Published in final edited form as:

Paediatr Perinat Epidemiol. 2010 May ; 24(3): 232–240. doi:10.1111/j.1365-3016.2010.01113.x.

Association of maternal prenatal depressive symptoms with child cognition at age 3 years

Alison C. Tse^a, Janet W. Rich-Edwards^{a,b,c}, Sheryl L. Rifas-Shiman^b, Matthew W. Gillman^{b,d}, and Emily Oken^b

^aDepartment of Epidemiology, Harvard School of Public Health

^bDepartment of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute

^cConnors Center for Women's Health and Gender Biology, Brigham and Women's Hospital

^dDepartment of Nutrition, Harvard School of Public Health

SUMMARY

We examined the association of prenatal depressive symptoms at mid-pregnancy with child cognition at age 3 years in Project Viva, a pre-birth cohort study of 1030 mother-child pairs in eastern Massachusetts. We measured maternal depressive symptoms using the Edinburgh Postnatal Depression Scale (EPDS), a self-report measure validated for use during pregnancy. Measures of child cognition included the Peabody Picture Vocabulary Test (PPVT) and the Wide Range Achievement of Visual Motor Abilities (WRAVMA). At mid-pregnancy, 81 mothers (7.9%) scored 13 or above on the EPDS, indicating probable depression. In the unadjusted model, children born to mothers with prenatal depressive symptoms had PPVT scores that were 3.8 points lower [95% confidence interval (CI) −7.1, −0.5]. With adjustment for sociodemographics, the association substantially attenuated [adjusted β for PPVT score = −0.7 (95% CI −3.6, 2.3)]. In both unadjusted and multivariable models, prenatal depressive symptoms were not associated with WRAVMA scores [adjusted β for total WRAVMA score = −0.5 (95% CI −3.0, 2.1)]. We found no evidence to suggest that maternal prenatal depression is independently associated with early child cognition.

INTRODUCTION

About one in every five women experiences depression during her lifetime.¹ The prevalence of depression in the perinatal period approaches, if not exceeds that among women in the general population. According to a recent meta-analysis, the prevalence of major and minor depression is 11.0% during the first trimester of pregnancy and 8.5% during the second and third trimesters.² Depressive symptoms or diagnosed depression during pregnancy have been associated in some studies with increased risk of spontaneous preterm birth,^{3, 4} reduced infant growth,⁵ and low birth weight,⁶ though not all data support such associations.^{7–9}

Limited extant data also suggest that prenatal depression may adversely affect child behavior. In a prospective study of 247 mother-child pairs, infants born to mothers with prenatal depressive symptoms had greater negative reactivity scores at 8 weeks of age when compared to those born to mothers without prenatal depressive symptoms, after controlling

for maternal postnatal psychological state and prenatal cortisol levels.¹⁰ In the Avon Longitudinal Study of Parents and Children (ALSPAC), maternal prenatal depressive symptoms at 18 and 32 weeks of pregnancy were associated with increased maternal report of child behavioral and emotional problems at age 4, independent of a number of covariates, including postpartum depression and markers of socioeconomic status (but not independent of prenatal anxiety).¹¹

In contrast to these consistent findings for behavioral outcomes, results for an association of prenatal depression with child cognition are conflicting, and few prospective studies have examined this topic. In a prospective study of 94 U.S. children evaluated at age 2 years, higher maternal prenatal depressive symptoms scores were associated with better mental and psychomotor development after adjustment for maternal education, infant sex, and postpartum depression.¹² Contrasting findings from ALSPAC suggested that persistent maternal prenatal depression (defined as depression at 18 and 32 weeks of gestation), but not prenatal depression at only one of these time points, was associated with slightly higher odds of developmental delay using a modified version of the Denver Developmental Screening Test at age 18 months (adjusted OR 1.34, 95% CI 1.11–1.62).¹³

There are several pathways by which maternal prenatal depression could influence child cognitive development. One hypothesis is that fetal programming might influence the fetal development of the hypothalamic pituitary adrenal axis (HPA axis).¹⁴ Studies in primates and rats suggest that maternal stress during sensitive periods of development may affect the prenatal programming of the fetal HPA axis. Prenatal depressive symptoms have been associated with elevated levels of plasma cortisol and corticotropin releasing hormone (CRH) in the mother.^{15, 16} Hormonal fluctuations during pregnancy associated with prenatal depression might lead to fetal programming of the fetal HPA axis, although this hypothesis is untested.

Mothers who are depressed during pregnancy may be more likely to practice unhealthy behaviors, including prenatal alcohol consumption^{17, 18} and smoking,^{19, 20} that might themselves affect child cognitive competence.^{21, 22} Shared predictors of prenatal maternal depression and child development, such as socioeconomic disadvantage could lead to a non-causal association between prenatal maternal depression and child development.^{23–25} Also previously associated with child development, prenatal anxiety is reportedly often comorbid with prenatal depression and thus too could act as a confounder.^{11, 26, 27} Prenatal depression is a strong predictor of postpartum depression,^{24, 26, 28} which itself has been associated with lower child cognitive development, perhaps due to poor maternal-child interactions.^{29, 30}

In the present study, our goal was to add to the limited literature surrounding prenatal depression and child cognitive development through the use of validated measures of prenatal depressive symptoms and child cognition, statistical control for multiple covariates, and a relatively large sample size. We hypothesized that prenatal depressive symptoms would be associated with poorer child cognition at age 3 years even after adjustment for potential confounders.

METHODS

Population and study design

The participants in this study were enrolled in Project Viva, a prospective pre-birth cohort study of 2128 mother-child pairs recruited from eight obstetric offices of Harvard Vanguard Medical Associates, a multi-specialty group practice in the Eastern Massachusetts area.³¹

Eligibility criteria for Project Viva included singleton pregnancy, enrollment no later than 22 weeks of gestation, intention to remain in the geographical area, and fluency in English.

We obtained informed consent, administered a brief interview, and provided a take-home self-administered questionnaire during the first study visit, which occurred following the initial prenatal clinical visit. We administered a brief interview and provided a questionnaire at the second study visit, which occurred at 26 to 28 weeks' gestation. Within 3 days after delivery, we briefly interviewed the mother and performed measurements on the newborn. Further maternal and child information was collected in person at age 6 months and via a mailed questionnaire at age one year. At age 3 years, we conducted an in-person study visit in the home or research office during which we conducted a developmental assessment. Institutional review boards from all participating sites approved the study.

Of the 1579 children eligible for the in-person study visit at age 3 years, 1263 completed the age 3 year study visit, of whom 1143 completed the Peabody Picture Vocabulary Test (PPVT) and/or the Wide Range Achievement of Visual Motor Abilities (WRAVMA). We excluded participants who were missing information on the Edinburgh Postnatal Depression Scale (EPDS) score at mid-pregnancy ($n=147$). We also excluded participants who were missing information on maternal education, maternal race, maternal PPVT score, or fetal growth ($n=18$). Following exclusions, the total sample sizes consisted of 1030 for the child PPVT score analysis and 990 for the child WRAVMA score analysis. Compared to the mothers excluded from this analysis, the women included in this analysis were less likely to have prenatal depressive symptoms (7.9% vs. 10.9%, $p<0.05$), and their infants had higher mean PPVT scores (104.4 vs. 100.0, $p<0.0001$) but similar WRAVMA scores (102.4 vs. 100.2, $p=0.08$). Mothers included in this analysis were also slightly older (mean age 32.6 vs. 31.1 years, $p<0.0001$) and more likely to have a college education (74% vs. 55%, $p<0.0001$) and a yearly household income of \$40,000 or more (90% vs. 79%, $p<0.0001$).

Prenatal depressive symptoms

Prenatal depression is a clinical diagnosis that can only be assigned using a diagnostic interview by a trained clinician. Though we were unable to clinically diagnose depression due to participant burden and cost in this large cohort, we used a standardized self-administered questionnaire to assess prenatal depressive symptoms. At the mid-pregnancy visit (mean=27.9, SD=2.0 weeks of gestation), we assessed prenatal depressive symptoms using the Edinburgh Postnatal Depression Scale (EPDS), a ten-item questionnaire that has been validated for use in the prenatal and postpartum periods and excludes somatic symptoms common to both normal pregnancy and depression.^{32, 33} We categorized women as having had depressive symptoms during pregnancy if they scored 13 or above on the EPDS at the mid-pregnancy visit, which indicates both major and minor forms of depression during pregnancy. Although the EPDS threshold for probable prenatal depression varies throughout the literature,³⁴ this cut-off has been used in this cohort^{15, 24} and other large cohorts that have measured prenatal and postpartum depressive symptoms^{26, 35}.

Child cognition

Trained research assistants blinded to the depression status of the mother assessed child cognition at age 3 years using the Peabody Picture Vocabulary Test (PPVT) and the Wide Range Assessment of Visual Motor Ability (WRAVMA) in either the child's home or a research office. The PPVT is an age-standardized measure of receptive vocabulary for use in children and adults aged 2.5 years and above.³⁶ PPVT scores correlate strongly with verbal and full scale IQ ($r\geq 0.90$) on the Weschler Intelligence Scale for Children-III.³⁶ The PPVT is standardized to have a mean score of 100 and standard deviation of 15 for each population of interest. The WRAVMA is an age-normed test of visual motor development which is

moderately correlated with IQ ($r \sim 0.60$) and is used in children and adults aged 3 years and above.³⁷ It consists of three tests of visual motor development: visual-spatial (matching test), visual-motor (drawing test), and the fine motor skills (pegboard test) which are used to generate a total standard score.³⁷ Previous work in this cohort demonstrated that the PPVT and WRAMA were sensitive to the effects of prenatal mercury exposure and fish consumption.³⁸

Covariates

We measured covariates using a combination of questionnaires and interviews. We collected self-reported maternal race/ethnicity, age, education, parity, household income, pregnancy intention, partnership status, partner education, alcohol use, and smoking habits at the time of study enrollment. Pregnancy intention was assessed with the following question: 'Regarding this pregnancy (a) I was actively trying to become pregnant (b) I was not actively trying, but I was glad to become pregnant (c) I wanted to be pregnant someday, but not now; or (d) I did not want to be pregnant now or at any time in the future'. To measure pregnancy related anxiety, we included a self-report scale that used 7 of the 10 items previously used by Rini et al.³⁹ in the questionnaire at enrollment. The seven items included asked women about concerns such as the baby's growth and development, having a hard or difficult labor, developing medical problems during pregnancy, and fear regarding the health of the baby.

We calculated gestation length from the last menstrual period, or from the second trimester ultrasound if the two estimated differed by greater than 10 days. Data on child sex, birth weight, and delivery date were obtained from the medical record. We derived birth weight for gestational age z-value (fetal growth) based on US national reference data.⁴⁰ Depressive symptoms were assessed at 6 months postpartum using the EPDS. We also queried mothers about social support from family and friends at 6 months postpartum and breastfeeding duration, maternal employment, and child daycare attendance at 12 months postpartum. We measured maternal PPVT score at the 3-year study visit.

Analysis

We first examined the distribution of prenatal depressive symptoms by parental and child characteristics by comparing percentages for categorical covariates and means for continuous covariates. We then used multivariate linear regression to assess the associations of prenatal depressive symptoms with child cognition scores while controlling for covariates.

In addition to prenatal depressive symptoms, we included maternal PPVT score and child age, primary language, and sex in our first model, based upon the reasoning that these factors would be immutable predictors of child cognition. Because our primary aim was to determine the independent association of prenatal depressive symptoms with child cognition, we next included variables that we hypothesized might act as confounders a priori, focusing particularly on maternal and child characteristics that have been independently associated with both prenatal depression and child cognition in previous studies. We thus controlled for sociodemographics of the family (i.e. household income, maternal education, race/ethnicity, and age, and partner status and education) and pregnancy related factors (i.e. pregnancy intention and parity). We added as a group these potential confounders in this second model. We then later removed each of these confounders one by one from the model to determine which of these variables acted as the largest confounder in our associations of interest. Because further adjustment for maternal employment and daycare attendance at one year and social support at six months did not change our estimates for prenatal depressive symptoms substantially, we did not include them in our models. Similarly, we did not

include pregnancy related anxiety in our models because it did not change our point estimates for prenatal depressive symptoms markedly when we added it to our confounder adjusted models.

Finally, in model 3, we further adjusted for potential pathway variables, namely fetal growth, gestational age, alcohol use, prenatal smoking, breastfeeding, and postpartum depression to examine whether any observed association between prenatal depression and child cognition might be mediated through these factors. Prenatal depression was hypothesized to influence child cognition through each of these potential pathways variables added in model 3. In contrast, those predictors of child cognition such as parental education and parity that occurred prior to prenatal depression were likely confounders and not intermediates in the pathway.

To test whether associations between prenatal depressive symptoms and child cognition scores differed by socioeconomic position, we added cross-product terms between prenatal depressive symptoms and maternal education to our confounder adjusted model (model 2). In secondary analyses, we treated the EPDS as a continuous score and next used a cut-off of 15 or above in our fully adjusted models to test the sensitivity of our results to varying definitions of prenatal depressive symptoms.

RESULTS

In our study population, 23% of mothers were non-white, 95% were married or cohabiting, and 74% were college graduates (Table 1). Mean (SD) maternal age was 32.6 (4.8) years. At mid-pregnancy, 81 women (8%) scored 13 or above on the EPDS, indicating the presence of prenatal depressive symptoms. As previously reported in this study population, 24 women with a lower income, younger age, unwanted pregnancy, and single partner status had a higher prevalence of prenatal depressive symptoms. The presence of prenatal depressive symptoms was also associated with postpartum depressive symptoms. Although white mothers were less likely than non-white mothers to have prenatal depressive symptoms, we previously demonstrated that this differential was explained by the higher socioeconomic position of the white mothers. 24

Mean (SD) child PPVT score was 104.4 (14.5) and mean (SD) child WRAVMA total score was 102.4 (11.3). As described in earlier work, child characteristics that were associated with lower cognition scores included first born child, higher fetal growth (birth weight adjusted for gestational age), female sex, and older age at testing, though many of the confidence intervals overlapped. 38

In the unadjusted model (Table 2), children born to mothers who had prenatal depressive symptoms had PPVT scores that were 3.8 points lower than those born to mothers who did not have prenatal depressive symptoms [95% confidence interval (CI) -7.1, -0.5]. When we adjusted for child age, sex, primary language, and maternal PPVT score, the association only attenuated marginally [$\beta = -3.3$ (95% CI -6.3, -0.2)]. However, when we further adjusted for parental demographics, we observed marked attenuation of the association [$\beta = -0.7$ (95% CI -3.6, 2.3)]. By removing each of the sociodemographic confounders separately, we found that parity, followed by partner education, changed the strength of the association the most (data not shown). In our final model, adjustment for potential pathway variables did not materially alter the association (Table 2).

We observed no association between prenatal depressive symptoms and WRAVMA total scores in either the unadjusted or adjusted models (Table 2). Furthermore, prenatal depressive symptoms were not associated with the visual-spatial, visual-motor, or fine motor

skills subtests of the WRAVMA in either the adjusted or unadjusted models (data not shown).

When we added cross-product terms between prenatal depressive symptoms and maternal education to our confounder adjusted models, we found p-values for the global test of significance of these interaction terms that were insignificant for both the WRAVMA ($p=0.54$) and PPVT ($p=0.31$). In secondary analyses when we treated EPDS at mid-pregnancy as a continuous score, we did not find associations with total PPVT score [fully adjusted $\beta = -0.2$ (95% CI $-0.4, 0.02$)] or total WRAVMA score [fully adjusted $\beta = -0.1$ (95% CI $-0.3, 0.1$)]. When we used a cut-off of 15 or above on the EPDS at mid-pregnancy to define the presence of prenatal depressive symptoms, we also found similar results to when we used a cut-off of 13 or above [fully adjusted β for total PPVT = -0.7 (95% CI $-4.4, 3.0$), fully adjusted β for total WRAVMA = -1.3 (95% CI $-4.5, 1.9$)].

DISCUSSION

In this study of over 1000 mother-child pairs, we found an apparent association between prenatal maternal depressive symptoms at mid-pregnancy and child receptive vocabulary that was almost entirely explained by sociodemographic characteristics of the family. We found no associations between prenatal depressive symptoms and measures of visual motor ability.

Our findings do not support our original hypothesis of an independent association of prenatal depressive symptoms with decreased child cognition. The strongest sociodemographic confounder in the association between prenatal depressive symptoms and child PPVT scores was parity. Higher birth order has been reported widely in the literature as a predictor of lower cognition scores.⁴¹ However, the causal nature of these findings has been debated as more recent research comparing the IQs of children of different birth order within families suggests that previous study findings may have been due to confounding by factors that vary between families, such as SES, maternal health, and family size.⁴¹⁻⁴²

One possible explanation for lower PPVT scores in children born to mothers who had depressive symptoms during pregnancy may have been, at least in part, a result of socioeconomic disadvantage rather than prenatal depression per se. In support of this, partner education appeared to change the estimates of the association between prenatal depressive symptoms and child PPVT scores to a degree that was second in magnitude only to parity. Several studies have reported an association between socioeconomic position and childhood cognition (as measured by IQ) independent of confounding by pregnancy characteristics and birth weight.^{23, 25} Previous research suggests that the association between socioeconomic disadvantage and poorer child cognitive development may be mediated by decreased cognitive stimulation, parenting style, physical environment of the home, or poor child health at birth.⁴³ However, we were unable to test the impact of home environment and other such factors on child development in this large cohort.

A sparse literature exists with which to compare the results of our study. In a small ($n=94$) prospective study of well-nourished and financially stable women, depressive symptoms at 24 weeks gestation were assessed using a composite of the depression subscale of Profile of Moods Scale (POMS) and the Center for Epidemiological Studies Depression Scale (CES-D).¹² In that analysis, which did not adjust for socioeconomic factors other than maternal education, more depressive symptoms were associated with higher scores on both the Mental Development Index and Psychomotor Development Index of the Bayley Scales of Infant Development at age 2 years. The authors hypothesized that mild to moderate levels of psychological distress might have led to enhanced fetal development in healthy populations.

Differences between our findings and those of DiPietro and colleagues may be due to their use of a measure of depressive symptoms which has not been validated for use in pregnant women and which contains items that overlap with symptoms of a normal, healthy pregnancy. In contrast, we used the Edinburgh Postnatal Depression Scale, which focuses on the cognitive and affective symptoms of depression, avoiding the loss of specificity that may result from emphasis on physical symptoms common to normal pregnancy.^{3, 32, 33} Our findings also contrast with those from ALSPAC, in which having elevated EPDS scores at both 18 and 32 months of gestation (but not at a single time point) was associated with lower scores on a modified version of the Denver Developmental Screening Test at age 18 months.¹³ However, this measure of child development was based on maternal self-report, which might be susceptible to reporter bias since depressed mothers might be less likely to accurately report or recognize their child's abilities. In contrast, we used the PPVT, and the WRAVMA, standardized instruments of child cognition that were both conducted by trained research assistants.

In Project Viva, the majority of mothers were relatively well educated and of higher incomes. Thus, the results of this study may not generalize to more disadvantaged children, who may not have the same opportunities to catch up developmentally during early life. In addition the results of this study may not generalize to the geographic area of Project Viva participants or the overall U.S. population since study participants are not necessarily representative of these populations. Although it was not feasible for us to assess depression status with a clinical interview in this large study, we used the Edinburgh Postnatal Depression Scale, a measure of depressive symptoms validated for use during pregnancy. We also controlled for confounding by a number of sociodemographic, behavioral, and clinical factors, allowing us to assess the association of prenatal depression with early child cognition independent of these factors. Another notable strength of our study is its large sample size, which would have increased our ability to detect an association if one were present.

However, our study has several potential limitations. We only measured prenatal depressive symptoms at a single time point. We may thus have missed some mothers with depression that occurred at an earlier or later time. This may warrant further research since the timing of prenatal insults on fetal neurodevelopment may be important.⁴⁴ By measuring depressive symptoms at mid-pregnancy, we also did not take into account the duration of depression during pregnancy. The severity and duration of depressive symptoms during pregnancy may play an important role in child development.⁴⁵ As in the case with all observational studies, we were unable to adjust for all potential factors that might influence child cognition. We adjusted for postnatal depression only at age 6 months, which is notable because postpartum depression at later time points has been associated with cognitive, emotional, and behavioral outcomes.^{46, 47} In addition, while we adjusted for pregnancy related anxiety, we did not have information on general anxiety during pregnancy. We cannot rule out the possibility of selection bias as the women included in our study were less likely to have prenatal depressive symptoms as compared to the entire cohort. However, in order for such attrition to have caused bias, this loss to follow-up must also have been jointly dependent on child cognition scores, which is not empirically verifiable.

CONCLUSIONS

We found no evidence that prenatal depressive symptoms assessed at about 28 weeks of gestation were independently associated with child cognitive development at age 3 years. Our findings suggest that prenatal depressive symptoms are unlikely to negatively affect the cognitive development of their children. Future studies should be conducted to examine the

impact of duration, timing, and severity of prenatal depression on child cognition using both validated measures of maternal depressive symptoms and child cognitive development.

Acknowledgments

FUNDING

This work was supported by the National Institutes of Health [grant numbers HD34568, HL69425, HL77504, and HL68041].

REFERENCES

1. Kessler RC, McGonagle KA, Swartz M, Blazer DG, Nelson CB. Sex and depression in the National Comorbidity Survey. I: Lifetime prevalence, chronicity and recurrence. *Journal of Affective Disorders*. 1993; 29:85–96. [PubMed: 8300981]
2. Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression: a systematic review of prevalence and incidence. *Obstetrics and Gynecology*. 2005; 106:1071–1083. [PubMed: 16260528]
3. Dayan J, Creveuil C, Marks MN, Conroy S, Herlicoviez M, Dreyfus M, et al. Prenatal depression, prenatal anxiety, and spontaneous preterm birth: a prospective cohort study among women with early and regular care. *Psychosomatic Medicine*. 2006; 68:938–946. [PubMed: 17079701]
4. Orr ST, James SA, Blackmore Prince C. Maternal prenatal depressive symptoms and spontaneous preterm births among African-American women in Baltimore, Maryland. *American Journal of Epidemiology*. 2002; 156:797–802. [PubMed: 12396996]
5. Stewart RC. Maternal depression and infant growth: a review of recent evidence. *Maternal and Child Nutrition*. 2007; 3:94–107. [PubMed: 17355442]
6. Paarlberg KM, Vingerhoets AJ, Passchier J, Dekker GA, Heinen AG, van Geijn HP. Psychosocial predictors of low birthweight: a prospective study. *British Journal of Obstetrics and Gynaecology*. 1999; 106:834–841. [PubMed: 10453835]
7. Berle JO, Mykletun A, Daltveit AK, Rasmussen S, Holsten F, Dahl AA. A linkage study from The Nord-Trøndelag Health Study (HUNT) and Medical Birth Registry of Norway. Neonatal outcomes in offspring of women with anxiety and depression during pregnancy. *Archives of Women's Mental Health*. 2005; 8:181–189.
8. Suri R, Altshuler L, Hellemann G, Burt VK, Aquino A, Mintz J. Effects of antenatal depression and antidepressant treatment on gestational age at birth and risk of preterm birth. *The American Journal of Psychiatry*. 2007; 164:1206–1213. [PubMed: 17671283]
9. Andersson L, Sundstrom-Poromaa I, Wulff M, Astrom M, Bixo M. Neonatal outcome following maternal antenatal depression and anxiety: a population-based study. *American Journal of Epidemiology*. 2004; 159:872–881. [PubMed: 15105180]
10. Davis EP, Glynn LM, Schetter CD, Hobel C, Chiciz-Demet A, Sandman CA. Prenatal exposure to maternal depression and cortisol influences infant temperament. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2007; 46:737–746. [PubMed: 17513986]
11. O'Connor TG, Heron J, Glover V. Antenatal anxiety predicts child behavioral/emotional problems independently of postnatal depression. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2002; 41:1470–1477. [PubMed: 12447034]
12. DiPietro JA, Novak MF, Costigan KA, Atella LD, Reusing SP. Maternal psychological distress during pregnancy in relation to child development at age two. *Child Development*. 2006; 77:573–587. [PubMed: 16686789]
13. Deave T, Heron J, Evans J, Emond A. The impact of maternal depression in pregnancy on early child development. *BJOG : An International Journal of Obstetrics and Gynaecology*. 2008; 115:1043–1051. [PubMed: 18651886]
14. Mulder EJ, Robles de Medina PG, Huizink AC, Van den Bergh BR, Buitelaar JK, Visser GH. Prenatal maternal stress: effects on pregnancy and the (unborn) child. *Early Human Development*. 2002; 70:3–14. [PubMed: 12441200]

15. Rich-Edwards JW, Mohllajee AP, Kleinman K, Hacker MR, Majzoub J, Wright RJ, et al. Elevated mid-pregnancy corticotropin-releasing hormone is associated with prenatal, but not postpartum, maternal depression. *The Journal of Clinical Endocrinology and Metabolism*. 2008; 93(5):1946–1951. [PubMed: 18303075]
16. Lundy BI, Jones NA, Field T, Nearing G, Davalos M, Pietro P, et al. Prepartum depression effects on neonates. *Infant Behavior and Development*. 1999; 22:121–137.
17. Marcus SM, Flynn HA, Blow FC, Barry KL. Depressive symptoms among pregnant women screened in obstetrics settings. *Journal of Women's Health*. 2003; 12:373–380.
18. Pajulo M, Savonlahti E, Sourander A, Helenius H, Piha J. Antenatal depression, substance dependency and social support. *Journal of Affective Disorders*. 2001; 65:9–17. [PubMed: 11426516]
19. Orr ST, Newton E, Tarwater PM, Weismiller D. Factors associated with prenatal smoking among black women in eastern North Carolina. *Maternal Child Health Journal*. 2005; 9:245–252.
20. Zhu SH, Valbo A. Depression and smoking during pregnancy. *Addictive Behaviors*. 2002; 27:649–658. [PubMed: 12188598]
21. Willford J, Leech S, Day N. Moderate prenatal alcohol exposure and cognitive status of children at age 10. *Alcoholism, Clinical and Experimental Research*. 2006; 30:1051–1059.
22. Olds DL, Henderson CR Jr, Tatelbaum R. Intellectual impairment in children of women who smoke cigarettes during pregnancy. *Pediatrics*. 1994; 93:221–227. [PubMed: 8121734]
23. Tong S, Baghurst P, Vimpani G, McMichael A. Socioeconomic position, maternal IQ, home environment, and cognitive development. *The Journal of Pediatrics*. 2007; 151:284–288. [PubMed: 17719939]
24. Rich-Edwards JW, Kleinman K, Abrams A, Harlow BL, McLaughlin TJ, Joffe H, et al. Sociodemographic predictors of antenatal and postpartum depressive symptoms among women in a medical group practice. *Journal of Epidemiology and Community Health*. 2006; 60:221–227. [PubMed: 16476752]
25. Lawlor DA, Batty GD, Morton SM, Deary IJ, Macintyre S, Ronalds G, et al. Early life predictors of childhood intelligence: evidence from the Aberdeen children of the 1950s study. *Journal of Epidemiology and Community Health*. 2005; 59:656–663. [PubMed: 16020642]
26. Heron J, O'Connor TG, Evans J, Golding J, Glover V. The course of anxiety and depression through pregnancy and the postpartum in a community sample. *Journal of Affective Disorders*. 2004; 80:65–73. [PubMed: 15094259]
27. Brouwers EPM, van Baar AL, Pop VJM. Maternal anxiety during pregnancy and subsequent infant development. *Infant Behavior and Development*. 2001; 24:95–106.
28. O'hara MW, Swain AM. Rates and risk of postpartum depression—a metaanalysis. *International Review of Psychiatry*. 1996; 8:37–54.
29. Grace SL, Evindar A, Stewart DE. The effect of postpartum depression on child cognitive development and behavior: a review and critical analysis of the literature. *Archive of Women's Mental Health*. 2003; 6:263–274.
30. Murray L, Fiori-Cowley A, Hooper R, Cooper P. The impact of postnatal depression and associated adversity on early mother-infant interactions and later infant outcome. *Child Development*. 1996; 67:2512–2526. [PubMed: 9022253]
31. Gillman MW, Rich-Edwards JW, Rifas-Shiman SL, Lieberman ES, Kleinman KP, Lipshultz SE. Maternal age and other predictors of newborn blood pressure. *The Journal of Pediatrics*. 2004; 144:240–245. [PubMed: 14760269]
32. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *The British Journal of Psychiatry*. 1987; 150:782–786. [PubMed: 3651732]
33. Murray DM, Cox JL. Screening for depression during pregnancy with the Edinburgh depression scale. *Journal of Reproductive and Infant Psychology*. 1993; 11:119–125.
34. Matthey S, Henshaw C, Elliott S, Barnett B. Variability in use of cut-off scores and formats on the Edinburgh Postnatal Depression Scale: implications for clinical and research practice. *Archive of Women's Mental Health*. 2006; 9:309–315.

35. Milgrom J, Gemmill AW, Bilszta JL, Hayes B, Barnett B, Brooks J, et al. Antenatal risk factors for postnatal depression: a large prospective study. *Journal of Affective Disorders*. 2008; 108:147–157. [PubMed: 18067974]
36. Dunn, LM.; Dunn, LM.; American Guidance, S. PPVT-III : Peabody Picture Vocabulary Test. Circle Pines Minn: American Guidance Service; 1997.
37. Adams, W.; Sheslow, D. Wide Range Assessment of Visual Motor Abilities. Wilmington, DE: Wide Range, Inc.; 1995.
38. Oken E, Radesky JS, Wright RO, Bellinger DC, Amarasiriwardena CJ, Kleinman KP, et al. Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort. *American Journal of Epidemiology*. 2008; 167:1171–1181. [PubMed: 18353804]
39. Rini CK, Dunkel-Schetter C, Wadhwa PD, Sandman CA. Psychological adaptation and birth outcomes: the role of personal resources, stress, and sociocultural context in pregnancy. *Health Psychology*. 1999; 18:333–345. [PubMed: 10431934]
40. Oken E, Kleinman KP, Rich-Edwards J, Gillman MW. A nearly continuous measure of birth weight for gestational age using a United States national reference. *BMC Pediatrics*. 2003; 3:6. [PubMed: 12848901]
41. Rodgers JL. What causes birth order-intelligence patterns? The admixture hypothesis, revived. *The American Psychologist*. 2001; 56:505–510. [PubMed: 11413874]
42. Wichman AL, Rodgers JL, MacCallum RC. A multilevel approach to the relationship between birth order and intelligence. *Personality and Social Psychology Bulletin*. 2006; 32:117–127. [PubMed: 16317193]
43. Guo G, Harris KM. The mechanisms mediating the effects of poverty on children's intellectual development. *Demography*. 2000; 37:431–447. [PubMed: 11086569]
44. Talge NM, Neal C, Glover V. Antenatal maternal stress and long-term effects on child neurodevelopment: how and why? *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2007; 48:245–261.
45. Brennan PA, Hammen C, Andersen MJ, Bor W, Najman JM, Williams GM. Chronicity, severity, and timing of maternal depressive symptoms: relationships with child outcomes at age 5. *Developmental Psychology*. 2000; 36:759–766. [PubMed: 11081699]
46. Stein A, Malmberg LE, Sylva K, Barnes J, Leach P. The influence of maternal depression, caregiving, and socioeconomic status in the post-natal year on children's language development. *Child: Care, Health, and Development*. 2008; 34:603–612.
47. Murray L, Sinclair D, Cooper P, Ducournau P, Turner P, Stein A. The socioemotional development of 5-year-old children of postnatally depressed mothers. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 1999; 40:1259–1271.

Table 1

Parental and child characteristics according to prenatal depressive symptoms at mid-pregnancy among 1030 mother-child pairs in Project Viva. ^a

	Overall	Prenatal depressive symptoms	
	(n = 1030)	Yes (EPDS score ≥ 13) (n = 81)	No (EPDS score <13) (n = 949)
	Mean (SD) or n (%)	Mean (SD) or %	Mean (SD) or %
Parental characteristics			
Maternal education			
High school or less	61(6%)	10%	6%
Some college	204 (20%)	25%	19%
Bachelor's degree	338 (38%)	31%	38%
Graduate degree	377 (37%)	35%	37%
Annual household income			
≤\$40,000	102 (10%)	26%	9%
\$40,001–70,000	223 (23%)	26%	23%
≥\$70,001	655 (67%)	47%	68%
Maternal race/ethnicity			
Black	102 (10%)	17%	10%
Hispanic	42 (4%)	7%	4%
Other	91 (9%)	11%	9%
White	790 (78%)	64%	78%
Maternal age (years)	32.6 (4.8)	31.3 (5.6)	32.7 (4.7)
Maternal PPVT score	106.6 (14.3)	105.3 (16.5)	106.7 (14.2)
Maternal smoking			
Former	221 (22%)	14%	23%
Smoked during pregnancy	97 (10%)	14%	9%
Never	693 (69%)	72%	68%
Alcohol use			
Any during pregnancy	122 (12%)	10%	12%
None	893 (88%)	90%	88%
Parity			
Multiparous	529 (51%)	54%	51%
Primiparous	501 (49%)	46%	49%
Pregnancy intention			
Trying to become pregnant	672 (67%)	57%	68%
Not trying but glad	279 (28%)	28%	28%
Wanted someday but not now	36 (4%)	9%	3%
Did not want ever	14 (1%)	7%	1%
Postpartum depressive symptoms at 6 months			

	Overall	Prenatal depressive symptoms	
	(<i>n</i> = 1030)	Yes (EPDS score ≥ 13) (<i>n</i> = 81)	No (EPDS score < 13) (<i>n</i> = 949)
	Mean (SD) or <i>n</i> (%)	Mean (SD) or %	Mean (SD) or %
No (EPDS score ≥ 13)	824 (93%)	74%	94%
Yes (EPDS score < 13)	63 (7%)	26%	6%
Partner status			
Not married or cohabiting	52 (5%)	20%	4%
Married or cohabiting	978 (95%)	80%	96%
Partner education			
High school or less	103 (11%)	11%	11%
Some college	177 (18%)	17%	18%
Bachelor's degree	367 (38%)	32%	38%
Graduate degree	323 (33%)	41%	33%
Child characteristics			
Gestational age			
< 37 weeks	58 (6%)	5%	6%
≥ 37 weeks	972 (94%)	95%	94%
Fetal growth (z-value)	0.25 (0.92)	0.20 (0.93)	0.25 (0.92)
Age at testing (months)	39.3 (3.5)	39.3 (4.3)	39.3 (3.4)
Sex			
Male	502 (49%)	47%	49%
Female	528 (51%)	53%	51%
Primary language			
Other language	29 (3%)	4%	3%
English	1001 (97%)	96%	97%
Breastfeeding duration			
≤ 1 month	199 (20%)	23%	20%
1 to <6 months	244 (25%)	22%	25%
6 to <12 months	278 (28%)	22%	28%
≥ 12 months	276 (28%)	34%	27%

EPDS, Edinburgh Postnatal Depression Scale; PPVT, Peabody Picture Vocabulary Test.

^a Participant numbers do not always add up to total sample size due to missing values.

Table 2

Associations of maternal prenatal depressive symptoms with child cognition test scores at age 3 years.

Model	Difference in mean PPVT score ^a (95% confidence interval)	Difference in mean total WRAVMA score ^b (95% confidence interval)
Unadjusted: Prenatal depressive symptoms	-3.8 (-7.1, -0.5)	-1.4 (-4.0, 1.2)
Model 1: Prenatal depressive symptoms + child sex + child age + child primary language ^b + maternal PPVT score	-3.3 (-6.3, -0.2)	-1.4 (-3.9, 1.1)
Model 2: Model 1 + maternal education + maternal race + maternal age + household income + parity + pregnancy intention + partner status of the mother + partner education	-0.7 (-3.6, 2.3)	-0.5 (-3.0, 2.1)
Model 3: Model 2 + postpartum depressive symptoms + breastfeeding duration + gestational age + fetal growth + prenatal smoking + prenatal alcohol use	-1.0 (-3.9, 1.9)	-0.6 (-3.1, 1.9)

PPVT, Peabody Picture Vocabulary Test; WRAVMA, Wide Range Assessment of Visual Motor Abilities.

^a Difference refers to linear regression coefficient comparing children born to mothers who had prenatal depressive symptoms [Edinburgh Postnatal Depression Scale (EPDS) at mid-pregnancy ≥ 13] vs. children born to mothers who did not have prenatal depressive symptoms (EPDS at mid-pregnancy < 13).

^b Child primary language not included in the WRAVMA models.