Lower Allopregnanolone in Pregnancy Predicts Postpartum Depression

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Background. Current evidence is mixed on the role of progesterone and its metabolites in perinatal mood and anxiety disorders.

Methods. Progesterone (P4) and allopregnanolone (ALLO) levels were measured by ELISA in 61 pregnant women with mood disorders at four time points across pregnancy and postpartum. Postpartum depression (PPD) was identified by clinician interview (DSM-IV criteria). Severity of symptoms was measured by the Inventory of Depressive Symptomatology (IDS-SR) and its anxiety subscale (IDS-SR-ANX). PPD biomarkers were previously identified by DNA methylation changes at two loci (HP1BP3 and TTC9B). We used generalized linear mixed effects models with random intercept to estimate the relationship between hormones and depression score (or clinical depression) while accounting for within-person correlation of outcomes over time.

Results. Women who met DSM-IV criteria for PPD had lower levels of ALLO in pregnancy (2.60, 95% CI 2.19-3.01) when compared to women who did not meet criteria (3.50, 95% CI 2.80-4.20) (p=.022). Similarly, those with higher levels of pregnancy ALLO had lower odds of moderate to severe depression (IDS-SR>39) (p=.026). These effects were driven by women who were not depressed in

pregnancy but later developed PPD. Higher levels of progesterone in pregnancy predicted lower anxiety in the postpartum, as measured by scores on IDS-SR (ANX) (β = -0.055, p=.018). In addition, HP1B3 methylation status was significantly associated with the change in allopregnanolone across pregnancy, and this association was driven by women who antenatally euthymic (p =.028).

Conclusions/Discussion. Our principal finding was a significant association between allopregnanolone levels in pregnancy and the later development of PPD. Our findings differ from previous research, possibly because we measured hormones at several points in pregnancy and in a population with high rates of clinician-assessed depression at most points during the study.

Keyword: postpartum depression, reproductive hormones, allopregnanolone

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