# What is the relationship between Neuro-Immune Circuits and Neurodevelopmental and Psychiatric Disorders?

## **Neuro-Immune Circuits and Brain Disorders:** Immune–brain crosstalk as a shared pathway in disease

Neuro-immune circuits are the bidirectional communication loops between immune cells/molecules and neural circuits. Across many studies, disrupted versions of these circuits are repeatedly linked with both neurodevelopmental (e.g., autism, Tourette's, ADHD) and psychiatric disorders (e.g., schizophrenia, depression).

### Core Roles of Neuro-Immune Circuits

- Immune signals (cytokines, complement, inflammasomes) and cells (microglia, astrocytes, monocytes) are **essential for normal brain development**, including synapse formation, pruning, and circuit refinement (Zengeler & Lukens, 2021; Lukens & Eyo, 2022; Westacott & Wilkinson, 2022; Martino et al., 2020; Gagliano et al., 2025).
- Microglia and other innate immune components help **sculpt neural circuitry** and maintain CNS homeostasis across life (Zengeler & Lukens, 2021; Lukens & Eyo, 2022; Hu et al., 2022).

#### Key Immune Mechanisms Implicated

| Mechanism / pathway | Example relevance to disorders | Citations |
|---|---|---|
| Microglial activation & synaptic pruning | ASD, schizophrenia, depression | (Zengeler & Lukens, 2021; Lukens & Eyo, 2022; Hughes et al., 2022; Matta et al., 2019; Raju & Smith, 2025; Westacott & Wilkinson, 2022; Hu et al., 2022) |
| Pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) | Alter circuits; link to mood, cognition | (Pape et al., 2019; Novellino et al., 2020; Nusslock et al., 2024; Szabo et al., 2025; Hong et al., 2016) |
| Complement & innate immune genes | Critical periods, ASD/SCZ risk | (Westacott & Wilkinson, 2022; Chen et al., 2022) |
| Maternal immune activation (e.g., infections) | Fetal brain disruption → ASD/SCZ | (Raju & Smith, 2025; Szabo et al., 2025; Bilbo et al., 2017) |
| Gut–microbiota–immune–brain axis | ASD, depression, anxiety, schizophrenia, Tourette/ADHD | (Zhou et al., 2025; Hughes et al., 2022; Martino et al., 2020; Matta et al., 2019; Prata et al., 2017; Hours et al., 2025) |

FIGURE 1 Major neuro-immune mechanisms tied to disorders

### Neurodevelopmental Disorders

- Autism: strong evidence for **innate immune dysfunction, neuroinflammation, and microglial dysregulation**, linked to altered synaptic connectivity and behavior (Zengeler & Lukens, 2021; Lukens & Eyo, 2022; Hughes et al., 2022; Matta et al., 2019; Hughes et al., 2024; Hu et al., 2022).
- Tourette, OCD, ADHD: immune pathways shape early circuit formation; **hyper-reactive immune/neuroinflammatory states** may drive symptom fluctuations (Martino et al., 2020; Gagliano et al., 2025).
- Maternal immune activation, via pathways like **P2X7–NLRP3–IL-1β**, can disrupt neuronal migration, synapse formation, and BBB integrity, increasing ASD/SCZ risk (Szabo et al., 2025; Bilbo et al., 2017).

### Psychiatric Disorders Across the Lifespan

- Schizophrenia, bipolar disorder, depression, PTSD and others share **chronic low-grade inflammation, microglial activation, and dysregulated immune-related gene expression** in brain tissue (Pape et al., 2019; Novellino et al., 2020; Chen et al., 2022; Nusslock et al., 2024; Hong et al., 2016; Prata et al., 2017).
- In depression, inflammatory signals alter **threat, reward, and executive circuits**, creating neuroimmune feedback loops that sustain symptoms and comorbid physical illness (Nusslock et al., 2024).
- Cross-disorder transcriptomic work shows that **immune-related gene networks co-operate with neuronal networks**, forming shared modules across ASD, SCZ, MDD, AD, and PD (Chen et al., 2022).

### Conclusion

Neuro-immune circuits are not peripheral to brain disorders—they are deeply embedded in how neural networks develop, function, and fail. Dysregulated immune signaling (especially microglial activity, cytokines, complement, and maternal or gut-driven inflammation) is a common pathway that links diverse neurodevelopmental and psychiatric conditions and is a major target for future diagnostics and therapies.



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