Archival Report

Biological Psychiatry

# Prepartum and Postpartum Maternal Depressive Symptoms Are Related to Children's Brain Structure in Preschool

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## ABSTRACT

**BACKGROUND:** Perinatal maternal depression is a serious health concern with potential lasting negative consequences for children. Prenatal depression is associated with altered brain gray matter in children, though relations between postpartum depression and children's brains and the role of white matter are unclear.

**METHODS:** We studied 52 women who provided Edinburgh Postnatal Depression Scale (EPDS) scores during each trimester of pregnancy and at 3 months postpartum and their children who underwent magnetic resonance imaging at age 2.6 to 5.1 years. Associations between maternal depressive symptoms and magnetic resonance imaging measures of cortical thickness and white matter structure in the children were investigated.

**RESULTS:** Women's second trimester EPDS scores negatively correlated with children's cortical thickness in right inferior frontal and middle temporal regions and with radial and mean diffusivity in white matter emanating from the inferior frontal area. Cortical thickness, but not diffusivity, correlations survived correction for postpartum EPDS. Postpartum EPDS scores negatively correlated with children's right superior frontal cortical thickness and with diffusivity in white matter originating from that region, even after correcting for prenatal EPDS.

**CONCLUSIONS:** Higher maternal depressive symptoms prenatally and postpartum are associated with altered gray matter structure in children; the observed white matter correlations appear to be uniquely related to the postpartum period. The reduced thickness and diffusivity suggest premature brain development in children exposed to higher maternal perinatal depressive symptoms. These results highlight the importance of ensuring optimal women's mental health throughout the perinatal period, because maternal depressive symptoms appear to increase children's vulnerability to nonoptimal brain development.

*Keywords:* Brain development, Diffusion imaging, Magnetic resonance imaging, Maternal depression, Postpartum, Pregnancy

http://dx.doi.org/10.1016/j.biopsych.2015.12.004

Depression is common during the perinatal period, with approximately 18% of women experiencing depression sometime during pregnancy (7% to 13% per trimester), and 13% reporting postpartum depression (1–5). Exposure to prenatal and/or postnatal maternal depression is associated with negative child outcomes, including increased risk for poor emotional regulation, mental health problems, and cognitive, behavior, or motor delays (6–11). Though many effects of prenatal depression are attenuated after controlling for postpartum depression (12), prenatal depressive symptoms are independently associated with lower intelligence (13) and behavioral problems (14–16) in children. Relations between perinatal depression and many child outcomes are moderated by socioeconomic status and sex; male and female children of mothers who experience stress during pregnancy exhibit different outcomes (17–19), and children from families of high socioeconomic status tend to show less severe effects of maternal depression than children from low socioeconomic status families (20,21).

Understanding the brain abnormalities associated with perinatal depressive symptoms can highlight brain regions sensitive to such effects and provide information about potential mechanisms linking maternal depression with negative behavioral and cognitive outcomes. Volumetric and diffusion magnetic resonance imaging (MRI) are common ways of assessing gray and white matter structure. Gray and white matter change significantly during the preschool period as part of normal brain maturation (22,23), and abnormalities are often associated with negative childhood outcomes, including learning disabilities (24) and externalizing and internalizing disorders (25,26). Despite the importance of understanding brain abnormalities, few studies have examined associations between maternal depression and children's brain structure. One study demonstrated lower anisotropy and axial diffusivity in the amygdala of neonates (5–17 days old) born to mothers with higher prenatal maternal depressive symptoms compared with lower depressive symptoms (27).

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ISSN: 0006-3223

The same infants showed associations between prenatal maternal depressive symptoms and white matter microstructure in right frontal connections including the inferior fronto-occipital and uncinate fasciculi (28). Another study showed correlations between increased maternal prenatal depression and reduced cortical thickness in the right prefrontal lobe of school-aged children; cortical thickness also mediated correlations between maternal depressive symptoms and children's externalizing behaviors (29). To our knowledge, no studies have investigated the effects of postpartum maternal depressive symptoms on children's brain structure, despite the strong associations between postpartum depression and children's outcomes (6). Furthermore, the few studies linking prenatal maternal depression and children's brain structure to date are limited to infants or school-aged children, leaving a critical gap in knowledge of brain abnormalities during early childhood, a period of rapid structural brain development (30) and a time when many of the behavior problems associated with perinatal depression become apparent (31).

The goal of this study was to investigate the associations between perinatal depressive symptoms and brain structure in preschool-aged children. Specifically, we used multimodal MRI to investigate gray and white matter structure in children born to mothers with a range of perinatal depressive symptoms. Given previous reports of cortical thickness alterations, we began with a whole-brain analysis of associations between cortical thickness in children and maternal perinatal depressive symptoms. We then followed up with a targeted investigation of white matter tracts emanating from affected cortical regions to determine whether white matter structure in underlying areas is also associated with maternal depressive symptoms. Because earlier findings relating depressive symptoms and children's brain outcomes were specific to the second trimester (29), we examined correlations in each trimester of pregnancy separately.

## METHODS AND MATERIALS

### Participants

Participants were 52 women recruited during pregnancy and the children (32 male/20 female) from those pregnancies. Women and children were recruited from an ongoing, prospective study examining maternal nutrition, mental health, and offspring outcomes (32). Table 1 summarizes characteristics of the women and children, including maternal age at child's birth, maternal postsecondary education (used as a proxy for socioeconomic status), breastfeeding status at 3 months postpartum, and child's gestational age and weight at birth. At the time of MRI scanning, children were aged 2.6 to 5.1 years (3.6 ± .5 years).

### Depressive Symptoms

Symptoms of maternal depression were assessed using the Edinburgh Postnatal Depression Scale (EPDS), a measure validated for assessment of depressive symptoms both prepartum and postpartum (33,34). Women completed the EPDS once during each trimester of pregnancy (first trimester: 11 ± 2.5 weeks, $n = 23$; second trimester: 17 ± 2.2 weeks, $n = 47$; third trimester: 32 ± 1.1 weeks, $n = 51$) and at 2 to 3 months postpartum (11 ± 2.3 weeks, $n = 52$); scores are reported in Table 1. Due to the timing of their enrollment in the study, 29 women did not complete the EPDS in their first trimester. Five women were missing second trimester scores, and one woman was missing a third trimester score. Depressive symptom scores across time points were highly correlated ($r = .48–.68$, all $p < .006$). Breastfeeding status was not related to depressive symptoms at any time point.

The EPDS is a screening tool for perinatal depression rather than a diagnostic instrument, though scores >12 are usually consistent with a physician diagnosis of major depressive disorder (33). Screening cutoffs range from 10 to 14 and are typically 1 to 2 points higher in pregnancy than postpartum (35). In our sample in the first trimester, only one woman scored ≥10 on the EPDS (she scored 16). In the second trimester, eight women scored ≥10, four women scored ≥12, and three women scored ≥14 on the EPDS. In the third trimester, three women scored ≥10, two women scored ≥12, and one woman scored ≥14. In the postpartum period, four women scored ≥10, three women scored ≥12, and one woman scored ≥14. Therefore, depending on the cutoff used, 4% of women met criteria for further follow-up during the first trimester, 6% to 17% met criteria for further follow-up during the second trimester, 2% to 6% met criteria for further follow-up during their third trimester, and 2% to 8% met screening criteria for postpartum depression. One woman was taking an antidepressant during pregnancy.

### Imaging

Brain imaging occurred at the Alberta Children's Hospital on a GE 3T MR750w (General Electric, Waukesha, Wisconsin) using a 32-channel head coil. During their scan, children were either awake and watching a movie or sleeping naturally. T1-weighted anatomical imaging was acquired using a spoiled gradient echo sequence with .9 × .9 × .9 $mm^3$ spatial resolution, echo time/repetition time = 3.8/8.2 ms. Diffusion tensor imaging (DTI) data were acquired using single-shot spin-echo echo planar imaging with 30 diffusion encoding gradient directions at b = 750 $s/mm^2$ and 5 images at

**Table 1. Descriptive Information for Women and Their Children**

| | Range | Mean ± SD | *n* |
|---|---|---|---|
| Women | | | |
| Age at child's birth (years) | 26–38 | 32.1 ± 3.0 | 52 |
| Postsecondary education (years) | 0–10 | 4.7 ± 2.9 | 52 |
| EPDS first trimester | 0–16 | 4.7 ± 3.6 | 23 |
| EPDS second trimester | 0–16 | 4.7 ± 4.2 | 47 |
| EPDS third trimester | 0–17 | 4.8 ± 3.2 | 51 |
| EPDS postpartum | 0–19 | 4.4 ± 4.1 | 52 |
| Breastfeeding/formula at 3 months postpartum | 28 exclusive breastfeeding, 6 mixed, 17 formula | | 51 |
| Children | | | |
| Sex | 20 female; 32 male | | 52 |
| Gestational age at birth (weeks) | 35.0–41.9 | 39.2 ± 1.4 | 52 |
| Birth weight (g) | 2230–4610 | 3369 ± 473 | 52 |
| Age at scan (years) | 2.6–5.1 | 3.6 ± .5 | 52 |

EPDS, Edinburgh Postnatal Depression Scale.