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Epigenetic mechanism of maternal post-traumatic stress disorder in delayed rat offspring development: dysregulation of methylation and gene expression

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ABSTRACT. Maternal post-traumatic stress disorder (PTSD) increases the risk of adverse neurodevelopmental outcomes in the child. Epigenetic alternations may play an essential role in the negative effects of PTSD. This study was aimed to investigate the possible epigenetic alterations of maternal PTSD, which underpins the developmental and behavioral impact. 24 pregnant Sprague-Dawley (SD) rats were randomly grouped into PTSD and control groups. Open-field tests (OFTs), elevated pull maze (EPM) assays, gene expression profile chip tests, and methylated DNA immunoprecipitation sequencing (MeDIP-Seq) were performed on the offsprings 30 days after birth. The results

showed that PTSD offsprings had lower body weights and OFT scores than control offsprings. Enzyme-linked immunosorbent assays showed that serotonin receptor (5-HT) and dopamine levels were significantly lower in PTSD offsprings than in control offsprings. In contrast, corticosterone levels were higher in the PTSD group than in the control group. In a comparison of the PTSD group versus the control group, 4,160 significantly differentially methylated loci containing 30,657 CpGs were identified; 2,487 genes, including 13 dysmethylated genes, were validated by gene expression profiling, showing a negative correlation between methylation and gene expression ($R = -0.617$, $P = 0.043$). In conclusion, maternal PTSD could delay the physical and behavioral development of offsprings, and the underlying mechanism could contribute to changes in neurotransmitters and gene expression, owing to dysregulation of whole-genome methylation. These findings could support further clinical research on appropriate interventions for maternal PTSD to prevent methylation dysregulation and developmental retardation.

Key words: Post-traumatic stress disorder; Epigenetics; Behavior; Environmental enrichment; Neurodevelopment