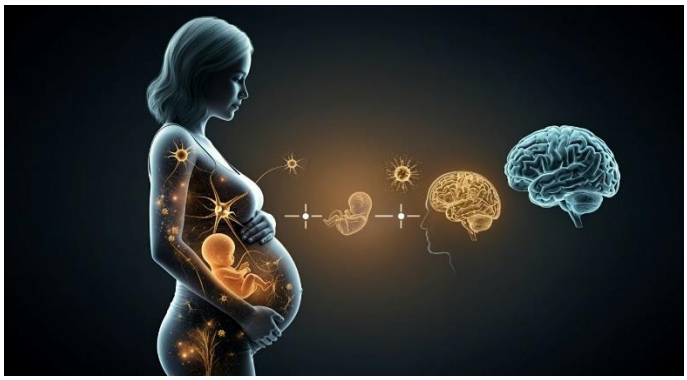
By Sex Prenatal Immune Origins of Brain Aging Differ

A team led by researchers from Harvard Medical School explored how prenatal exposure to maternal pro-inflammatory cytokines affected memory-related brain circuits and immune functions in offspring over the course of 50 years.

The study examined sex-specific differences in brain activity and memory performance and linked fetal immune disruptions to long-term impacts on health, particularly cognitive and immune resilience in midlife.



Study

The present study examined the long-term effects of prenatal maternal immune activity on memory and immune functions in offspring.

The researchers used data from a prenatal cohort recruited between 1959 and 1966, focusing on 204 participants who were evenly divided based on sex and were approximately 50 years old.

Maternal serum samples collected from the prenatal cohort during the late second or early third trimester were analyzed for pro-inflammatory cytokines, particularly interleukin (IL)-6 and tumor necrosis factor-alpha (TNF-α), given their roles in brain development. The researchers also measured anti-inflammatory cytokine IL-10, but found it did not have a significant effect, highlighting the specificity of pro-inflammatory cytokines.

The participants were categorized based on their prenatal exposure levels.

The adult offspring underwent clinical evaluations, neuropsychological testing, and functional brain imaging. Their memory performance was assessed using tasks such as the Face-Name Associative Memory Exam and Selective Reminding Test.

Additionally, brain activity and connectivity during memory encoding were evaluated through functional magnetic resonance imaging (MRI), with a focus on regions such as the hippocampus and ventrolateral prefrontal cortex.

The researchers also conducted sex-specific analyses to assess interactions between maternal cytokine exposure and brain activity, controlling for socioeconomic and demographic factors.

Reproductive histories and hormonal assessments from the female participants were used to categorize them based on reproductive stages, enabling examination of postmenopausal effects.

Additionally, offspring immune function in midlife was evaluated using markers such as the NLRP3 inflammasome score. NLRP3 or nucleotide-binding and oligomerization domain (NOD)-, leucine-rich repeat (LRR)-, and pyrin domain-containing protein 3 is a protein linked to inflammatory responses to toxins, injury, or antigens.

Findings

The results indicated that prenatal exposure to maternal pro-inflammatory cytokines had sex-specific, long-term effects on the immune function and memory circuits in the offspring.

Elevated maternal IL-6 and TNF-α levels were associated with decreased performance in memory tasks and altered brain activity, particularly in the hippocampus and ventrolateral prefrontal cortex, in male offspring. These effects were linked to poorer task-evoked brain responses during memory encoding and reduced functional activity.

In women, the effects of prenatal exposure were revealed post-menopause, with higher levels of maternal cytokines correlating with diminished memory performance and altered connectivity between memory-related brain regions.

Interestingly, no significant associations were observed in premenopausal or perimenopausal women, indicating that reproductive aging amplifies these impacts.

Furthermore, the study identified immune function changes in midlife. Elevated prenatal cytokine exposure was associated with increased inflammasome activity in the offspring, especially in female offspring after menopause, which suggested a retained hyperimmune state. This heightened immune response is also correlated with poorer episodic memory performance.

Additionally, standardized childhood academic performance at age 7 was linked to adult memory outcomes, suggesting the predictive value of early cognitive indicators for lifelong cognitive health. This emphasizes the role of prenatal conditions in shaping not only immediate but also long-term cognitive trajectories.

In contrast to the pronounced effects of IL-6 and TNF-α, no significant effects were observed for IL-10, underscoring the critical influence of pro-inflammatory cytokines on memory and immune outcomes.

Conclusion

Overall, the results suggested that prenatal exposure to maternal inflammatory cytokines had an enduring impact on memory and immune functions in offspring, with distinct sex-specific effects that emerge across the lifespan. Male offspring showed earlier deficits, while the effects were amplified post-menopause in women.

These findings reported the role of early immune disruptions in shaping lifelong cognitive and immune resilience and emphasized the need for targeted interventions to mitigate risks associated with prenatal inflammatory exposures. Although the study is comprehensive, the authors acknowledge limitations, including the focus on a single time point of cytokine measurement and sample size constraints for some analyses.

These findings provide a foundation for future research exploring the link between prenatal immune activity and aging-related disorders such as Alzheimer's disease.

Source:

https://www.news-medical.net/news/20241124/From-womb-to-midlife-Prenatal-immune-disruptions-reshape-memory-and-cognitive-aging.aspx