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demonstrated associations with measurable behavioral outcomes in toddlers.

**Funding Source:** Stanford Precision Health and Integrated Diagnostics seed funding

**Keywords:** Epigenetics, Early Life Stress, Intergenerational Transmission

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**High Worry in Pregnancy, Neuroactive Steroid Dysregulation, and Postpartum Depression**

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**Background:** Worry has been identified as a key component of anxiety in pregnant and postpartum women, and our group has previously shown that women who are high worriers in pregnancy are nearly four times as likely to develop postpartum depression as those who are average or low worriers. Biological correlates of high worry in pregnancy are unknown, and we sought to examine whether levels of progesterone and two of its metabolites were related to high worry in pregnancy.

**Methods:** Pregnant women (N=114) with and without anxiety disorders were followed at four visits across pregnancy and postpartum. Psychological scales and a blood draw were done at each visit. Levels of three neuroactive steroids (progesterone (P4), allopregnanolone (ALLO), and its 5-alpha, 3-beta isomer (ISO)) steroids were analyzed at each time point using gas chromatography-mass spectrometry and compared using Student’s t-test.

**Results:** Women with high worry (identified as a score >/= 60 on the Penn State Worry Questionnaire) comprised 21% of the sample. High worry in the second trimester was associated with higher levels of both ALLO and ISO (p = 0.009 and p=0.003, respectively). At the third trimester, the ratio of P4 to its metabolites was higher in women who went on to develop postpartum depression (ALLO NS, ISO p=0.018).

**Conclusions:** These findings indicate that dysregulation of progesterone metabolism in pregnancy may be associated with high worry in pregnancy and the subsequent development of postpartum depression. Further analysis will include additional molecules in the progesterone metabolism pathway.

**Funding Source:** NIMH K23 MH110607

**Keywords:** Pregnancy, Neuroactive Steroid, Worry, Postpartum Depression

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**Prenatal Stress and the Microbiome in the Time of COVID- A Prospective Cohort Study**

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**Background:** Given the emerging importance of the role of the gut microbiota-brain-axis in mediating prenatal stress-induced neurodevelopmental outcomes, a prospective cohort study was conducted. The COVID-19 Pandemic occurred halfway through study recruitment (n=35). The study aims to a) evaluate perceived stress across gestation, b) determine whether maternal microbiome composition changes with stress, and c) discern the influence of the COVID-19 pandemic on maternal stress, psychometric scores, and alterations in the microbiome.

**Methods:** This longitudinal study design includes five time points across pregnancy and the post-partum period, at which biological samples were collected and psychometrics administered. Samples include maternal rectal and vaginal swabs. Psychometrics include measures of perceived stress, anxiety, depression, sleep, diet, and childhood adversity. Study participants identify as 62.9% White and 31.4% Black or African American. Finally, PacBio full-length 16S rRNA sequencing using SMRT Cell technology is used to identify the maternal rectal and vaginal microbial communities.

**Results:** Participants delivering during the pandemic reporting greater perceived stress (p<0.05). Of note, there were no significant differences in anxiety or depressive symptoms across gestation in the pre-pandemic participants as compared to participants during the pandemic. During the second trimester, increased depression associated with increased rectal alpha diversity, and increased perceived stress was associated with increased levels of Prevotella, Sneathia, and Gardnerella in the rectal samples. In contrast, participants with increased depressive symptoms during the third trimester had reduced vaginal alpha diversity measures at delivery.

**Conclusions:** Findings suggest maternal perceived stress and depressive symptoms are associated with alterations in maternal microbiota.

**Keywords:** Gut Microbiome, Prenatal Maternal Stress, Gut-Brain Axis

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**SYMPOSIUM**

**Sex Differences in Neuroinflammation, Aging, and Alzheimer’s Disease**

Chair: Holly Hunsberger

**Sex-Specific Onset of Sundowning Behavior in an Alzheimer’s Mouse Model**

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**Background:** Circadian rhythm is dampened in Alzheimer’s disease (AD) patients. In addition to cognitive decline, AD patients (~50%) become confused, agitated, and anxious in the evening, often referred to as “sundowning.” However, the mechanisms underlying this increased anxiety-like behavior (e.g., sundowning) remain unclear.

**Methods:** Using the elevated plus maze (EPM) as a proxy for sundowning behavior, we tested the ArcCreERT2 x EYFP x AD