·Review·

Diffusion magnetic resonance imaging for Brainnetome: A critical review

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Abstract: Increasing evidence shows that the human brain is a highly self-organized system that shows attributes of small-worldness, hierarchy and modularity. The "connectome" was conceived several years ago to identify the underpinning physical connectivities of brain networks. The need for an integration of multi-spatial and -temporal approaches is becoming apparent. Therefore, the "Brainnetome" (brain-net-ome) project was proposed. Diffusion magnetic resonance imaging (dMRI) is a non-invasive way to study the anatomy of brain networks. Here, we review the principles of dMRI, its methodologies, and some of its clinical applications for the Brainnetome. Future research in this field is discussed.

Keywords: brain mapping; neural networks; magnetic resonance imaging; imaging

1 Introduction

Over the past two decades we have learned that, rather than individual regions, a group of intensively interacting brain areas are involved in even simple cognitive processes[1,2]. Thus, the entire brain can be characterized as a highly self-organized network[3]. This conceptualizing strategy has been analogously exploited in such other facets of our society as social networks and computer networks[3]. One or several sub-networks of the brain are disrupted in neurological or psychiatric disease, as evidenced in major depressive disorder (MDD)[4], bipolar disorder[5], Alzheimer's disease (AD)[6], and schizophrenia[2,5], as well as in normal development[7,8] and aging[9].

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The term "human connectome" was proposed to emphasize "a comprehensive structural description of the network of elements and connections forming the human brain"[3,10,11]. Subsequently, many studies emerged to explore the networks of the human brain, comprising data collection and the development of toolkits[11,12] to investigate healthy development and neuropsychiatric diseases[2,5-9]. Extending the connectome, the Brainnetome was conceived to reveal not only physical structural connectivities but also functional connectivities by various levels of *in-vivo* imaging methods and *ex-vivo* imaging/staining techniques. The Brainnetome seeks not only a static description of the network state at a certain time point, but also to describe the dynamic processes throughout natural development and neuropsychiatric evolution[13,14].

This review focuses on one of the most promising techniques, diffusion magnetic resonance imaging (dMRI), and its use for modeling and analysis in the

Brainnetome. dMRI is a widely used *in-vivo* imaging technique that explores neuronal microstructure by probing the diffusion of water molecules. To date, it is the only non-invasive method for revealing the micro-geometry of nervous tissues and exploring white matter fiber connectivities in living human subjects. Increasing numbers of reports reveal altered networks of white matter microstructure (WMM) in neuropsychiatric disorders, such as MDD[4], bipolar disorder[15], AD[16], schizophrenia[17] and epilepsy[18], as well as in development[7,8] and healthy aging[9]. Currently, two critical questions concerning WMM networks remain: how to define the nodes of networks, a crucial point in network construction[19], and how to identify WMM connections given two pre-defined nodes. The latter includes two sequential questions: how to model the distribution of water molecules within an individual voxel[20] and how to define the tractography based on the modeled distribution function[21].

First we introduce how to model the local diffusion function within individual voxels, from diffusion tensor imaging (DTI) to high angular resolution diffusion imaging (HARDI). Then, tractography methods are reviewed, and the limitations of local deterministic streamlining and its possible improved variants are discussed. Next, extant WMM network analysis and its clinical applications are charted. Finally, some unsolved problems in dMRI are discussed, and useful free software is recommended in the appendix. We provide a brief overview of the principles of dMRI and how its use in anatomical brain network analysis has evolved during the past decades, and then consider the realm of clinical applications of the dMRI-based Brainnetome, for both the developing brain and the brain with neuropsychiatric disease.

2 Principles of dMRI and diffusion distribution modeling

2.1 Diffusion-weighted imaging (DWI) and DTI The diffusion of water molecules is constrained by the surrounding structures including cells, axonal membranes, myelin sheaths, and surrounding tissue. Statistically, water molecules diffuse rapidly along and slowly across, neuronal fibers. Thus, quantitatively modeling the diffusion of water molecules among white matter fibers is crucial to understanding neuronal microstructure and fiber direction.

The classical diffusion gradient sequence used in dMRI is the pulsed gradient spin-echo sequence proposed by Stejskal and Tanner[22]. This sequence has 90° and 180° gradient pulses with duration time δ and separation time Δ. To eliminate the dependence of spin density, at least two measurements of DWI signals are needed, *S(b)* with the diffusion weighting factor b in the following equation introduced by Le Bihan *et al.*[23], and $S(0)$ with $b = 0$ which is the baseline signal without any gradient.

$$b = \gamma^2 \delta^2 (\Delta - \frac{\delta}{3}) \|\mathbf{G}\|^2 \quad (1)$$

In equation 1 for the value of b, γ is the proton gyromagnetic ratio, $\mathbf{G} = \|\mathbf{G}\|\mathbf{u}$ is the diffusion sensitizing gradient pulse with norm $\|\mathbf{G}\|$ and direction u. $\tau = \Delta - \frac{1}{3}\delta$ is normally used to describe the effective diffusion time[23,24]. With *S(b)* and the pulsed gradient spin echo sequence the diffusion weighted signal attenuation *E(b)* is given by the Stejskal-Tanner equation[22],

$$E(b) = \frac{S(b)}{S(0)} = \exp(-bD) \quad (2)$$

where D is the apparent diffusion coefficient (ADC) reflecting the properties of the surrounding tissues. Note that in the general case D is also dependent on $\mathbf{G}$ in a complex way; however, free diffusion in DTI assumes D is only dependent on the direction of $\mathbf{G}$, i.e. $\mathbf{u} = \mathbf{G}/\|\mathbf{G}\|$. Early work in dMRI reported that, in the ADC, D is dependent on the gradient direction $\mathbf{u}$ and was used in two or three DWI images in different directions to detect the properties of tissues[25,26]. Basser *et al.* introduced the diffusion tensor[24] to represent the ADC as $D(\mathbf{u}) = \mathbf{u}^T\mathbf{D}\mathbf{u}$, where $\mathbf{D}$ is called the diffusion tensor, which is a 3 × 3 symmetric positive definite matrix independent of $\mathbf{u}$. This method is called DTI and is the most common in dMRI. In DTI, the signal *E(b)* is represented as

$$E(b) = \exp(-b\mathbf{u}^T\mathbf{D}\mathbf{u}). \quad (3)$$

The diffusion tensor $\mathbf{D}$ can be estimated from measured diffusion signal samples $\{E(b_i)\}$ through a simple least-squares method or a weighted least-squares method[24],

or more complex methods which consider positive definite constraints or Rician noise[27-29]. If a single *b*-value is used, the optimal *b*-value for tensor estimation is reported to range between 0.7 and 1.5 × 10^{-3} s/mm^2 [30,31], and normally, ~20 DWI images are used in DTI for clinical studies. A schema of the sampling scheme normally used in DTI is shown in Fig. 3A. Useful indices can be obtained from the tensor **D**, and the most important are fractional anisotropy (FA) and mean diffusivity (MD)[32] defined as follows (Fig. 1):

$$\mathrm{FA}=\frac{\sqrt{3}\left\|\mathbf{D}-\frac{1}{3}\mathrm{Trace}(\mathbf{D})I\right\|}{\sqrt{2}\|\mathbf{D}\|}=\sqrt{\frac{3}{2}}\sqrt{\frac{(\lambda_1-\bar{\lambda})^2+(\lambda_2-\bar{\lambda})^2+(\lambda_3-\bar{\lambda})^2}{\lambda_1^2+\lambda_2^2+\lambda_3^2}} \quad (4)$$

$$\mathrm{MD}=\bar{\lambda}=\frac{1}{3}\mathrm{Trace}(\mathbf{D})=\frac{\lambda_1+\lambda_2+\lambda_3}{3} \quad (5)$$

where $\{\lambda_i\}_{i=1}^3$ represents the three eigenvalues of **D** and $\bar{\lambda}$ is the mean eigenvalue. MD and FA have been used in many clinical applications[21,33], such as a study of MD in stroke[34].

2.2 HARDI DTI modeling for dMRI is an intuitive way to chart the distribution of water molecules where aligned fibers occur. Unfortunately, when fibers cross within the voxel (as well as fanning and kissing), the simple Gaussian model in DTI is unable to correctly characterize the structure of the distribution (Fig. 2). One-third to two-thirds of the imaging voxels in the brain contain crossing fibers, making it urgently necessary to develop accurate modeling techniques in dMRI.

The diffusion process in each voxel is fully characterized by the diffusion probability density function called the ensemble average propagator (EAP) denoted as $P(\mathbf{R})$, which describes the ensemble mean probability in the voxel that the water molecules move with the displacement vector R under the effective diffusion time τ. By introducing the **q** vector defined as $\mathbf{q}=q\mathbf{u}=(2\pi)^{-1}\gamma\delta G$, b is given as $b = 4\pi^2\tau q^2$. Under the narrow pulse assumption in the pulsed gradient spin echo sequence, the EAP is the 3-D Fourier transform of the diffusion signal $E(\mathbf{q})$[35], i.e.,

$$P(\mathbf{R})=F\{E(\mathbf{q})\}(\mathrm{R})=\int_{\mathbf{R}^3}E(\mathbf{q})\exp(-2\pi i\mathbf{q}^T\mathbf{R})d\mathbf{q}. \quad (6)$$

The EAP of free diffusion in DTI has a Gaussian distribution[24]. However, the EAP in the general case is more complex. EAPs in different regions of the brain reflect different microstructures and reveal fiber directions. The term HARDI was first proposed by Tuch *et al.*[36,37], who reported a finer angular resolution sampling scheme than the conventional DTI scheme. The original HARDI term[36,37] means single-shell sampling (only one *b*-value) (Fig. 3C). Some researchers have proposed estimating orientation distribution functions or EAPs in multiple-shell sampling[38-41]. Thus the term HARDI now refers to all modeling methods beyond DTI.

Since the EAP is the Fourier transform of the DWI signal, diffusion spectrum imaging (DSI) was proposed to estimate the EAP using a fast Fourier transform from exhaustive signal samples[42]. This is impractical because DSI needs about 500 DWIs with a large range of *b*-values up to 17 000 s/mm^2. The sampling scheme in DSI is shown in Fig. 3B. Q-ball imaging (QBI)[43,44], as well as its derived

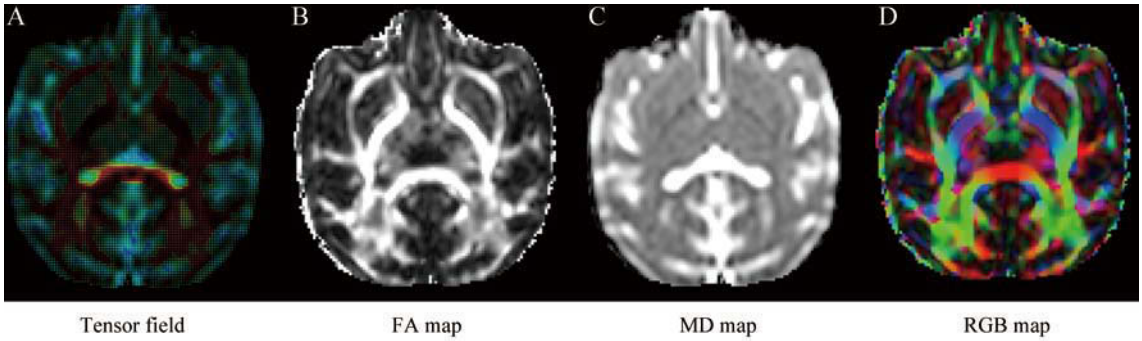

Fig. 1. Tensor field and scalar maps estimated from monkey data with b = 1 500 s/mm^2 (images created based on the data provided by Dr. Chunshui Yu from Xuanwu Hospital, Capital Medical University, Beijing, with permission). FA, fractional anisotropy; MD, mean diffusivity; RGB, red-green-blue.

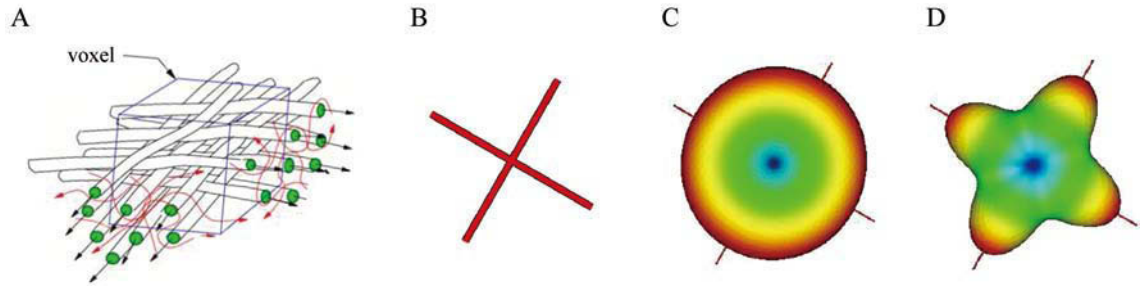

Fig. 2. Diffusion MRI modeling in the case of crossing fibers. A: Inside a voxel, the fibers are crossing instead of one bundle of directed fibers. B: Diagram to delineate the distribution of fibers inside the voxel. C: Traditional diffusion tensor imaging modeling fails to reveal the crossing structures. D: A possible model depicting the diffusion directions (adapted from Dr. Descoteaux's thesis[20]).

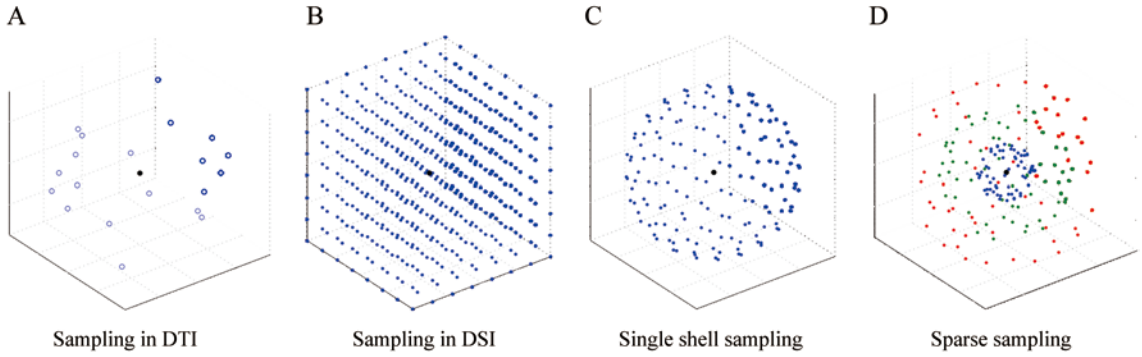

Fig. 3. Several kinds of sampling in q-space. The black dot in q = (0, 0, 0)T is the baseline image without a diffusion gradient. Note that although we showed sampling in R3, normally only samples in a half-space are used, e.g. qz≥0. A: sampling used in diffusion tensor imaging (DTI), normally <20 DWI images are used; B: dense Cartesian sampling used in diffusion spectrum imaging (DSI); C: single shell sampling; D: sparse sampling.

forms, to estimate varied orientation distribution functions (ODFs) from single shell data (Fig. 3C), has the merits of small sampling and fast solution and thus has been widely exploited in HARDI[45-49]. Considering that it cannot handle multiple-shell data, Cheng *et al.* proposed a HARDI method called analytical spherical polar Fourier imaging (SPFI) to estimate both the EAP profile and two kinds of ODFs from arbitrarily sampled data[50,51]. This works well, especially for data with high noise, low anisotropy, and non-exponential decay. The estimated EAP and two kinds of ODFs estimated using SPFI from monkey data, where the crossing angles of fibers are almost 90° are shown in Fig. 4. This agrees with the recent findings of Wedeen *et al.* who also identified well-aligned WMM as a grid-like structure[52].

3 Tractography for WMM and network construction

Tractography integrates voxel-wise orientations to describe a fiber tract that connects related voxels. Tractographic methods can be classified as local or global, deterministic or probabilistic, model-based or model-free. The most widely used is the tensor streamline[53,54], which uses the local deterministic method and considers local orientation as the principal direction of tensors in DTI. The tensor streamline essentially solves an ordinary differential equation with a given principal vector field. Several issues need to be considered in this algorithm. The tensors in sub-voxel positions need to be interpolated. An FA threshold and orientation angle threshold also need to be set as the stop condition so that the tracts cannot reach grey matter

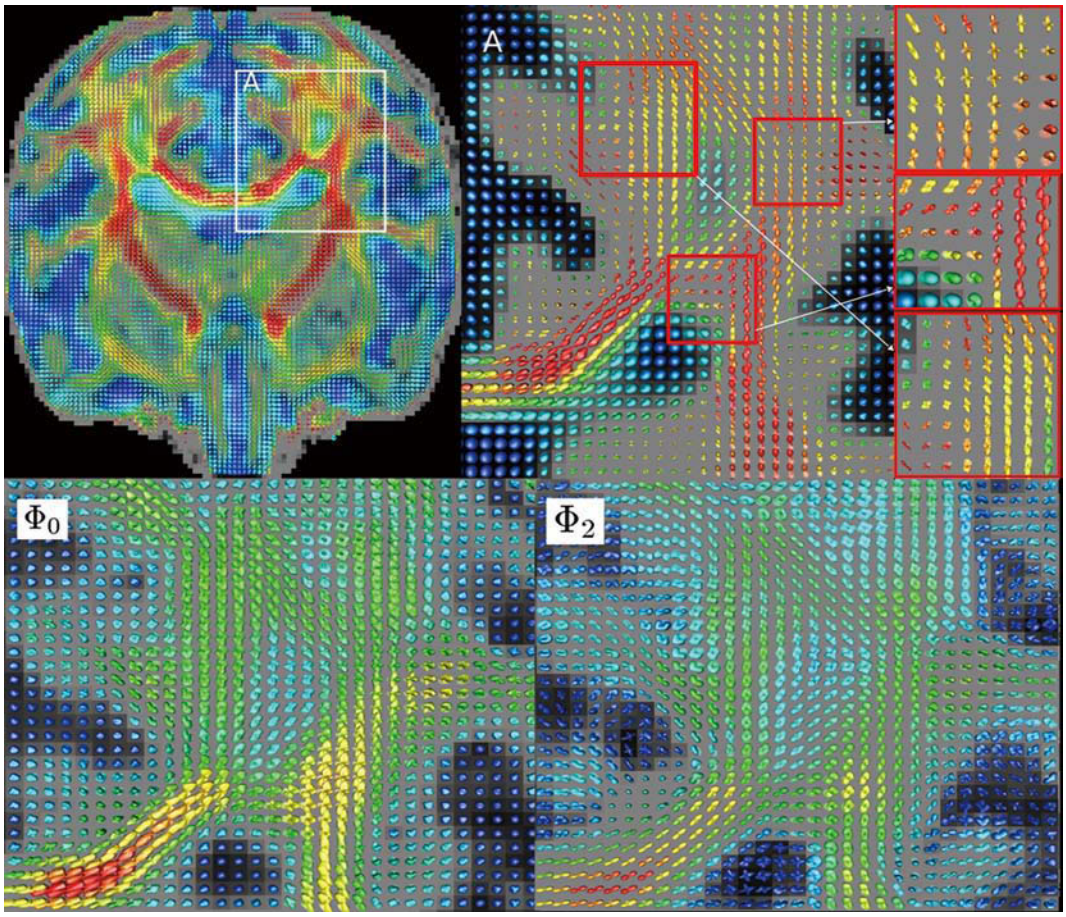

Fig. 4. Ensemble average propagator and two kinds of orientation distribution functions estimated using analytical spherical polar Fourier imaging from monkey data (images created based on the data provided by Dr. Chunshui Yu from Xuanwu Hospital, Capital Medical University, Beijing, with permission).

with a low FA, and so that the local direction near the tract cannot change too much.

In addition to the intrinsic modeling errors of tensor streamline tracking, this method cannot yield a probabilistic trust region for the acquired tracts. Therefore, it has been generalized into a multi-tensor/ODF streamline by considering the local orientation as the principal, or through the use of multi-tensors[55], or by considering the maxima of ODFs[20,56,57]. Globally optimized tractography[58-65] was also proposed and has performed better than local tractographic methods. The uncertainty and prior probability can be incorporated into a Bayesian formalization to obtain the posterior probability of the particular values in a given local diffusion model[66,67]. Based on the posterior probability, deterministic tracking can be performed many times to finally obtain a probability between two regions[67].

If we know the white matter fiber tracts of the entire brain, given two pre-defined regions of interest (ROIs) as the start and end, we can readily specify the connecting fiber tracts between the ROIs. This is the basis for constructing an anatomical network based on the dMRI technique. There are many types of pre-defined ROIs, anatomical[68-70], functional[71-73], or mixed[74]. In addition, when examination is confined to a specific sub-network (as detailed in the following section), localized fiber tracts can be selected by the ROIs, such as anterior cingulate cortex[75,76], prefrontal cortex[77], and motor areas[78]. We can also leverage fiber clustering methods[79,80], or mutually combine with fMRI[81,82] to group fiber tracts that predict different connectivity

paths. There are many network studies from the perspective of dMRI for Brainnetome to investigate, in both healthy and neuropsychiatric subjects. Gong *et al.* used a probabilistic tracking method to examine the relationship between the properties of the global network and age and sex in normal subjects[83]. Yan *et al.* also investigated the relationship between the small-worldness of the network and sex and brain size[84]. The global efficiency of the dMRI network was also found to be positively correlated with the intelligence quotient[85].

4 dMRI network-based applications in neuropsychiatric disease

As the connecting path between sub-/cortical areas, WMMs act as transportation routes for information exchange between gray matter. The dysfunctions in neuropsychiatric disease usually reflect various alterations of white matter[4,86]. The anatomical network derived from dMRI is not merely confined to local WMM lesions, but provides a whole-brain connectivity metric on how neuropsychiatric disease affects WMM[87]. Such an approach to investigate neuropsychiatric diseases comports well with the associative nature of brain functions[2].

Recently, there have been increasing numbers of dMRI network-based studies of neuropsychiatric diseases[88], such as MDD[4], bipolar disorder[15], normal aging[9], AD[16], schizophrenia[17], epilepsy[18], language disorders[89], motor disorders[90], and recovery of function after a stroke and other traumatic brain injuries[91,92]. From the network perspective, research on neuropsychiatric disease using dMRI can be classified into three types: specific node-based, regional network-based and global network-based. We present a brief review of current research progress and trends concerning neuropsychiatric disease from the perspective of the dMRI technique-based Brainnetome.

Some studies have concentrated on specific hub nodes in the white matter path, which are usually thought to reflect WMM degeneration. For example, ROIs were placed onto the anterior/posterior cingulum to assess the asymmetry of left/right FA values in schizophrenia[93]. Periventricular white matter was evaluated to investigate the progress of dementia in mild cognitive impairment and AD[94]. To characterize the status and the trend of deterioration in patients with brain tumors, ROIs were intuitively placed around the tumor[95] or tumor-affected WMM, such as at the internal capsule in motor dysfunctions caused by malignant glioma[96]. To quantify the process of normal aging, FA values were also assessed in the cerebral cortex[97] and subcortical nuclei[98].

To specifically identify a certain dysfunction in neuropsychiatric diseases, often only one or several localized networks is studied. The default mode network (DMN) is one of the most important sub-networks of the brain, which is intrinsically a new paradigm to describe the functional activity during the resting state[99]. Using DTI and fMRI, Teipel *et al.*[100] and Greicius *et al.*[101] showed that functional connectivity across the entire DMN is based on a distinct pattern of anatomical connectivity within the cerebral white matter. In addition, some psychiatric diseases, such as schizophrenia[102], AD[103-105], and epilepsy[106], also demonstrate a decreased WMM connectivity within the DMN. In a recent review[4], Hulvershorn *et al.* used a dMRI-derived network to systematically review the dysfunctional connectivity in pediatric MDD. A similar study on adolescent MDD was also reported[75]. Gutman *et al.* studied the action of deep brain stimulation on different targets by examining the connectivity patterns of the DMN regions[107]. In epilepsy, McDonald *et al.* found that multiple tracts associated with memory and language functions are impaired, and the extent of the deterioration correlates with verbal memory performance[108]. Other manifestations of sub-networks are also attractive, such as the language[109,110] and prefrontal-cingulate-insula[111] networks during maturation, the cortico-striatal network in aging[112] and epilepsy, the prefrontal-limbic network in MDD[113-115], the motor[78] and frontal-temporal[116] networks in epilepsy, the language[117,118] network in dyslexia, and the cortico-subcortical network in autism[119], AD[120], stroke[121,122], and schizophrenia[123]. Those individual sub-networks allow specification of the underlying dysmodulation of functional units occurring in a neuropsychiatric state.

Globally exploring changes across the entire brain

network would help to locate possible lesions or alterations. As an aging disorder of diffuse lesions across the brain, AD has received attention worldwide. In view of the promising ability of dMRI to detect possible lesions, the Alzheimer's Disease Neuroimaging Initiative (ADNI) study (http://adni.loni.ucla.edu/about-data-samples/) has included DTI data collection in its second phase. Meanwhile, research on network-based automatic recognition of mild cognitive impairment, regarded as an early stage of AD, has also emerged[87]. Wang *et al.* found disrupted small-world networks and a negative correlation between small-worldness and clinical measures in schizophrenia[124], consistent with a report by Commoun *et al.*[125]. Disrupted topological organization was also found in the WMM network of AD patients[126]. Li *et al.* discovered that the early blind, in contrast to either the late blind or normal controls, have low fiber density and poor global efficiency of the network[127]. Weinstein *et al.* used tractography and tract-based spatial statistics to examine the lesions along associative WMM fibers, which seem helpful in explaining some behavioral impairments in autism[128]. Müller argued that autism is a "distributed disorder" that requires various levels of study (genetic, neuroanatomical, neurofunctional, behavioral). In tracing the cause, should one seek a localized neurological abnormality, a single functional network, or a single cognitive-behavioral domain[129]? Müller's arguments are also applicable to other neuropsychiatric diseases, including Huntington disease[130], traumatic brain injury[91,92], and others[8,88].

5 Future directions of dMRI for Brainnetome

In summary, dMRI is a promising imaging technique that can non-invasively trace WMMs, currently on an imaging scale of millimeters. Thus, it can extract direct connectivities among the cortical/subcortical regions. This crucially paves the way for anatomical network analysis. Training, as well as neuronal degeneration, can alter WMM. Intensive training of normal controls for ~6 weeks changes WMM through induction of long-term potentiation (LTP)[131]. Excitingly, a more recent study showed that short-term training for only two hours results in microstructural changes in the brain that can be detected by a general DTI framework[132]. This demonstrates that the dMRI technique is able to recapitulate the evolution of a network within a relatively short time-scale. This is why we emphasize the properties of dynamic evolution in the Brainnetome concept, in contrast to the previous connectome[13]. By using the HARDI technique, Wedeen *et al.* identified well-aligned WMM as a grid-like structure[52], and Raj *et al.* showed the classic WMM patterns of common dementias[133]. All have demonstrated great potential for dMRI to explore the underlying structural mysteries of the brain.

However, there are still critical questions that urgently need to be answered before dMRI can be reliably used in clinical diagnosis.

There are major challenges for diffusion modeling and tractography[134,135]. First, DWI signals are very noisy, especially for signals with high *b*-values. Thus, scanners need to be improved to generate high-quality DWI images, and enhanced de-noising is also required. Second, for the sake of balance among the signal-to-noise ratio and diffusive intensity, and scanning time as well, we usually fail to identify fibers crossing white matter[20,36,43]. Third, group study in dMRI is normally performed on registered scalar maps with FA or MD values in DTI, not the whole tensor field in DTI nor the probability function field in HARDI. Thus, registration methods for the tensor field and probability function field are needed to accommodate individual differences[136]. Better statistical analyses are needed to compare tensor-valued or probability function-valued images, not just scalar maps. In addition, after achieving tractography for each subject, how to perform reliable group studies on the detected tracts remains obscure[135].

After accomplishing tractography, dMRI network construction and analysis still encounter many problems[135]. The network nodes are usually pre-defined by atlases, although different atlases may yield significantly different results in the subsequent network analysis[19]. Furthermore, different numbers of seed points used within ROIs yield varied network properties[137]. Even along the same WMM path, different positions of initiating ROIs may affect the network construction[138]. Bassett *et al.* disclosed conserved

and variable architectures of anatomical networks between the DTI and DSI techniques[139]. Also, different thresholds for determining the existence of connectivities may result in different network topologies. Most work on network analysis relies on statistical tests on the derived scalar indices, such as small-worldness. This inevitably loses much information when whole networks are replaced with scalar indices. Optimized measurements and more powerful statistical comparisons for brain networks are anticipated.

In recent years, the multi-modality imaging strategy has received much attention owing to its ability to dissect imaged objects from different aspects, and this can provide new perspectives to understand networks from complementary sources of information. For anatomical network analysis, dMRI has also been combined with other imaging techniques. Direct fusion with other modalities of MRI imaging, such as structural and functional MRI[4,140], is useful for image alignment thanks to homogeneous registration. By introducing genomic imaging, we hope to understand the genetic mechanisms of network evolution and thus individuals' cognitive functions[141-143]. dMRI network analysis has also been combined with electroencephalography[144], magnetoencephalography[145], positron emission tomography[146] and magnetic resonance spectroscopy[147].

Reproducibility and reliability are crucially important for network construction based on the dMRI technique, and they overwhelmingly determine whether dMRI can be used to objectively differentiate neuropsychiatric status among different subjects or at different time points[148]. Many researchers have tried to investigate the reproducibility and reliability of the acquired networks through different imaging protocols[139,149,150], different imaging sites[151,152], and different parameters for constructing networks[19,153]. However, this is still an open question for the Brainnetome era[12].

Although currently it is hard to achieve a complete anatomical network of the brain due to the obstacles described above and other unforeseen difficulties, the already obtained and apparently promising clues can help us approach the physical infrastructural neural network for Brainnetome[3,154]. Brainnetome has sparked promising research and clinical applications for both developmental and neuropsychiatric conditions[2,5-9]. The emerging Brainnetome era needs multidisciplinary collaboration[12].

Appendix. Some useful tools for diffusion MRI (dMRI) data processing, network construction and image/network visualization, and the related source links

Name	Brief description of functions related to dMRI for Brainnetome
FSL	Eddy current correction, tensor estimation, deterministic tracking, probabilistic tracking, TBSS, QBI, SD
	http://www.fmrib.ox.ac.uk/fsl/index.html
3D Slicer	DTI, tracking, Rician noise removal, deterministic tracking, stochastic tracking
	http://www.slicer.org
MRI Studio	Tensor and multi-tensor estimation, deterministic tracking
	https://www.mristudio.org
CAMINO	Tensor and multi-tensor estimation, QBI, SD, PASMRI, Monte-Carlo simulation, tensor registration
	http://www.cs.ucl.ac.uk/research/medic/camino
Trackvis	Tensor estimation, fiber tracking, DSI, QBI
	http://www.trackvis.org
MRtrix	DTI, QBI, SD, fiber tracking
	http://www.nitrc.org/projects/mrtrix
DTI-TK	Tensor estimation, tensor registration, image format conversion
	http://dti-tk.sourceforge.net/pmwiki/pmwiki.php

Appendix. (Continued)

Brain Connectivity Toolbox	Matlab-based routines for computing network properties https://sites.google.com/a/brain-connectivity-toolbox.net/bct
DTI Tracking System	DTI data processing, tracking (determined/probabilistic), statistical analysis and visualization. Batch-processing support http://www.brainnetome.org/software.html, http://www.brainnetome.org/wiki
Brainnetome Toolkit	Matlab-based GUI, with functions computing most network properties, including degree, clustering, efficiency/shortest-path, small-worldness, betweenness, assortative, resilience, *etc*, and visualization of networks http://www.brainnetome.org/software.html, http://www.brainnetome.org/wiki

DSI, diffusion spectrum imaging; DTI, diffusion tensor imaging; PASMRI, persistent angular structure MRI; QBI, Q-ball imaging; SD, spherical deconvolution. For the suggested steps on data processing, network construction and visualization, more details can be found at the wiki of the Brainnetome website (http://www.brainnetome.org/wiki).

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