Prenatal PTSD is predicted by the interaction of early life adversity, current stressors, and chronic HPA activity: Preliminary results from the BE SAFE Pregnancy Study

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Background

- Pregnancy is a key period in which maternal life history can impact the developing fetus and infant through the maternal-fetal endocrine milieu and later maternal care.[1]
- Blunted HPA response to stress has been associated with early life adversity and PTSD, but acute stressors can also result in higher HPA activation and the onset of PTSD symptoms. [3-5]
- Hair cortisol is a measure of chronic HPA activation validated in pregnant women. Hair cortisol has been inconsistently associated with mental health and chronic stress in pregnant and non-pregnant samples, potentially due to the interacting effects of early life adversity, current stress, and chronic HPA activity. [2,6]

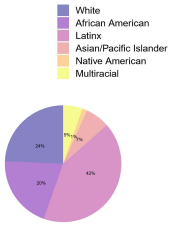
Methods

Participants (n=98)

- A low-income, ethnically diverse community sample of 101 pregnant women in their 2nd or 3rd trimester were enrolled in the BE-SAFE Pregnancy Study at Zuckerberg San Francisco General. 100 completed psychosocial questionnaires and 76 provided hair samples. 2 were excluded due to abnormal cortisol values and steroid use.

Table 1. Sample Characteristics

	Mean(sd)
Age	29.0 (6.5)
Education years	12.7 (2.8)
Weeks Pregnant	28.0 (8.1)
PCL5 Total Score	25.0 (17.8)
Prenatal Stressors	2.6 (1.9)
ACES Score	4.3 (2.8)
Hair Cortisol ng/ml	54.7 (167.6)
Below Federal Poverty Line	59.5%



Early Life Adversity and Current Stressors

- Adverse Childhood Events Questionnaire (ACES):10 items assessing maltreatment and family dysfunction prior age 18.
- Current Stressors:10 traumatic/stressful life events experienced during the pregnancy [7]

PTSD during pregnancy

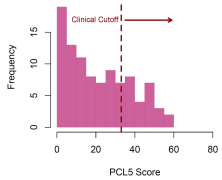
- Posttraumatic Stress Disorder Check List for the DSM-5 (PCL5): 20 items assessing symptom severity, scores range 0-80.

Chronic HPA Activity

A 3cm sample of scalp hair was washed in isopropanol, weighed (>5g), and pulverized. Cortisol

Data Analysis: A Bayesian approach

- The PTSD score was discrete, overdispersed, and bound between 0 and 80; **best modeled as a beta-binomial distribution**
- Bayesian models fit using MCMC in R and RStan; regularizing priors impose conservatism on parameters
- Early life adversity and prenatal stressors modelled as **monotonic effects**, capturing non-linearity in predictors
- Bayesian imputation of missing data reduces bias and increases statistical power
- Model comparison using approximate leave-one-out-cross-validation (LOO-CV)



Additive Risk Model: Early life adversity, current stress, and hair cortisol cumulatively increase risk of prenatal PTSD

$$PTSD \sim \alpha + \textbf{\textit{Current Stress}} + \textbf{\textit{Early Life Adversity}} + \textbf{\textit{Hair Cortisol}} + weeks + age + African\ American + Spanish + education$$

Multiplicative Risk Model: Early adversity and current stress interact with HPA activity to increase risk of prenatal PTSD

$$PTSD \sim \alpha + \textbf{\textit{Current Stress*Early Life Adversity*Hair Cortisol}} + weeks + age + African\ American + Spanish + education$$

The intersection of life-course adversity, chronic HPA activity, and prenatal PTSD

Fig 1. Posterior effect sizes

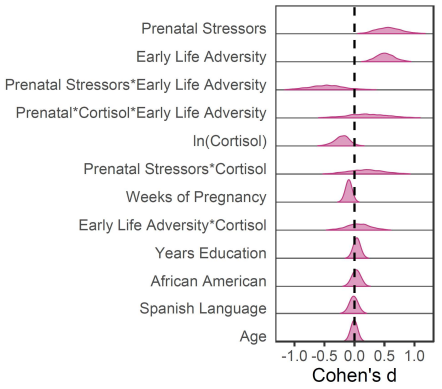


Fig 2. Women with low hair cortisol have higher risk regardless of current stress

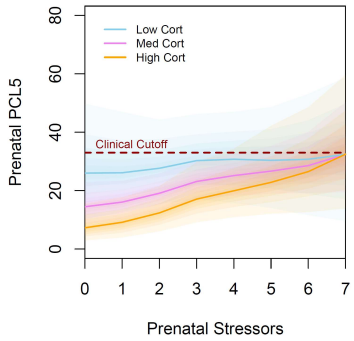
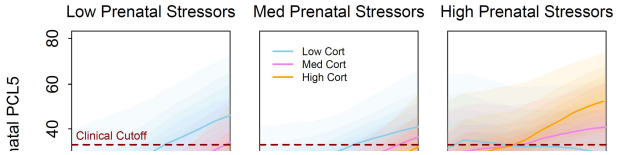


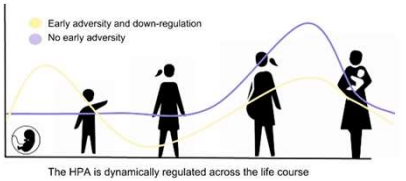
Fig 3. When current stress is high, the effect of early life adversity on PTSD risk is weak



Results

- Model comparison (LOO-CV) suggested that the **multiplicative risk model outperformed the additive risk model.**
- Early life adversity and current stressors each predict prenatal PTSD, as did the interaction between them, such that women with high prenatal stress have higher risk of PTSD regardless of earlier adversity.
- Lower hair cortisol had a direct effect on PTSD risk, as did the interaction between hair cortisol and prenatal stressors, such that women with low hair cortisol and high early life adversity have the greatest risk of PTSD. However, these relationships are 'washed out' by the immediate effects of high levels of current stressors on PTSD symptomatology.

Discussion



The HPA is dynamically regulated across the life course

- We suggest here a generative, Bayesian model for identifying interacting risk factors leading to PTSD in pregnancy to account for multiple pathways towards mood disorder
- Hypothesized life history tradeoffs/intergenerational effects of psychosocial stress during development should be evaluated in a life course context
- Our approach may have further clinical relevance as additional risks of prenatal HPA blunting (e.g., preterm birth) are identified.[8]

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