What are the relationships among Neuro-Developmental and Psychiatric Disorders with Addiction and Common Neuro-Immune Pathways?

Neurodevelopmental, Psychiatric Disorders, Addiction, and Shared Neuro-Immune Pathways

Multiple lines of research suggest that neurodevelopmental disorders (NDDs), major psychiatric conditions, and addiction are linked by overlapping immune and inflammatory mechanisms in the brain and body. These shared pathways may help explain why these disorders often co-occur across the lifespan.

Shared Neuro-Immune Mechanisms Across Disorders

- **Innate immunity and chronic inflammation:** Dysregulated microglia, astrocytes, and blood–brain barrier function, with chronic low-grade inflammation, are seen across neurodegenerative and psychiatric disorders including depression, schizophrenia, ASD and PTSD (Novellino et al., 2020; Pape et al., 2019; Hassamal, 2023).
- **Common pathways:** Recurrent involvement of **pro-inflammatory cytokines** (IL-1β, IL-6, TNF-α), NF-κB, MAPK, and PI3K–Akt/mTOR signaling is reported in NDDs and mood/psychiatric disorders (Gagliano et al., 2025; Han et al., 2021; Namba et al., 2021; Chen et al., 2025; Hassamal, 2023; Shahi et al., 2025).
- **Neuroinflammation as a convergent "multiple-hit" pathway:** Genetic vulnerability plus infections, stress, or toxins can break immune tolerance, drive neuroinflammation, and disturb developing neural circuits, yielding syndromes labeled as NDDs or early-onset psychiatric disorders (Gagliano et al., 2025; Han et al., 2021; Martino et al., 2020; Namba et al., 2021; Shahi et al., 2025).

Examples of Common Neuro-Immune Features

Feature / Pathway	Disorders Implicated	Citations
Microglial activation, cytokines	ASD, ADHD, SCZ, depression, TS/OCD	(Gagliano et al., 2025; Novellino et al., 2020; Han et al., 2021; Martino et al., 2020; Pape et al., 2019; Hassamal, 2023; Shahi et al., 2025)
Maternal immune activation	ASD, ADHD, TS	(Gagliano et al., 2025; Diao et al., 2026; Han et al., 2021)
NF-κB / inflammasome (NLRP3)	ASD, ADHD, SCZ, BD, OCD, TS	(Chen et al., 2025; Shahi et al., 2025)
PI3K–Akt signaling	NDDs, immune disorders	(Xiu et al., 2024; Chen et al., 2025)
Gut–brain–immune axis	ASD, ADHD, epilepsy	(Martino et al., 2020; Chen et al., 2025)

FIGURE 1 Shared immune pathways across brain disorders.

Neurodevelopmental–Immune Links and Progression to Psychiatric States

- **NDD-specific immune profiles:** Children with ASD, ADHD, and intellectual disability show a characteristic pattern: depleted compensatory immune-regulatory system, increased IL-1 signaling, macrophage polarization, and altered chemokines, clustering into subtypes dominated by **neurogenesis, Th1 polarization, or IL-1 signaling** (Sreenivas et al., 2023; Liu et al., 2025; Herrera-Imbroda et al., 2023; Hofford et al., 2018; Shahi et al., 2025).
- **Genetic overlap with immune disorders:** Large GWAS show substantial polygenic sharing and pleiotropic loci between NDDs and autoimmune/immune disorders, enriched for neural signaling and inflammatory pathways (Gagliano et al., 2025; Han et al., 2021; Breunig et al., 2024; Xiu et al., 2024).
- **NDDs and mood disorders:** Shared mechanisms include neurotransmitter dysregulation (dopamine, serotonin), neuroinflammation, and HPA-axis changes, with overlapping alterations in prefrontal and amygdala circuits for emotion and control (Nusslock et al., 2024; Bertollo et al., 2025; Hassamal, 2023).

Addiction, Depression, Psychosis, and Neuro-Immune Crosstalk

- **Substance use disorders (SUDs):** Drugs of abuse alter peripheral and central immune signaling, changing cytokines and glial activity, which in turn affect synaptic plasticity and reward circuits; neuroimmune signaling is proposed as a treatment target for SUDs (Namba et al., 2021; Smiley & Wood, 2022; Hofford et al., 2018).
- **Depression and SUD comorbidity:** Inflammation biases brain networks toward **heightened threat, blunted reward, and weak executive control**, increasing risk for both depression and substance use and promoting self-medicating, pro-inflammatory behaviors (Nusslock et al., 2024; Namba et al., 2021; Smiley & Wood, 2022; Hassamal, 2023).
- **Psychosis and drug abuse:** Both psychosis and SUDs show overlapping pro-inflammatory lipids and proteins (cytokines, chemokines, endocannabinoids, eicosanoids), suggesting a common origin in abnormal neurodevelopment driven partly by neuroinflammation (Herrera-Imbroda et al., 2023; Pape et al., 2019; Hassamal, 2023).

Transdiagnostic Perspective and Future Directions

- Several reviews argue for a **transdiagnostic "immunoneuropsychiatry" framework**, where subgroups of ASD, ADHD, schizophrenia, mood disorders, TS/OCD, and SUDs are pathogenically related via microglial activation, cytokines, autoantibodies, and barrier dysfunction (Gagliano et al., 2025; Novellino et al., 2020; Martino et al., 2020; Namba et al., 2021; Pape et al., 2019; Chen et al., 2025; Hassamal, 2023; Shahi et al., 2025).
- This supports exploring **immunomodulatory and gut–brain axis–targeted treatments** and rethinking diagnostic boundaries based on shared neuro-immune signatures (Gagliano et al., 2025; Novellino et al., 2020; Martino et al., 2020; Namba et al., 2021; Xiu et al., 2024; Pape et al., 2019; Chen et al., 2025; Shahi et al., 2025).

Summary

Neurodevelopmental disorders, major psychiatric illnesses (depression, bipolar disorder, psychosis), and addiction frequently share common neuro-immune pathways. These include chronic low-grade inflammation, microglial and cytokine dysregulation, maternal immune activation, gut–brain–immune interactions, and overlapping genetic risk with immune diseases. Such shared mechanisms likely contribute to high comorbidity and may open routes to immune-targeted, transdiagnostic prevention and treatment strategies.

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