

# Is Paternal Immune Activation a newly emerging pathway with respect to Neurodevelopmental and Psychiatric Disorders that needs additional research?

## Paternal Immune Activation: An Emerging but Understudied Risk Pathway

Most immune-development work has focused on **maternal** immune activation (MIA), which is now a well-established, cross-disorder risk factor. The papers here repeatedly emphasize the maturity of the MIA field and the need for further refinement, but they do **not** yet provide comparable data for paternal immune activation. That gap itself supports the idea that paternal pathways are *emerging* and under-researched.

### How Established Is Maternal (vs. Paternal) Immune Activation?

- Multiple reviews describe MIA as a **critical, well-established risk factor** for neurodevelopmental disorders (ASD, ADHD, schizophrenia, Tourette syndrome, anxiety) and a **“disease primer”** for a broad spectrum of CNS disorders (Estes & McAllister, 2016; Han et al., 2021; Hall et al., 2023; Lins, 2021; Aguilar-Valles et al., 2020; Tang et al., 2025; Bergdolt & Dunaevsky, 2019; Kwon et al., 2022; Guma et al., 2019; Haddad et al., 2020; Conway & Brown, 2019; Woods et al., 2021).
- Papers stress that the MIA field, although relatively young, has already “become a major focus” of neurodevelopmental pathology research and has **“steadily more compelling”** evidence (Estes & McAllister, 2016; Aguilar-Valles et al., 2020; Tang et al., 2025; Guma et al., 2019; Conway & Brown, 2019; Woods et al., 2021).

### Focus of Current Work (Predominantly Maternal)

Main theme	What is emphasized	Citations
Risk scope	Links to ASD, schizophrenia, ADHD, Tourette, anxiety, broad NDDs	(Careaga et al., 2017; Han et al., 2021; Hall et al., 2023; Estes & McAllister, 2016; Quagliato et al., 2021; Lins, 2021; Aguilar-Valles et al., 2020; Tang et al., 2025; Bergdolt & Dunaevsky, 2019; Kwon et al., 2022; Guma et al., 2019; Haddad et al., 2020; Conway & Brown, 2019; Woods et al., 2021)
Mechanisms	Cytokines, microglial activation, disrupted neurogenesis/migration, epigenetic priming	(Estes & McAllister, 2016; Aguilar-Valles et al., 2020; Tang et al., 2025; Bergdolt & Dunaevsky, 2019; Kwon et al., 2022; Guma et al., 2019; Massrali et al., 2022; Woods et al., 2021)
Field status	“Nascent” but rapidly advancing, with urgent need for mechanistic and preventive research	(Estes & McAllister, 2016; Aguilar-Valles et al., 2020; Tang et al., 2025; Guma et al., 2019; Haddad et al., 2020; Conway & Brown, 2019; Bilbo et al., 2017)

FIGURE 1 Current work centers on maternal pathways

## Indirect Indications That Paternal Pathways Are Underexplored

- Several reviews explicitly highlight **maternal and paternal age** as risk modifiers for ASD, schizophrenia, psychosis, and ADHD, but mechanistic work is far more developed for maternal immune processes than for paternal factors (Hall et al., 2023).
- MIA reviews repeatedly call the field “in its infancy” and emphasize unmet needs around **gene–environment interactions, epigenetics, and intergenerational effects** (Estes & McAllister, 2016; Aguilar-Valles et al., 2020; Bergdolt & Dunaevsky, 2019; Guma et al., 2019; Conway & Brown, 2019; Bilbo et al., 2017; Woods et al., 2021). These are precisely the domains in which paternal immune activation and sperm-mediated epigenetic effects would operate, yet they are not detailed in these articles, implying a research gap rather than a negative finding.

## Need for Additional Research

Across these papers, calls for **long-term prospective human studies**, better mechanistic models, and integration of epigenetics and other parental factors are common (Estes & McAllister, 2016; Aguilar-Valles et al., 2020; Bergdolt & Dunaevsky, 2019; Guma et al., 2019; Haddad et al., 2020; Conway & Brown, 2019; Bilbo et al., 2017; Woods et al., 2021). None provide systematic data on paternal immune activation, indicating that:

- Immune-mediated **paternal** contributions remain largely uncharacterized.
- Understanding how pre-conception paternal immune states and epigenetic changes influence offspring NDD and psychiatric risk is a **logical next step** extending the established MIA framework.

## Conclusion

Within current neuroimmune research, immune-based paternal effects can reasonably be considered a **newly emerging and under-studied pathway**. The literature here solidly establishes maternal immune activation as a major risk mechanism and repeatedly calls for expanded work on related, multi-parental, and epigenetic routes—strongly suggesting that paternal immune activation is a promising area that requires substantial additional research.

*These search results were found and analyzed using Consensus, an AI-powered search engine for research. Try it at <https://consensus.app>. © 2026 Consensus NLP, Inc. Personal, non-commercial use only; redistribution requires copyright holders' consent.*

## References

- Aguilar-Valles, A., Rodrigue, B., & Matta-Camacho, E. (2020). Maternal Immune Activation and the Development of Dopaminergic Neurotransmission of the Offspring: Relevance for Schizophrenia and Other Psychoses. *Frontiers in Psychiatry*, 11. <https://doi.org/10.3389/fpsy.2020.00852>
- Bergdolt, L., & Dunaevsky, A. (2019). Brain changes in a maternal immune activation model of neurodevelopmental brain disorders. *Progress in Neurobiology*, 175, 1–19. <https://doi.org/10.1016/j.pneurobio.2018.12.002>
- Bilbo, S., Block, C., Bolton, J., Hanamsagar, R., & Tran, P. (2017). Beyond infection - Maternal immune activation by environmental factors, microglial development, and relevance for autism spectrum disorders. *Experimental Neurology*, 299, 241–251. <https://doi.org/10.1016/j.expneurol.2017.07.002>
- Careaga, M., Murai, T., & Bauman, M. (2017). Maternal Immune Activation and Autism Spectrum Disorder: From Rodents to Nonhuman and Human Primates.. *Biological psychiatry*, 81 5, 391-401. <https://doi.org/10.1016/j.biopsych.2016.10.020>

- Conway, F., & Brown, A. (2019). Maternal Immune Activation and Related Factors in the Risk of Offspring Psychiatric Disorders. *Frontiers in Psychiatry*, 10. <https://doi.org/10.3389/fpsy.2019.00430>
- Estes, M., & McAllister, A. (2016). Maternal immune activation: Implications for neuropsychiatric disorders. *Science*, 353, 772 - 777. <https://doi.org/10.1126/science.aag3194>
- Guma, E., Guma, E., Plitman, E., Plitman, E., & Chakravarty, M. (2019). The role of maternal immune activation in altering the neurodevelopmental trajectories of offspring: a translational review of neuroimaging studies with implications for autism spectrum disorder and schizophrenia.. *Neuroscience and biobehavioral reviews*. <https://doi.org/10.1016/j.neubiorev.2019.06.020>
- Haddad, F., Patel, S., & Schmid, S. (2020). Maternal Immune Activation by Poly I:C as a preclinical Model for Neurodevelopmental Disorders: A focus on Autism and Schizophrenia.. *Neuroscience and biobehavioral reviews*. <https://doi.org/10.1016/j.neubiorev.2020.04.012>
- Hall, M., Willis, D., Rodriguez, E., & Schwarz, J. (2023). Maternal immune activation as an epidemiological risk factor for neurodevelopmental disorders: Considerations of timing, severity, individual differences, and sex in human and rodent studies. *Frontiers in Neuroscience*, 17. <https://doi.org/10.3389/fnins.2023.1135559>
- Han, V., Patel, S., Jones, H., Nielsen, T., Mohammad, S., Hofer, M., Gold, W., Brilot, F., Lain, S., Nassar, N., & Dale, R. (2021). Maternal acute and chronic inflammation in pregnancy is associated with common neurodevelopmental disorders: a systematic review. *Translational Psychiatry*, 11. <https://doi.org/10.1038/s41398-021-01198-w>
- Kwon, H., Choi, G., & Huh, J. (2022). Maternal inflammation and its ramifications on fetal neurodevelopment.. *Trends in immunology*. <https://doi.org/10.1016/j.it.2022.01.007>
- Lins, B. (2021). Maternal immune activation as a risk factor for psychiatric illness in the context of the SARS-CoV-2 pandemic. *Brain, Behavior, & Immunity - Health*, 16. <https://doi.org/10.1016/j.bbih.2021.100297>
- Massrali, A., Adhya, D., Srivastava, D., Baron-Cohen, S., & Kotter, M. (2022). Virus-Induced Maternal Immune Activation as an Environmental Factor in the Etiology of Autism and Schizophrenia. *Frontiers in Neuroscience*, 16. <https://doi.org/10.3389/fnins.2022.834058>
- Quagliato, L., De Matos, Ú., & Nardi, A. (2021). Maternal immune activation generates anxiety in offspring: A translational meta-analysis. *Translational Psychiatry*, 11. <https://doi.org/10.1038/s41398-021-01361-3>
- Tang, Q., Wang, X., Yang, F., Liang, L., Li, Y., Liu, W., Zhou, R., & , B. (2025). Pathophysiological associations between maternal immune activation and neurodevelopmental disorders in offspring: a comprehensive review. *Frontiers in Endocrinology*, 16. <https://doi.org/10.3389/fendo.2025.1681190>
- Woods, R., Lorusso, J., Potter, H., Neill, J., Glazier, J., & Hager, R. (2021). Maternal immune activation in rodent models: A systematic review of neurodevelopmental changes in gene expression and epigenetic modulation in the offspring brain.. *Neuroscience and biobehavioral reviews*. <https://doi.org/10.1016/j.neubiorev.2021.07.015>