Autism-related behaviors in children exposed prenatally to maternal preeclampsia and polycystic ovary syndrome.

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Background: Males are more likely to be diagnosed with autism and it has been suggested that perturbations in the hormonal milieu during prenatal development may contribute to sex-dependent vulnerability for autism and other neurodevelopmental disorders. While this area of research has primarily focused on testosterone produced by the fetus, we present data supporting the notion that maternal testosterone may cross the placenta and affect the developing brain.

Objective: Data from 270 mother-infant dyads in the nuMoM2b Study were analyzed to study the relationship between maternal testosterone during pregnancy and risk for neurodevelopmental disorders.

Design/Methods: Mothers reported diagnoses of preeclampsia, a gestational condition characterized by hypertension, and polycystic ovary syndrome (PCOS), characterized by enlarged ovaries, as both are associated with elevated maternal testosterone in the third trimester. Mothers completed the Children's Empathizing Quotient (EQ-C) and the Social Communication Questionnaire (SCQ), on which a score of ≥10 indicates risk for autism. Using a retrospective matched case-control design, children of mothers who had been diagnosed with preeclampsia and/or PCOS (n = 58) were matched with healthy controls based on maternal age at delivery, maternal ethnicity, and infant gestational age at birth.

Results: Maternal testosterone in the second trimester was higher in women with preeclampsia and/or PCOS, but only among those carrying a female fetus (p = 0.01). Maternal preeclampsia and/or PCOS did not affect second trimester maternal estradiol levels, nor did it impact umbilical cord blood testosterone or estradiol levels at birth. Children, especially females, born to mothers with preeclampsia and/or PCOS had significantly lower EQ-C scores (p = 0.05), higher SCQ total scores (p = 0.01) and were more likely to meet the at-risk cutoff on the SCQ, with an unadjusted odds ratio of 5.53 (p = 0.03). These children also exhibited greater hyperactivity (p = 0.04). While maternal testosterone was not associated with EQ-C scores, we found that maternal testosterone was positively associated with higher total scores on the childhood SCQ (p = 0.002) and that mothers of children who met the SCQ at-risk cutoff had higher testosterone (p = 0.003). Contrary to our hypothesis, we did not find group differences in placental aromatase.

Conclusions: In this sample, the effects of maternal preeclampsia and/or PCOS on child neurobehavioral outcomes are most robust among female children. The elevated levels of maternal testosterone, especially in female-carrying pregnancies, may explain the female susceptibility to the adverse effects of prenatal exposure to maternal preeclampsia and/or PCOS.