Brain Network Disease

> Brain network diseases are neurological or psychiatric conditions arising from dysfunction in the brain's structural or functional connectivity, rather than from localized damage alone.

Concept	Explanation
Brain Networks	Interconnected brain regions that work together to perform cognitive or motor tasks
Structural Connectivity	Physical white matter tracts (mapped via DTI/tractography)
Functional Connectivity	Temporally correlated activity between brain areas (fMRI, EEG, MEG)
Disconnectivity	Loss or dysfunction of network communication
Diaschisis	Remote functional impairment caused by a focal lesion

Examples of Brain Network Diseases

Disease	Affected Network(s)	Manifestation
Alzheimer's Disease	Default Mode Network (DMN)	Memory loss, disorientation
Epilepsy	Thalamocortical and other circuits	Seizures due to network hyperexcitability
Parkinson's Disease	Basal ganglia-thalamocortical loops	Tremor, rigidity, cognitive slowing
Schizophrenia	Salience, frontoparietal, DMN	Hallucinations, delusions, cognitive deficits
Autism Spectrum Disorder	Social brain network	Atypical social interaction and communication
Stroke (with diaschisis)	Variable depending on location	Deficits extend beyond lesion site
Functional Neurological Disorder	Limbic-attention-motor network	Non-lesional motor or sensory symptoms

Tools for Studying Brain Networks

- **fMRI** – Functional connectivity via BOLD signal (task or resting state)
- **DTI (Diffusion Tensor Imaging)** – Structural mapping of white matter
- ⚡ **EEG / MEG** – Temporal resolution of network activity
- **Graph Theory** – Models brain as nodes and edges (connectomics)
- **Connectome** – Global map of brain connectivity

Clinical Relevance: Understanding brain network dysfunction helps:

- Guide **non-lesional epilepsy surgery**

- Explain **cognitive and behavioral syndromes** beyond structural lesions
- Design **neuromodulation therapies** (DBS, TMS) targeting entire circuits
- Understand recovery via **neural plasticity and compensation**

Idiopathic generalized epilepsy (IGE) is a brain network disease, but the location of this network and its relevance for treatment remain unclear. Ji et al. combine the locations of brain abnormalities in IGE (131 coordinates from 21 studies) with the human connectome to identify an IGE network. They validated this network by showing alignment with structural brain abnormalities previously identified in IGE and brain areas activated by generalized epileptiform discharges in simultaneous electroencephalogram-functional magnetic resonance imaging. The topography of the IGE network aligns with brain networks involved in motor control and loss of consciousness consistent with generalized seizure semiology. To investigate therapeutic relevance, they analyzed data from 21 patients with IGE treated with deep brain stimulation (DBS) for generalized seizures. Seizure frequency reduced a median 90% after DBS and stimulation sites intersect an IGE network peak in the centromedian nucleus of the thalamus. Together, this study helps unify prior findings in IGE and identify a brain network target that can be tested in clinical trials of brain stimulation to control generalized seizures [1].

1)
Ji GJ, Fox MD, Morton-Dutton M, Wang Y, Sun J, Hu P, Chen X, Jiang Y, Zhu C, Tian Y, Zhang Z, Akkad H, Nordberg J, Joutsa J, Torres Diaz CV, Groppa S, Gonzalez-Escamilla G, Toledo M, Dalic LJ, Archer JS, Selway R, Stavropoulos I, Valentin A, Yang J, Isbaine F, Gross RE, Park S, Gregg NM, Cukiert A, Middlebrooks EH, Dosenbach NUF, Turner J, Warren AEL, Chua MMJ, Cohen AL, Larivière S, Neudorfer C, Horn A, Sarkis RA, Bubrick EJ, Fisher RS, Rolston JD, Wang K, Schaper FLWVJ. A generalized epilepsy network derived from brain abnormalities and deep brain stimulation. Nat Commun. 2025 Mar 24;16(1):2783. doi: 10.1038/s41467-025-57392-7. PMID: 40128186.