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# Higher prenatal dietary glycemic index in the third trimester of pregnancy is associated with infant negative affect at 6 months

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**The dietary glycemic index (GI) reflects post-prandial plasma glucose generation rate, with higher-GI foods rapidly increasing blood sugar. Prenatal consumption of high-GI foods is associated with offspring risk for obesity and metabolic disorders. The impact of prenatal dietary GI exposure on infant neurodevelopment remains unclear. Maternal dietary intake, percent adiposity, and insulin resistance were prospectively assessed during the second and third trimesters in a sample of women with healthy, singleton pregnancies ($N = 302$). Infant negative affect was prospectively assessed at six months using observer ratings (Still Face Paradigm) and caregiver-reports (Infant-Behavior Questionnaire-Revised). Structural equation models assessed the independent effects of second and third trimester maternal dietary GI, adiposity, insulin resistance on infant negative affect, adjusted for relevant covariates. Higher third, but not second, trimester dietary GI was associated with increased observer-rated infant negative affect ($\beta = 0.14$, $p = .04$) and with higher caregiver-reported infant sadness ($\beta = 0.17$, $p = .01$), suggesting a programming effect of prenatal dietary GI on infant neurodevelopment. Targeted interventions that decrease dietary GI in later pregnancy may prove more effective for optimizing infant behavioral health compared to longer-term changes needed to alter metabolic state. Identifying modifiable early contributors to infant negative affect supports proactive strategies for mitigating future psychopathology risk.**

**Keywords** Behavioral health, Dietary quality, Infant temperament, Prenatal diet, Prenatal programming, Negative affect

The intrauterine environment has enduring consequences for infant development[1,2], with growing evidence suggesting that prenatal environmental factors influence fetal brain development and thus shape infant temperament and behavioral trajectories[3–7]. Negative affect (NA)—the range of negative emotions indicating distress, discomfort, or dissatisfaction[8]—is a temperament trait of particular interest due to its emergence during early infancy as an indicator of socioemotional development[9]. Sustained and intense temperamental NA is associated with anxiety disorders, depression, and other psychological conditions[10–13]. Mounting evidence suggests that high infant NA is an early indicator of psychological vulnerability to later developmental psychopathology[14]. Prenatal nutrition and maternal metabolic state, including pre-pregnancy body mass index (BMI) and gestational weight gain (GWG), have been associated with child neurodevelopmental outcomes[15], with infants born to mothers with higher pre-gravid BMIs exhibiting increased NA[16], as well as difficulties with emotional regulation later in life[17,18]. Pre-gravid BMI and higher GWG are also associated with infant risk for neuropsychiatric disorders[19–21], including risk for autism[22–25], attention deficit hyperactivity disorder (ADHD)[22,26], and affective disorders[26–28]. However, the mechanisms underlying the associations between maternal BMI and child neurodevelopment are unclear and have not been fully examined. Differences in prenatal

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nutrition[29], exposure to different metabolic hormones (i.e. insulin[15] and adipokines[30]), and increased exposure to chronic inflammation[31] have all been postulated to play a role. [*Note.* In this work, the term 'maternal' is used to refer to individuals who are pregnant or have given birth to a child. We acknowledge that it may not fully describe the experiences of all individuals who fulfill the role of birthing parents].

Fetal exposure to hyperglycemia and hyperinsulinemia is also associated with neurodevelopmental consequences[32–34]. As fetal glucose requirements increase over the course of a typical pregnancy, maternal glucose uptake is naturally restricted to ensure adequate glucose availability for the fetus[35]. Upregulation of pancreatic processes leads to concomitant increases in maternal insulin secretion[36]. The effects of high glucose exposure and maternal insulin resistance on fetal body composition and cardiometabolic outcomes are well-documented[37–40]. Growing evidence suggests that prenatal exposure to hyperglycemia, as in gestational diabetes mellitus (GDM), is associated with an increased risk for neuropsychiatric disease in offspring[41], including risk for autism[42,43] and ADHD[44,45].

While emerging evidence indicates that chronic maternal metabolic conditions such as obesity and insulin resistance may influence infant temperament, the impact of acute metabolic events—specifically maternal post-prandial glucose surges—on infant neurodevelopment is understudied. Unlike chronic hyperglycemia, transient post-prandial spikes in glucose and increased variability in plasma glucose levels may pose a different set of challenges and possible risks to the developing fetus, potentially triggering rapid alterations in fetal insulin levels and metabolic responses, the effects of which may extend to the developing brain. One study examining the role of post-prandial glucose exposure on fetal brain activity using fetal magnetoencephalography (fMEG) in healthy pregnancies showed that fetuses of pregnant women with insulin resistance (but not GDM) had longer brain response latencies to auditory stimuli following an oral glucose tolerance test (OGTT), when compared to fetuses of pregnant women with greater insulin sensitivity[46]. Another study by the same group showed that the fetuses of pregnant women with GDM had slower post-prandial responses to auditory stimuli (measured by fMEG following an OGTT), when compared to fetuses from non-GDM pregnancies undergoing the same evaluation[47].

Adequate prenatal nutrition is essential for supporting fetal development and reducing risk for cardiometabolic disease[48–50] and psychopathology[51]. Conversely, certain prenatal dietary patterns are associated with increased offspring risk for disease[52] and disorder[16]. Preclinical evidence suggests that prenatal dietary patterns high in saturated fats and sugar may have programming effects on offspring temperament[53–56]. There is growing evidence for prenatal dietary programming of neurodevelopment in humans[57]. For example, fetal exposure to prenatal diets high in total and saturated fats is associated with lower surgency and orienting/regulation at four-months[58]. Similarly, in contexts of higher prenatal stress, prenatal diets with lower omega-3:omega-6 ratios were linked to lower orienting/regulation in six-month-olds[59], while prenatal diets low in antioxidants were linked to higher NA in 30-month-olds[60]. Together, these findings suggest that prenatal dietary patterns play a critical role in programming infant temperament.

The glycemic index (GI) is an indicator of diet quality that measures the amount and timing of post-prandial blood glucose release caused by individual foods[61]. Notably, results from other studies suggest that maternal pre-gravid BMI may not be associated with the GI, indicating its distinct contribution to the fetal environment[62,63]. Primarily derived from maternal carbohydrate intake, glucose is a significant energy source for the growing fetus, particularly the developing brain[64]. Diets high in refined carbohydrates have a higher GI, leading to sharper post-prandial glucose peaks, which may exacerbate the metabolic burden on the developing fetal brain. Higher-GI diets are linked to increased obesity and metabolic disorder risk in adults[65,66] and emerging evidence suggests that fetal exposure to higher-GI diets during gestation is correlated with alterations in infant birthweight, body fat composition, and risk for metabolic disorders[67–70]. The consequences of higher-GI prenatal diets on infant neurobehavioral development are less well-understood. However, recent evidence shows that offspring exposed to maternal periconceptual diets with a high glycemic load ([GL] a metric that considers both the quality of the carbohydrate [as in the GI] *and* the quantity or portion size of the carbohydrate) exhibit more caregiver-reported signs of anxiety and inhibition as toddlers (approximately 14 months)[71]. These findings highlight the potential long-term consequences of maternal prenatal dietary patterns on infant temperament. Earlier work suggests that a three-day average for prenatal dietary GI is predictive of maternal plasma glucose concentrations[62]. In the present study, we collect three days of dietary GI in the second trimester and three days of dietary GI in the third trimester (six total), allowing us to examine the trimester-specific effects of dietary GI on offspring temperament development. Several recent reviews point out that the maternal prenatal diet is a modifiable risk factor[72,73]. However, despite its potential to inform intervention methods, to our knowledge, the association between maternal prenatal dietary GI and temperament in infancy has not been previously examined.

Prior to probing mechanistic effects and developing dietary interventions for optimizing the intrauterine environment, the independent effects of prenatal diet, adiposity, and insulin resistance require clarification. Using structural equation modeling (SEM), a powerful statistical tool for examining the distinct contributions of many factors to an outcome, we examined the following:

1. *Research Question 1: What are the distinct contributions of prenatal maternal dietary GI, adiposity, and insulin resistance on infant NA?*
2. *Research Question 2: How does the prenatal timing of maternal dietary GI, adiposity, and insulin resistance influence infant NA?*

To answer these questions, we estimated two SEMs (one examining maternal variables captured in the second trimester, the other examining maternal variables captured in the third trimester). Each model simultaneously accounted for the effects of prenatal maternal dietary GI, adiposity, and insulin resistance on infant NA at six months.

In the current study, we assessed infant NA using both observer ratings and caregiver reports. Assessing NA in both contexts is essential for gaining a comprehensive understanding of infant NA, as observer ratings and caregiver reports of this temperament dimension convey distinct information[74]. Observer reports offer an unbiased perspective, minimizing the influence of contextual factors, while caregiver ratings provide insights into the nuances of behavior within the familial setting. By utilizing both assessment methods, we capture a fuller spectrum of infant behavior, accounting for variations across contexts and ensuring a more holistic interpretation of temperament traits. Additionally, we adopt a fine-grained approach to infant temperament assessment, including carefully examining specific NA temperament domains, a key direction in identifying the specific emotional processes essential to understanding precursors of psychopathology[75]. Given evidence from preclinical[53–56] and human studies[16] that maternal dietary quality and adiposity may have distinct programming effects on infant sadness (propensity to display unhappiness or distress) and fear (distressed reaction to novel or unfamiliar situations), the sadness and fear domains of NA were of specific interest in this study.

## Methods

Data came from an ongoing, prospective longitudinal study examining the influence of maternal perinatal nutrition, adiposity, and metabolic state on infant neurodevelopment[76,77]. Participants were recruited beginning in 2018 at Oregon Health & Science University (OHSU). Participants reported their dietary intake, completed an in-laboratory body composition assessment, and provided a fasting blood sample during the second (24–26 weeks' gestation) and third (37–39 weeks' gestation) trimesters. When infants were approximately six months old, caregivers completed infant temperament questionnaires and infants were observed for expressions of emotional regulation including NA, as part of a standardized battery of tests. See Fig. 1 for a study timeline. This study was conducted according to Declaration of Helsinki guidelines and was approved by the OHSU Institutional Review Board. All participants provided written informed consent.

### Participants

The present study included 302 participants. All pregnancies occurred between 2018 and 2021. Exclusionary criteria included: multiples pregnancies, known fetal anomaly or genetic condition affecting brain development or behavior, current substance use, use of medications affecting inflammation or with teratogenic effects, history of second- or third-trimester pregnancy loss and medical conditions affecting inflammation or confounded with obesity (e.g., Diabetes Type I/II, cancer, kidney disease, polycystic ovarian syndrome, bariatric surgery history, autoimmune diseases). See detailed recruitment information in Supplemental Methods and in Supplementary Fig. 1.

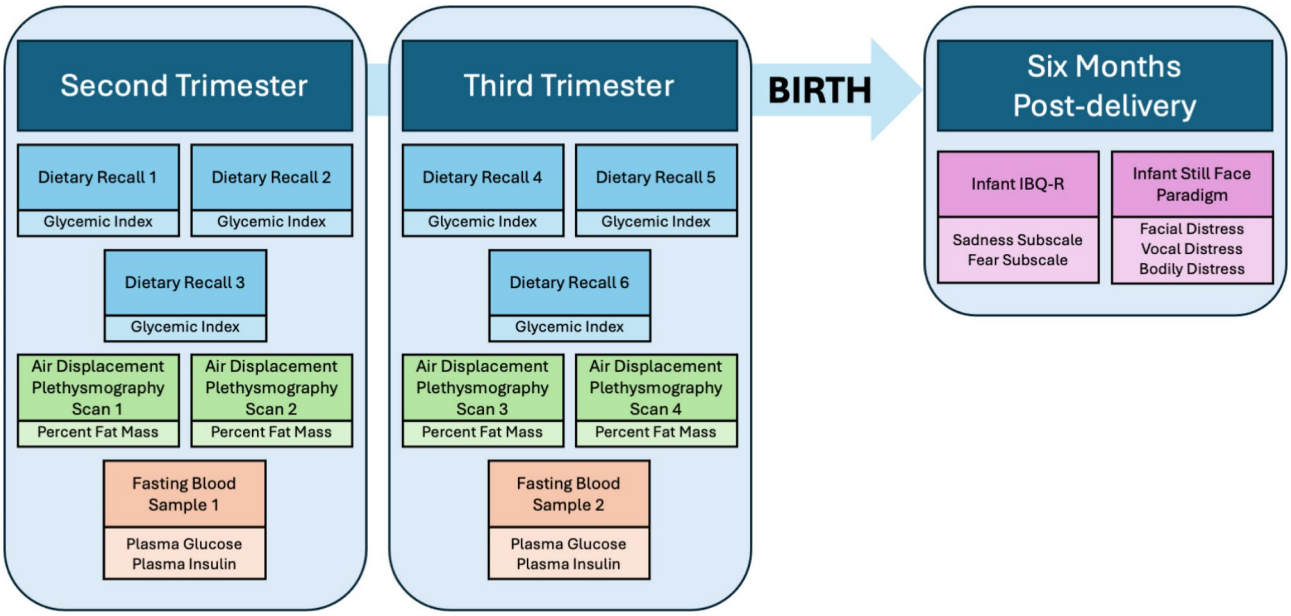


**Fig. 1**. Study timeline. Three 24-hour dietary recalls were conducted at each trimester (six total), as well as two body composition scans per trimester (four total) using air displacement plethysmography. A fasting blood sample was obtained during the second and third trimester (two total) from which HOMA-IR values were derived. Six months following delivery of infants, caregivers completed the Infant Behavior Questionnaire-Revised (IBQ-R) and infants were assessed using the Still Face Paradigm to determine infant temperament tendencies and propensities for negative affect.

## Measures

*Dietary glycemic index*

Prenatal dietary intake was measured by six unannounced, non-consecutive 24-hour recalls during the second and third trimester (3 recalls/trimester). Trained dietitians conducted recalls via the multi-pass method to record participant food and drink intake during the previous day[78]. The recalls were conducted over a two-week period, including two weekdays and one weekend day. The Nutrition Data System for Research software (NDSR, versions 2018–2020; University of Minnesota, Minneapolis, Minnesota) was used to calculate the daily GI values for each participant by comparing the foods reported during recall to published sources[79]. Methods for assigning GI values to foods with unpublished values are described elsewhere[80,81]. All interviewers completed a training program and met qualification standards established in the Oregon Clinical and Translational Research Institute Bionutrition Unit for using the NDSR software. All the GI values are expressed in relation to glucose (glucose = 100). The average GI values for the second and third trimesters were computed by summing the GI values of all foods reported on each recall day within a trimester and then averaging within each trimester. The second and third trimester GI averages were used in analyses.

*Adiposity*

Air displacement plethysmography was utilized via the BodPod® Body Composition tracking system (Life Measurement, Inc.) to measure second and third trimester body fat[82,83]. Participants fasted overnight and prior to testing and avoided exercise for three hours prior to testing. Participants wore skin-tight clothing and a swimming cap for testing. Following standard procedures, two 60-second measures were collected during both the second and third trimesters and the two measures were averaged within each trimester. As body fluid increases during pregnancy[84], estimates of fat and lean mass were adjusted according to a validated equation[85] and the adjusted second and third trimester pregnancy percent fat mass averages were utilized in analyses.

*Insulin resistance*

Fasting blood samples (44 mLs) captured via venipuncture during the second and third trimester were assayed for plasma glucose (mg/dL, colorimetric method—Stanbio Laboratories Inc., Boerne, TX 78006; mean coefficients of variation [%CV]; inter-assay: 2.8%, intra-assay: 1.5%, range: 20–450 mg/dL) and insulin (mU/L, commercially-available ELISA kits—Mercodia AB, Uppsala, Sweden; %CV: inter-assay: 6.1%, intra-assay: 2.9%, range: 1-200 mU/L). The degree of maternal insulin resistance was calculated as the Homeostatic Model Assessment for Insulin Resistance [HOMA-IR[86]), using the following equation: HOMA-IR = [fasting insulin (mU/L) x fasting glucose (mg/dL)] / 405. Extreme HOMA-IR scores (values > 6 SD above the mean) for two participants at each timepoint were excluded due to suspected non-fasting.

## Infant outcomes

*Observer ratings of negative affect: Still-Face Paradigm*

Infant NA was assessed using the Still-Face Paradigm (SFP), a validated observational measure[87] of infant distress during short-term disruptions in caregiver-infant interactions[88]. Blinded coders scored infants' facial, vocal, and bodily distress during the Still Face episode of the SFP and the proportion of facial, vocal, and bodily distress exhibited by infants was calculated. Intensity modifiers (high, medium, low) were utilized to capture the intensity of SFP reactions. To focus on more pronounced reactions and allow for examination of heightened distress, the high- and medium-intensity codes were collapsed into a single category termed "medium-high" intensity to capture peak reactivity, as has been done previously[89]. See detailed coding information in the Supplementary Methods.

Prior to hypothesis testing, results from a confirmatory factor analysis (CFA) supported considering the medium-high intensity distress measures (facial, vocal, and bodily distress) together as a latent variable representing overall infant NA (all loadings > 0.76, $ps < 0.0001$). See detailed information in the Supplementary Methods and Supplementary Table 1.

*Caregiver ratings of negative affect: Infant Behavior Questionnaire-Revised*

Maternal reports of infant NA were measured using the Infant Behavior Questionnaire-Revised (IBQ-R). The IBQ-R is a widely-used, standardized instrument designed to explore the behavioral characteristics and temperament ratings of 3–12 month-olds[8]. Given their alignment with the dimensions of NA observed in the SFP and their value in identifying tendencies toward internalizing distress[90], we focused our analyses solely on the sadness and fear subscales. The sadness subscale ($\alpha = 0.80$) includes six items regarding behaviors reflecting sadness in infants, including questions regarding how often infants cry, show a gloomy facial expression, whimper or whine, or appear sad, downcast, or unhappy. The fear subscale ($\alpha = 0.92$) includes six items regarding behaviors indicative of fear in infants, including becoming startled, displaying shyness, and avoiding novel situations. See detailed IBQ-R information in the Supplementary Methods.

Due to the COVID-19 pandemic occurring during data collection for this study, we shifted to remote data collection methods[76] after pandemic onset and continued to offer remote options after pandemic restrictions were relaxed. Thus, location of assessment (remote or in-person) and perceived stress during pregnancy (Perceived Stress Scale[91]) were considered in all analyses. See *Covariates* section below for details. Notably, a review of medical records indicated that no participants tested positive for COVID-19 during pregnancy.

## Covariates

Covariates were considered based on their potential to influence maternal dietary or metabolic health during pregnancy, infant behavioral outcomes, or maternal temperament ratings[7,91–96]. *Maternal age* at last menstrual period was considered ($M = 31.94$ years, range = 17.84–40.28 years), along with parity. *Parity* values in our sample

included 0 ($n$ = 170, 56.3%), 1 ($n$ = 91, 30.1%), 2 ($n$ = 24, 7.9%), 3 ($n$ = 7, 2.3%), and 4 ($n$ = 2, 0.7%), or Unknown ($n$ = 17, 5.6%) and were categorized into primiparous ($n$ = 170, 56.3%) or multiparous ($n$ = 124, 41.1%). Eight participants (2.6%) had missing or unreported parity data. *Maternal race and ethnicity* were also considered. Participants identified as Asian ($n$ = 24, 7.9%), Black ($n$ = 4, 13.2%), Multiracial ($n$ = 32, 10.6%), Native American ($n$ = 3, 0.9%), Pacific Islander ($n$ = 1, 3.3%), White ($n$ = 235, 77.7%), Other ($n$ = 2, 0.7%) or Missing/Not Reported/Unknown ($n$ = 10, 3.3%). Participants also reported whether they identified as Hispanic ($n$ = 25, 8.3%), non-Hispanic ($n$ = 277, 9.2%), with 9 participants (3.0%) missing data. Given the low rates of specific racial/ethnic groups, race and ethnicity were combined and categorized into White, non-Hispanic ($n$ = 221, 73.2%) or racial/ethnic minority ($n$ = 81, 26.8%) for analyses. *Prenatal stress*, measured using the Perceived Stress Scale (PSS)[97] during the second and third trimesters of pregnancy, was also considered as a covariate. *Synthetic insulin use* (Yes = 15, 5.05%; No = 279, 92.4%) was also considered. As two participants reported metformin use during pregnancy, a combined variable of prenatal synthetic insulin/metformin use was used as a covariate in analyses, with twenty-four participants (7.9%) having missing or unreported data. We also considered self-reported *prenatal vitamin use*, with any prenatal vitamin supplementation in the second or third trimester (Yes = 270, 89.4%; No = 9, 3.0%) considered as a covariate in analyses. Twenty-three participants (7.6%) had missing or unreported prenatal vitamin use data. Participants self-reported information about their *socioeconomic status* at enrollment and at 37-weeks' gestation, including total household income, via the following question, "Which of these categories best describes your total combined family income for the past 12 months?" Categories included: 1 = Less than $5000, 2=$5,000 through $11,999, 3=$12,000 through $15,999, 4=$16,000 through $24,000, 5=$25,000 through $34,000, 6=$35,000 through $49,999, 7=$50,000 through $74,000, 8=$75,000 through $99,999, 9=$100,000 through $199,999, 10=$200,000 through $299,999, 11=$300,000 and greater. The mean value from each of these brackets was calculated and divided by the number of people living in the household and used in analyses. For those reporting $300,000 and greater ($n$ = 17, 5.6%), $300,000 was used in calculations. For those reporting less than $5,000 ($n$ = 2, 0.7%), $5,000 was used in calculations.

*Infant birthweight* was captured at delivery and birthweight percentiles were considered in analyses. Infants in our study were classified as being at or below the 10th percentile ($n$ = 21, 7.0) or at or above the 90th percentile ($n$ = 39, 12.9%), based on recommendations provided by the World Health Organization[98]. All other infants' birthweights were between the 10th and 90th percentile ($n$ = 237, 78.5%). Birthweight percentiles were missing for five individuals (1.7%). All postnatal assessments occurred when infants were approximately six months of age ($M_{age}$: 6.39 months, SD: 0.55 months; Mode: 6.01 months; Range: 5.32–9.17 months); however, due to the range, *infant age* at assessment was considered as a covariate. Observational assessments of infant temperament were conducted either in-laboratory ($n$ = 90, 29.8%) or remotely over video conferencing software ($n$ = 160, 53.0%). Thus, we considered *assessment location* as a covariate in all analyses involving the SFP. The *Center for Epidemiological Studies Depression Scale (CES-D)*[99] was used to capture maternal mood at six months post-delivery and maternal CES-D score at six months post-delivery was included as a covariate in all models examining maternal-reports of infant NA. Analyses also considered *infant feeding practices* at six months assessed at via the Infant Feeding and Sleeping Questionnaire[100] (e.g., Are you currently breastfeeding or feeding your child pumped breast milk?; Yes: $n$ = 226, 74.8% of sample). Forty-six participants (15.2%) had missing or unreported data for this variable.

*Sensitivity analyses: Gestational diabetes mellitus diagnosis and dietary glycemic load*

A subset of participants was diagnosed with gestational diabetes mellitus (GDM; Yes: $n$ = 27, 8.9%). While primary analyses incorporated prenatal use of synthetic insulin (a recommended GDM-management strategy[101]), we conducted sensitivity analyses covarying GDM diagnosis status. The predictor variables considered in this sensitivity analysis remained consistent with the primary analyses, including maternal adiposity, HOMA-IR, and dietary GI captured during the second and third trimesters of pregnancy.

To examine whether portion size, in addition to carbohydrate quality, contributes to infant NA, we also conducted sensitivity analyses incorporating second and third trimester maternal dietary GL in place of dietary GI. Other predictor variables remained consistent with the primary analyses, including maternal adiposity and HOMA-IR during the second and third trimesters of pregnancy.

## Analytic strategy

A major goal of this study was to examine the unique contributions of each focal predictor (maternal dietary GI, adiposity, and HOMA-IR) on infant NA. One challenge associated with disentangling these unique effects is that these metrics of maternal metabolic state are typically correlated with one another. To address this, we elected to test our hypotheses using structural equation modeling (SEM), a statistical framework that allowed us to estimate the intercorrelations among focal variables while simultaneously examining their unique effects on infant NA. Models were estimated using M*plus* (v.8; Muthen & Muthen, 1998–2021) using the robust maximum likelihood estimator, which can accommodate non-normal data by adjusting standard errors using the Huber-White sandwich estimator. Missing data were addressed using full information maximum likelihood (FIML), consistent with best practices for handling missing data[102]. This allowed us to utilize all available data in our analyses ($N$ = 302). Model fit was assessed by examining the comparative fit index (CFI; adequate fit was considered as CFI ≥ 0.90), the Tucker Lewis index (TLI; adequate fit was considered as TLI ≥ 0.90), the standard root mean square residual (SRMR; adequate fit was considered as SRMR ≤ 0.05), and the root mean squared error of the approximation (RMSEA; adequate fit was considered as RMSEA ≤ 0.08)[103,104]. The M*plus cluster* command was used to account for non-independent observations (i.e., participants who were followed across multiple pregnancies; $n$ = 5).

Candidate covariates included maternal age, parity, minoritized race/ethnicity, prenatal stress, synthetic insulin/metformin use, prenatal vitamin use, household income (adjusted for household size), infant birthweight

percentiles, and age at six-month assessment, SFP assessment location, maternal CES-D score at six months The following approach was used to address our research questions:

1. *Bivariate Correlations*, *t-Tests*, *ANOVA*, *and Covariate Selection*. Bivariate correlations examined the associations among focal variables. Associations between focal variables and candidate continuous covariates were assessed using bivariate correlations, while *t*-tests were used to compare continuous focal variables across dichotomous categorical covariates. For covariates with more than two categories, comparisons were conducted using one-way ANOVA. Covariates with significant associations ($p < .05$) with prenatal adiposity, dietary GI, HOMA-IR values, or infant NA were incorporated into models used to test our research questions.
2. *Research Questions 1 and 2*: Research Question 1 (*What are the distinct contributions of prenatal maternal dietary GI*, *adiposity*, *and insulin resistance on infant NA?*) was addressed using an SEM in which observer ratings of infant NA as well as caregiver-reported infant sadness and fear were simultaneously regressed on maternal dietary GI, adiposity, and HOMA-IR during pregnancy. Dietary GI, adiposity, and HOMA-IR were allowed to covary. Covariates identified in Step 1 were included in this model, with paths estimated from each covariate to dietary GI, adiposity, HOMA-IR, and infant NA. To address Research Question 2 (*How does the prenatal timing of maternal dietary GI*, *adiposity*, *and insulin resistance influence infant NA?*), models were run twice: once considering second trimester variables and again considering third trimester variables. Given its direct role in influencing HOMA-IR, prenatal use of synthetic insulin use was included in all models. To preserve model parsimony, for all other candidate covariates, non-significant paths from covariates were removed from final models.

## Results

### Descriptive statistics

Demographic information and descriptive statistics appear in Table 1.

| Focal Variables | Mean (SD) or % | Range or *n* |
|---|---|---|
| *Second Trimester* | | |
| Adiposity (% body fat mass) | 33.65% (6.67%) | 15.00 – 54.00% |
| Dietary Glycemic Index | 57.28 (3.70) | 47.13–68.11 |
| HOMA-IR[1] | 1.05 (0.81) | 0.08–4.47 |
| *Third Trimester* | | |
| Adiposity (% body fat mass) | 33.16% (5.94%) | 21.00 – 52.00% |
| Dietary Glycemic Index | 57.07 (4.02) | 47.21–66.89 |
| HOMA-IR | 1.86 (1.70) | 0.22–11.75 |
| *Postnatal Infant Behavioral Assessment* | | |
| Facial distress (SFP[2]) | 0.13 (0.24) | 0.00–1.00 |
| Vocal distress (SFP) | 0.12 (0.22) | 0.00–1.00 |
| Bodily distress (SFP) | 0.21 (0.25) | 0.00–1.00 |
| Sadness subscale (IBQ-R[3]) | 3.33 (0.84) | 1.13–6.00 |
| Fear subscale (IBQ-R) | 2.41 (0.88) | 1.14–5.81 |
| **Covariates** | | |
| Maternal Age (years) | 31.94 (4.23) | 17.84–40.28 |
| Maternal Race/Ethnicity (% racial/ethnic minority) | 26.8% | *n* = 81 |
| Parity (% multiparous) | 41.1% | *n* = 124 |
| Maternal Perceived Stress Scale (2T[4]) | 10.94 (5.70) | 0.00–25.00 |
| Maternal Perceived Stress Scale (3T[5]) | 12.33 (5.86) | 0.00–27.00 |
| Gestational Diabetes Mellitus (% with diagnosis) | 8.9% | *n* = 27 |
| Prenatal Insulin Use (% using synthetic insulin) | 5.0% | *n* = 15 |
| Prenatal Supplement Use (% using prenatal vitamins) | 89.4% | *n* = 270 |
| Total Household Income | $139,557 ($80,474) | $5,000 – $300,000 |
| Total Number of People in Household | 2.81 (1.12) | 1–8 |
| Infant Birthweight (grams) | 3380.30 (490.12) | 1630.00–5230.00 |
| Breastfeeding Status (% breastfeeding at postnatal assessment) | 74.8% | *n* = 226 |
| Maternal CES-D[6] Score at Postnatal Assessment | 8.17 (7.70) | 0.00–42.00 |
| Infant Age at Postnatal Assessment (months) | 6.39 (0.55) | 5.32–9.17 |
| Postnatal Assessment Location (% conducted in-lab) | 29.8% | *n* = 90 |

**Table 1**. Descriptive statistics. [1]HOMA-IR = Homeostatic Model of Insulin Resistance (higher scores indicate more insulin resistance). [2]SFP = Still Face Paradigm. [3]IBQ-R = Infant Behavior Questionnaire—Revised. [4]2T = Second trimester. [5]3T = Third trimester. [6]CES-D = Center for Epidemiological Studies Depression Scale.

## Bivariate correlations

Second trimester HOMA-IR was positively correlated with observer ratings of infant NA at six months ($r = .20$, $p = .01$) and caregiver rated infant fear from the IBQ-R ($r = .23$, $p = .003$). Caregiver rated infant sadness from the IBQ-R was correlated with greater third trimester GI ($r = .14$, $p = .04$). See Table 2 for detailed correlations between focal variables and continuous covariates.

## *T*-tests and ANOVA

Comparisons of focal variables (e.g., second and third trimester adiposity [% body fat mass], dietary GI, and HOMA-IR values, as well as infant NA and the sadness and fear subscales) were conducted using *t*-tests for two-category covariates and one-way ANOVA for covariates with three categories. Detailed comparisons are provided in the Supplementary Methods and Supplementary Tables 2–5.

Participants with a GDM diagnosis exhibited significantly higher adiposity (second trimester: $p < .001$, third trimester: $p < .001$), higher dietary GI (second trimester: $p = .02$, third trimester: $p = .04$), and higher HOMA-IR values (second trimester: $p < .001$, third trimester: $p < .001$), compared to those without a GDM diagnosis. Similarly, compared to those not using synthetic insulin, participants using synthetic insulin had higher adiposity (second trimester: $p < .001$, third trimester: $p < .001$), higher dietary GI (second trimester: $p = .03$, third trimester: $p = .004$), and higher HOMA-IR values (second trimester: $p = .01$, third trimester: $p < .001$). Compared to those who continued breastfeeding at six months postpartum, participants who discontinued breastfeeding had higher adiposity (second trimester: $p < .001$, third trimester: $p = .002$), higher third trimester dietary GI (second trimester: $p = .14$, third trimester: $p < .001$), and higher second trimester HOMA-IR values (second trimester: $p < .001$, third trimester: $p = .64$). Infants tested remotely during the SFP exhibited higher NA, compared to those tested in the laboratory ($p < .001$).

## Maternal adiposity, dietary GI, and HOMA-IR and infant NA

Observer-rated and caregiver-reported infant NA was first regressed on second trimester maternal HOMA-IR, dietary GI, and adiposity and then again on third trimester variables. All final models fit the data adequately. Results from final models are detailed below.

*Second trimester variables and Observer-Reports and Caregiver-Ratings of infant NA*

The second trimester model fit the data adequately ($\chi^2(df = 20) = 32.52$, $p = .04$; CFI = 0.98; TLI = 0.95; SRMR = 0.03; RMSEA = 0.05). After accounting for the intercorrelations among second trimester adiposity, dietary GI, and HOMA-IR, as well as between observer-rated infant NA and caregiver-reported infant fear sadness and fear, there was a significant association between second trimester HOMA-IR and caregiver-reported infant fear at six months (β = 0.27, [95% CI: 0.09, 0.46], $p = .003$). Second trimester PSS, synthetic insulin and/or metformin use, and SFP assessment location were retained as covariates in the final model. See Fig. 2 for details. There were no other significant associations between second trimester HOMA-IR and other measures of infant NA (Observer-reported NA: β = 0.23, $p = .11$; Sadness subscale: β=-0.003, $p = .98$). There were no significant

| | 1. | 2. | 3. | 4. | 5. | 6. | 7. | 8. | 9. | 10. | 11. | 12. | 13. | 14. | 15. | 16. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Adiposity (% body fat mass [2T[1]]) | - | | | | | | | | | | | | | | | |
| 2. Glycemic Index (2T) | 0.08 | - | | | | | | | | | | | | | | |
| 3. HOMA-IR[2] (2T) | **0.52** | -0.07 | - | | | | | | | | | | | | | |
| 4. Adiposity (% body fat mass [3T[3]]) | **0.94** | **0.18** | **0.50** | - | | | | | | | | | | | | |
| 5. Glycemic Index (3T) | **0.19** | **0.38** | 0.09 | **0.20** | - | | | | | | | | | | | |
| 6. HOMA-IR (3T) | **0.43** | -0.01 | **0.35** | **0.37** | 0.00 | - | | | | | | | | | | |
| 7. Infant Negative Affect (SFP[4]) | 0.06 | 0.01 | **0.20** | -0.05 | 0.10 | -0.01 | - | | | | | | | | | |
| 8. Infant Sadness (IBQ-R[5]) | -0.04 | 0.08 | -0.09 | 0.07 | **0.14** | -0.02 | -0.02 | - | | | | | | | | |
| 9. Infant Fear (IBQ-R) | 0.14 | 0.03 | **0.23** | 0.09 | -0.03 | 0.00 | 0.06 | **0.25** | - | | | | | | | |
| 10. Maternal Age (years) | -0.04 | -0.03 | -0.09 | -0.02 | -0.08 | **-0.21** | -0.11 | **-0.16** | **-0.14** | - | | | | | | |
| 11. PSS[6] (2T) | 0.13 | 0.12 | -0.09 | 0.09 | 0.05 | 0.04 | 0.11 | **0.24** | -0.01 | **-0.12** | - | | | | | |
| 12. PSS (3T) | **0.18** | 0.10 | -0.02 | **0.19** | 0.13 | 0.12 | -0.001 | **0.17** | 0.04 | -0.11 | **0.58** | - | | | | |
| 13. Total Household Income[7] | **-0.21** | -0.07 | **-0.16** | -0.14 | **-0.24** | -0.04 | -0.07 | -0.06 | -0.03 | 0.25 | **-0.12** | -0.09 | - | | | |
| 14. Infant Birthweight (grams) | 0.01 | 0.00 | -0.11 | -0.06 | -0.04 | -0.10 | **0.17** | -0.04 | -0.05 | **0.12** | 0.01 | 0.03 | -0.07 | - | | |
| 15. Maternal CES-D[8] at Postnatal Assessment | 0.15 | **0.19** | -0.02 | 0.12 | 0.13 | 0.11 | 0.11 | **0.15** | **0.14** | **-0.23** | **0.53** | **0.54** | **-0.16** | 0.01 | - | |
| 16. Infant Age at Postnatal Assessment (months) | -0.03 | -0.04 | -0.04 | -0.04 | 0.10 | -0.05 | 0.03 | -0.12 | 0.00 | -0.06 | 0.01 | 0.12 | -0.03 | -0.11 | 0.05 | - |

**Table 2**. Bivariate correlations between study variables. [1]2T = Second trimester; [2]HOMA-IR = Homeostatic Model of Insulin Resistance (higher scores indicate more insulin resistance); [3]3T = Third trimester; [4]SFP = Still Face Paradigm; [5]IBQ-R = Infant Behavior Questionnaire—Revised; [6]PSS = Perceived Stress Scale; [7]Adjusted by number of people in household; [8]CES-D = Center for Epidemiological Studies Depression Scale. Significant correlations are bolded. The metabolic and dietary measures exhibited stability across trimesters, as evidenced by significant positive correlations between second and third trimester adiposity ($r = .94$, $p < .001$), GI ($r = .38$, $p < .001$), and HOMA-IR ($r = .35$, $p < .001$).

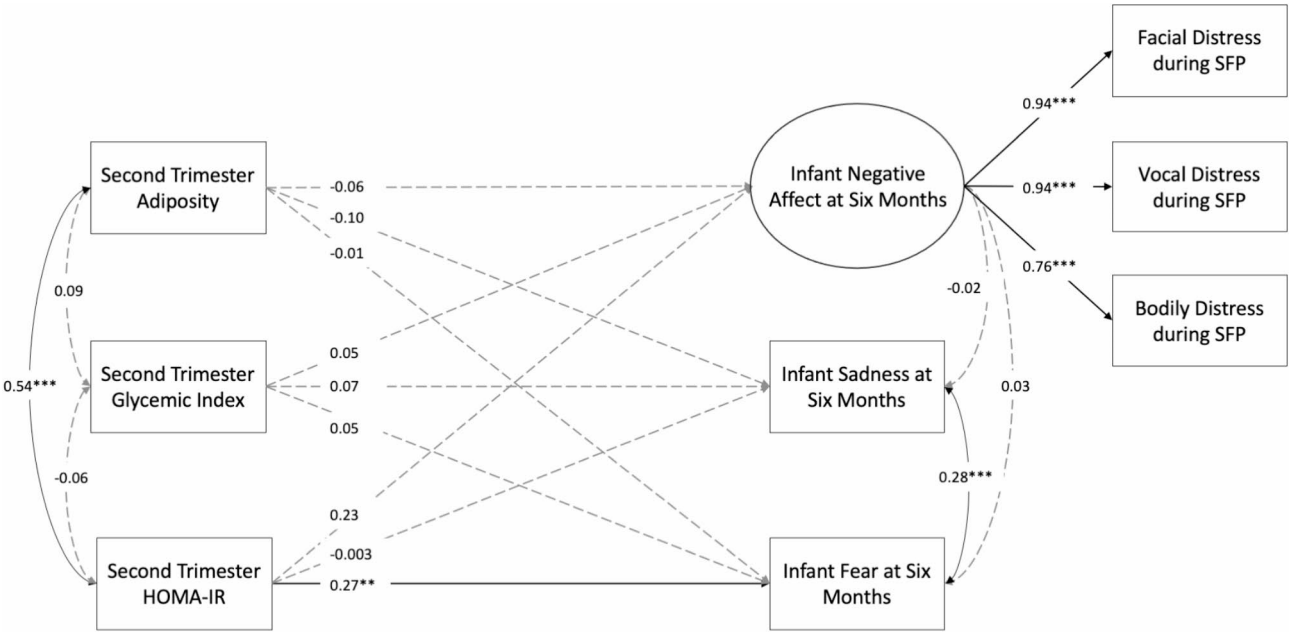


**Fig. 2**. Second trimester HOMA-R predicts caregiver-reported infant fear at six months ($N = 302$). Results from structural equation model testing the independent effects of second trimester maternal adiposity, dietary glycemic index, and homeostatic model of insulin resistance (HOMA-IR) on observer and caregiver ratings of infant NA at six months. This model fit the data adequately (Model fit statistics: $\chi^2(df = 20) = 32.52$, $p = .04$; CFI = 0.98; TLI = 0.95; SRMR = 0.03; RMSEA = 0.05). Second trimester HOMA-IR independently predicted caregiver-reported infant fear at six months (β = 0.27, [95% CI: 0.09, 0.46], $p = .003$). Final model estimates were adjusted for second trimester perceived stress scale (β = 0.24, [95% CI: 0.11, 0.36], $p < .0001$), synthetic insulin and/or metformin use (βs > -0.08, $ps < 0.61$), and assessment location (β = 0.24, [95% CI: 0.10, 0.37], $p = .001$). *$p < .05$, **$p < .01$, ***$p < .001$.

associations between second trimester adiposity on infant NA (Observer-reported NA: β=-0.06, $p = .54$; Sadness subscale: β=-0.10, $p = .37$; Fear subscale: β=-0.01, $p = .88$) or between second trimester dietary GI and infant NA (Observer-reported NA: β = 0.05, $p = .36$; Sadness subscale: β = 0.07, $p = .31$; Fear subscale: β = 0.05, $p = .47$).

*Third trimester variables and Observer-Reports and Caregiver-Ratings of infant NA*

The third trimester model fit the data adequately ($\chi^2(df = 29) = 61.58$, $p = .001$; CFI = 0.95; TLI = 0.91; SRMR = 0.03; RMSEA = 0.06). After accounting for the intercorrelations among third trimester adiposity, GI, and HOMA-IR, as well as between observer-rated infant NA and caregiver-reported infant fear sadness and fear, there was a significant association between third trimester dietary GI and observer-ratings of NA at six months (β = 0.14, [95% CI: 0.01, 0.27], $p = .04$). There was also a significant association between third trimester dietary GI and caregiver-reported infant sadness at six months (β = 0.17, [95% CI: 0.04, 0.29], $p = .01$). Maternal age, third trimester PSS, synthetic insulin and/or metformin use, infant age at NA testing, and SFP assessment location were retained as covariates in the final model. See Fig. 3 for details. There were no significant associations between third trimester dietary GI and caregiver-reported infant fear (β=-0.04, $p = .64$). There were no significant associations between third trimester adiposity and infant NA (Observer-reported NA: β=-0.11, $p = .12$; Sadness subscale: β=-0.004, $p = .97$; Fear subscale: β = 0.10, $p = .26$) or third trimester HOMA-IR and infant NA (Observer-reported NA: β = 0.04, $p = .50$; Sadness subscale: β=-0.17, $p = .20$; Fear subscale: β = 0.01, $p = .93$).

Sensitivity analyses examined whether these effects survived considering whether participants were diagnosed with GDM ($n = 27$). Results were consistent in significance, magnitude, and direction with the main models reported. See Supplementary Results and Supplementary Tables 6–7 for detailed results. Sensitivity analyses also examined whether the observed effects were associated with portion size by assessing the association between maternal dietary GL on infant NA. Results from these models were non-significant. See Supplementary Results and Supplementary Tables 8–9 for detailed results.

## Discussion

Maternal diet and metabolic health during pregnancy exert profound programming effects on offspring developmental trajectories, including future psychopathological risk[29,33,105]. Identifying the distinct programming roles of maternal prenatal nutrition, body composition, and insulin sensitivity on infant risk for neurodevelopmental disorders is critical for identifying key intervention targets and timepoints, and necessarily requires the consideration of their complex interplay. Here, we examined the associations between prenatal maternal dietary GI, adiposity, and HOMA-IR and infant NA, an early risk factor for future psychopathology. We sought to disentangle the unique contributions of each factor on infant NA at six months. Our findings

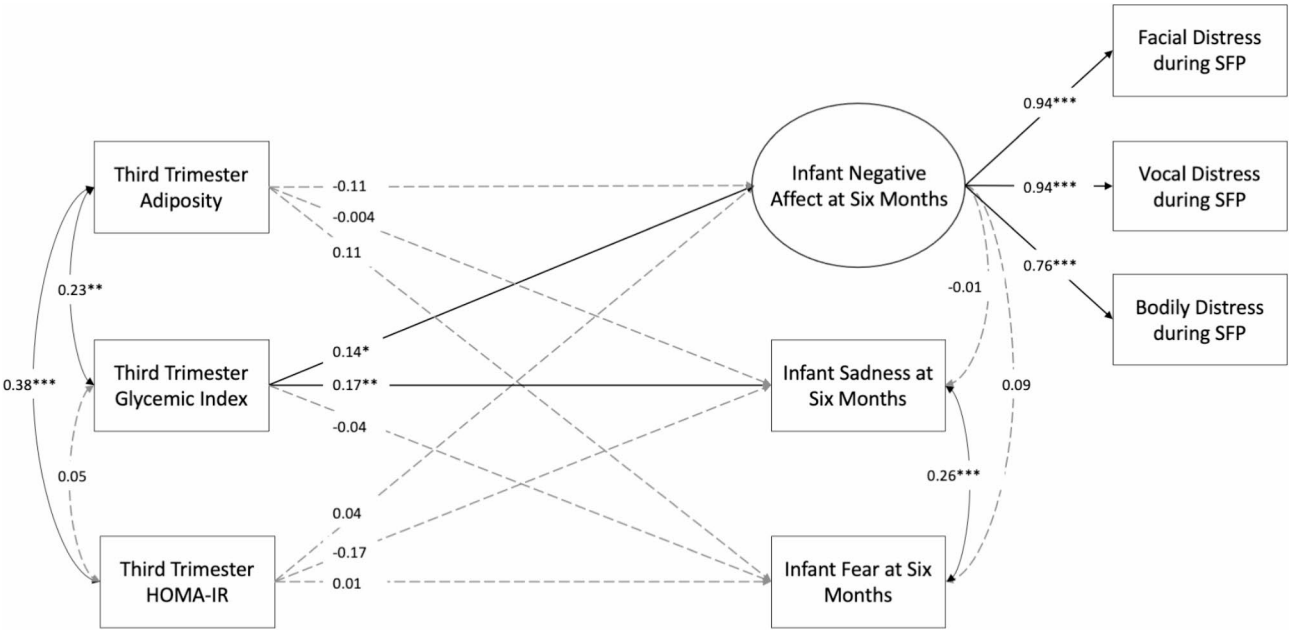


**Fig. 3**. Third trimester dietary glycemic index predicts observer-reported infant negative affect and caregiver-reported infant sadness at six months ($N = 302$). Results from structural equation model testing the independent effects of third trimester maternal adiposity, dietary glycemic index (GI), and homeostatic model of insulin resistance (HOMA-IR) on observer and caregiver ratings of infant NA at six months. This model fit the data adequately ($\chi^2(df = 29) = 61.58$, $p = .001$; CFI = 0.95; TLI = 0.91; SRMR = 0.03; RMSEA = 0.06). Third trimester dietary GI independently predicted observer-ratings of NA at six months (β = 0.14, [95% CI: 0.01, 0.27], $p = .04$). There was also an association between third trimester dietary GI and caregiver-reported infant sadness at six months (β = 0.17, [95% CI: 0.04, 0.29], $p = .01$). Final model estimates were adjusted for maternal age (β = -0.14, [95% CI: -0.27, -0.01], $p = .04$), perceived stress scale (β = 0.16, [95% CI: 0.04, 0.28], $p = .01$), synthetic insulin and/or metformin use (βs > 0.12, $p$s < 0.21), infant age at NA testing (β = -0.16, [95% CI: -0.29, -0.04], $p = .01$), and assessment location (β = 0.25, [95% CI: 0.11, 0.39], $p = .0001$). *$p < .05$, **$p < .01$, ***$p < .001$.

revealed a significant link between higher third trimester dietary GI and increased infant NA, an association observed in both maternal-reports of infant sadness, a fine-grained temperament domain of NA, and observer-ratings of infant behavioral NA, underscoring the robustness of this effect. These same associations were not observed for variables captured in the second trimester, suggesting a potential sensitive period for when dietary GI-related fetal programming of infant NA occurs.

Accumulating preclinical[53–56] evidence and evidence from human studies[16] suggests that maternal dietary quality and adiposity may have programming effects on infant NA, and particularly, on high rates of sadness and fear, which are associated with later psychopathology[106]. Caregiver-reported measures in this study suggested that prenatal high-GI diet's effects on infant NA may be specific to infant sadness, suggesting that offspring exposed to higher-GI prenatal diets may have broad tendencies toward future internalizing disorders.

That the third, but not second, trimester dietary GI was associated with infant NA highlights the importance of considering timing effects when examining prenatal maternal dietary influences on infant neurodevelopment[107,108]. The timing and impact of maternal dietary GI on fetal neurodevelopment are especially pertinent as maternal glucose serves as the primary fuel source to the fetal brain[64]. The unique metabolic demands of the third trimester may create an environment in which higher-GI diets exert more pronounced effects on infant development[109]. The fetal brain may have heightened vulnerability to nutritional influences during the third trimester due to its substantial energy requirements throughout this period[109]. The third trimester is a period of rapid maturation, including synaptogenesis and synaptic refinement[110,111]. This interpretation is supported by the increased nutrient demands during the third trimester[112], including for polyunsaturated fatty acids and choline, both of which are critical for brain development[113,114]. In contrast, the second trimester is marked by neurogenesis and neuronal migration[110], including rapid growth of fetal white matter, deep subcortical structures, and the cerebellum[115], potentially laying the neural groundwork as a precursor to the more intricate aspects of emotional regulation. We note our finding of a significant effect of second, but not third, trimester HOMA-IR on caregiver-reported infant fear at six months, which may suggest that the various aspects of infant temperament, and domains of NA in particular, are impacted differentially by maternal metabolic health factors at different times during pregnancy.

The distinction between insulin resistance, reflecting chronic glycemic control[116], and dietary GI, reflecting plasma glucose concentrations following specific food intake[117] is crucial. Both adiposity and insulin resistance may result from chronic high GI food consumption; however, chronic but steady increases in insulin resistance and accumulation of adipose tissue may allow for gradual fetal adaptation to the intrauterine environment,

whereas frequent glucose exposure fluctuations from higher-GI diets[118] may present a less optimal fetal environment, leading to distinct programming effects on the fetus.

Our findings contribute to mounting evidence that maternal diet during the periconceptual and perinatal periods plays a critical programming role in infant and toddler temperament and behavioral outcomes[58–60,71]. Previous research demonstrated that higher maternal dietary GL at a single timepoint surrounding conception was associated with reductions in toddler socioemotional functioning measured using the Infant-Toddler Social and Emotional Assessment[71]. We extend these findings in our study by repeatedly measuring maternal dietary GI throughout pregnancy using six 24-hour dietary recalls and identifying an association between third trimester maternal dietary GI and infant caregiver-rated and observer-reported NA at six months. Taken together, these studies suggest that the glycemic quality of the maternal diet during these key periods has programming effects on offspring neurodevelopmental health, with maternal consumption of a more glycemic periconceptual and prenatal diet associated with increased risk for offspring developmental psychopathology.

Beyond glycemic measures, other components of the prenatal maternal diet are emerging as important to infant temperament and behavioral health, While pregnant women's self-reported 24-hour total dietary fat intake did not appear to influence caregiver-reported NA, it was associated with lower orienting/regulation and surgency in four month olds[58]. In addition to the total amount of fat consumed, evidence highlights the importance of the *type* of fatty acid consumed, with higher maternal dietary omega-3:omega-6 ratio captured via a FFQ early in pregnancy linked to higher caregiver-reported infant orienting/regulation at six months old, but only in contexts of higher maternal prenatal stress[59]. Higher plasma concentrations of omega-3 fatty acids during the third trimester are also associated with lower infant NA at six months, measured via maternal-reports and observer-ratings[16]. Furthermore, maternal dietary antioxidant consumption has also been linked to child behavior, with higher consumption of dietary antioxidants measured via FFQ in early pregnancy associated with higher caregiver-reported surgency (e.g., vitamin C and selenium) and caregiver-reported effortful control (e.g., vitamin C) in 30-month-olds[60]. The same study found that an association between prenatal stress and caregiver-reported NA in offspring was exacerbated among children of mothers with lower prenatal antioxidant intake.

Mechanistic studies in animal models further underscore that maternal dietary patterns (especially diets high in fat and sugar) influence offspring susceptibility to depressive- or anxiety-like phenotypes[53,56,119]. Taken together, these studies emphasize the important role of maternal prenatal diet composition in programming offspring temperament and behavioral health, with specific dietary components appearing to differentially affect offspring neurodevelopmental domains throughout the phases of pregnancy, underscoring the role of maternal diet as a key, modifiable factor in fetal programming of emotional development and regulation.

It is important to consider what the dietary GI reflects. The dietary GI reflects how quickly the blood glucose increases following the consumption of an individual food. Notably, our use of a three-day average of the dietary GI during pregnancy is supported by prior work that shows that the dietary GI is predictive of important markers of maternal carbohydrate metabolism, including both plasma glucose and glycosylated hemoglobin (hemoglobin A1c [HbA1c])[62], a form of hemoglobin chemically linked to glucose, representing the average blood glucose over the prior 2–3 months[120]. In non-pregnant samples, studies show that the dietary GI is also predictive of other glycemic response indicators[121]. Prior work also indicates that the prenatal dietary GI is associated with infant birth outcomes[62]. Dietary GI is associated with fluctuations in blood glucose[118], which might have unique implications for fetal development.

Another measure of glycemic impact is the dietary GL, which adjusts for serving size and the span of the blood glucose increase. We found that maternal prenatal dietary GI but not GL in the third trimester was predictive of infant NA at six months (Supplementary Results and Supplementary Tables 8–9), suggesting that the glycemic nature of the food consumed has developmental programming effects on the fetus, rather than the serving size or the numbers of calories of the glycemic foods consumed. Prior work shows that maternal dietary GL has a weaker association with glycosylated hemoglobin in pregnant women and does not have an association with plasma glucose or with infant birth outcomes[62]. However, this may not offer a full explanation, as the aforementioned study examining the role of maternal dietary GL on offspring socioemotional development showed that higher maternal periconceptual dietary GL was associated with anxiety and inhibition in toddlers[71]. It is worth noting, however, that in this prior study only a single capture of maternal dietary GL was utilized, and was calculated using a food frequency questionnaire concerning eating habits during the last menstrual period before pregnancy, which may be a limited representation of the day-to-day maternal diet. It is also possible that this discrepancy in findings between maternal dietary GI in our study and maternal dietary GL in the previous study is due to participant difficulties in accurately recalling and/or reporting portion sizes, as opposed to simply recalling the specific foods they consumed, limiting the fidelity of the dietary GL measure. Discrepancies between study outcomes when assessing dietary GI versus dietary GL may also be explained by studies in pregnant women show that there is a chronic underreporting of daily energy intake, particularly among women with higher BMIs[122,123]. Dietary GI and GL have also been associated with methylation of different genes in cord blood[124], which may result in different pathways toward similar temperament and behavioral outcomes, offering another potential explanation of these findings.

Consideration of the precise molecular mechanisms underlying these associations is needed. One compelling mechanism is inflammation, with higher-GI foods triggering an inflammatory response via repeatedly elevating maternal blood glucose concentrations and impacting fetal neurodevelopment[125]. Alternatively, or in addition, oxidative stress may result from fluctuating maternal blood glucose levels[126,127], leading to cellular damage and potential consequences for the developing fetal brain. Dietary influences on cord blood DNA methylation patterns[124] may also indicate cascading epigenetic effects on infant neurodevelopment. Another interesting possibility is that the maternal prenatal diet may alter the maternal microbiome, which may have programming effects on infant temperament, as in two recent studies[128,129].

Study strengths include our use of objective measures including repeated, nutritionist-conducted 24-hour recalls (three days in the second and third trimesters [six total]), BodPod® assessment of adiposity, and determining HOMA-IR from blood samples captured within two weeks of the other measures. Our data collection procedures allowed us to examine trimester-specific effects, resulting in the findings that second trimester HOMA-IR predicts infant fear, while third trimester dietary GI predicts infant NA, highlighting the need for more studies examining the timing of prenatal influences on infant neurodevelopment. Another strength is our use of a three-day average to measure prenatal dietary GI which has been previously shown to be predictive of glucose measured in maternal plasma[62]. Previous evidence indicates that prenatal dietary GI influences neonatal body composition outcomes, with neonates of mothers who consumed low-GI diets giving birth to infants with lower weights[69]. The data presented in this study extend these findings by examining the influence of prenatal dietary GI on infant neurodevelopmental outcomes in six months olds. Our study also incorporated longitudinal dietary data from the second and third trimesters, as well as infant feeding practices at six months (74.8% of infants were still breastfed at six months). SEM is a strong analytic approach used to disentangle each predictor's independent contributions while controlling for confounding covariates[130]. Furthermore, by incorporating well-established methods of assessing objective (SFP)[87,88] and subjective (IBQ-R) NA[8], we comprehensively assessed infant temperament, bolstering the findings.

Limitations should also be considered. First, as the observed effects were relatively small in magnitude, these findings should be replicated in larger samples. Future research should explore the underlying mechanisms and long-term implications of these associations, including considering the role of the postnatal diet, which has important implications for infant development[105]. Future studies specifically examining perinatal dietary trajectories from conception through the postpartum period are warranted to better characterize the timing effects of nutrition on child temperament and behavior. Future work may benefit from using continuous glucose monitoring during pregnancy as a tighter measure of the daily fluctuations in blood glucose to further clarify the associations between the prenatal dietary GI and infant temperament development. Future studies evaluating the contributions of the prenatal dietary GI and GL on offspring neurodevelopmental outcomes may also benefit from using more frequently assessed dietary recalls, using dietary recalls assessed at other times during the periconceptual or perinatal period, or using weighed food diaries as alternatives.

In conclusion, this study underscores the significance of maternal dietary quality during pregnancy, particularly third trimester dietary GI, in optimizing infant neurodevelopmental health. Clinically, maternal body composition and pancreatic physiology may represent more challenging intervention targets, unlike the glycemic nature of the diet itself, which may be more readily modifiable[131]. Developing targeted dietary interventions that involve exchanging high-GI foods for lower-GI replacements may be a feasible means of enhancing infant neurodevelopmental health and well-being. To the extent that infant NA is associated with future psychopathology, our findings represent important preliminary evidence for the third trimester as a critical window for maternal dietary quality to exert programming effects on infant temperament and point to the dietary GI as a potential intervention target for reducing risk for future psychiatric concerns. These findings have implications for clinical practice and public health and highlight the value of recommending maternal dietary modifications at specific pregnancy stages.

## Data availability

The data that support the findings of this study are openly available via the National Institute of Mental Health Data Archive (https://nda.nih.gov/), collection C2996.

Received: 26 February 2024; Accepted: 24 February 2025
Published online: 11 March 2025

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## Acknowledgements

This work was supported by the National Institutes of Health/National Institute of Mental Health (ELS and JTN, Grant Number: R01 MH117177), (JTN and ELS, Grant Number: R01 MH124824), (HCG, Grant Number: K01 MH120507). The project was also supported by the National Center for Advancing Translational Sciences (Grant Numbers: UL1 TR002369 and TL1 TR002371), the National Institute on Alcohol Abuse and Alcoholism (Grant Number: T32 AA007468), and by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (Grant Number: K12 AR084221). The funders played no role in the writing of this manuscript, or in the decision to submit the article for publication. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. None of the data have been previously published. The authors would like to acknowledge the contributions of the Prenatal And Child Health (PEACH) study research staff that collected the data represented in the study. We would also like to express our appreciation to the participants in the study. All authors have read and agreed to the published version of the manuscript.

## Author contributions

Conceptualization, E.K.W., H.C.G. and E.L.S.; methodology, E.K.W., J.C.A., J.T.N., H.C.G., and E.L.S.; formal analysis, E.K.W., H.C.G., and E.L.S.; resources, J.T.N., H.C.G., and E.L.S.; data curation, E.K.W., O.N., J.C.A., A.E., A.H., H.C.G., and E.L.S. writing—original draft preparation, E.K.W.; writing—review and editing, O.N., J.C.A., A.E., A.H., J.T.N., H.C.G., and E.L.S.; visualization, E.K.W.; supervision, E.L.S.; project administration, J.T.N., H.C.G., and E.L.S.; funding acquisition, E.K.W., J.T.N., H.C.G., and E.L.S.

## Declarations

### Competing interests
The authors declare no competing interests.

### Additional information
**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-91886-0.

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