Transcriptomics, the Immune System and Neurodevelopmental and Psychiatric Disorders

Transcriptomics, the Immune System, and Neurodevelopmental/Psychiatric Disorders

Transcriptomic studies show that immune-related gene expression is widely altered in neurodevelopmental and major psychiatric disorders. These changes often converge on **innate immune pathways**, interact with neuronal networks, and may be shaped by gene–environment interactions.

Shared Immune–Transcriptomic Themes Across Disorders

- Large brain datasets across ASD, schizophrenia (SCZ), bipolar disorder (BD), MDD, Alzheimer's and Parkinson's disease show >60% of curated immune-related genes altered in at least one disorder, with shared changes dominated by innate immunity and neuroimmune–neuronal co-expression networks (Chen et al., 2022; , 2022; Chen et al., 2022).
- Cross-disorder analyses of ASD, SCZ and BD find >25% of the transcriptome altered, including microglial, astrocyte and interferon-response modules that define neural–immune mechanisms (Gandal et al., 2018; Hernandez et al., 2020).
- Integrative NDD atlases and regression/NDD cohorts consistently identify inflammatory and immune-response pathways as a common axis, alongside translational, mitochondrial and synaptic changes (Nishida et al., 2025; Khavari et al., 2020; Han et al., 2025; Koetsier et al., 2025).

Examples of Immune/Neural Pathway Involvement

Disorder / context	Immune feature	Neural feature	Citations
ASD (brain/blood, multi-omics)	Upregulated IL-1β, IFN-γ, immune genes	Downregulated synaptic genes	(Meng et al., 2025; Nishida et al., 2025; Koetsier et al., 2025; Tomaiuolo et al., 2023)
SCZ/BD/MDD (brain)	Innate immune / interferon modules	Disease-specific neuronal networks	(Chen et al., 2022; Gandal et al., 2018; Priyanka et al., 2025; , 2022; Chen et al., 2022)
PANS, tics/OCD	Altered innate immune pathways; reduced TNF/IL-6 responses	Acute-onset neuropsychiatric symptoms, regression	(Jones et al., 2021; Han et al., 2025)

FIGURE 1 Immune–transcriptomic alterations across disorders and tissues

Gene–Environment and Developmental Links

- Oxidative stress in differentiating neurons drives strong upregulation of immunity-related genes and disruption of neurodevelopmental pathways linked to SCZ (Nishida et al., 2025).
- Maternal inflammation and autoimmunity associate with tics/OCD in offspring, and maternal and Tourette brain transcriptomes share enriched innate immune pathways (Khavari et al., 2020; Jones et al., 2021).
- Complement C4 is elevated in SVZ of SCZ and ASD, with ASD genes enriched for adaptive, and SCZ for innate immune functions (Mou et al., 2022).
- Several studies emphasize immune–epigenetic–ribosomal interfaces as a mechanism by which infections and other exposures disturb neurodevelopment (Nishida et al., 2025; Khavari et al., 2020; Han et al., 2025; Xiu et al., 2024; Koetsier et al., 2025).

Genetic Architecture, Causality, and Targets

- Many immune transcriptomic changes are not strongly explained by common GWAS variants, suggesting substantial environmental contribution (Chen et al., 2022).
- Nonetheless, genetic work shows shared polygenic architecture between NDDs and immune diseases, converging on inflammatory and PI3K–Akt pathways (Xiu et al., 2024), and immune biomarkers with potential causal roles in SCZ, BD, depression and AD (Dardani et al., 2024; Stacey et al., 2025).
- Immune-related transcription factors (e.g., IRF, NFKB family) and hubs such as IRF3, RACK1, and specific cytokine/immune receptors emerge as candidate mechanistic and therapeutic targets (Meng et al., 2025; Dardani et al., 2024; Gandal et al., 2018; Priyanka et al., 2025; Tomaiuolo et al., 2023; Stacey et al., 2025).

Conclusion

Across neurodevelopmental and psychiatric disorders, transcriptomics consistently shows immune dysregulation—especially of innate immune and interferon-related pathways—tightly intertwined with synaptic, neuronal, and translational processes. These patterns point to a complex gene–environment interface, where infections, oxidative stress, and other inflammatory states act on susceptible genetic backgrounds to alter brain and peripheral immune programs. Immune-focused biomarkers and targets are emerging, but disentangling causality and refining disorder- and cell type–specific interventions remain key challenges.

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