What Is the Physiological Basis of Functional Connectivity & What Can It Tell Us?

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I will review evidence that spontaneous, i.e. not stimulus- or task-driven, activity in the brain is not noise, but orderly and organized at the level of large scale systems in a series of functional networks that maintain at all times a high level of coherence. These networks of spontaneous activity correlation, or resting state networks (RSN), measured with fMRI are closely related to the underlying anatomical connectivity, but their topography is also gated by the history of prior task activation. Network coherence does not depend on covert cognitive activity, but its strength and integrity relates to behavioral performance. In the healthy brain, individual variability in cognitive functions, or learning a new task, and even the predisposition to learn are correlated with specific patterns of functional connectivity within/across networks. In the diseased brain, specific abnormalities, even in structurally normal regions, correlate with behavioral deficits. Functional connectivity therefore has the potential to become a clinically helpful tool to assess brain function in any disease state that impairs neuronal communication. An important challenge for the future is to understand the temporal structure of RSNs at rest and their coordination during tasks. Initial high temporal resolution studies with electro-corticography (ECoG) or magneto-encephalography (MEG) suggest that fMRI RSNs are heterogeneous in the frequency domain: with different networks or even different parts of the same network oscillating at different frequencies. Computational studies show that one of such dynamics, the anti-correlation between networks, depends on noise driven transitions between different multi-stable cluster synchronization states. These multi-stable states emerge because of transmission delays between regions that are modeled as coupled oscillators systems. Large-scale systems dynamics are useful for keeping different functional sub-networks in a state of heightened competition, which can be stabilized and fired by even small modulations of either sensory or internal signals.