Fetal Exposure to Maternal Depressive Symptoms is Associated with Cortical Thickness in Late Childhood

Supplemental Information

Assessment of Prenatal Depression

Prenatal maternal depression was evaluated using the short form of the Center for Epidemiological Studies Depression Inventory (CESD) (1). On a 4-point scale, women indicated how often they experienced a symptom during the past week ranging from "barely or none of the time" to "most of the time." Responses to each of the nine items were scored from 0-3. Two of the items were reverse scored so the final (total) score could range from 0 to 27, with a higher score indicating greater self-reported depressive symptoms. This measure has both internal consistency (Kuder-Richardson = .87) and validity (1). Short form scores correlate 0.97 with the original scale. The CESD is a commonly used instrument for the study of depression in the general population, in patients with a variety of disorders and has been validated in samples of pregnant women (2). Scores on the CESD during pregnancy are associated with birth outcome, post partum depression and infant development (3-7). Among our participants, prenatal depression significantly ($F_{(1.9,138.8)} = 5.57$, $p < 0.005$) increased over the course of gestation (19 weeks GA, 5.4 (4.1); 25 weeks GA, 5.7 (4.1); 31 weeks GA, 6.9 (4.6)). The increase in ratings of depression as gestation progressed is in contrast to the decrease in anxiety that is specific to pregnancy across gestation (8-9).

Salivary Cortisol Assessment

Saliva samples were collected in the early afternoon at each prenatal visit, at least one hour after the participant had eaten using a Salivette sampling device (Sarstedt, Numbrecht, Germany). Saliva samples were spun and stored at -70°C until assayed. Thawed samples were centrifuged at 3000 rpm for 15 minutes before assay. Levels were determined by a competitive

luminescence immunoassay (LIA; IBL-America, Minneapolis, MN) with detection limits of 0.015 µg/dl. The cross reactivity of the assay was <2.5% with cortisone, prednisone and corticosterone and <0.1% with other naturally occurring steroids. The intra- and inter-assay coefficients of variance were 5.5% and 7.6%, respectively. Data reduction for the LIA assay was done by an automated four-parameter logistics computer program (software Mikro Win 2000; Berthold Microplate Luminometer). Samples were assayed in duplicate, averaged, residualized for time of day and log transformed to reduce skewedness.

Results for Maternal Prenatal Depression and Salivary Cortisol

The correlations at each gestational interval between maternal depressive symptoms and the residualized and transformed maternal cortisol levels were not significant (19 weeks GA, r = -0.03; 25 weeks GA, r = -0.09; 31 weeks GA, r = 0.13).

Conclusions about the Cortisol Signal to the Fetus

Our results did not support the HPA mechanism as a maternal signal to the fetus of depressive symptoms. However, rather than conclude that maternal cortisol is not a signal to the fetus of maternal depressive symptoms we suggest that methodological limitations in our assessments of maternal cortisol concentrations (based on a single sample at each pregnancy assessment) might have prevented detection of a significant association with maternal mood. In support of this, we have shown that when maternal cortisol is measured repeatedly over the course of the day in an ambulatory setting, maternal psychosocial state and cortisol concentrations are associated, but they are not associated when measured once in the laboratory (10).

Levels of Maternal Prenatal and Concurrent Depression

Maternal prenatal depressive scores were positively skewed (all below 0.96) with no evidence of kurtosis (all below 0.60). The number of current maternal depressive symptoms was significantly positively skewed (2.97) and radically kurtotic (12.04) reflecting the absence of depressive symptoms. All of the measures of maternal prenatal depressive symptoms were significantly correlated.

Controlling for Current Levels of Maternal Depression at the Time of Child MRI

Because of partially shared variance (~20%) between prenatal and current maternal reports of depressive symptoms, and because of evidence that a depressed mother influences her child's behavior and its developing brain, all analyses were repeated using current depressive symptoms as a covariate. Clustering of current depression scores are in the "no symptom" range so these results should be interpreted with caution. Nevertheless, after controlling for current levels of depression, the direction of findings and structures affected are not changed, but the percentage of the areas affected by gestational exposure to maternal depression is slightly but not significantly reduced.

Controlling for Birth Outcome

In our cohort of relatively healthy pregnant women, prenatal symptoms of depression were not significantly associated with either length of gestation (r's = -.15 to -.21, p's > .08) or birth weight (r's = -.01 to .09, p's > .40). However, because fetuses of depressed mothers have been reported to be small on all biophysical parameters (11-13), born early and are small for gestational age (14, 15), are hyperactive and have higher heart rate and greater heart rate variability than fetuses of euthymic women (16-18), are hypotonic and exhibit decreased sensitivity to repeated stimulation (19) and because it is well-established that there are

persisting neurological consequences of the trauma related adverse birth outcomes (20), all of our results were adjusted to account for birth outcome.

Supplemental References

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