# Models of Network Spread and Network Degeneration in Brain Disorders

## *Supplemental Information*

### Diffusion MRI to Connectivity

The key steps and methods in network extraction are now well established (1–3). The original 6-direction diffusion tensor imaging (DTI) (4) has given way to modern high-angular-resolution diffusion imaging (HARDI) sequences that overcome several challenges of conventional DTI, *viz* poor orientation resolution, inability to detect crossing or kissing fibers, and inability to measure non-Gaussian diffusion processes (5, 6). Several algorithms for reconstruction of fiber orientation from HARDI acquisitions are available, including Q-ball imaging (5, 7), diffusion spectrum imaging (8), spherical deconvolution (9, 10), 3D curve inference (11) and diffusion kurtosis imaging (12). **Tractography** refers to the computational algorithms needed to connect voxels in brain dMRI data along the directions of putative fibers. *Deterministic* tractography (13, 14) and *probabilistic* tractography (15) are both popular methods, and new algorithmic advances have yielded *global* tractography algorithms (16–18). An excellent review article is (19). **Anatomic brain networks** were first extracted from tractography by (2, 8, 20) and the requisite processing pipelines are now well established, following (2, 21). As illustrated in Figure S1, this involves coregistering subject MRI and dMRI onto a standard atlas, e.g. Desikan-Killiany atlas (22); segmentation into gray, white and CSF; and parcellation into gray matter structures. Parcels are used to establish the seed and target regions for tractography, and the connectivity between the two is given by summing the probabilities of the streamlines.

### Graph Theory Analysis

Characteristic graph metrics to examine differences in network topology are now widely available and published. These network metrics include global (network-wide) metrics like connection density, global

efficiency, clustering coefficient, small-worldness, average shortest path length, modularity, etc. Several metrics have local counterparts, i.e. can be defined at the node or edge level, including: Local connection strength, local efficiency and local modularity. A widely cited open resource available in MATLAB for computing these metrics is the Brain Connectivity Toolbox (BCT) as described in (23). Specific network statistics have been examined extensively in prior reviews, see (1, 3, 24, 25).

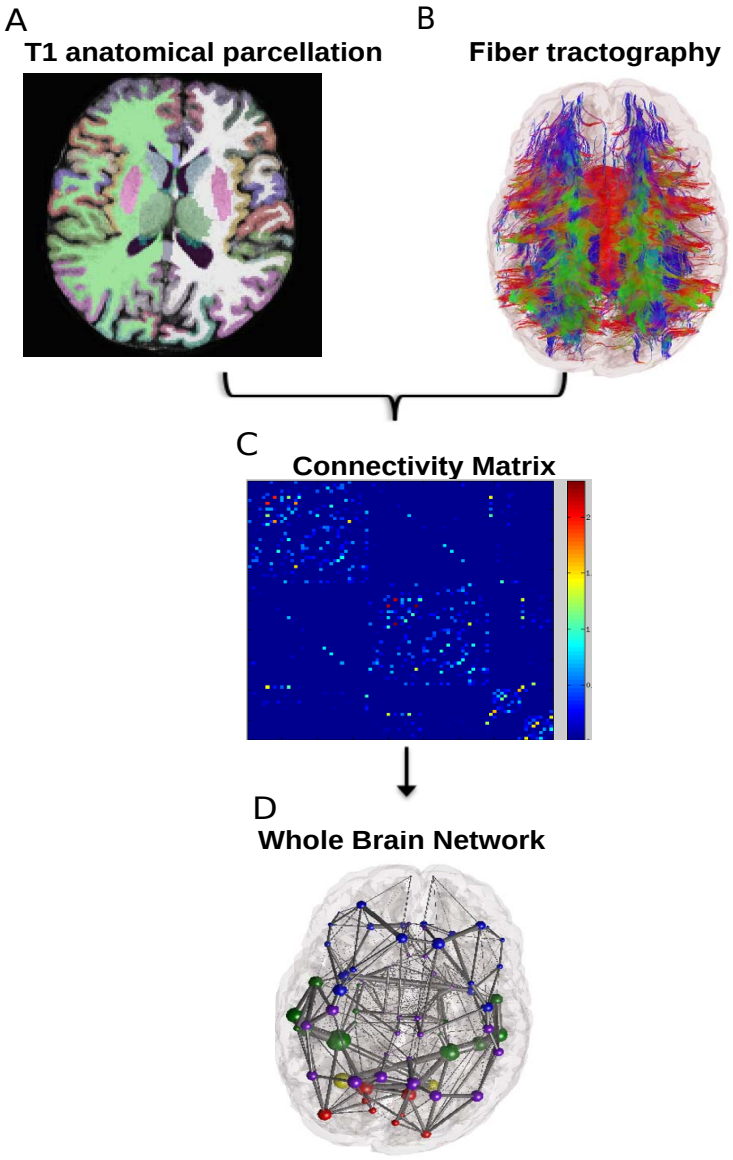


**Figure S1**: General pipeline of connectome extraction, from T1-MRI and dMRI, to coregistration, atlas-based parcellation to tractography, and finally culminating in a connectivity matrix representing the whole brain network.

**Supplemental References**


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