Does Maternal Immune Activation have broad relevance across Neurodevelopmental and Psychiatric Disorders?

While not the sole cause, **maternal immune activation (MIA) appears broadly relevant** to multiple neurodevelopmental and psychiatric disorders.

Does maternal immune activation increase risk for neurodevelopmental and psychiatric disorders? N = 20

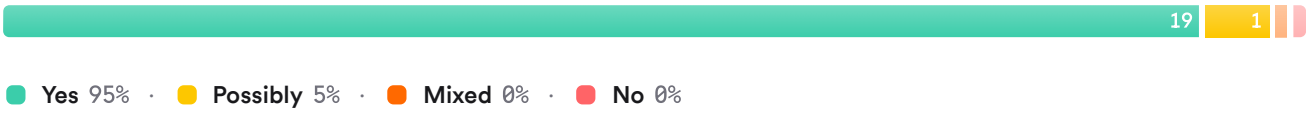

FIGURE 1 Consensus that maternal inflammation increases NDD risk

Maternal immune activation refers to systemic inflammation during pregnancy from infection or other inflammatory states. Across human and animal work, it is repeatedly linked to higher risk of several neurodevelopmental and psychiatric outcomes, though effects are modest and depend on timing, severity, and other risk factors.

Disorders Implicated

- **Autism spectrum disorder (ASD)** and **schizophrenia** are most consistently associated with maternal infection and inflammation in epidemiological studies and MIA animal models (Estes & McAllister, 2016; Careaga et al., 2017; Brown & Meyer, 2018; Gumusoglu & Stevens, 2019; Bergdolt & Dunaevsky, 2019; Szabo et al., 2025; Haddad et al., 2020; Otero & Antonson, 2022; Tang et al., 2025).
- **ADHD** and **Tourette syndrome** are also linked to maternal inflammatory states (obesity, pre-eclampsia, smoking, stress, autoimmune disease, asthma, low SES) (Han et al., 2021; Tang et al., 2025; Woods et al., 2022).
- **Bipolar disorder** shows associations with maternal infection/inflammation in cohort studies (Brown & Meyer, 2018).
- Reviews describe MIA as a **shared early risk factor** for a “broad spectrum” of CNS disorders and psychoses, not just ASD and schizophrenia (Estes & McAllister, 2016; Brown & Meyer, 2018; Gumusoglu & Stevens, 2019; Otero & Antonson, 2022; Tang et al., 2025; Mueller et al., 2020).

Examples of MIA-Linked Outcomes

Disorder group	Types of maternal inflammatory exposures linked	Citations
ASD, schizophrenia	Viral/bacterial infection, autoimmune disease, fever, obesity, stress	(Estes & McAllister, 2016; Careaga et al., 2017; Brown & Meyer, 2018; Gumusoglu & Stevens, 2019; Bergdolt & Dunaevsky, 2019; Szabo et al., 2025; Haddad et al., 2020; Han et al., 2021; Otero & Antonson, 2022; Tang et al., 2025)

Disorder group	Types of maternal inflammatory exposures linked	Citations
ADHD, Tourette	Obesity, pre-eclampsia, smoking, stress, autoimmune disease, asthma, low SES	(Han et al., 2021; Woods et al., 2022; Tang et al., 2025)
Broader psychoses	Prenatal infection → dopaminergic changes, psychosis-relevant behaviors	(Aguilar-Valles et al., 2020; Gumusoglu & Stevens, 2019; Bergdolt & Dunaevsky, 2019; Otero & Antonson, 2022; Mueller et al., 2020)

FIGURE 2 Maternal exposures linked to multiple disorders

Shared Mechanisms Across Disorders

- MIA elevates cytokines (e.g., IL-6, IL-1β, TNF-α, IL-17A) that cross the placenta, alter placental function, activate fetal microglia, and disrupt neurogenesis, migration, and cortical circuitry (Han et al., 2021; Boulanger-Bertolus et al., 2018; Szabo et al., 2025; Haddad et al., 2020; Aguilar-Valles et al., 2020; Otero & Antonson, 2022; Tang et al., 2025).
- These changes produce overlapping behavioral phenotypes in animals (social deficits, sensorimotor gating problems, anxiety- and depression-like behaviors, cognitive changes) relevant to ASD, schizophrenia, mood and anxiety disorders (Gumusoglu & Stevens, 2019; Bergdolt & Dunaevsky, 2019; Haddad et al., 2020; Brown & Meyer, 2018; Otero & Antonson, 2022; Bilbo et al., 2017).

Heterogeneity and “Priming” Rather Than Determinism

- MIA is described as an **early “priming” event** that increases vulnerability, often requiring genetic risk or later “second hits” (stress, drugs, additional immune insults) for disorders to emerge (Szabo et al., 2025; Estes & McAllister, 2016; Brown & Meyer, 2018; Meyer, 2019; Otero & Antonson, 2022; Mueller et al., 2020).
- Many offspring remain resilient; outcomes vary by timing, intensity, sex, genetics, microbiome, and environment (Meyer, 2019; Hall et al., 2023; Mueller et al., 2020).

Conclusion

Across human and animal research, maternal immune activation is a broad, non-specific risk factor that can bias neurodevelopment toward multiple psychiatric and neurodevelopmental disorders rather than any single diagnosis. Its impact is probabilistic and shaped by many interacting biological and environmental factors.

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/fpsyt.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

Boulanger-Bertolus, J., Pancaro, C., & Mashour, G. (2018). Increasing Role of Maternal Immune Activation in Neurodevelopmental Disorders. *Frontiers in Behavioral Neuroscience, 12*. https://doi.org/10.3389/fnbeh.2018.00230

Brown, A., & Meyer, U. (2018). Maternal Immune Activation and Neuropsychiatric Illness: A Translational Research Perspective.. *The American journal of psychiatry, 175 11*, 1073-1083. https://doi.org/10.1176/appi.ajp.2018.17121311

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

Estes, M., & McAllister, A. (2016). Maternal immune activation: Implications for neuropsychiatric disorders. *Science, 353*, 772 - 777. https://doi.org/10.1126/science.aag3194

Gumusoglu, S., & Stevens, H. (2019). Maternal Inflammation and Neurodevelopmental Programming: A Review of Preclinical Outcomes and Implications for Translational Psychiatry.. *Biological psychiatry, 85 2*, 107-121. https://doi.org/10.1016/j.biopsych.2018.08.008

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

Han, V., Patel, S., Jones, H., & Dale, R. (2021). Maternal immune activation and neuroinflammation in human neurodevelopmental disorders. *Nature Reviews Neurology, 17*, 564 - 579. https://doi.org/10.1038/s41582-021-00530-8

Meyer, U. (2019). Neurodevelopmental Resilience and Susceptibility to Maternal Immune Activation.. *Trends in neurosciences*. https://doi.org/10.1016/j.tins.2019.08.001

Mueller, F., Scarborough, J., Schalbetter, S., Richetto, J., Kim, E., Couch, A., Yee, Y., Lerch, J., Vernon, A., Weber-Stadlbauer, U., & Meyer, U. (2020). Behavioral, neuroanatomical, and molecular correlates of resilience and susceptibility to maternal immune activation. *Molecular Psychiatry, 26*, 396 - 410. https://doi.org/10.1038/s41380-020-00952-8

Otero, A., & Antonson, A. (2022). At the crux of maternal immune activation: Viruses, microglia, microbes, and IL-17A. *Immunological Reviews, 311*, 205 - 223. https://doi.org/10.1111/imr.13125

Szabo, D., Otrokocsi, L., & Sperlágh, B. (2025). The role of maternal infections in neurodevelopmental psychiatric disorders: focus on the P2X7/NLRP3/IL-1β signalling pathway. *Journal of Neuroinflammation, 22*. https://doi.org/10.1186/s12974-025-03509-0

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., Fletcher, J., ElTaher, H., McEwan, F., Harris, I., Kowash, H., D'Souza, S., Harte, M., Hager, R., & Glazier, J. (2022). Maternal immune activation and role of placenta in the prenatal programming of neurodevelopmental disorders. *Neuronal Signaling, 7*. https://doi.org/10.1042/ns20220064