mass index. Insulin sensitivity = QUICKI [24]. Conversion from metric to SI units: glucose (mg/dL X 0.0555 = mmol/L), insulin (μU/mL X 6 = pmol/L). Data are unadjusted mean (SD); all differences between White and Black groups are nonsignificant (p > 0.05).

Figure 1 depicts PYY₃₋₃₆ (1A), CCK (1B), GLP-1 (1C), PP (1D), and GIP (1E) concentrations in Black and White women. For CCK, the main effect of race was significant ($p = 0.03$) indicating higher mean CCK in White compared with Black women. For GLP-1 there was a significant race-by-time interaction ($p = 0.04$), as the mean GLP-1 value at 30 minutes was higher in White women than Black women but there was no significant difference at 0 or 120 minutes. There was a significant race-by-time interaction for GIP ($p = 0.02$). The two groups were no different at 0 and 30 minutes, but Black women had a significantly higher mean GIP at 120 minutes than did White women. There were no significant differences for PYY₃₋₃₆ ($p = 0.10$) or PP ($p = 0.37$), although differences were in the expected direction.

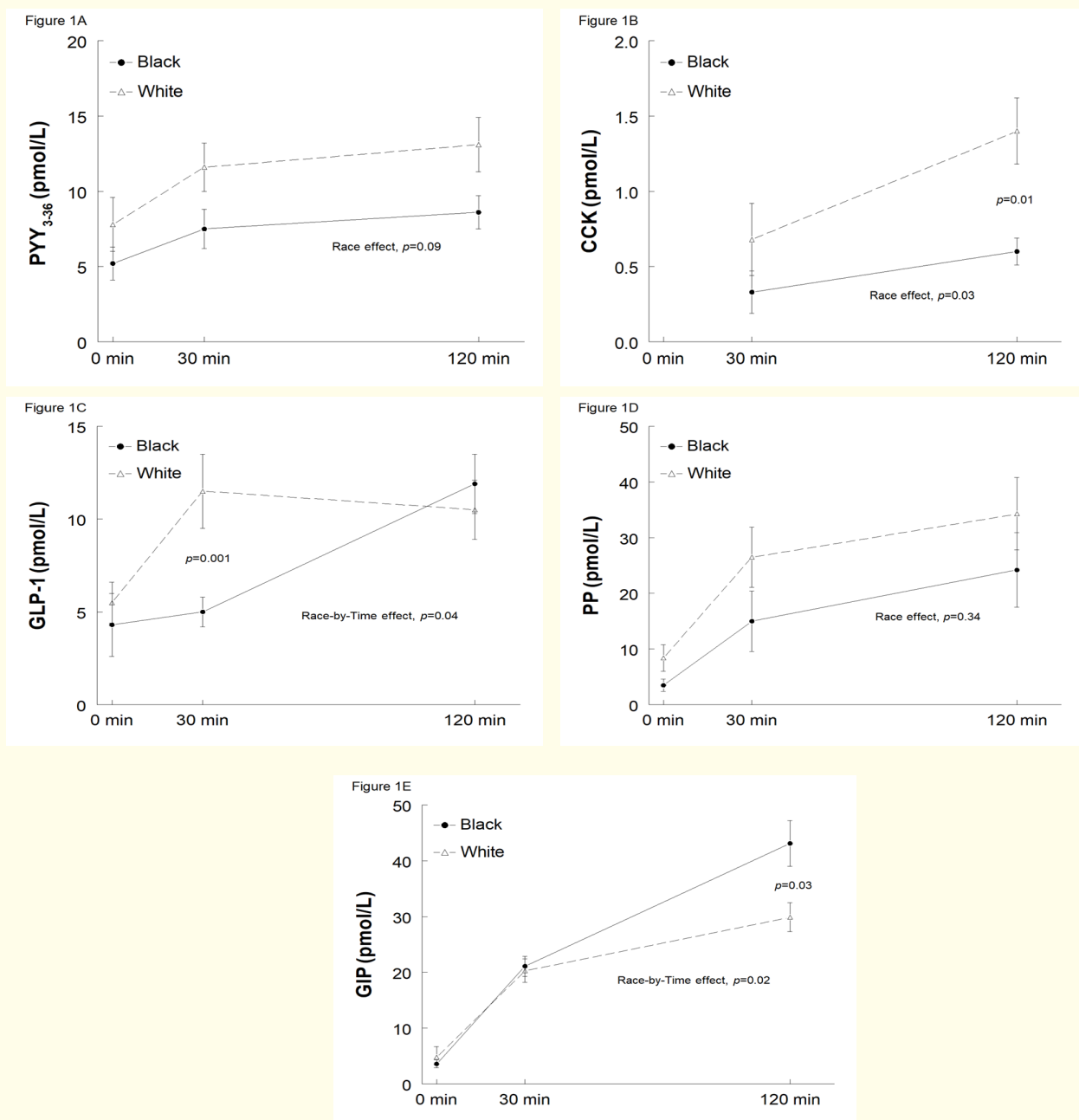


Figure 1A-1E: Fasting (min 0) and postprandial (min 30 and 120) plasma peptide-YY (PYY, 1A), cholecystikin (CCK, 1B), glucagon-like peptide-1 (GLP-1, 1C), pancreatic polypeptide (PP, 1D), and gastric inhibitory polypeptide (GIP, 1E) in Black (closed circle) and White (open triangle) women. Data are depicted as raw mean \pm standard error. Conversion to SI units: PYY (pg/mL \times 0.25 = pmol/L), GLP-1 (pg/mL \times 0.3032 = pmol/L), PP (pg/mL \times 0.239 = pmol/L), GIP (pg/mL \times 0.2006 = pmol/L).

Discussion

Previous studies have shown diminished PYY₃₋₃₆ in overweight [11] and obese [9] Black women and in Black youth [12] compared to their White counterparts. In the current study, the postprandial release of CCK and GLP-1 was blunted in Black compared to White women, suggesting a more global level of dysfunction in postprandial satiety signaling that reflects a common underlying mechanism. Because the release of these gut-derived peptides is macronutrient sensitive, the observed differences could reflect racial differences in fatty acid sensing, uptake, and metabolism that ultimately could contribute to greater adiposity in Black women.

CD36 is a membrane glycoprotein that detects long-chain fatty acids and mediates their uptake. CD36 responds most to long-chain fatty acids, particularly oleic, linoleic and docosahexaenoic acids in olive, seed, and marine oils [25] and less to fatty acids with shorter length [26]. CD36 is expressed in many tissues including adipose tissue, muscle and the gastrointestinal (GI) tract. CD36 is needed for the satiety response to a dietary fat load [27]; in addition, it senses fat concentration in taste buds of the tongue [28], improves hepatic insulin sensitivity [29] and promotes adipocyte differentiation and adipogenesis [30]. Thus, defective CD36 functioning may contribute to a positive energy balance and adiposity by causing inadvertent overconsumption of fat because of limited ability to taste fat, increasing hepatic insulin resistance and thereby promoting hunger and weight gain, and reducing resting energy expenditure and postprandial thermogenesis. Notably, low CD36 activity may lead to reduced satiety cueing because ingested fat is sensed less efficiently in the GI tract.

Polymorphisms in *CD36* occur at a relatively high frequency in people of African ancestry, and certain common variants reduce CD36 protein expression and function. For example, homozygous carriers of the -31118 A variant have a six-fold higher fat-tasting threshold than people without it [28]. About one of five people of African Ancestry has two copies of the CD36 -31118 A variant (rs1761667) [31]. It is plausible that race differences in satiety peptide release are reflective of a greater proportion of homozygous carriers of the CD36 risk allele, which is associated with blunted fatty acid uptake (rs1761667), among Black women in our studies.

Contrary to our hypothesis, postprandial GIP concentration was higher in Black compared to White women. In the larger sample of 40 women, the postprandial insulin response was greater in obese black compared to obese white women after the low glycemic meal and tended to be greater in normal weight black women compared to normal weight white women after both high and low glycemic meal challenges [7]. The higher GIP observed in the subset of Black women thus is consistent with its primary role in inducing insulin secretion. In addition, PP did not differ significantly between the two groups, however the direction of the effect was consistent with our hypothesis (Black, 13.8 pmol/L vs. White, 23.0 pmol/L).

All findings reported here should be viewed cautiously in light of the very small sample size and the limited data points used to evaluate the postprandial response, especially for CCK. Much work remains to elucidate whether the observed racial differences in peripheral circulating hormone levels 1) replicate in the population at large and, if so, what are the underlying mechanisms; and 2) translate into functional differences in central satiety signaling that yield meaningful differences in food intake and, if so, do they explain any of the excess obesity morbidity among Black women. Future studies that compare gut satiety peptide release following a long-chain versus a medium-chain fatty acid challenge in Black and White women with and without the rs1761667 variant could provide the foundation from which to examine these larger questions. Prior findings linking blunted satiety responsiveness in African-American girls with brain-derived neurotrophic factor promoter methylation [32] suggest that expanded genetic and epigenetic analyses in Black and White women are warranted. Supplementing these investigations with measures of energy expenditure and gastric emptying rate and more stringent assessments of body composition would greatly inform our understanding of these complex phenomena at the individual person level. Ultimately, this work could assist with the development of individualized interventions through the application of nutritional genomics [33] to reduce racial disparities in obesity as well as the overall societal burdens associated with obesity.

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