## Applications of Brain Network Analysis in Clinical Neuroscience Paul M. Matthews

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By the mid-twentieth century, Karl Lashley's "mass action principle", which explained clinical deficits in terms of the volume of brain affected, and the localisationist hypotheses of Jean-Martin Charcot were reconciled by connectionist models. As more recently expressed in a graph theoretical framework by Olaf Sporn and others, this approach recognizes that the brain is organized as connected hubs with hierarchical modularity (Sporns). These hubs show rich local (and sparser long-range) connectivities to display "small world" behaviours.

The recent ability to characterize microstructural (e.g., diffusion tensor imaging) and physiological (e.g., resting state fMRI [rsfMRI], MEG) signals from the brain that show complementary structures have transformed this conception into a powerful heuristic for clinical neuroscience. It already is having a practical impact. For example, classical syndromic nosology for psychiatric disease is being challenged by a neurobiological systems-based framework conceptualizing disease in terms of network dysfunction. Relationships between different manifestations is view in terms of differences in relative weighting of dysfunction- or adaptive compensatory activity- in brain networks. Different presentations of dementia are well distinguished and changes in network activity over time provide a possible way of monitoring disease evolution. More widespread manifestations of focal processes and the dynamics of changing interactions have been mapped in epilepsy. The robustness of formulations is being tested- and largely is supported by- crossmodal studies. For example, discriminant network changes in Parkinson's disease and related disorders have been explored usefully with both FDG PET and fMRI

Emerging applications are building on modeling to create a "virtual brain" that promises to guide interventions. In the first instance, these interventions likely would be interference methods, such as TMS. However, as they become better annotated with additional data, networks may guide new drug development by relating molecular to systems pharmacodynamics and suggesting functional biomarkers of reponse.

Understanding of network plasticity and dynamics also is providing a rationale for new forms of brain-machine interfaces. The potential to image network dynamics will help in the design of tools to enable this, e.g., by identifying network nodes capable of greater adaptive change.

Proc. Intl. Soc. Mag. Reson. Med. 23 (2015)