

Abstract Information

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Address :	UGSF UMR8576 CNRS University of Lille University of Lille
Participation :	symposium
Title of the Symposium :	Early life stress, Sex differences, and Maternal influences: Insights into Brain and Behavioral Disorders
Category :	Invited Speakers
Thematic Area :	Neuroendocrine Systems, Biological Rhythms and sleep
Title :	The intergenerational inheritance of early life stress is transmitted by maternal care via oxytocin.
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Abstract : Perinatal stress (PRS) in rats induces enduring alterations that can be predicted by reduced maternal behavior due to gestational stress. This study examined the intergenerational effects of PRS by mating first-generation (F1) PRS-exposed female rats with naïve males and evaluating the phenotypes of both F1 and second-generation (F2) offspring. PRS was associated with diminished maternal behavior in F1 mothers and F0 grandmothers. Both F1 and F2 offspring exhibited consistent changes in behaviors, linked to neurobiological alterations affecting stress responses across generations. Notably, F2 offspring were not directly exposed to restraint stress during gestation, suggesting an indirect transmission of PRS effects via maternal care.

Given the established role of maternal care in epigenetic transmission, we investigated epigenetic modifications influenced by maternal behavior. Differential gene expression patterns were identified across F1 and F2 generations, implicating key pathways related to glutamatergic synaptic transmission and the regulation of stress systems. These findings highlight the interplay between maternal care and epigenetic mechanisms in shaping the offspring's hypothalamic-pituitary-adrenal (HPA) axis function.

Postpartum treatments with carbetocin (an oxytocin analog) or the probiotic *Lactobacillus reuteri*, known to enhance oxytocin system activity and consequently maternal care, successfully reversed PRS-induced long-term effects in F1 and F2 offspring. These

interventions restored normal maternal care and mitigated neurobehavioral and epigenetic alterations.

The results underscore the critical role of maternal care in mediating the intergenerational transmission of PRS effects and the plasticity of these outcomes through targeted interventions. Moreover, the findings emphasize the therapeutic potential of modulating the oxytocinergic system to counteract the adverse consequences of PRS, offering promising avenues for addressing stress-related neuropsychiatric disorders across generations.