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Exploring the network dynamics underlying brain activity during rest

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ABSTRACT

Since the mid 1990s, the intriguing dynamics of the brain at rest has been attracting a growing body of research in neuroscience. Neuroimaging studies have revealed distinct functional networks that slowly activate and deactivate, pointing to the existence of an underlying network dynamics emerging spontaneously during rest, with specific spatial, temporal and spectral characteristics. Several theoretical scenarios have been proposed and tested with the use of large-scale computational models of coupled brain areas. However, a mechanistic explanation that encompasses all the phenomena observed in the brain during rest is still to come.

In this review, we provide an overview of the key findings of resting-state activity covering a range of neuroimaging modalities including fMRI, EEG and MEG. We describe how to best define and analyze anatomical and functional brain networks and how unbalancing these networks may lead to problems with mental health. Finally, we review existing large-scale models of resting-state dynamics in health and disease.

An important common feature of resting-state models is that the emergence of resting-state functional networks is obtained when the model parameters are such that the system operates at the edge of a bifurcation. At this critical working point, the global network dynamics reveals correlation patterns that are spatially shaped by the underlying anatomical structure, leading to an optimal fit with the empirical BOLD functional connectivity. However, new insights coming from recent studies, including faster oscillatory dynamics and non-stationary functional connectivity, must be taken into account in future models to fully understand the network mechanisms leading to the resting-state activity.

Contents

Abbreviations: fMRI, functional magnetic resonance imaging; MEG, magnetoencephalography; EEG, electroencephalography; BOLD, blood oxygen level dependent; BLP, band-limited power; RSN, resting-state network; DMN, default mode network; ICA, independent component analysis; AAL, automated anatomical labeling; ROI, region of interest; DTI/DSI, diffusion tensor/spectrum imaging.

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1. Brain activity during rest

Someone who is awake but not consciously performing any task, physical or mental, is said to be resting. In this state, unlike sleeping, the person is conscious and ready to respond promptly to any sort of external stimulation or cognitive requirement. One could say that the person is somehow on *stand-by*: although still and quiet, she is awake, ready to suddenly chase a fly that lightly lands on her arm, or to immediately turn her head towards the least disturbing sound. Notably, while the person is resting and the body is static, the brain instead seems to be actively engaged, exhibiting slow spatiotemporally organized fluctuations of neuronal activity. The patterns of brain activity observed during quiet wakeful rest are distinguishable from the ones observed during goal-directed behaviour or when the brain falls asleep (Deco et al., 2013a; Kalcher et al., 2013; Larson-Prior et al., 2011; Mennes et al., 2011).

Several studies have speculated on the link between this resting brain activity and underlying high-order cognitive processes such as moral reasoning, self-consciousness, remembering past experiences or planning for the future (Buckner et al., 2008; Lou et al., 1999; Morcom and Fletcher, 2007; Saxe and Kanwisher, 2003; Wagner et al., 2005). However, findings of resting brain patterns in anesthetized monkeys (Vincent et al., 2007) and, more recently, in rats (Lu et al., 2012), points to a more fundamental origin of resting brain activations (Fig. 1) (even if animals may also have a need for self representations).

To date, the blood-oxygen-level dependent (BOLD) signal used in functional magnetic resonance imaging (fMRI) has been the first and most widely used technique in studies of brain activity during rest (Biswal et al., 1995, 2010). But evidence of coordinated spontaneous activity has been detected in data collected with other functional imaging techniques such as optical imaging (Arieli et al., 1996), positron-emission tomography (PET) (Raichle et al., 2001), electroencephalography (EEG) (Goldman et al., 2002; Laufs et al., 2003; Moosmann et al., 2003), electrophysiology (Leopold et al., 2003) and more recently magnetoencephalography (MEG) (Brookes et al., 2011; de Pasquale et al., 2010). All these techniques have their own specificities, sensitivities and spatio-temporal resolutions and the data may be affected by different kinds of physiological signals and artefacts (see Section 2). As such, it is crucial to take into account the type of signal being measured by each technique in order to understand the neurophysiological meaning of resting-state activity and how it relates at multiple spatial and temporal scales.

Explorations into the organization of resting-state activity in the brain have revealed the existence of temporally correlated activity – or functional connectivity – between different voxels in the brain, some belonging to brain areas specific for different tasks, defining the so-called resting state networks (RSNs). Despite the evidence from the empirical side, the significance of functional connectivity in brain activity during rest remains under debate. Over the last years, a growing number of theoretical and experimental studies have aimed to investigate the origin of the correlation patterns defining RSNs using different neuroimaging techniques. However, it is still not clear whether RSNs are an epiphenomenon or not. Studies using diffusion-MRI to detect white matter pathways in the living brain have inspected the relationship between RSNs and the underlying map of long-range axonal connections (Hagmann et al., 2008; Sporns et al., 2000) (see Section 3). Importantly, a remarkable match has been found between the neuroanatomical network and resting-state functional connectivity, indicating that functional connections between brain areas may be mediated through white-matter fibres. Bottom-up computational models can be used to simulate the interactions between brain areas in the structural network and compare the results with empirical functional data. Although the empirical data is typically contaminated by physiological signals (which vary strongly across the human brain and therefore are difficult to remove entirely), a good fit with the model results (free from any type of physiological and behavioural artefacts) indicates that at least some part of resting-state functional connectivity originates from neural interactions in the white-matter network. In Section 4 we review the existing models of resting-state activity obtained through different reduction lines.

To understand the mechanisms leading to the dynamics observed in the brain at rest, one can look at the brain as a dynamical system. Indeed, the complex space–time structure of the brain's wiring diagram, together with a myriad of biochemical processes, form a dynamical framework capable of holding an infinite number of mental states over which cognition unfolds (Kelso, 2012; Tononi et al., 1994). The existence of different input-dependent stable states in the brain has been evident since the first human electrophysiological recordings, which revealed that strong