

Gene expression in postpartum depression within pharmacologically –induced (GnRHa) depressive symptoms and SERT variability

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Background - Sex-steroid hormone fluctuations may increase risk for depressive symptoms in postpartum depression (PPD). Serum hormone levels are not associated with risk for PPD; however, in women with a predisposing risk to PPD, administration of estradiol (E2), either experimentally or via natural pregnancy, is required to elicit depressive symptoms following hormone withdrawal.

Dr. Frøkjær (Frøkjær, V.G., et al, 2015) demonstrated a significant positive association between changes in neocortical serotonin transporter (SERT) binding and changes in depression scores from baseline following a pharmacologically induced biphasic ovarian hormone response by Gonadotrophin-releasing hormone agonists (GnRHa) relative to placebo. We identified a specific set of genes in late pregnancy predicting later PPD development using genome-wide gene expression profiling in prospectively derived antenatal blood from the highly sex-steroid stimulated state in third trimester of pregnancy (Mehta, D., et al, 2014), suggesting an enhanced sensitivity to estrogen signaling predisposes to PPD. Guintivano et al (Guintivano, J., et al, 2014) demonstrated an increased sensitivity of DNA methylation changes in response to estrogen that predisposes to PPD.

Methods - Longitudinal genome-wide data from 63 women (31 GnRHa treated and 30 placebo treated) was evaluated. Gene expression was measured using the Illumina Human HT12v4 arrays and DNA methylation was assessed using the Illumina 450k arrays using standard experimental protocols and custom statistical pipelines as described previously (Mehta et al, PNAS, 2013).

Results and Conclusions - PPD gene expression biomarker set identified the subset of women demonstrating sensitivity to GnRHa intervention and these markers were associated with brain SERT responses to GnRHa. Epigenetic signatures identified subsets of women demonstrating sensitivity to GnRHa intervention in terms of the emergence of depressive symptoms or brain SERT responses to GnRHa. Further functional analysis is currently underway to investigate the underlying biological pathways.

Keywords - Postpartum depression, gene expression, pharmacological treatment