Parental Obesity and Early Childhood Development

Edwina H. Yeung, PhD,[a] Rajeshwari Sundaram, PhD,[b] Akhgar Ghassabian, MD, PhD,[a] Yunlong Xie, PhD,[c] Germaine Buck Louis, PhD, MS[d]

abstract

BACKGROUND: Previous studies identified associations between maternal obesity and childhood neurodevelopment, but few examined paternal obesity despite potentially distinct genetic/epigenetic effects related to developmental programming.

METHODS: Upstate KIDS (2008–2010) recruited mothers from New York State (excluding New York City) at ∼4 months postpartum. Parents completed the Ages and Stages Questionnaire (ASQ) when their children were 4, 8, 12, 18, 24, 30, and 36 months of age corrected for gestation. The ASQ is validated to screen for delays in 5 developmental domains (ie, fine motor, gross motor, communication, personal-social functioning, and problem-solving ability). Analyses included 3759 singletons and 1062 nonrelated twins with ≥1 ASQs returned. Adjusted odds ratios (aORs) and 95% confidence intervals were estimated by using generalized linear mixed models accounting for maternal covariates (ie, age, race, education, insurance, marital status, parity, and pregnancy smoking).

RESULTS: Compared with normal/underweight mothers (BMI <25), children of obese mothers (26% with BMI ≥30) had increased odds of failing the fine motor domain (aOR 1.67; confidence interval 1.12–2.47). The association remained after additional adjustment for paternal BMI (1.67; 1.11–2.52). Paternal obesity (29%) was associated with increased risk of failing the personal-social domain (1.75; 1.13–2.71), albeit attenuated after adjustment for maternal obesity (aOR 1.71; 1.08–2.70). Children whose parents both had BMI ≥35 were likely to additionally fail the problem-solving domain (2.93; 1.09–7.85).

CONCLUSIONS: Findings suggest that maternal and paternal obesity are each associated with specific delays in early childhood development, emphasizing the importance of family information when screening child development.

[a]*Epidemiology Branch,* [b]*Biostatistics and Bioinformatics Branch,* [c]*Glotech, Inc, and* [d]*Office of the Director, Division of Intramural Population Health Research,* Eunice Kennedy Shriver *National Institute of Child Health and Human Development, Rockville, Maryland*

Dr Yeung conceptualized the analysis, supervised the data collection, performed data analysis, and drafted the initial manuscript; Drs Xie and Sundaram performed statistical analysis; Dr Ghassabian interpreted the data; Dr Buck Louis designed the study, interpreted the data, and obtained funding; and all authors critically reviewed the manuscript and approved the final manuscript as submitted.

DOI: 10.1542/peds.2016-1459

Accepted for publication Nov 3, 2016

Address correspondence to Edwina Yeung, PhD, Epidemiology Branch, Division of Intramural Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, 6710B Rockledge Dr, Rm 3122, MSC 7004, Bethesda, MD 20817. E-mail: yeungedw@mail.nih.gov

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

WHAT'S KNOWN ON THIS SUBJECT: A high proportion (20%–30%) of adults is obese. Studies have observed associations between maternal obesity and childhood development with increased risks of diagnosed disorders, such as autism, but few accounted for paternal BMI despite epigenetic modifications associated with obesity.

WHAT THIS STUDY ADDS: In this first US study to prospectively examine both maternal and paternal obesity, maternal obesity was associated with delays in fine motor development, whereas paternal obesity was associated with delays in personal-social functioning, suggesting independent associations.

To cite: Yeung EH, Sundaram R, Ghassabian A, et al. Parental Obesity and Early Childhood Development. *Pediatrics.* 2017;139(2):e20161459

Approximately 1 in 5 pregnant women in the United States enter into pregnancy with a BMI ≥30.[1] Concerns have risen that prepregnancy obesity may be adversely associated with childhood neurodevelopment.[2,3] Potential mechanisms include exposure to inflammation during prenatal brain development, adipokine dysregulation, micronutrient insufficiency, hyperglycemia, and abnormal development of the serotonin system.[2,4]

Evidence regarding the role of maternal obesity on childhood neurodevelopment was recently reviewed.[2,3] Most longitudinal cohorts observed negative associations between maternal obesity or increased prepregnancy BMI and childhood development despite variations in the outcomes studied and a wide age range of assessment.[5–14] A few studies showed inconsistent evidence.[15–17] Related studies have also examined gestational weight gain (GWG) with inconsistent findings.[9,18–20]

Although maternal obesity has been the primary focus of research,[5–13] evolving evidence suggests a possible role for paternal obesity.[19,21] In particular, de novo mutations and potential shifts in epigenetic programming in sperm and in placenta increase with paternal BMI.[22–24] Paternal BMI is also important to explore, as it could demonstrate specificity of associations. Associations similar to maternal BMI may suggest residual confounding from socioeconomic or shared postnatal influences.[25] On the other hand, dissimilar associations can support true intrauterine programming specific to maternal BMI.

Given few studies of childhood neurodevelopment had paternal BMI information,[12,13,15,19] and none being from the United States, our objective was to evaluate associations between parental obesity and early childhood development up to 3 years of age. We accounted for sociodemographic and lifestyle factors and examined associations with GWG. We hypothesized that both maternal and paternal obesity would be associated with delays in early childhood development.

METHODS

Study Design and Population

The Upstate KIDS Study recruited 5034 women ~4 months after a delivery in New York State (excluding New York City) between 2008 and 2010. The cohort was originally established to investigate the association between couples' fecundity and early childhood growth and development.[26] Thus, infants conceived by infertility treatment and multiples were oversampled.[26] The primary cohort consists of all singletons and 1 randomly selected twin of each pair. Triplets and quadruplets (n = 134 from 45 mothers) were excluded due to low numbers and a lack of established guidance on appropriate GWG for mothers in this group.[27] The New York State Department of Health and the University at Albany (State University of New York) Institutional Review Boards approved the study, and entered into a reliance agreement with the National Institutes of Health. Parents provided written informed consent.

Developmental Assessment

Development was measured by using the Ages and Stages Questionnaire (ASQ), which is a validated screening instrument for identifying developmental delays.[28,29] The ASQ encourages parents to perform activities with their children and then respond to questions capturing 5 developmental domains (ie, fine motor, gross motor, communication, personal-social functioning, and problem-solving ability). Parents completed the ASQ at 4 to 6, 8, 12, 18, 24, 30, and 36 months of age, corrected for gestational age.[30,31] We implemented the ASQ second edition[31] at ages 4 to 12 months and the third edition[30] from 18 months onward. Each questionnaire item was scored. Failing scores were defined as scores 2 SDs below the mean for the child's age per ASQ instructions.[30,31] Parents were contacted to administer a follow-up screen for any failed domain(s) by using an age-appropriate ASQ as recommended by the instrument.[29] The child was considered to have failed the domain only if she or he also failed the follow-up screen or if the parent was not reachable. Screening instruments were considered valid only if completed in the specified age windows.[30,31] A total of 3759 singletons and 1062 nonrelated twins with ASQ data who returned for ≥1 time point were included in the analyses (n = 168, 3% excluded).

Parental Obesity and GWG

At enrollment, mothers completed a questionnaire about health status and lifestyle. Questions included information regarding both parents' height and weight, maternal weight before pregnancy, and total GWG. Maternal prepregnancy weight, weight at delivery, and height also were extracted from electronic birth certificates. Prepregnancy weight and height were used to calculate prepregnancy BMI. Birth certificate information for maternal BMI was prioritized and augmented with maternal self-reported information where missing (1.6%). Paternal BMI was calculated from weight and height as reported by mothers. BMI categories were based on World Health Organization cutoffs (as specified in Table 1) except 148 underweight mothers were grouped with normal weight.

GWG was calculated as the delivery weight minus prepregnancy weight

TABLE 1 Baseline Characteristics by Maternal Prepregnancy BMI Status in Upstate KIDS (Primary Cohort)

	All	Normal Weight, BMI <25.0	Overweight, BMI 25.0–29.9	Obese Class I, BMI 30.0–34.9	Obese Class II/III, BMI ≥35.0
n (%)	4821	2317 (48)	1234 (26)	639 (13)	631 (13)
Maternal characteristics					
Prepregnancy BMI	27.06 (6.83)	21.85 (1.97)	27.21 (1.40)	32.26 (1.43)	40.62 (5.01)
Maternal age, y[a]	30.46 (6.06)	30.40 (6.11)	30.93 (6.15)	30.27 (5.92)	29.94 (5.76)
Paternal age, y[a]	33.14 (6.84)	33.12 (6.79)	33.52 (7.05)	32.49 (6.50)	33.11 (6.90)
Non-Hispanic white, *n* (%)	3888 (81)	1876 (81)	985 (80)	528 (83)	499 (79)
Maternal education,[a] *n* (%)					
Less than high school	289 (6)	143 (6)	68 (6)	45 (7)	33 (5)
High school or GED equivalent	620 (13)	268 (12)	138 (11)	88 (14)	126 (20)
Some college	1463 (30)	564 (24)	385 (31)	239 (37)	275 (44)
College	1064 (22)	567 (25)	273 (22)	119 (19)	105 (17)
Advanced degree	1385 (29)	775 (33)	370 (30)	148 (23)	92 (14)
Private insurance,[a] *n* (%)	3617 (75)	1779 (77)	944 (77)	468 (73)	426 (68)
Married/Living as married,[a] *n* (%)	4079 (88)	1989 (90)	1042 (88)	537 (88)	511 (84)
Previous live birth,[a] *n* (%)	2612 (55)	1137 (50)	545 (44)	259 (41)	233 (37)
Infertility treatment, *n* (%)	1422 (30)	682 (29)	350 (28)	190 (30)	200 (32)
Any alcohol during pregnancy,[a] *n* (%)	586 (12)	332 (14)	142 (12)	63 (10)	49 (8)
Smoked during pregnancy,[a] *n* (%)	680 (14)	297 (13)	164 (13)	97 (15)	122 (19)
Preexisting diabetes,[a] *n* (%)	47 (1)	5 (0.2)	11 (1)	11 (2)	20 (3)
Gestational diabetes,[a] *n* (%)	459 (10)	135 (6)	120 (10)	81 (13)	123 (19)
Gestational hypertension,[a] *n* (%)	512 (11)	145 (6)	148 (12)	78 (12)	141 (22)
Multivitamin use,[a] *n* (%)	3224 (69)	1591 (71)	828 (69)	410 (66)	395 (64)
Fish oil (omega-3 fatty acid) use,[a] *n* (%)	722 (15)	400 (18)	184 (15)	66 (11)	72 (12)
Paternal BMI[a]	28.24 (5.45)	26.81 (4.40)	28.36 (5.02)	29.86 (6.00)	31.56 (7.00)
Normal/underweight, *n* (%)	1176 (27)	695 (34)	278 (25)	121 (21)	82 (15)
Overweight, *n* (%)	1854 (43)	982 (48)	492 (44)	191 (34)	189 (33)
Obesity (class I), *n* (%)	811 (19)	281 (13)	235 (21)	156 (28)	139 (25)
Obesity (class II/III), *n* (%)	451 (11)	97 (5)	103 (10)	97 (17)	154 (27)
Postpartum depression score[a]	2.69 (2.80)	2.49 (2.69)	2.72 (2.73)	2.95 (3.00)	3.13 (3.02)
Postpartum depression,[a] *n* (%)	983 (21)	421 (19)	245 (21)	155 (25)	162 (26)
Breastfeeding at discharge,[a] *n* (%)	3760 (79)	1884 (82)	974 (80)	471 (74)	431 (69)
Children's characteristics					
Male infant, *n* (%)	2494 (52)	1181 (51)	636 (52)	340 (53)	337 (53)
Singleton, *n* (%)	3759 (78)	1829 (79)	956 (77)	498 (78)	476 (75)
Birth weight, g[a]	3173 (695)	3119 (664)	3212 (708)	3242 (682)	3227 (777)
Gestational age, wk	38.04 (2.48)	38.07 (2.44)	38.06 (2.49)	38.06 (2.47)	37.84 (2.63)
Small for gestational age, *n* (%)	621 (14)	330 (15)	137 (12)	72 (13)	82 (15)
GWG, kg[a]	32.3 (16.3)	35.6 (13.8)	33.8 (15.6)	28.9 (16.5)	21.0 (20.3)
Excessive GWG, *n* (%)	2105 (44)	762 (33)	713 (58)	385 (60)	245 (39)
Adequate GWG, *n* (%)	1661 (34)	998 (43)	362 (29)	144 (23)	157 (25)
Inadequate GWG, *n* (%)	1040 (22)	548 (24)	157 (13)	109 (17)	226 (36)
Age at last ASQ, mo[a]	24.26 (13.11)	25.01 (12.99)	24.27 (13.08)	22.86 (13.34)	22.89 (13.15)

Values are mean (SD) unless otherwise indicated. Mean (SD) for continuous variables; *n* (%) for categorical. Missing data: paternal BMI (*n* = 529, 11%), multivitamin/fish oil use during pregnancy (*n* = 132, 3%), insurance status (*n* = 4), parity (*n* = 35, 0.7%), marital status (*n* = 203, 4.2%), drinking (*n* = 1), smoking (*n* = 1), postpartum depression (*n* = 170, 3.5%), breastfeeding at discharge (*n* = 52, 1%). GWG defined by 2009 Institute of Medicine guidelines[27]: Inadequate GWG is <12.5 kg for underweight women, <11.5 kg for normal-weight women, <7.0 kg for overweight women, and <5.0 kg for obese women (classes I and II) delivering singletons. Low GWG is <17.0 kg for underweight and normal-weight women, <14.0 kg for overweight women, and <11.0 kg for obese women (classes I and II) delivering twins. Adequate GWG is between 12.5 and 18.0 kg for underweight women, between 11.5 and 16.0 kg for normal-weight women, between 7.0 and 11.5 kg for overweight women, and between 5.0 and 9.0 kg for obese women (classes I and II) delivering singletons. Adequate GWG is between 17.0 and 25.0 kg for underweight and normal-weight women, between 14.0 and 23.0 kg for overweight women, and between 11.0 and 19.0 kg for obese women (classes I and II) delivering twins. Excessive GWG is >18.0 kg for underweight women, >16.0 kg for normal-weight women, >11.5 kg for overweight women, and >9.0 kg for obese women (classes I and II) delivering singletons. Excessive GWG is >25.0 kg for underweight and normal-weight women, >23.0 kg for overweight women, and >19.0 kg for obese women (classes I and II) delivering twins.

[a] $P < .05$ difference by analysis of variance or χ^2.

from birth certificates and total weight gain from maternal report used only where missing (2.4%). GWG was categorized based on the Institute of Medicine criteria for inadequate and excessive weight gain specified for plurality and obesity categories.[27]

Covariates

Covariate information came from vital records (ie, maternal and paternal age, insurance status, plurality, parity, birth weight, and gestational age) or by baseline maternal report with retrospectively reported information on the pregnancy at 4 months postpartum (ie, marital status, race, education, pregnancy smoking, alcohol use, multivitamin use, and fish oil [omega-3 fatty acid] supplementation). Pregnancy complications were identified

by using available data sources including maternal report, birth certificates, and New York State's Statewide Planning and Research Cooperative System. Townsend index, a measure of socioeconomic deprivation, was calculated based on census information.[32,33]

Statistical Methods

Participant characteristics relative to maternal obesity categories were compared by using χ^2 and *t* tests among the primary cohort. We evaluated the associations between parental BMI categories with failing any ASQ domain (yes/no) and separately by each of the 5 domains. We used generalized linear mixed models with a logit function and random effect to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) of these associations.[34] These models use children's repeated ASQ pass/fail information over time. To assess a potential nonlinear trajectory, we estimated the odds of failure relative to categorical time. The ORs denote the association between BMI category and odds for failing an ASQ accounting for time of assessment and other covariates. Fixed effects were assessed with robust SEs. Results were further stratified by plurality. Sampling weights were applied to account for the study's design of oversampling infants conceived with infertility treatment and twins.[26] Weights were based on New York State birth certificate data for all infants born during the period of recruitment. Longitudinal methods accounted for varying developmental stages over follow-up, allowing flexibility of children to fail at any point in time.

Parental BMI was first examined by comparing overweight and obese groups with the normal/underweight groups. We separately investigated obese class I and obese class II/III groups. Maternal obesity was examined with and without adjustment for paternal BMI. Paternal obesity was examined in a similar fashion. The interaction of the 2 was examined by creating a 9-category variable that crossed maternal and paternal BMI categories such that children whose parents both had BMI ≤25 served as the reference group and children with both parents of BMI ≥35 was the highest exposure group. GWG was modeled with the adequate weight gain group as reference.

A priori factors known to be associated with development[35,36] and associated with maternal obesity were adjusted for, including maternal age, race/ethnicity, education, insurance, married/living as married, previous live birth, and pregnancy smoking. We did not adjust for infertility treatment because we previously did not identify associations.[29] Fish oil supplementation, multivitamin use, and the Townsend index were added in separate models but did not alter associations and were not retained in final statistical models (data not shown). Multiple imputations completed missing data on paternal BMI (11%), marital status (*n* = 4%), fish oil (3%), multivitamin use (3%), parity (*n* <1%), drinking (*n* <1%), smoking (*n* <1%), and insurance status (*n* <1%). We imputed missing covariate data by generating 25 imputed data sets by using the MICE algorithm in R.[37] The procedure specifies the multivariate imputation model on a variable-by-variable basis by a set of conditional densities, one for each incomplete variable. Auxiliary variables informing imputation included all parental variables from Table 1 (except breastfeeding and postpartum depression). We assumed that the data are missing at random; that is, missing with respect to observed data accounted for in our models. All other analyses were conducted with SAS version 9.4 (SAS Institute, Inc, Cary, NC).

RESULTS

Maternal obesity was associated with lower socioeconomic status and higher paternal BMI (Table 1). It was also related to greater likelihood of smoking, being diagnosed with gestational diabetes or hypertension, and lower likelihood of alcohol intake, multivitamin use, and fish oil supplementation during pregnancy. Loss to follow-up was low (<6%) but responses differed by obesity status (Supplemental Table 6). A higher percentage of the children of obese women failed the ASQ than children of nonobese women.

In unadjusted analyses, maternal obesity (BMI ≥30) was associated with higher odds of failing most domains but only the fine motor domain remained significant after adjustment for covariates and paternal BMI (adjusted odds ratio [aOR] 1.67; 1.12–2.47) (Table 2). Associations of similar magnitude with the fine motor domain were observed among singletons (1.69; 1.10–2.58) and twins (1.97; 1.07–3.64; Supplemental Table 7). No associations were observed for the overweight category of prepregnancy BMI 25 to 30. Although associations reached significance at class II/III obesity category, risks were elevated for class I as well (aOR 1.60; 0.97–2.64), suggesting an overall association between obesity more generally (BMI ≥30) than only at higher levels (BMI ≥35). The fine motor association with maternal obesity also was similar among boys (aOR 1.63) and girls (aOR 1.61, *P*-interaction = .83).

We then evaluated paternal obesity (BMI ≥30) and found a significant increased risk of failing the personal-social domain (aOR 1.75; 1.13–2.71) compared with children of normal-weight fathers (Table 3). Neither further adjustment for maternal obesity (aOR 1.71; 1.08–2.70) nor replacing maternal covariates with paternal information (ie, paternal age, education, and race) (aOR 1.71;

TABLE 2 Associations (aOR [95% CI]) Between Maternal Obesity and ASQ Fails in the Primary Cohort of Upstate KIDS

	Unadjusted	Model 1[a]	Model 1[a] + paternal BMI
Overweight (25≤BMI<30)			
Any fail	1.04 (0.79–1.37)	0.98 (0.75–1.29)	0.99 (0.75–1.30)
Fine	1.32 (0.89–1.96)	1.23 (0.83–1.82)	1.24 (0.83–1.84)
Gross	0.84 (0.53–1.33)	0.81 (0.51–1.29)	0.86 (0.53–1.37)
Communication	1.36 (0.89–2.09)	1.30 (0.86–1.97)	1.28 (0.84–1.95)
Personal-social	1.35 (0.91–2.00)	1.20 (0.82–1.76)	1.13 (0.77–1.66)
Problem solving	1.34 (0.87–2.07)	1.29 (0.83–1.98)	1.24 (0.80–1.91)
Obese (BMI ≥30)			
Any fail	1.35 (1.03–1.77)[b]	1.20 (0.92–1.57)	1.20 (0.91–1.59)
Fine	1.90 (1.28–2.82)[b]	1.67 (1.12–2.47)[b]	1.67 (1.11–2.52)[b]
Gross	1.18 (0.75–1.87)	1.10 (0.69–1.76)	1.26 (0.77–2.07)
Communication	1.60 (1.05–2.45)[b]	1.42 (0.93–2.16)	1.38 (0.89–2.14)
Personal-Social	1.49 (1.01–2.20)[b]	1.21 (0.83–1.78)	1.05 (0.70–1.57)
Problem solving	1.46 (0.94–2.27)	1.25 (0.81–1.93)	1.15 (0.73–1.80)
Obese class I (30≤BMI<35)			
Any fail	1.18 (0.84–1.67)	1.08 (0.77–1.50)	1.08 (0.77–1.52)
Fine	1.78 (1.07–2.94)[b]	1.57 (0.96–2.57)	1.60 (0.97–2.64)
Gross	1.21 (0.69–2.14)	1.15 (0.65–2.05)	1.26 (0.70–2.26)
Communication	1.29 (0.76–2.20)	1.21 (0.71–2.04)	1.14 (0.66–1.96)
Personal-social	0.99 (0.59–1.66)	0.84 (0.51–1.41)	0.80 (0.47–1.35)
Problem solving	0.95 (0.54–1.69)	0.85 (0.48–1.50)	0.81 (0.45–1.45)
Obese class II (BMI ≥35)			
Any fail	1.55 (1.11–2.18)[b]	1.35 (0.96–1.90)	1.36 (0.95–1.93)
Fine	2.04 (1.24–3.34)[b]	1.77 (1.08–2.93)[b]	1.82 (1.09–3.04)[b]
Gross	1.15 (0.63–2.11)	1.06 (0.56–1.98)	1.24 (0.64–2.38)
Communication	2.00 (1.15–3.48)[b]	1.71 (0.98–2.96)	1.63 (0.93–2.86)
Personal-social	2.14 (1.33–3.46)[b]	1.68 (1.05–2.68)[b]	1.43 (0.88–2.32)
Problem solving	2.15 (1.24–3.73)[b]	1.75 (1.02–3.01)[b]	1.61 (0.91–2.83)

[a] Model 1 = adjusted for maternal age, race, education, insurance, married, previous live birth, and pregnancy smoking.
[b] $P < .05$.

TABLE 3 Adjusted Associations (OR [95% CI]) Between Paternal Obesity and ASQ Fails in Upstate KIDS

Father Obese (Father's BMI ≥30)	Primary Cohort	Singletons	Twins
Any fail	1.08 (0.80–1.44)	1.09 (0.80–1.47)	1.10 (0.63–1.91)
Fine	0.97 (0.62–1.51)	0.96 (0.61–1.51)	1.08 (0.52–2.28)
Gross	0.77 (0.46–1.28)	0.75 (0.44–1.28)	1.08 (0.49–2.37)
Communication	1.18 (0.73–1.91)	1.17 (0.71–1.94)	1.18 (0.61–2.29)
Personal-social	1.75 (1.13–2.71)[a]	1.76 (1.12–2.77)[a]	1.16 (0.54–2.48)
Problem solving	1.33 (0.81–2.19)	1.32 (0.79–2.20)	1.14 (0.53–2.43)

Models adjusted for maternal age, race, education, insurance, married/living as married, previous live birth, and pregnancy smoking.
[a] $P < .05$.

1.11–2.65) affected the results. This association was primarily among singletons (aOR 1.76; 1.12–2.77) rather than twins (aOR 1.16; 0.54–2.48). Both class I and class II paternal obesity had similar associations with the personal-social domain (aOR 1.70; 1.01–2.86 and 1.77; 0.93–3.34, among singletons, respectively). No sex interactions were observed (data not shown).

Children of 2 parents with class II/III obesity (BMI ≥35) had higher odds of failing multiple domains (ie, fine motor, personal-social, and problem solving) even after adjusting for covariates compared with children of normal/underweight parents (Table 4). When a BMI of 30 (ie, any obesity) was used instead of 35 (ie, class II/III obesity) for both parents, the fine motor and personal-social domains remained significantly associated with higher odds (aOR 2.10; 1.13–3.93 and 2.12; 1.14–3.95, respectively), but the problem-solving domain was not (aOR 1.58; 0.79–3.18). Because of the smaller numbers of twins, we could not conduct analysis among them with 9 parental obesity groups.

Compared with adequate GWG, inadequate GWG was associated with increased risk of failing any developmental domain (aOR 1.40; 1.02–1.91), particularly among singletons (Table 5). Further adjusting for birth weight reduced the association (aOR 1.21; 0.86–1.71). Domain-specific fails did not reach statistical significance unless restricted to mothers who were normal weight. Among normal-weight women, inadequate GWG was

TABLE 4 Adjusted (OR [95% CI]) Between Parental Obesity and ASQ Fails in Upstate KIDS

	n	Any Fail	Fine Motor	Gross Motor	Communication	Personal-Social	Problem Solving
Primary cohort							
1 (maternal <25 and paternal <25)	776	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
2 (maternal 25–35 and paternal <25)	444	1.18 (0.77–1.81)	2.38 (1.26–4.49)[a]	0.86 (0.41–1.81)	1.14 (0.57–2.27)	1.51 (0.78–2.92)	1.25 (0.61–2.56)
3 (maternal 35+ and paternal <25)	99	1.38 (0.61–3.14)	1.48 (0.48–4.60)	1.29 (0.29–5.85)	1.70 (0.42–6.91)	1.16 (0.29–4.62)	1.63 (0.43–6.12)
4 (maternal <25 and paternal 25–35)	1421	1.01 (0.72–1.42)	1.16 (0.68–2.01)	0.75 (0.42–1.35)	0.78 (0.44–1.40)	1.45 (0.83–2.53)	1.10 (0.60–2.02)
5 (maternal 25–35 and paternal 25–35)	1199	1.02 (0.72–1.43)	1.25 (0.73–2.15)	0.70 (0.39–1.26)	1.13 (0.65–1.97)	1.55 (0.91–2.66)	1.32 (0.74–2.37)
6 (maternal 35+ and paternal 25–35)	369	1.06 (0.64–1.73)	1.52 (0.70–3.26)	0.73 (0.29–1.83)	1.20 (0.54–2.67)	2.32 (1.16–4.64)[a]	1.70 (0.76–3.82)
7 (maternal <25 and paternal 35+)	117	1.23 (0.56–2.72)	0.97 (0.26–3.57)	0.38 (0.05–2.81)	1.84 (0.61–5.49)	3.33 (1.22–9.03)[a]	1.62 (0.44–5.95)
8 (maternal 25–35 and paternal 35+)	224	0.83 (0.45–1.54)	1.09 (0.43–2.76)	0.94 (0.35–2.50)	1.13 (0.45–2.85)	1.04 (0.42–2.58)	0.82 (0.25–2.67)
9 (maternal 35+ and paternal 35+)	163	2.13 (1.17–3.91)[a]	3.54 (1.54–8.15)[a]	1.04 (0.35–3.12)	2.15 (0.74–6.20)	3.16 (1.33–7.52)[a]	2.93 (1.09–7.85)[a]
Singletons							
1 (maternal <25 and paternal <25)	633	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
2 (maternal 25–35 and paternal <25)	357	1.16 (0.75–1.80)	2.39 (1.24–4.58)[a]	0.82 (0.38–1.77)	1.11 (0.54–2.30)	1.48 (0.74–2.94)	1.25 (0.60–2.60)
3 (maternal 35+ and paternal <25)	79	1.33 (0.56–3.15)	1.48 (0.46–4.73)	1.24 (0.26–5.92)	1.79 (0.43–7.47)	1.09 (0.25–4.87)	1.60 (0.41–6.27)
4 (maternal <25 and paternal 25–35)	1107	0.99 (0.69–1.41)	1.16 (0.66–2.04)	0.72 (0.40–1.33)	0.76 (0.41–1.39)	1.43 (0.80–2.56)	1.07 (0.57–2.00)
5 (maternal 25–35 and paternal 25–35)	933	1.00 (0.70–1.42)	1.23 (0.71–2.16)	0.69 (0.37–1.27)	1.14 (0.64–2.03)	1.57 (0.89–2.75)	1.30 (0.71–2.37)
6 (maternal 35+ and paternal 25–35)	273	1.03 (0.62–1.71)	1.49 (0.67–3.31)	0.72 (0.28–1.87)	1.19 (0.52–2.74)	2.32 (1.13–4.75)[a]	1.65 (0.71–3.83)
7 (maternal <25 and paternal 35+)	90	1.18 (0.51–2.71)	0.88 (0.20–3.77)	0.32 (0.03–3.48)	1.80 (0.57–5.74)	3.28 (1.15–9.32)[a]	1.57 (0.40–6.13)
8 (maternal 25–35 and paternal 35+)	162	0.80 (0.42–1.52)	1.08 (0.41–2.83)	0.93 (0.34–2.59)	1.15 (0.44–3.01)	1.00 (0.38–2.65)	0.79 (0.23–2.75)
9 (maternal 35+ and paternal 35+)	124	2.06 (1.10–3.86)[a]	3.47 (1.46–8.25)[a]	0.96 (0.30–3.12)	2.18 (0.73–6.56)	3.31 (1.36–8.02)[a]	3.00 (1.10–8.20)[a]

Models adjusted for maternal age, race, education, insurance, married/living as married, previous live birth, and pregnancy smoking.

[a] $P < .05$.

associated with gross motor (aOR 2.45; 1.29–4.65) and personal-social fails (aOR 1.87; 1.05–3.34). These associations were also not significant after additional adjustment for birth weight (data not shown). Excessive GWG was protective among twins for the communication domain (0.44; 0.21–0.89).

DISCUSSION

To our knowledge, Upstate KIDS is the first study in the United States to evaluate both paternal and maternal BMI with respect to early childhood development among singletons and twins. Given that the prevalence of obesity is approximately double in the United States[1] as in Europe,[38] and that class II/III obesity (BMI ≥35) in both parents may be most concerning, the relevance of findings to a US population is important. Inclusion of twins was also unique, as previous investigations frequently excluded them. Our findings show that maternal and paternal obesity may be differentially associated with developmental domains: maternal obesity being associated with fine motor skills and paternal with personal-social development. The latter association, however, was observed only among singletons and not twins. When both parents had BMI of ≥35, an additional association with the problem-solving domain emerged.

Our finding regarding maternal obesity and fine motor developmental delay agree with results from other cohorts, which evaluated children's development at a younger age.[13] Psychomotor scores (and only those reflecting fine motor) were inversely associated with maternal BMI and not for paternal BMI.[13] The study also found an inverse association with cognitive scores.[13] However, our findings do not support a previous US study on maternal obesity. Specifically, at 2 years (n = 6850), the study found

TABLE 5 GWG and ASQ Fails in Upstate KIDS

	Primary Cohort	Singletons	Twins
Inadequate GWG			
Any fail	1.40 (1.02–1.91)[a]	1.38 (0.99–1.93)	1.06 (0.70–1.59)
Fine	1.52 (0.98–2.37)	1.56 (0.97–2.50)	0.84 (0.49–1.42)
Gross	1.53 (0.91–2.59)	1.53 (0.87–2.68)	1.28 (0.71–2.31)
Communication	1.37 (0.84–2.23)	1.37 (0.80–2.33)	0.73 (0.45–1.18)
Personal-social	1.46 (0.93–2.29)	1.47 (0.91–2.39)	0.95 (0.56–1.60)
Problem solving	1.04 (0.62–1.72)	1.02 (0.59–1.75)	1.08 (0.61–1.92)
Excessive GWG			
Any fail	0.96 (0.74–1.24)	1.01 (0.77–1.32)	0.70 (0.40–1.23)
Fine	0.99 (0.68–1.46)	1.04 (0.70–1.55)	0.90 (0.47–1.74)
Gross	0.87 (0.56–1.35)	0.91 (0.58–1.45)	0.93 (0.43–2.01)
Communication	0.81 (0.54–1.20)	0.84 (0.55–1.28)	0.44 (0.21–0.89)[a]
Personal-social	1.10 (0.76–1.60)	1.15 (0.77–1.70)	0.95 (0.46–1.92)
Problem solving	0.79 (0.52–1.19)	0.81 (0.53–1.24)	0.53 (0.23–1.22)

Models adjusted for maternal age, race, education, insurance, married/living as married, previous live birth, and pregnancy smoking + Maternal Obesity (3 categories).
[a] $P < .05$.

no association with psychomotor development (encompassing fine and gross motor) but observed a relation with delayed mental development.[5] We had previously found that maternal obesity was associated with delayed developmental milestones, such as a longer time to sitting alone and crawling[39]; however, no associations were found with later milestones involving standing or walking alone.[39] The lack of longer-term association is consistent with our current investigations of gross motor development. Apart from these studies, many studies measured cognitive abilities,[7–9,11,12,17,20] such as IQ or autism spectrum disorder (ASD),[10,14,19,21] which are difficult to directly compare with our results, as these neurodevelopmental phenotypes were not assessed in this study. We did not observe increased odds of problem-solving domain fails until both paternal and maternal weight were in the obese class II/III categories. Contrarily, 2 European birth cohorts did not find consistent associations between maternal overweight and child cognition and behavior as measured by several validated instruments.[15] The difference in findings may be explained by their assessing overweight rather than obesity, even though the latter seems to be more indicative of long-term impact, suggesting a threshold effect.[6] Residual confounding remains an issue. A large linkage study in Sweden observed that maternal obesity was associated with risk of offspring autism but not after analyses were restricted to siblings, suggesting associations may not be causal and that familial risk factors that are incompletely controlled for may still play a role.[19] Alternatively, some studies have found that childhood obesity itself may be related to poorer cognitive development.[40]

The potential mechanisms explaining how maternal obesity may affect offspring development, largely drawn from animal evidence, has been previously reviewed.[3,4] Inflammation remains a leading explanation. As adipocytes accumulate fatty acids and become enlarged (ie, adipocyte hypertrophy), mechanisms respond to restrict their size, including upregulating immune cells, which lead to increased inflammatory cytokines in both maternal and fetal circulation.[4] In a sheep experiment, fetuses of obese ewes had increased circulation of free fatty acids coupled with upregulation of inflammatory genes in their placentas compared with controls.[41] To further understand causal relationships, interventions to counter inflammation through dietary modification among obese pregnant women has been suggested.[2]

With regard to paternal obesity, we had few studies to compare with and none in the United States. Of the studies abroad that have examined paternal and maternal BMI, findings were generally null[13] or were similar to maternal obesity with authors concluding associations were due to residual confounding.[12,15] Surén and colleagues[21] found paternal rather than maternal obesity to be more strongly associated with risk of ASD. Our results cannot be directly compared with previous studies because we evaluated different domains of development by using the ASQ, a validated screening rather than diagnostic tool. Nevertheless, our findings provide suggestive evidence for a differential role of paternal obesity on the personal-social domain (attributes close to those evidenced in ASD). Research in embryo development suggests that there are potential mechanisms through epigenetic alterations to sperm that could have downstream impact.[42] The presence of pleiotropic genes that increases risk of both ASD and obesity may also explain observations.[21] That there also may be synergistic influence of class II/III obesity in both parents remains to be replicated.

Apart from uniquely having information on paternal BMI, Upstate KIDS was able to adjust for major confounders, including socioeconomic status. As with any observational design, we cannot eliminate residual bias or other selection-related factors. However, the specificity of the associations for maternal and paternal obesity suggests that associations were not wholly attributed to a shared family environment.[25] We used a validated screening tool demonstrated to identify early developmental delays,[28,43] but did not have systematic developmental assessments of all children. The ASQ's sensitivity has varied (75%–100%) depending on instrument compared.[28,30,44] Intraclass correlations 0.75 to 0.82 were observed for parental test-retest reliability.[30] As such, we recognize that some children may be misclassified on development. We also recognize that delays may not be permanent, and some children may outgrow them. However, as a screening instrument, the ASQ has been shown to be clinically useful in a general population and that additional pediatrician input may not necessarily increase prediction of developmental delay.[45] It also has been shown to help potentially identify children for earlier intervention, even if not all children go on to be eligible for services.[43] Making the ASQ available online might have aided in receiving timely responses and follow-up. We did not measure adiposity directly but relied on birth certificates and maternal report to calculate BMI. Birth certificate reports were closer to time of delivery, decreasing the impact of time on recall and therefore used. Birth certificates may underestimate obesity,[46] but such misclassification would lead to an underestimation of the true effect. It remains possible that reporting errors may be higher for paternal BMI, as it was ascertained from mothers. Although there was loss to follow-up,[29] generalized linear mixed effects models are robust to such losses under the missing at random assumption.[34] Our population, which was predominantly non-Hispanic white and highly educated, may not be generalizable to all populations, but the prevalence of obesity in the cohort was comparable with national data.

CONCLUSIONS

In this first examination of maternal and paternal obesity in the United States on early childhood development, maternal obesity was associated with delays in fine motor development and paternal obesity marginally associated with delays in personal-social functioning. The impact of higher levels of parental obesity (ie, having both parents with BMI ≥35, which constituted 3% of our cohort) was most striking for multiple domains. Findings emphasize the importance of family information when screening child development as, if replicated elsewhere, such information may help inform closer monitoring or earlier intervention.

ACKNOWLEDGMENTS

The authors thank all the Upstate KIDS participants and staff for their important contributions.

ABBREVIATIONS

aOR: adjusted odds ratio
ASD: autism spectrum disorder
ASQ: Ages and Stages Questionnaire
CI: confidence interval
GWG: gestational weight gain
OR: odds ratio

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Supported by the Intramural Research Program of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (contracts HHSN275201200005C, HHSN267200700019C). The sponsor played no role in the study design, data collection, data analysis or interpretation, writing of the manuscript, or the decision to submit the article for publication. Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

1. Fisher SC, Kim SY, Sharma AJ, Rochat R, Morrow B. Is obesity still increasing among pregnant women? Prepregnancy obesity trends in 20 states, 2003–2009. *Prev Med*. 2013;56(6):372–378
2. Rivera HM, Christiansen KJ, Sullivan EL. The role of maternal obesity in the risk of neuropsychiatric disorders. *Front Neurosci*. 2015;9:194
3. van der Burg JW, Sen S, Chomitz VR, Seidell JC, Leviton A, Dammann O. The role of systemic inflammation linking maternal BMI to neurodevelopment in children. *Pediatr Res*. 2016;79(1–1):3–12
4. Segovia SA, Vickers MH, Gray C, Reynolds CM. Maternal obesity, inflammation, and developmental programming. *Biomed Res Int*. 2014;2014:418975
5. Hinkle SN, Schieve LA, Stein AD, Swan DW, Ramakrishnan U, Sharma AJ. Associations between maternal prepregnancy body mass index and child neurodevelopment at 2 years of age. *Int J Obes*. 2012;36(10):1312–1319
6. Hinkle SN, Sharma AJ, Kim SY, Schieve LA. Maternal prepregnancy weight status and associations with children's development and disabilities at kindergarten. *Int J Obes*. 2013;37(10):1344–1351

7. Tanda R, Salsberry PJ, Reagan PB, Fang MZ. The impact of prepregnancy obesity on children's cognitive test scores. *Matern Child Health J*. 2013;17(2):222–229
8. Huang L, Yu X, Keim S, Li L, Zhang L, Zhang J. Maternal prepregnancy obesity and child neurodevelopment in the Collaborative Perinatal Project. *Int J Epidemiol*. 2014;43(3):783–792
9. Pugh SJ, Richardson GA, Hutcheon JA, et al. Maternal obesity and excessive gestational weight gain are associated with components of child cognition. *J Nutr*. 2015;145(11):2562–2569
10. Jo H, Schieve LA, Sharma AJ, Hinkle SN, Li R, Lind JN. Maternal prepregnancy body mass index and child psychosocial development at 6 years of age. *Pediatrics*. 2015;135(5). Available at: www.pediatrics.org/cgi/content/full/135/5/e1198
11. Basatemur E, Gardiner J, Williams C, Melhuish E, Barnes J, Sutcliffe A. Maternal prepregnancy BMI and child cognition: a longitudinal cohort study. *Pediatrics*. 2013;131(1):56–63
12. Bliddal M, Olsen J, Støvring H, et al. Maternal pre-pregnancy BMI and intelligence quotient (IQ) in 5-year-old children: a cohort based study. *PLoS One*. 2014;9(4):e94498
13. Casas M, Chatzi L, Carsin AE, et al. Maternal pre-pregnancy overweight and obesity, and child neuropsychological development: two Southern European birth cohort studies. *Int J Epidemiol*. 2013;42(2):506–517
14. Li M, Fallin MD, Riley A, et al. The association of maternal obesity and diabetes with autism and other developmental disabilities. *Pediatrics*. 2016;137(2):e20152206
15. Brion MJ, Zeegers M, Jaddoe V, et al. Intrauterine effects of maternal prepregnancy overweight on child cognition and behavior in 2 cohorts. *Pediatrics*. 2011;127(1). Available at: www.pediatrics.org/cgi/content/full/127/1/e202
16. Torres-Espinola FJ, Berglund SK, García-Valdés LM, et al; PREOBE team. Maternal obesity, overweight and gestational diabetes affect the offspring neurodevelopment at 6 and 18 months of age—a follow up from the PREOBE Cohort. *PLoS One*. 2015;10(7):e0133010
17. Heikura U, Taanila A, Hartikainen AL, et al. Variations in prenatal sociodemographic factors associated with intellectual disability: a study of the 20-year interval between two birth cohorts in northern Finland. *Am J Epidemiol*. 2008;167(2):169–177
18. Gage SH, Lawlor DA, Tilling K, Fraser A. Associations of maternal weight gain in pregnancy with offspring cognition in childhood and adolescence: findings from the Avon Longitudinal Study of Parents and Children. *Am J Epidemiol*. 2013;177(5):402–410
19. Gardner RM, Lee BK, Magnusson C, et al. Maternal body mass index during early pregnancy, gestational weight gain, and risk of autism spectrum disorders: results from a Swedish total population and discordant sibling study. *Int J Epidemiol*. 2015;44(3):870–883
20. Neggers YH, Goldenberg RL, Ramey SL, Cliver SP. Maternal prepregnancy body mass index and psychomotor development in children. *Acta Obstet Gynecol Scand*. 2003;82(3):235–240
21. Surén P, Gunnes N, Roth C, et al. Parental obesity and risk of autism spectrum disorder. *Pediatrics*. 2014;133(5). Available at: www.pediatrics.org/cgi/content/full/133/5/e1128
22. Murphy SK. Obesity: Paternal obesity—a risk factor for autism? *Nat Rev Endocrinol*. 2014;10(7):389–390
23. McPherson NO, Fullston T, Aitken RJ, Lane M. Paternal obesity, interventions, and mechanistic pathways to impaired health in offspring. *Ann Nutr Metab*. 2014;64(3–4):231–238
24. Binder NK, Beard SA, Kaitu'u-Lino TJ, Tong S, Hannan NJ, Gardner DK. Paternal obesity in a rodent model affects placental gene expression in a sex-specific manner. *Reproduction*. 2015;149(5):435–444
25. Ness AR, Griffiths AE, Howe LD, Leary SD. Drawing causal inferences in epidemiologic studies of early life influences. *Am J Clin Nutr*. 2011;94(suppl 6):1959S–1963S
26. Buck Louis GM, Hediger ML, Bell EM, et al. Methodology for establishing a population-based birth cohort focusing on couple fertility and children's development, the Upstate KIDS Study. *Paediatr Perinat Epidemiol*. 2014;28(3):191–202
27. Institute of Medicine. *Weight Gain During Pregnancy: Reexamining the Guidelines*. Washington, DC: National Academies Press; 2009
28. Schonhaut L, Armijo I, Schönstedt M, Alvarez J, Cordero M. Validity of the Ages and Stages Questionnaires in term and preterm infants. *Pediatrics*. 2013;131(5). Available at: www.pediatrics.org/cgi/content/full/131/5/e1468
29. Yeung EH, Sundaram R, Bell EM, et al. Examining infertility treatment and early childhood development in the Upstate KIDS Study. *JAMA Pediatr*. 2016;170(3):251–258
30. Squires J, Bricker D. *Ages & Stages Questionnaires, Third Edition (ASQ-3)*. Baltimore, MD: Brookes Publishing; 2009
31. Squires J, Potter L, Bricker D. *The ASQ User's Guide for the Ages & Stages Questionnaires: A Parent-Completed, Child-Monitoring System*. Baltimore, MD: Paul. H. Brookes Publishing Co; 1999
32. Townsend P, Phillimore P, Beattie A, eds. *Health and Deprivation: Inequality and the North*. London, UK: Croom Helm; 1988
33. Eibner C, Sturm R. US-based indices of area-level deprivation: results from HealthCare for Communities. *Soc Sci Med*. 2006;62(2):348–359
34. Molenberghs GV. *Models for Discrete Longitudinal Data*. New York, NY: Springer Science+Business Media, Inc; 2006
35. Potijk MR, Kerstjens JM, Bos AF, Reijneveld SA, de Winter AF. Developmental delay in moderately preterm-born children with low socioeconomic status: risks multiply. *J Pediatr*. 2013;163(5):1289–1295
36. Julvez J, Ribas-Fitó N, Torrent M, Forns M, Garcia-Esteban R, Sunyer J. Maternal smoking habits and cognitive development of children at age 4 years in a population-based birth cohort. *Int J Epidemiol*. 2007;36(4):825–832

37. van Buuren SG-OK. Multivariate imputation by chained equations in R. *J Stat Softw*. 2011;45(3):1–67

38. Gallus S, Lugo A, Murisic B, Bosetti C, Boffetta P, La Vecchia C. Overweight and obesity in 16 European countries. *Eur J Nutr*. 2015;54(5):679–689

39. Wylie A, Sundaram R, Kus C, Ghassabian A, Yeung EH. Maternal prepregnancy obesity and achievement of infant motor developmental milestones in the upstate KIDS study. *Obesity (Silver Spring)*. 2015;23(4):907–913

40. Liang J, Matheson BE, Kaye WH, Boutelle KN. Neurocognitive correlates of obesity and obesity-related behaviors in children and adolescents. *Int J Obes*. 2014;38(4):494–506

41. Zhu MJ, Du M, Nathanielsz PW, Ford SP. Maternal obesity up-regulates inflammatory signaling pathways and enhances cytokine expression in the mid-gestation sheep placenta. *Placenta*. 2010;31(5):387–391

42. McPherson NO, Bell VG, Zander-Fox DL, et al. When two obese parents are worse than one! Impacts on embryo and fetal development. *Am J Physiol Endocrinol Metab*. 2015;309(6):E568–E581

43. Guevara JP, Gerdes M, Localio R, et al. Effectiveness of developmental screening in an urban setting. *Pediatrics*. 2013;131(1):30–37

44. Gollenberg AL, Lynch CD, Jackson LW, McGuinness BM, Msall ME. Concurrent validity of the parent-completed Ages and Stages Questionnaires, 2nd Ed. with the Bayley Scales of Infant Development II in a low-risk sample. *Child Care Health Dev*. 2010;36(4):485–490

45. Rydz D, Srour M, Oskoui M, et al. Screening for developmental delay in the setting of a community pediatric clinic: a prospective assessment of parent-report questionnaires. *Pediatrics*. 2006;118(4). Available at: www.pediatrics.org/cgi/content/full/118/4/e1178

46. Park S, Sappenfield WM, Bish C, Bensyl DM, Goodman D, Menges J. Reliability and validity of birth certificate prepregnancy weight and height among women enrolled in prenatal WIC program: Florida, 2005. *Matern Child Health J*. 2011;15(7):851–859

Parental Obesity and Early Childhood Development

Edwina H. Yeung, Rajeshwari Sundaram, Akhgar Ghassabian, Yunlong Xie and Germaine Buck Louis

Pediatrics 2017;139;; originally published online January 2, 2017;
DOI: 10.1542/peds.2016-1459

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Parental Obesity and Early Childhood Development

Edwina H. Yeung, Rajeshwari Sundaram, Akhgar Ghassabian, Yunlong Xie and Germaine Buck Louis

Pediatrics 2017;139;; originally published online January 2, 2017;
DOI: 10.1542/peds.2016-1459