Title

An Exploration into Neurobiology of Postpartum Psychosis

Background

The neurobiology of postpartum psychosis (PPP) remains unclear. We studied some candidate gene loci including, Estrogen receptor alpha (ESR1), Hemicentin (HMNC1), Methyltransferase like 13 (METTL13), and Serotonin Transporter (5HTTLPR) gene polymorphisms for association with PPP. Cytokine changes were studied to assess the role of immunological factors in PPP.

Methods

Women with PPP (n=105) and healthy controls (n=102) were genotyped for the above mentioned SNPs. Real time-PCR and gel based methods were used for genotyping of ESR1 (rs9340799; rs2234693), HMCN1 (rs2891230), METTL13 (rs2232825) and 5-HTTLPR loci.

For the cytokine changes, women admitted with first-onset PPP (n=20) were compared against healthy postpartum (HPP, n=20), healthy non-postpartum (HNPP, n=20) and women with acute transient polymorphic psychosis (ATPP, n=20). Serum cytokines were measured using cytometric bead array.

Results

T allele of METTL13 (rs2232825) was significantly higher among PPP as compared to healthy controls (p=0.02). No significant associations were found with other SNPs.

IL-6 and IL-8 levels were significantly elevated in the PPP group as compared to HNPP (p = 0.05) but not with HPP. IL-17A was significantly elevated in the PPP when compared to HNPP (p=0.03).

Discussion

The postpartum period is known to be associated with significant hormonal changes. METTL13 activity is reported to regulate estrogen receptor induced gene transcription. Our results suggest that METTL13 rs2232825 locus or a linked functional locus may modulate the vulnerability to PPP. IL-17A is reported to enhance the expression of pro-inflammatory cytokines and resultant neuronal damage. Findings suggest a role for METTL13 and pro-inflammatory cytokines in manifestation of PPP.

References

1. Bergink V et al. Immune System Dysregulation in First-Onset Postpartum Psychosis. Biol Psychiatry. 2013;73(10):1000–7.

2. Mahon PB et al. Genome-wide linkage and follow-up association study of postpartum mood symptoms. Am J Psychiatry. 2009;166(11):1229–37.