

Maternal Metabolic Dysfunction: Unraveling the Mechanisms Driving Offspring Neurobehavioral Alterations

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Maternal metabolic health plays a fundamental role in shaping offspring brain development and long-term neurological function. The increasing prevalence of obesity and type 2 diabetes among women of reproductive age has raised important concerns regarding the developmental programming of neuropsychiatric and cognitive disorders. Although epidemiological and experimental studies consistently associate maternal metabolic dysfunction with an increased risk of anxiety, cognitive impairment, and metabolic disease in offspring, the underlying mechanisms remain incompletely understood. Our research aims to identify the molecular and cellular pathways linking adverse maternal metabolic environment to long-lasting changes in brain function. Using preclinical models of maternal obesity and multidisciplinary approaches combining behavioral phenotyping with molecular, histological, and functional analyses, we investigate how metabolic disturbances during pregnancy and lactation reshape key brain regions involved in cognition and emotional regulation, particularly the cortex and the hippocampus.

Our findings demonstrate that maternal obesity induces persistent anxiety-like behavior and memory deficits in adult offspring, accompanied by hippocampal remodeling involving neuroinflammatory and synaptic pathways. Importantly, these responses exhibit marked sexual dimorphism, with female offspring showing a stronger neuroinflammatory profile, whereas males display more pronounced alterations in synaptic plasticity-related proteins. These observations support the concept that distinct biological mechanisms underlie developmental programming in males and females.

By integrating metabolism, neuroinflammation, and neural plasticity, this work provides new insights into how maternal metabolic disorders influence offspring brain health and highlights potential therapeutic targets to prevent the long-term neurological consequences of obesity and diabetes during pregnancy.

Keywords: Maternal Obesity, Offspring, Neurobehaviour alterations

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