Changes in Sweet Taste Across Pregnancy in Mild Gestational Diabetes Mellitus: Relationship to Endocrine Factors

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Abstract
Gestational diabetes mellitus (GDM) is glucose intolerance diagnosed during pregnancy. Previous work suggested that women with GDM showed exaggerated preferences for sweet taste, but data were limited to a single time point during pregnancy. This study longitudinally assessed sweet taste changes across pregnancy in women who developed GDM (\(n = 15\)) as compared with women with normal glucose tolerance (NGT; \(n = 93\)) and nonpregnant controls (\(n = 19\)). A second objective was to relate sweet taste changes in GDM to fasting leptin and insulin profiles. Following an overnight fast, subjects evaluated strawberry-flavored milks varying in sucrose and fat content, as well as glucose solutions. Evaluations were made at 3 time points during pregnancy and during early postpartum. At 34–38 weeks gestation, women with GDM gave higher liking ratings to moderately sweetened (5% and 10% sucrose) strawberry milks than women with NGT. These differences were not related to alterations in the perception of the samples. At 24–28 weeks gestation, and in women with GDM only, fasting insulin was correlated with liking of the glucose solutions (\(R^2 = 0.63, P = 0.004\)) and fasting leptin was correlated with sweetness liking of the 10% sucrose milk (\(R^2 = 0.42, P = 0.017\)). These data suggest that women with GDM exhibit higher liking ratings for a sweet fat milk drink late in pregnancy. Also, higher hedonic ratings for sweet taste in GDM may be related to elevated leptin and insulin concentrations at midpregnancy. GDM may increase the desire for sweet taste that could influence dietary management of this disease.

Key words: gestational diabetes, insulin, leptin, sweet taste

Introduction
Gestational diabetes mellitus (GDM) is glucose intolerance first recognized during pregnancy (Metzger and Coustan 1998) that affects \(\sim 7\)% of all pregnant women (American Diabetes Association 2004b). The hallmarks of GDM include insulin resistance and a reduced capacity to secrete insulin from pancreatic islet cells, features it shares with Type 2 diabetes (T2DM; American Diabetes Association 2004a). The similarity between these 2 diseases is underscored by the observation that the risk of later development of T2DM is approximately 10-times higher in women with GDM in pregnancy as compared with women without GDM in pregnancy (Lee et al. 2007). A pregnancy complicated by GDM increases the risk of maternal complications such as hypertension and pre-eclampsia as well as fetal complications like macrosomia (excess fetal growth), which can lead to the need for cesarean delivery and delayed fetal lung maturity leading to neonatal respiratory distress at birth (Bowen 1992; American Diabetes Association 2004b). Optimizing glucose control can reduce pregnancy complications. Effective medical management of GDM is crucial for maintaining a healthy pregnancy to term. Diet manipulation is the first therapeutic approach followed by hypoglycemic medications or insulin if diet fails (American Diabetes Association 2004b). Nutritional therapy for GDM follows the same, general guidelines as those designed for nonpregnant individuals with T2DM (American Diabetes Association 2007). However, management of the pregnant diabetic is complicated by consideration for the nutritional needs of the developing fetus and compliance with current diet therapies is often poor (Armstrong et al. 2007).
1991; Langer 2002). Thus, there is an urgent need to develop better therapeutic intervention strategies for the management of GDM.

It has long been suspected that diabetes disrupts sweet taste function and increases the desire for sweet taste (Perros et al. 1996). Exaggerated preference for sweet foods could alter dietary behavior and affect diabetic control. Decreased taste acuity for glucose (Schelling et al. 1965; Lawson et al. 1979; Abbasi 1981; Perros et al. 1996) and sucrose (Lawson et al. 1979) has been observed in patients with T2DM compared with age-matched controls. Healthy, first-degree relatives of persons with T2DM also show diminished discrimination of glucose (Lawson et al. 1979; Settle 1981) suggesting that this deficit precedes the onset of disease symptoms. However, studies comparing hedonic ratings for sweet taste in individuals with and without T2DM have found only small differences (Dye and Koziatek 1981) or no differences between groups (Lawson et al. 1979; Tepper et al. 1996). Nevertheless, Tepper et al. (1996) showed that individuals with well-controlled T2DM consumed more total sweetness in the diet (from both carbohydrate and nonnutritive sweeteners) than age-matched controls (Tepper et al. 1996). Moreover, that same study (Tepper et al. 1996) found that peak preference ratings for sweetened beverages in laboratory taste tests were positively correlated with dietary intake of sweet foods in subjects with diabetes but not in age-matched controls.

Only one study has investigated sweet taste and dietary behavior in women with GDM (Tepper and Seldner 1999). Subjects in this study evaluated flavored milk samples that varied in sucrose content (0%, 5%, and 10%), and testing was conducted twice, at the beginning of the 3rd trimester (28–32 weeks gestation) and at 12-week postpartum. Results showed that during pregnancy, women with GDM liked the 10% sucrose, sweetened milk sample more than women without GDM. However, this difference arose from different response patterns in the 2 groups of women. Women without GDM liked the 10% sucrose-sweetened milk sample “less” during pregnancy than during postpartum, when their liking ratings returned to the same level as nonpregnant controls (CONT). In contrast, women with GDM showed no change in liking for the samples across the study, and liking ratings did not differ from those of CONT. These results suggest that GDM is associated with an exaggerated preference for sweet taste late in gestation, that is, absent in healthy pregnancy. The nutritional and clinical importance of this late-stage preference for sweet taste is unknown.

Tepper and Seldner (1999) also examined sweet taste responses to glucose solutions but no differences in liking or intensity ratings were found between women with GDM and the other groups. However, in women with GDM, plasma glucose 1 h after an oral glucose challenge was positively correlated with liking ratings for the glucose solutions as well as reported dietary intake of fruit/fruit juice. These relationships were absent in women without GDM.

Thus, in GDM, more severe glucose intolerance was associated with higher preferences for sweet carbohydrates (Tepper and Seldner 1999). There are presently no data relating changes in sweet taste to disruptions in endocrine parameters that underlie this disease.

The present study prospectively followed women who developed GDM and women who maintained normal glucose tolerance (NGT) over the course of pregnancy and into the early postpartum period. CONT were assessed at similar time intervals as the pregnant women. The primary objective was to compare the magnitude and time course of sweet taste changes in the 2 groups of pregnant women to determine if increased preference for sweet taste persisted into late pregnancy in GDM, as our earlier findings suggested. Both the dairy drinks and glucose solutions were investigated to make direct comparisons with our earlier work. The glucose solutions represent a pure sweet stimulus, and the dairy drinks represent a sweetened flavored mixture that approximates a real dairy beverage.

A second objective was to relate sweet taste to alterations in leptin and insulin in GDM. Insulin and leptin are purported to play a role in appetite and sweet taste preference in humans (Rodin et al. 1985; Gielkens et al. 1998; Karhunen et al. 1998; Raynaud et al. 1999) and elevations in these hormones have been associated with disruptions in sweet taste responses in animal models of diabetes (Kawai et al. 2000). The potential role of these 2 hormones in sweet taste in GDM has not been studied.

Subjects and methods

Subjects and recruitment

Healthy pregnant and nonpregnant women, 18–45 year of age, were recruited from the Women’s Ambulatory Clinic at Saint Peter’s University Hospital, New Brunswick, NJ. Recruitment was carried out and data were collected on a continuous, rolling basis over a 3-year period. Both normal weight (body mass index [BMI] = 19.8–24.9 kg/m²) and overweight (BMI = 25.0–30.0 kg/m²) women were included. Because a major risk factor for GDM is overweight prior to pregnancy (Jovanovic-Peterson and Peterson 1996), we oversampled overweight pregnant women in order to obtain a sufficient number of women who would eventually develop GDM. Exclusion criteria for all women included preexisting medical conditions (including Type 1 or T2DM), hypertension or impaired renal function, GDM in a previous pregnancy, and use of medications that interfere with taste or appetite (Schiffman 1991). Nonpregnant women had to be weight stable during the 3 month prior to the study, not following dietary restrictions (e.g., weight loss or low-sodium diets), have regular menstrual cycles, and be free of disordered eating (Garner et al. 1983). This study was approved by the Institutional Review Boards of Rutgers University, Saint Peter’s University Hospital, and the Robert Wood Johnson Medical School, New Brunswick, NJ.
Johnson Medical School of the University of Medicine and Dentistry of New Jersey. All subjects gave written consent and received monetary compensation for their participation.

Study design
A prospective study design was used in which pregnant women were enrolled at 16–20 weeks gestational age, before their GDM status was known. They were tested 3 times during pregnancy (at 16–20, 24–28, and 34–38 weeks gestation) and at 6–10 weeks after delivery. CONT were tested at similar intervals. The study collected information on sensory responses to sweet taste, food cravings, dietary intake, and endocrine profiles at each session. Responses to sweet taste and their associations with serum insulin and leptin are reported here. Other data are reported elsewhere (Belzer 2008).

All pregnant women are routinely screened for GDM at 24–28 weeks gestation using a 1-h, 50-g oral glucose challenge. Women with a positive screen (glucose >140 mg/dL) undergo a 3-h, 100-g oral glucose tolerance test to confirm their diagnosis (Carpenter and Coustan 1982). Thus, women who developed GDM during the course of this study were identified at 24–28 weeks gestational age. Also, women with GDM were referred to nutritional counseling at the time of their diagnosis and received diet therapy until the end of their pregnancies. A diabetic exchange diet plan was followed (Holler 1991). Women without GDM received standard nutritional guidance for pregnancy.

Test stimuli
Two sensory stimuli were used: strawberry-flavored milks that varied in sucrose and fat content and glucose solutions. Both stimuli were used in our previous study in GDM (Tepper and Seldner 1999). The flavored milks were prepared using methods described previously (Tepper and Seldner 1999). Nonfat dry milk (Carnation, Nestlé) was reconstituted using spring water according to package directions. Twelve samples were prepared by substituting 0%, 5%, or 10% (w:v) bland vegetable oil (Hunt-Wesson Inc.) and 0%, 5%, 10%, or 20% (w:v) sucrose (Fisher Scientific) to the nonfat milk. Strawberry flavor (International Flavors & Fragrances) and red food coloring (McCormick & Co. Inc.) were added. The samples were mixed in a blender until homogenized. The samples were designed to be visually similar but perceptually different in flavor and texture (Tepper et al. 1994). Five glucose solutions (0.01–0.16 M) were prepared with laboratory grade dextrose (Fisher Scientific) dissolved in spring water. All samples were prepared 1-day prior to testing and stored at 5 °C. They were brought to room temperature prior to testing.

Testing procedure
Both stimuli were rated for sweetness intensity and liking using 15-cm line scales where 0 = none and 15 = very strong (for intensity) and 0 = dislike extremely and 15 = like extremely (for liking). Additionally, the milk samples were rated for intensity and liking of creaminess and flavor.

All test sessions were conducted in the morning after a 10-h overnight fast. At the beginning of each session, a blood sample was obtained by venipuncture for analysis of selected hormones (serum insulin, leptin, cortisol, estrogen, progesterone) and serum glucose. Hormone analyses were performed using standard radioimmunoassay methods at the Diabetes Research Center of the University of Pennsylvania, and serum glucose was measured using the hexokinase method by a commercial laboratory (Accumed Diagnostics Laboratory). Details of the blood collections and analytical methods are reported elsewhere (Belzer 2008). Subjects were then seated in the testing room to evaluate the samples. Subjects were presented with 20 mL of each sample. They were instructed to taste then expectorate each sample and to completely rinse their mouths with water before proceeding to the next sample. All samples were identified with 3-digit codes and were presented randomly within stimulus type. The glucose samples were always presented first. To prevent sensory fatigue, the subjects rested for approximately 5 min between each class of stimulus. The taste ratings were completed in ~1 h. Following the sensory testing, subjects completed a food frequency questionnaire and a food cravings questionnaire.

Data analysis
Mixed model analysis with exchangeable intraperson correlation structure, determined by Akaike’s information criterion, was used to assess the temporal trends in the attribute ratings across sessions. All data were modeled as a function of subject group (GDM, NGT, or CONT), gestational age (16–20, 24–28, and 34–38 weeks gestation, and 6–10 weeks postpartum), and their interactions. Linear contrasts compared group differences during pregnancy and the postpartum session and between experimental periods within each subject group. BMI at entry was used as a covariate in the analyses. Added variable plots (Weisberg 1985) were used to graphically examine the linear associations between the sensory ratings and fasting endocrine concentrations and were also adjusted for BMI at entry. Partial correlation coefficients were calculated to assess the strength of the linear associations. All statistical analyses were conducted using SAS version 9.1 for the personal computer (SAS Institute Inc.). Statistical significance was set at $\alpha = 0.05$. Bonferroni correction was applied for multiple testing, as appropriate. The criterion, after correction, was set at $P < 0.017$.

Preliminary analysis of the glucose solutions revealed no differences in sweetness ratings across concentrations; therefore the glucose ratings were collapsed across concentrations and expressed as an average rating for each subject group at each time point. Similarly, review of the milk data revealed no group differences in the attribute ratings as a function of fat content of the samples. Therefore, the data were collapsed across fat.
concentrations for the final data analyses. This data reduction step produced a single concentration curve for each subject group at each time point. This approach was also used in our previous study to clarify the data presentation (Tepper and Seldner 1999).

Results

Subject characteristics

One hundred and eight pregnant women were enrolled in the study: 15 pregnant women were diagnosed with GDM and 93 pregnant women remained normal glucose tolerant throughout pregnancy. The CONT group was comprised of 19 nonpregnant women. More than 50% of the study participants were Hispanic (see Table 1). The overall prevalence rate for GDM was high (14%) relative to the general obstetric population (7%; American Diabetes Association 2004b) and overall attrition rate for the study was modest (33%). Because some women dropped out of the study prematurely and others did not complete all sessions, sample size for each group varied across the study. Sample sizes at each session are noted in the tables and figures.

All the women who developed GDM remained on nutritional therapy to term, and none required insulin or hypoglycemic agents to control their disease. Based on clinical monitoring, pregnancy outcomes, and repeated 1-h oral glucose tolerance tests (conducted as part of the study protocol), it was determined that all the women with GDM had mild diabetes, which was successfully controlled by diet alone. Selected parameters are shown in Table 1. Fasting glucose and insulin did not differ between the GDM and NGT group at either 24–28 or 34–38 weeks gestation. Fasting glucose values for the GDM group were within the normal range, which is typical of mild GDM (Butte 2000). At 24–28 week gestation, serum glucose and insulin were more elevated after the glucose challenge in the GDM group as compared with the NGT group, but serum glucose remained within a clinically acceptable range for women with GDM (Butte 2000). At 34–38 weeks gestation, serum glucose but not serum insulin was more elevated after the glucose challenge in the GDM group relative to the NGT group. Additionally, pregnancy outcomes were favorable in the women with GDM, maternal weight gain was lower in the GDM relative to the NGT group, and infant birthweight and prevalence of caesarean delivery were similar in the 2 groups of women.

Flavored milk ratings

Intensity ratings for sweetness, creaminess, and overall flavor of the flavored milks (collapsed across fat concentrations) are shown in Figure 1. Mixed model analysis revealed that the intensity of sweetness, creaminess, and flavor increased significantly across sucrose concentrations for all subject groups, after controlling for intake BMI (P < 0.0001). However, the shapes of these functions did not differ between sessions or by subject group. Thus, neither pregnancy nor GDM altered the intensity ratings for sweetness, creaminess, or flavor of the samples.

Liking ratings for sweetness, creaminess, and overall flavor of the samples averaged across fat concentrations are shown in Figure 2. Mixed model analysis revealed that all groups showed significant curvilinear relationships between the liking ratings and increasing sucrose concentration of the samples, after controlling for BMI at intake (P < 0.0001).

Table 1  Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>GDM</th>
<th>NGT</th>
<th>CONT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total enrollment</td>
<td>15</td>
<td>93</td>
<td>19</td>
</tr>
<tr>
<td>BMI at entry (kg/m²)</td>
<td>28.8 ± 2.6a</td>
<td>27.0 ± 3.5a</td>
<td>24.5 ± 0.5b</td>
</tr>
<tr>
<td>Agea</td>
<td>29.2 ± 3.1</td>
<td>26.2 ± 0.7</td>
<td>27.1 ± 1.3</td>
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<tr>
<td>Ethnicity (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>60</td>
<td>52</td>
<td>79</td>
</tr>
<tr>
<td>Caucasian</td>
<td>20</td>
<td>20</td>
<td>11</td>
</tr>
<tr>
<td>African American</td>
<td>13</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Asian</td>
<td>0</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>24–28 weeks gestation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin—fasting (µU/mL)a</td>
<td>27.5 ± 3.4a</td>
<td>20.2 ± 1.4a,b</td>
<td>11.5 ± 3.4b</td>
</tr>
<tr>
<td>Insulin—postchallenge (µU/mL)b</td>
<td>113.0 ± 11.2a</td>
<td>79.7 ± 4.7b</td>
<td>54.2 ± 10.7b</td>
</tr>
<tr>
<td>Glucose—fasting (mmol/L)a</td>
<td>4.6 ± 0.2</td>
<td>4.2 ± 0.1</td>
<td>4.5 ± 0.2</td>
</tr>
<tr>
<td>Glucose—postchallenge (mmol/L)b</td>
<td>7.9 ± 0.4a</td>
<td>5.8 ± 0.2a</td>
<td>5.3 ± 0.4b</td>
</tr>
<tr>
<td>34–38 weeks gestation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin—fasting (µU/mL)b</td>
<td>24.8 ± 3.7</td>
<td>23.5 ± 1.5</td>
<td>13.1 ± 3.5</td>
</tr>
<tr>
<td>Insulin—postchallenge (µU/mL)b</td>
<td>121.0 ± 13.7a</td>
<td>98.5 ± 5.4a</td>
<td>62.5 ± 11.2b</td>
</tr>
<tr>
<td>Glucose—fasting (mmol/L)b</td>
<td>4.2 ± 0.2</td>
<td>4.4 ± 0.1</td>
<td>4.6 ± 0.2</td>
</tr>
<tr>
<td>Glucose—postchallenge (mmol/L)b</td>
<td>8.2 ± 0.5a</td>
<td>6.4 ± 0.2a</td>
<td>5.7 ± 0.4b</td>
</tr>
<tr>
<td>Pregnancy weight gain (kg)a</td>
<td>8.3 ± 1.5a</td>
<td>13.9 ± 0.6a</td>
<td></td>
</tr>
<tr>
<td>Cesarean delivery (%)</td>
<td>27</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Gestational age (weeks)a</td>
<td>40.0 ± 0.6</td>
<td>39.4 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>Infant birthweight (g)a</td>
<td>3321 ± 125</td>
<td>3325 ± 53</td>
<td></td>
</tr>
</tbody>
</table>

aValues are means ± standard error of the mean. Values in the same row with different italicized superscripts are different at P < 0.05.
bValues are means (±standard error of the mean) estimated by mixed model analysis, adjusted for BMI at entry. Values in the same row with different italicized superscripts are different at P < 0.017 after Bonferroni correction.
Overall, the shapes of these functions did not differ by session or subject group (no session or group main effect). However, at 34–38 weeks gestation, linear contrasts revealed several differences in the liking ratings between women with GDM and the other groups. The GDM group liked the sweetness, creaminess, and flavor of the 5% sucrose sample more than the CONT group ($P$ values = 0.005–0.015). The GDM group also liked the creaminess and flavor of the 5% sucrose sample ($P = 0.008$ and 0.006, respectively) as well as the creaminess of the 10% sucrose sample ($P = 0.013$) more than the NGT group. There were no group differences at any other time point in the study.

**Glucose ratings**

Mixed model analysis for main effects showed that averaged sweetness intensity ratings declined across sessions ($P < 0.0001$) but did not vary by group. In contrast, averaged sweetness liking ratings varied by group ($P = 0.002$) but not across sessions. Visual inspection of the liking data revealed that the 2 groups of pregnant women gave higher liking ratings to the glucose solutions than did the CONT women, but the GDM group did not differ in liking ratings from the NGT group. Because GDM did not further exaggerate the liking ratings for glucose, the 2 groups of pregnant women were combined for further analysis.

Figure 3 shows the general effect of pregnancy on the averaged intensity and liking ratings of the glucose solutions. In the combined pregnant group, averaged sweetness intensity ratings at 16–20 weeks gestation were higher than at all other sessions ($P = 0.02$, $P < 0.001$, and $P < 0.01$, respectively), and in the CONT group, averaged sweetness intensity at 16–20 weeks gestation was higher than that same measure at 24–28 weeks and 34–38 weeks gestation ($P = 0.02$ and $P < 0.01$, respectively). The combined pregnant group liked the averaged glucose solutions more than the CONT group at 24–28 weeks and 34–38 weeks gestation ($P = 0.03$ and $P = 0.02$, respectively).

**Correlations between sensory ratings and serum leptin and insulin**

Linear associations were examined between sensory ratings and fasting leptin and insulin values for all subject groups at all sessions, but no relationships were observed for the intensity ratings. However, 2 sets of relationships emerged for the liking ratings.
Leptin and sweetness liking of the 10% sucrose milks

Among women with GDM, fasting leptin was positively correlated with sweetness liking ratings of the 10% sucrose-sweetened sample at 24–28 weeks gestation ($R^2 = 0.42$, $P = 0.017$) but not at any other time point during the study. Scatter plots of these relationships are shown in Figure 4. There were no significant associations between these 2 parameters for the other groups of women at any time point during the study ($R^2 = 0.00–0.27$, $P = 0.02–0.83$). The relationship between leptin and sweetness liking ratings of the 10% sucrose sample approached significance in the CONT group at the first test session (corresponding to 16–20 weeks gestation), but the $R^2$ was low ($R^2 = 0.27$), and no associations were observed for this group at other time points during the study.

Insulin and averaged sweetness liking of the glucose solutions

Among women with GDM, fasting insulin and averaged sweetness liking of the glucose solutions were positively correlated at 24–28 weeks gestation ($R^2 = 0.63$, $P = 0.004$) but not at other time points (see Figure 5). No significant relationships between these variables were observed in the other groups of women at any time point during the study ($R^2 = 0.00–0.36$, $P = 0.05–0.90$).

Discussion

The main objective of this study was to assess sensory ratings for sweetened stimuli across pregnancy in women who developed GDM compared with women with NGT. At 34–38 weeks gestation, the GDM group liked moderately sweetened (5% and 10% sucrose) flavored milks more than the NGT group for several of the attributes tested. Also at 34–38 weeks gestation, women with GDM liked the 5% sucrose sample more than the CONT group. No differences were found between women with GDM and the other groups at any other time point during the study. The present findings support our previous results showing that when tested at 28–32 weeks gestational age, women with GDM gave higher liking ratings than women without GDM to these same
flavored milks at 5% and 10% sucrose concentration (Tepper and Seldner 1999). Taken together, the data from both studies suggest that women with GDM express an increased preference for moderately sweetened milks after gestational week 28, which persists into late pregnancy. There was no suggestion, in the present data, that increased preference for the flavored milks preceded the development of GDM. It is noteworthy that the women with GDM preferred the moderately sweetened samples but not the sweetest sample (20% sucrose). In fact, there was a visible peak in the liking ratings for the milk samples at 24–28 weeks gestation that did not occur at subsequent time points. However, this same pattern was also observed in the CONT group suggesting the presence of a session (i.e., training) effect on the glucose ratings. Experimental error does not appear to explain these findings as the subjects were recruited and tested on an ongoing basis in this study, and each woman was tested on a separate day. Moreover, intensity ratings for the milk samples did not vary across sessions in any subject group. Thus, the reason for this decline in glucose intensity rating in our study remains unexplained.

The results of the current study and our previous work in GDM (Tepper and Seldner 1999) contradict earlier studies in T2DM showing that sweet taste acuity is blunted in the latter disease (Lawson et al. 1979; Perros et al. 1996). A variety of factors could contribute to this disparity. Persons with T2DM are generally older than women with GDM, and the effects of age on taste function are well known (reviewed in Hays and Roberts 2006). Moreover, T2DM is a chronic, degenerative disease that affects neurological functioning including the taste system. Some of the taste deficits seen in T2DM may be due to neurological complications that worsen with disease duration (Abbasi 1981). Finally, most (Schelling et al. 1965; Lawson et al. 1979; Abbasi 1981; Perros et al. 1996) but not all studies (Settle 1981) reporting diminished taste perception in T2DM evaluated threshold acuity. We did not conduct threshold testing in our present or previous work and therefore might have missed small deficits in taste acuity associated with GDM. Nevertheless,
GDM did not alter the perceived intensity of glucose in aqueous solutions or sucrose in milk samples when presented across a wide range of concentrations and tested in 2 different cohorts of women. One interpretation of these findings is that sweet taste perception is not compromised in GDM as it is in T2DM. Women with GDM are both diabetic and

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**Figure 4** Added variable plots of liking ratings of sucrose-sweetened milk versus fasting serum leptin, with the effect of initial BMI removed. The association was positive and significant in women with GDM at 24–28 weeks gestation. There were no other significant associations in any group at any other time point.

**Figure 5** Added variable plots of liking ratings of glucose solutions versus fasting serum insulin, with the effect of initial BMI removed. The association was positive and significant in women with GDM at 24–28 weeks gestation. There were no other significant associations in any group at any other time point.
pregnant, and the combined effects of these 2 physiological states may result in different perceptual experiences of sweet taste than what is observed in persons with T2DM. This possibility should be examined in future studies.

The second objective of this study was to relate changes in sweet taste to circulating leptin and insulin concentrations. We previously reported in this same cohort of women that fasting leptin tended to rise earlier in GDM pregnancy (at 24–28 weeks gestation) than it did in healthy pregnancy (at 34–38 weeks gestation) and that this early rise in leptin coincided with the development of insulin resistance and the emergence of diabetic symptoms in women with GDM (Belzer 2008, Belzer et al. 2009). We examined associations between these 2 hormones and the sensory ratings, and 2 relationships were found. In women with GDM, but not in the other groups, liking of the 10% sucrose flavored milk was highly correlated with fasting serum leptin, and also, averaged sweetness liking of the glucose solutions was highly correlated with fasting serum insulin. These relationships were only observed at 24–28 weeks gestation. These novel findings suggest that leptin and insulin might play a role in the preference for sweet taste in GDM, but the importance of this relationship is presently unclear.

There is substantial evidence from animal studies of a role for leptin in sweet taste. For example, leptin is coexpressed in fungiform and vallate papillae with α-gustducin in mice (Shigemura et al. 2003). Leptin injection in lean mice selectively suppresses chorda tympani and glossopharyngeal responses to sweet taste as well as lick rates for sucrose and saccharin (Kawai et al. 2000). Interestingly, administration of leptin reduces neural responses to sweet taste in the ob/ob mouse (a strain that lacks leptin) but not the db/db mouse (a strain that lacks a functional leptin receptor). Enhanced chorda tympani responses to sugars have also been reported in rats made obese by lesions of the ventromedial hypothalamus or by high-fat feeding (Shimizu et al. 2003). Both types of rats exhibit metabolic abnormalities that closely resemble those seen in human obesity and T2DM, namely, hyperinsulinemia and hyperleptinemia. Thus, it is conceivable that increased preference for sweet stimuli might correlate with the development of hyperleptinemia and the emergence of insulin resistance at 24–28 weeks gestational age in women who are diagnosed with GDM. Also of relevance are recent data from nondiabetic humans showing that changes in sweet taste recognition thresholds are synchronized with the diurnal variation in leptin (Nakamura et al. 2008). Whether this shift in taste acuity is accompanied by changes in sweet taste preference across the day and is altered in T2DM and GDM remains an intriguing question for future research.

This study had several strengths and limitations. Although sample size for women with GDM was relatively small, the prevalence rate for GDM in this predominantly Hispanic sample was 14%, almost double the rate observed in the general obstetric population (American Diabetes Association 2004b). The dropout rate was also modest (33%) given the length of each woman’s participation to study completion (ca. 33 weeks). The women studied here developed mild GDM, and controlled their disease by diet, alone. Results might have been more robust if they had a more severe form of GDM. However, insulin and oral hypoglycemic agents are known to interfere with taste function (Schiffman 1991) and their use might have complicated the interpretation of the findings. We note, however, that the high success rate of diet therapy observed here is atypical in clinical practice (Langer 2002). Presumably there was a strong selection bias in this study in that women who were more likely to comply with diet therapy were also those more likely to volunteer for the study. Thus, the extent to which the present findings can be extrapolated to the general obstetric population with GDM is unknown and requires further study.

In conclusion, the major finding of this study was that at 34–38 weeks gestational age, women with GDM gave higher liking ratings to moderately sweetened flavored milks than pregnant women with NGT. This increased preference occurred in the absence of changes in the perceived intensity of the samples, at a time when diet restrictions were in effect and diabetic symptoms were well controlled. It is possible that the diet restrictions contributed to this hedonic shift. Laitinen et al. (1991) previously showed that diet therapy altered the preference for some sweet foods in individuals newly diagnosed with T2DM, although, the effects were different from those observed here. As diet therapy progressed, the preference for sweet juices decreased and the preference for fatty foods (milk and cheese) did not change in patients with T2DM. We note, however, that in our previous study, increased preference for the flavored milks was observed in women with GDM who were tested before diet therapy began (Tepper and Seldner 1999). Thus, the diet restrictions might have contributed to increased preference for the sweetened dairy drinks in GDM but was probably not the driving force for these changes. Another possible explanation for our findings is that the overall duration of insulin resistance, rather than its severity, contributes to this late pregnancy rise in sweet preference in GDM. We also observed positive correlations between specific measures of sweet taste preference and serum leptin and insulin in women with GDM. However, these relationships were observed earlier in pregnancy, at 24–28 weeks gestational age, when diabetic symptoms were untreated and these hormones were at maximal concentrations. Thus, it appears that the mechanisms underlying these endocrine taste correlates are different from those underlying the group difference in liking of the milk samples. These studies are the first to prospectively examine and document changes in sweet taste in GDM pregnancy. Additional studies are needed to understand the medical implications of these changes and to elucidate the mechanisms involved.

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