TRANSGENERATIONAL PROGRAMMING OF NEUROLOGICAL DISORDERS BY PRENATAL STRESS

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Introduction: The perinatal environment represents a critical determinant for the susceptibility to neurological disease in later life. While perinatal factors are known to affect one generation, effects of adverse experience may be transmitted to subsequent generations. Here we investigated the genetic, epigenetic, and behavioural manifestations of adverse experience in a new rat model of multigenerational prenatal stress.

Methods: Mild stress was induced during rat pregnancy in mothers (P0), daughters (F1) and granddaughters (F2). Non-stressed pregnant dams served as controls. Sensorimotor development and maturation of offspring was tested from postnatal days 9-110. Furthermore, brain and blood tissues were collected from newborns for transcriptome and microRNAome analyses.

Results: Prenatal stress modulated the expression of miRNAs and genes implicated in human neurological and psychiatric disease. Putative targets for altered miRNAs included genes related to neurotrophic factors, neurotransmission, stress response, and genes involved with miRNA biogenesis pathway. Alterations in gene and miRNA expression were accompanied by characteristic behavioural profiles in prenatally stressed rats that persisted into adulthood. Multigenerational prenatal stress had cumulative effects on gene and miRNA profiles and caused larger delays in developmental milestones.

Conclusion: Our findings suggest that prenatal stress across several generations may cumulatively affect offspring health and development by modulating miRNAs related to neuroplasticity and cell survival. Gene expression profiles point towards genetic risk factors of multiple sclerosis, Parkinson's disease, and psychiatric conditions. These findings pioneer the transgenerational origins of neurological disease and propose that experience across several generations may program the risk of neurological disorders.