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Review article

Small-world human brain networks: Perspectives and challenges

Xuhong Liao[a,b,c], Athanasios V. Vasilakos[d], Yong He[a,b,c,*]

[a] National Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, Beijing 100875, China
[b] IDG/McGovern Institute for Brain Research, Beijing Normal University, Beijing 100875, China
[c] Beijing Key Laboratory of Brain Imaging and Connectomics, Beijing Normal University, Beijing 100875, China
[d] Department of Computer Science, Electrical and Space Engineering, Lulea University of Technology, 97187 Lulea, Sweden

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ABSTRACT

Modelling the human brain as a complex network has provided a powerful mathematical framework to characterize the structural and functional architectures of the brain. In the past decade, the combination of non-invasive neuroimaging techniques and graph theoretical approaches enable us to map human structural and functional connectivity patterns (i.e., connectome) at the macroscopic level. One of the most influential findings is that human brain networks exhibit prominent small-world organization. Such a network architecture in the human brain facilitates efficient information segregation and integration at low wiring and energy costs, which presumably results from natural selection under the pressure of a cost-efficiency balance. Moreover, the small-world organization undergoes continuous changes during normal development and ageing and exhibits dramatic alterations in neurological and psychiatric disorders. In this review, we survey recent advances regarding the small-world architecture in human brain networks and highlight the potential implications and applications in multidisciplinary fields, including cognitive neuroscience, medicine and engineering. Finally, we highlight several challenging issues and areas for future research in this rapidly growing field.

1. Introduction

The human brain is a formidably complex system, in which approximately 86 billion neurons (Azevedo et al., 2009) interact through approximately 150 trillion synapses (Pakkenberg et al., 2003). Explaining the emergent coherent brain function unfolding on complicated structural pathways is a great challenge for neuroscientists. Recently, there has been an explosion of studies modelling the brain as complex networks that consist of neural units (e.g., neurons and brain regions) linked by structural connectivity (i.e., structural wiring) or functional connectivity (i.e., coherent temporal activities) (Bassett and Bullmore, 2006; Bullmore and Sporns, 2009, 2012; Craddock et al., 2013; He and Evans, 2010; Park and Friston, 2013; Reijneveld et al., 2007). The characterization of the human brain from a network perspective provides a comprehensive understanding of the structural and functional architectures of the human brain. Mapping and quantifying the connectivity patterns of the human brain (i.e., the human connectome) have become important topics in the field of neuroscience (Kelly et al., 2012; Sporns et al., 2005; Van Essen et al., 2012).

To date, significant progress has been made in neuroimaging technologies, such as electroencephalography (EEG), magnetoencephalography (MEG) and multi-modal magnetic resonance imaging (e.g., structural MRI, diffusion MRI and functional MRI), which enable non-invasive mapping of the human connectome. Graph theory-based network analysis helps demonstrate the intrinsic topological organization of human brain networks, such as small-worldness, modular organization and highly connected or centralized hubs (Bullmore and Sporns, 2009, 2012; He and Evans, 2010; Kaiser, 2011; Meunier et al., 2010; van den Heuvel and Sporns, 2013b). The small-world model is of special interest when describing human brain networks, because it supports efficient information segregation and integration with low energy and wiring costs, and it is well suited for complex brain dynamics (e.g., a high rate of information transmission) (Watts and Strogatz, 1998). Recent studies indicate that the small-world topological organization of brain networks undergoes changes during development and ageing (Cao et al., 2016b; Collin and van den Heuvel, 2013; Gao et al., 2016), as well as in the case of brain disorders (Dai and He, 2014; Filippi et al., 2013; Fornito and Bullmore, 2015; Fornito et al., 2012b; Gong and He, 2015; Stam, 2014; Xia and He, 2011), and that these changes provide novel insights into the biological mechanisms in health and disease. Moreover, advances in small-world brain models

* Corresponding author at: National Key Laboratory of Cognitive Neuroscience and Learning, IDG/McGovern Institute for Brain Research, Beijing Key Laboratory of Brain Imaging and Connectomics, Beijing Normal University, Beijing 100875, China.
E-mail address: yong.he@bnu.edu.cn (Y. He).

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may spur innovations in engineering, thereby enabling the design of more-efficient and more-powerful chips, computers and other devices than what existed previously (Bassett et al., 2010; Eliasmith et al., 2012; Furber, 2016; Machens, 2012; Merolla et al., 2014; Rueckert, 2016).

This review primarily focuses on the recent advances in small-world human brain networks, through the utility of non-invasive neuroimaging data and graph theory-based network analysis. The remaining sections are organized as follows. Section 2 provides background on human brain network analyses and the small-world model, including the construction of brain networks and graph theoretical approaches. Section 3 summarizes recent small-world human brain network studies using empirical or theoretical approaches. Sections 4–6 discuss the potential implications and applications in multidisciplinary science, such as cognitive neuroscience, medicine and engineering. Finally, Section 7 highlights challenging issues and areas for future research in this rapidly growing field.

2. Background

2.1. Brain network construction

Diverse biological, technological and social systems can be modelled as networks, which consist of a set of nodes that represent the constituent units of the system, and edges that denote the interactions between nodes (Barabási, 2011; Boccaletti et al., 2006). For example, in the World Wide Web, the nodes may be webpages, whilst the edges may be the hyperlinks between them. In brain networks, the nodes can be neurons, neuronal populations or brain regions, depending on the spatial scales of interest, and the edges represent the structural or functional connectivity that links the nodes. To date, most in vivo human brain network studies have primarily focused on the large-scale networks of brain regions, which can be constructed as follows (Fig. 1):

(1) Node definition. Nodes can be defined in various ways according to the neuroimaging data considered (Fig. 1a), such as EEG electrodes, MEG sensors or reconstructed brain sources of EEG/MEG signals using biophysical models (Lopes da Silva, 2004). In MRI studies, regions of interest may be defined according to anatomical landmarks (Tzourio-Mazoyer et al., 2002), functional significances (Dosenbach et al., 2010; Power et al., 2011), connectivity profiles (Cohen et al., 2008; Craddock et al., 2012; Fan et al., 2016), multi-modal parcellation (Glasser et al., 2016) and random parcellation (Zalesky et al., 2010), as well as a single imaging voxel with a high spatial resolution (~millimetres) (Hayasaka and Laurienti, 2010; Liang et al., 2013; Liao et al., 2013; Valencia et al., 2009) (Fig. 1b) . In most cases, brain networks involve tens to hundreds of nodes, with the exception of voxel-wise brain networks that comprise at least thousands of nodes (i.e., voxels). Notably, it is still an open question regarding how to choose the most appropriate node definition while addressing a specific scientific question (Bullmore and Bassett, 2011; Kaiser, 2011; Rubinov and Sporns, 2010; Sporns, 2014). In general, structurally constrained schemes are preferred used in structural network studies, whereas functional defined schemes are preferred in functional network studies. When exploring the structure–function relationship, the parcellations obtained through multi-modal neuroimaging data or randomized parcellations may serve as appropriate candidates. Besides, cross-validation using different parcellations is encouraged to address whether the findings are not driven by a specific brain parcellation.

(2) Edge definition. The structural and functional connectivity of the human brain may be inferred through in vivo neuroimaging techniques (Fig. 1c). In general, structural connectivity refers to the anatomical pathways between brain regions, which form a biological route for information transfer and communication. Specifically, by using diffusion MRI to measure the anisotropic diffusion of water molecules in brain tissues, structural connectivity may be inferred as the interregional white matter fibre tracts reconstructed through deterministic or probabilistic tractography methods (Behrens et al., 2003; Mori et al., 1999; Parker et al., 2003). Additionally, structural connectivity can also be defined as the structural covariance inferred from the across-individual covariation of regional morphological measurements (e.g.,

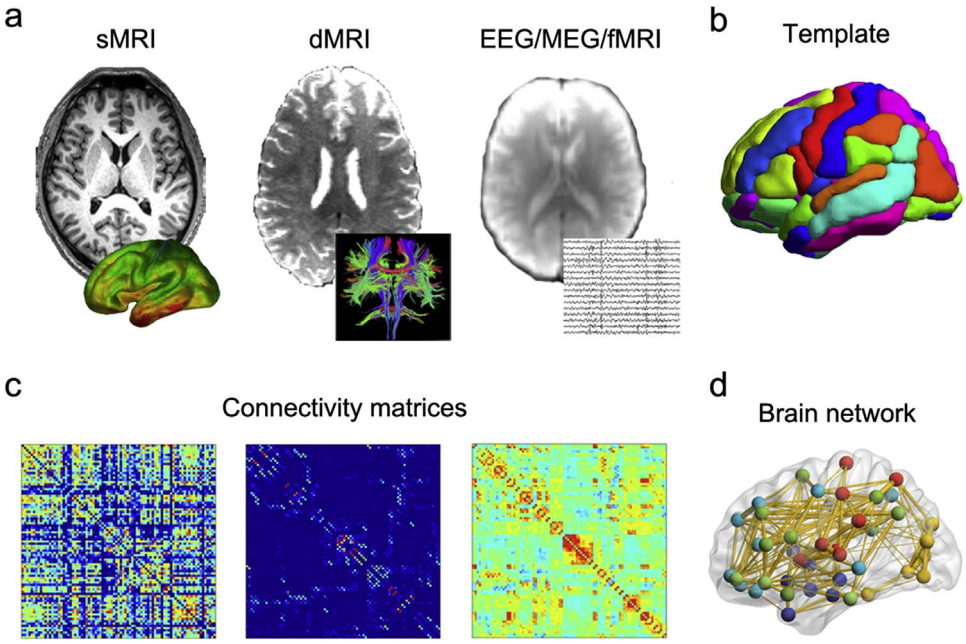

Fig. 1. Illustration of brain network construction. (a) Multi-modal neuroimaging data used for the estimation of structural and functional connectivity, including structural MRI (left), diffusion MRI (middle) and EEG, MEG and functional MRI data (right). sMRI, structural MRI; dMRI, diffusion MRI; fMRI, functional MRI; EEG, electroencephalography; MEG, magnetoencephalography. (b) Brain template used for the node definition. The brain nodes can be defined in a variety of ways, such as EEG electrodes, MEG sensors, anatomical and/or functional information-based divisions, random divisions and imaging voxels. (c) Structural and functional connectivity matrices representing the relationship between each pair of nodes. The structural connectivity can be inferred as across-individual covariation in regional morphological measures observed by structural MRI (left) or white matter fibre tracts reconstructed from diffusion MRI (middle). The functional connectivity between two nodes is estimated as the statistical coherence between the nodal time courses observed by EEG, MEG or functional MRI (right). (d) Visualization of the human brain network using the BrainNet Viewer package (Xia et al., 2013).