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MATERNAL PRENATAL ANXIETY AND EPIGENETIC MODIFICATION GLUCOCORTICOID RECEPTOR GENE: THE SHAPING OF THE BIOLOGICAL STRESS RESPONSE

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Background: The methylation status of the human glucocorticoid receptor gene NR3C1 in newborns has been reported to be sensitive to prenatal maternal mood. This study investigates both the association between maternal cortisol and emotional state during pregnancy and the methylation state of the promoter region of NR3C1 gene.
Methods: We examined 83 pregnant women. Psychological data and diurnal cortisol data were assessed to evaluate maternal stress once each trimester. DNA methylation at different loci of the NR3C1 gene, including exon 1B, 1D and 1F, was analyzed in genomic DNA from cord blood mononuclear cells.
Results: Univariable analyses indicated pregnancy related anxiety to be the strongest psychological parameter throughout pregnancy. Most significant findings concerned 1F. Particularly the methylation state of CpG9 was significantly associated with maternal emotional wellbeing. In a multivariable model the proportion of variance in methylation state of F9 explained (PVE) by pregnancy related anxiety was 7.8% (p=0.023) during T1.
Furthermore different CpG-units located at the nerve growth factor inducible protein A (NGFI-A) binding sites of 1F were associated with maternal anxiety [(F20.21: PC PRAQ and fear of integrity in T1: respectively PVE:8.9% and PVE:9.0%; Fear of delivery T2: PVE:8.0%, Fear of integrity T2: PVE:6.0% and STAI T2: PVE:5.9%) - (F12.13: PC PRAQ T1: PVE:6.9%, fear of integrity T2: PVE:6.0% and fear of delivery T2: PVE:8.0%)] and cortisol (F38.39: PVE: 8.9%) in T3.
Conclusion: These data indicate that prenatal maternal emotional state, particularly pregnancy related anxiety, are associated with the methylation state of the NR3C1 gene in the child.

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