Neuroactive Steroid Metabolism in Early Pregnancy Depression and Anxiety in Low-Income Women of Color

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Abstract

Background
• Between 6.5%-12.9% of women experience perinatal depression (PND), with comorbid anxiety (PNA) in ~50% of cases.1-2
• Rates are even higher in women of color (20% PND, 10% PNA).3
• Progesterone (P4) and its neuroactive steroid (NAS) metabolites change across the perinatal period.
• Lower concentrations of Allopregnanolone (ALLO), a negative allosteric modulator of the GABA_A receptor, have been associated with perinatal depression in 3rd trimester and postpartum women.4-6
• No studies have investigated this relationship in early pregnancy and in relation to anxiety in a diverse sample.

Aims
Aim: To investigate a variety of NAS in depressed or anxious, and non-depressed or anxious women at two early perinatal timepoints.

Methods
• 50 pregnant women (56% Black, 28% Latina) provided 2 blood samples for GC-MS analysis of NAS (positive allosteric modulators (ALLO, Pregnanolone) and negative allosteric modulators (Isoallopregnanolone and Epipregnanolone)).
• Ratios of these NAS to P4 served as a marker of NAS metabolism, the primary predictor variables.
• Women completed the CAT-MH which yielded diagnoses of MDD or GAD, the primary dependent variables, at 2 timepoints.

Visit 1: ~<16 weeks gestation
Visit 2: ~28 weeks gestation

• Logistic mixed effects models assessed the relationship between NAS ratios and MDD/GAD.

Results

Figure 1. Logged ratios of (a) ALLO, (b) PA, (c) ISOALLO, and (d) EPI to P4 by depression screening (negative = 0, positive = 1) in the second trimester only. Levels of P4 are also shown (e). Continuous depression severity scores in relation to NAS ratio to P4 are shown for each metabolite in (f).

Figure 2. Logged ratios of (a) ALLO, (b) PA, (c) ISOALLO, and (d) EPI to P4 by anxiety screening (negative = 0, positive = 1) in the second trimester only. Levels of P4 are also shown (e). Continuous anxiety severity scores in relation to NAS ratio to P4 are shown for each metabolite in (f).

Conclusions
• Increased metabolism of P4 to its NAS isomers is associated with affective disorders earlier in pregnancy. The direction of these associations differ from later pregnancy, where lower levels of ALLO are associated with PND. This relationship was strongest in women with MDD or GAD in both the first and second trimesters.
• Hypothesis 1: There is a dynamic, inverse effect of NAS on mood in early pregnancy compared to late pregnancy in response to acute increases in NAS synthesis, where GABA_A receptors are not able to properly adapt their subunit expression & sensitivity, resulting in discoordination between NAS and GABA_ARs.
• Hypothesis 2: Depression during pregnancy acts as an acute stressor, increasing NAS synthesis. As depression and pregnancy continue, the stressor becomes “chronic”, resulting in decreased NAS synthesis. Future work is needed to determine if the increase in NAS metabolism precedes or is a consequence of MDD and the extent to which comorbid GAD may influence the directionality of this association.

References


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