Does the Dysregulation of Microglia in Maternal Immune Activation dysregulate not only Innate Immunity but also Adaptive Immunity over the Lifespan?

Yes, MIA dysregulates **both innate and adaptive immunity** over the lifespan, though adaptive evidence is preliminary.

Does dysregulation of microglia in maternal immune activation dysregulate both innate and adaptive immunity over the lifespan? N = 7

Yes 100% · Possibly 0% · Mixed 0% · No 0%

FIGURE 1 Research consensus on MIA-driven innate and adaptive immune dysregulation

Maternal immune activation (MIA) persistently alters microglial innate immune reactivity from embryonic development through adulthood, with effects on adaptive immune cell populations emerging as a parallel but less-characterized consequence (Hayes et al., 2022; Schaafsma et al., 2017; Davis et al., 2025).

Persistent Innate Immune Dysregulation

MIA induces a long-lived **decrease in microglial immune reactivity** (blunting) across the developmental trajectory, accompanied by changes in chromatin accessibility and reduced transcription factor occupancy (Hayes et al., 2022; Mastenbroek et al., 2024). This blunted response diminishes microglial contributions to inflammatory states and impairs overlapping functional pathways including interferon signaling, phagocytosis, and protein localization (Hayes et al., 2022). Adult whole-brain microglia from MIA-exposed offspring display a persistent reduction in pro-inflammatory activation upon LPS re-challenge, yet hippocampal microglia show the opposite pattern—an increased inflammatory response—demonstrating region-specific divergence in innate immune programming (Schaafsma et al., 2017). The blunted phenotype reflects epigenetic reprogramming akin to **innate immune memory**, where prenatal immune priming alters the microglial response to secondary insults later in life (Mastenbroek et al., 2024; Chamera et al., 2020).

Evidence Strength	Claim
Strong	MIA causes a long-lived decrease in microglial immune reactivity (blunting) from neonatal stages through adulthood, confirmed by multiple independent groups across LPS and poly(I:C) models (Hayes et al., 2022; Schaafsma et al., 2017; Hayes et al., 2022; Traetta & Tremblay, 2022; Liu et al., 2026)
Strong	MIA persistently alters microglial transcriptomes and phagocytic function into adulthood, with epigenetic reprogramming underlying altered responses to secondary immune challenges (Mattei et al., 2017; Mastenbroek et al., 2024; Mattei et al., 2017; Mastenbroek et al., 2024)

Evidence Strength	Claim
Moderate	MIA alters peripheral adaptive immune cell distribution, including cytotoxic CD8+ T cell populations in thymus, spleen, lymph, and brain, suggesting crosstalk between innate and adaptive arms (Davis et al., 2025)

FIGURE 2 Evidence strength for MIA-driven innate and adaptive immune dysregulation claims

Mechanisms of Innate Immune Programming

The epigenetic landscape of microglia is durably reshaped by MIA, with more open chromatin regions but fewer transcription factors occupying them, consistent with a **trained immunity** mechanism (Mastenbroek et al., 2024; Hayes et al., 2022). Single-cell RNA-sequencing reveals that MIA does not generate a distinct microglial subpopulation but rather decreases the contribution to inflammatory microglia states (Hayes et al., 2022). MIA also shifts microglial phenotype from M1 toward mixed M1/M2-like subpopulations in fetal and neonatal brains, upregulating pleiotropic cytokines (Loayza et al., 2022). Neuron-microglia communication axes—particularly **CX3CL1-CX3CR1 and CD200-CD200R**—are disrupted by MIA, sensitizing offspring to exaggerated microglial activation upon a second immune hit in adulthood (Chamera et al., 2020; De Cossío et al., 2021; Chamera et al., 2020). Prenatal replacement of MIA microglia with naive microglia ameliorates immune blunting and restores striatal circuit development, confirming that aberrantly formed microglia are causally responsible for long-term innate immune dysfunction (Hayes et al., 2022).

Adaptive Immunity and Innate-Adaptive Crosstalk

Evidence for adaptive immune dysregulation is more limited but emerging. MIA alters the distribution of **cytotoxic CD8+ T cells** in both the periphery and brain, with elevated CD8+ T cells in the thymus but reduced populations in the spleen, lymph, and brain of adult offspring (Davis et al., 2025). These peripheral adaptive immune changes may contribute to alterations in microglial morphology in the prefrontal cortex, potentially accounting for sociability and repetitive-like behavioral deficits (Davis et al., 2025). Maternal intestinal T helper 17 cells, educated by endogenous microbes, serve as key drivers of IL-17A signals capable of reaching the fetal brain and causing neuropathologies, directly linking maternal adaptive immunity to offspring neurodevelopmental outcomes (Otero & Antonson, 2022). However, sterile immunostimulants commonly used in MIA models fail to capture the full biologically relevant **innate and adaptive inflammatory sequelae** induced by live pathogen infection, limiting translational conclusions about adaptive immune involvement (Otero & Antonson, 2022).

Lifespan Persistence and Limitations

Dimension	Finding	Key Caveat
Innate immune blunting	Persists from neonatal stage through adulthood across multiple brain regions (Hayes et al., 2022; Traetta & Tremblay, 2022)	Direction of change varies by brain region (whole brain vs. hippocampus) (Schaafsma et al., 2017)
Microglial transcriptome	Altered expression persists into adulthood but effect size is relatively small (Mastenbroek et al., 2024)	Contradictory results across MIA models, timing, and readouts (Smolders et al., 2018; Breach et al., 2021)

Dimension	Finding	Key Caveat
Adaptive immune cells	CD8+ T cell redistribution in periphery and brain of adult offspring (Davis et al., 2025)	Single study; mechanism linking peripheral T cells to CNS microglia not established (Davis et al., 2025)
Sex-specific effects	MIA blunts microglial reactivity and disrupts synaptic pruning predominantly in males (Liu et al., 2026)	Female-specific outcomes underexplored (Liu et al., 2026)

FIGURE 3 Lifespan persistence of MIA immune effects with key caveats

The evidence strongly supports that MIA dysregulates microglial innate immunity across the lifespan through epigenetic priming and immune blunting, while adaptive immune involvement—though demonstrable through altered T cell distributions and maternal Th17 cell signaling—remains preliminary and requires further investigation to establish causal links between peripheral adaptive immunity and CNS microglial dysfunction.

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References

Breach, M., Dye, C., Joshi, A., Platko, S., Gilfarb, R. A., Krug, A., Franceschelli, D., Galan, A., Dodson, C. M., & Lenz, K. (2021). Maternal allergic inflammation in rats impacts the offspring perinatal neuroimmune milieu and the development of social play, locomotor behavior, and cognitive flexibility. *Brain, behavior, and immunity, 95*, 269 - 286. https://doi.org/10.1016/j.bbi.2021.03.025

Chamera, K., Szuster-Głuszczak, M., Trojan, E., & Basta-Kaim, A. (2020). Maternal Immune Activation Sensitizes Male Offspring Rats to Lipopolysaccharide-Induced Microglial Deficits Involving the Dysfunction of CD200–CD200R and CX3CL1–CX3CR1 Systems. *Cells, 9*. https://doi.org/10.3390/cells9071676

Davis, L., Ince, L. M., Gullapalli, S., & Fonken, L. (2025). Neuroimmune and behavioral changes elicited by maternal immune activation in mice are ameliorated by early postnatal immune stimulation. *Brain, behavior, and immunity, 127*, 375 - 386. https://doi.org/10.1016/j.bbi.2025.03.005

De Cossío, L. F., Lacabanne, C., Bordeleau, M., Castino, G., Kyriakakis, P., & Tremblay, M. (2021). Lipopolysaccharide-induced maternal immune activation modulates microglial CX3CR1 protein expression and morphological phenotype in the hippocampus and dentate gyrus, resulting in cognitive inflexibility during late adolescence.. *Brain, behavior, and immunity*. https://doi.org/10.1016/j.bbi.2021.07.025

Hayes, L. N., An, K., Carloni, E., Li, F., Vincent, E., Trippaers, C., Paranjpe, M., Dölen, G., Goff, L., Ramos, A., Kano, S.-I., & Sawa, A. (2022). Prenatal immune stress blunts microglia reactivity, impairing neurocircuitry. *Nature, 610*, 327 - 334. https://doi.org/10.1038/s41586-022-05274-z

Liu, C., Li, T., Ji, J.-J., Li, Z., Samsom, J. N., Liu, K., Lu, Q., Zhu, W., & Liu, F. (2026). Maternal immune activation causes sex-specific impairment of microglial function during prefrontal cortex development.. *Brain, behavior, and immunity, 136*, 106770. https://doi.org/10.1016/j.bbi.2026.106770

Loayza, M., Lin, S., Carter, K., Ojeda, N., Fan, L., Ramarao, S., Bhatt, A., & Pang, Y. (2022). Maternal immune activation alters fetal and neonatal microglia phenotype and disrupts neurogenesis in mice. *Pediatric Research, 93*, 1216-1225. https://doi.org/10.1038/s41390-022-02239-w

Mastenbroek, L. J. M., Kooistra, S., Eggen, B., & Prins, J. R. (2024). The role of microglia in early neurodevelopment and the effects of maternal immune activation. *Seminars in Immunopathology, 46*. https://doi.org/10.1007/s00281-024-01017-6

Mattei, D., Ivanov, A., Ferrai, C., Jordan, P., Guneykaya, D., Buonfiglioli, A., Schaafsma, W., Przanowski, P., Deuther-Conrad, W., Brust, P., Hesse, S., Patt, M., Sabri, O., Ross, T., Eggen, B., Boddeke, E., Kamińska, B., Beule, D., Pombo, A., . . . Wolf, S. (2017). Maternal immune activation results in complex microglial transcriptome signature in the adult offspring that is reversed by minocycline treatment. *Translational Psychiatry, 7*. https://doi.org/10.1038/tp.2017.80

Otero, A., & Antonson, A. M. (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

Schaafsma, W., Basterra, L. B., Jacobs, S., Brouwer, N., Meerlo, P., Schaafsma, A., Boddeke, E., & Eggen, B. (2017). Maternal inflammation induces immune activation of fetal microglia and leads to disrupted microglia immune responses, behavior, and learning performance in adulthood.. *Neurobiology of disease, 106*, 291-300. https://doi.org/10.1016/j.nbd.2017.07.017

Smolders, S., Notter, T., Smolders, S., Rigo, J., & Brône, B. (2018). Controversies and prospects about microglia in maternal immune activation models for neurodevelopmental disorders.. *Brain, behavior, and immunity, 73*, 51-65. https://doi.org/10.1016/j.bbi.2018.06.001

Traetta, M. E., & Tremblay, M. (2022). Prenatal inflammation shapes microglial immune response into adulthood.. *Trends in immunology*. https://doi.org/10.1016/j.it.2022.10.009