Brain Hyper- and/or Hypo-Connectivity in Neurodevelopmental, Psychiatric, Addiction, Brain Injury, Neurologic and Neurodegenerative Disorders

Brain Hyper- and Hypoconnectivity Across Brain Disorders: A Cross-Diagnostic Overview

Across many neurodevelopmental, psychiatric, addiction, neurologic, and neurodegenerative conditions, brain changes are increasingly understood as **network-level "dysconnectivity"** rather than isolated lesions. Resting-state and structural connectivity studies show repeatable patterns of both **hyperconnectivity** (stronger-than-normal coupling) and **hypoconnectivity** (weaker-than-normal coupling) in large-scale networks.

Patterns Across Major Brain Networks

Psychiatric disorders

- Shared pattern: **DMN–FPN hyperconnectivity** and **DMN–salience / salience–FPN hypoconnectivity**, associated with generalized cognitive deficits (Sha et al., 2019; Sha et al., 2018).
- Depression: **Hyperconnectivity within DMN** and between DMN and FPN; **hypoconnectivity within FPN** and between FPN and attention/salience networks (Kaiser et al., 2015; Sha et al., 2019).
- PTSD: Trauma-related **DMN hypoconnectivity** and AN–DMN hypoconnectivity; PTSD-specific **hyperconnectivity** between affective, somatomotor, and DMN regions (Bao et al., 2021).
- Structural white-matter networks in schizophrenia, bipolar disorder, and MDD show **shared reductions in global efficiency and connectivity strength** with graded severity (HC > MDD > BD > SZ) (Repple et al., 2022; De Lange et al., 2018; Hansen et al., 2022).

Addiction (substance + behavioral)

- SUD/behavioral addictions show **hyperconnectivity** in reward and salience circuits (amygdala–basal ganglia, thalamus–midbrain, insula, parahippocampal regions) (Tolomeo & Yu, 2022).
- Network-level meta-analyses show **hypoconnectivity in limbic, salience, and FPN**, with mixed hyper/hypoconnectivity in DMN (Taebi et al., 2022).
- Behavioral addictions: disrupted inhibition/salience and cingulate–thalamus–striatal systems, including combined structural and rsFC abnormalities (Zeng et al., 2023; Chen et al., 2024).

Neurologic and Neurodegenerative disease

- Traumatic brain injury and multiple sclerosis: frequent **functional hyperconnectivity**, especially early, interpreted as an adaptive or compensatory response (Hillary et al., 2014; Hillary & Grafman, 2017; Aswendt & Hoehn, 2022).
- Mild cognitive impairment and Alzheimer's disease: shift toward **hypoconnectivity** as degeneration progresses (Hillary et al., 2014; Herzog et al., 2022).
- High-order analyses in AD and frontotemporal dementia show widespread **hypoconnectivity with focal hyperconnectivity** in hubs (amygdala, insula, frontal gyrus), suggesting compensatory processes that wane with progression (Herzog et al., 2022).
- Cross-disorder analyses identify **central, long-range, hub connections** as "hotspots" for disconnectivity across multiple psychiatric and neurological disorders (De Lange et al., 2018; Heuvel & Sporns, 2019; Hansen et al., 2022; Cauda et al., 2018).

Conceptual Themes

Hyper- vs hypoconnectivity dynamics

Phase / severity	Typical pattern	Example conditions	Citations
Early / mild insult	Predominant **hyperconnectivity** (often in hubs) as compensatory response	TBI, MS, early neurodegeneration	(Hillary et al., 2014; Hillary & Grafman, 2017; Aswendt & Hoehn, 2022)
Progressive / advanced	Increasing **hypoconnectivity**, loss of integration	AD, advanced dementia, broad neurodegeneration	(Hillary et al., 2014; Herzog et al., 2022)
Chronic psychiatric & addiction	Mixed patterns: hyper within DMN/reward; hypo among control, salience, attention networks	MDD, PTSD, SUD, BA	(Sha et al., 2019; Kaiser et al., 2015; Tolomeo & Yu, 2022; Taebi et al., 2022; Bao et al., 2021; Chen et al., 2024)

FIGURE 1 Illustrative phases of hyper- and hypoconnectivity across disorders

Shared Network Principles

- Many disorders preferentially affect **highly connected hubs and integrative pathways**, making them cross-disorder "vulnerability points" (Heuvel & Sporns, 2019; De Lange et al., 2018; Hansen et al., 2022; Cauda et al., 2018).
- Polyconnectomic and meta-connectomic approaches show **generalizable whole-brain connectivity signatures** that cut across multiple psychiatric and neurodegenerative diagnoses (Libedinsky et al., 2024; Sha et al., 2018; Zhang et al., 2021).

Conclusion

Across diverse brain disorders, hyper- and hypoconnectivity cluster in a small set of large-scale networks (DMN, FPN, salience, limbic/reward, sensorimotor). Early or milder insults often show hub-focused hyperconnectivity that may be compensatory, while more chronic or degenerative stages are marked by widespread hypoconnectivity and reduced network efficiency. Shared vulnerability of central hubs and integrative connections helps explain overlapping symptoms and supports network-based, transdiagnostic models of brain disease.

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