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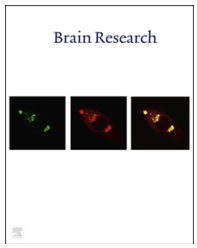

Research Report

Human brain asymmetry in microstructural connectivity demonstrated by diffusional kurtosis imaging

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ABSTRACT

Structural asymmetry of whole brain white matter (WM) pathways, i.e., the connectome, has been demonstrated using fiber tractography based on diffusion tensor imaging (DTI). However, DTI-based tractography fails to resolve axonal fiber bundles that intersect within an imaging voxel, and therefore may not fully characterize the extent of asymmetry. The goal of this study was to assess structural asymmetry with tractography based on diffusional kurtosis imaging (DKI), which improves upon DTI-based tractography by delineating intravoxel crossing fibers. DKI images were obtained from 42 healthy subjects. By using automatic segmentation, gray matter (GM) was parcellated into anatomically defined regions of interest (ROIs). WM pathways were reconstructed with both DKI- and DTI-based tractography. The connectivity between the ROIs was quantified with the streamlines connecting the ROIs. The asymmetry index (AI) was utilized to quantify hemispheric differences in the connectivity of cortical ROIs and of links interconnecting cortical ROIs. Our results demonstrated that leftward asymmetrical ROIs and links were observed in frontal, parietal, temporal lobes, and insula. Rightward asymmetrical ROI and links were observed in superior frontal lobe, cingulate cortex, fusiform, putamen, and medial temporal lobe. Interestingly, these observed structural asymmetries were incompletely identified with DTI-based tractography. These results suggest that DKI-based tractography can improve the identification of asymmetrical connectivity patterns, thereby serving as an additional tool in the evaluation of the structural bases of functional lateralization.

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1. Introduction

Even though both hemispheres of the human brain share similar topographic and surface anatomy, quantitative studies have demonstrated hemispheric asymmetries that are related to functional lateralization (Hugdahl, 2005; Toga and Thompson, 2003). For example, language and auditory processing region, which have been known for leftward functional lateralization, show a larger volume on the left hemisphere (Foundas et al., 1998; Geschwind and Levitsky, 1968; Steinmetz, 1996; Watkins et al., 2001). The close association between hemispheric asymmetry and functional lateralization suggests that structural asymmetry may constitute the structural basis for functional lateralization. Similarly, structural asymmetry is altered by pathological conditions that preferentially lead to isolated neurological deficits. Abnormal patterns of structural asymmetries have been observed in patients with dyslexia (Hynd et al., 1990; Larsen et al., 1990), schizophrenia (Crow et al., 1989; Petty, 1999), autism (Herbert et al., 2005; Hier et al., 1979), and Alzheimer's disease (Derflinger et al., 2011; Geroldi et al., 2000).

Previous studies have assessed structural asymmetry using volumetric MRI measured on cortical and subcortical gray matter (GM) regions. Nonetheless, the regional volumetric measurement does not assess neural circuitry architecture. Because brain functions involve physiological processes that are supported by neural network architecture, the identification of connectivity asymmetries may provide a deeper understanding of the structural and functional properties of the human brain.

Recent advances in diffusion MRI (dMRI) acquisition and post-processing allow the quantitative mapping of whole brain neural connectivity, known as the brain connectome (Hagmann et al., 2006). The neural connectivity is established through white matter tracts interconnecting cortical and subcortical regions. The orientation of white matter tracts in each image voxel is determined based on the measured anisotropic diffusion. The white matter tracts are then connected across image voxels by assuming the orientational coherence along the tracts, called tractography. Our group previously demonstrated structural asymmetry of neural network architecture in older individuals (Bonilha et al., 2014) using the connectome reconstructed from tractography based on diffusion tensor imaging (DTI) (Le Bihan, 2003; Mori and van Zijl, 2002). DTI assumes a single fiber orientation in an image voxel. Nonetheless, an image voxel is at a macroscopic millimeter scale and likely contain white matter tracts on the order of micrometers with multiple orientations, i.e. crossing fibers. Some subcortical areas have been shown to be densely populated by crossing fibers, such as the corona radiata, optic radiation, and the medial and posterior temporal lobes (Behrens et al., 2007; Wedeen et al., 2008). Thus, DTI-based tractography is limited in these areas (Tuch, 2004; Wedeen et al., 2005), and the connectome derived from DTI-based tractography may not fully identify asymmetrical neural circuitry involving fiber crossing areas.

To address the problem, in this study, we employ the connectome reconstructed from diffusional kurtosis imaging (DKI) tractography (Jensen et al., 2005; Jensen et al., 2014) to study the structural asymmetry of the human brain. Compared to conventional DTI (with $b=1000$ s/mm^2), DKI employs multiple b-values (up to 2000 s/mm^2) to quantify the non-Gaussianity of water diffusion, called kurtosis, which may provide additional information about tissue microstructure (Jensen and Helpern, 2010). DKI has been shown to better represent crossing fibers than DTI (Jensen et al., 2014). We

Table 1 – Values of asymmetry index (AI) of significantly asymmetrical ROIs across all subjects ($N=42$)—mean (standard deviation). The AI quantifies the hemispheric asymmetry in the ROI connectivity derived from DTI- and DKI-based tractography; positive AI indicates leftward asymmetry, and negative AI indicates rightward asymmetry. The significant asymmetry was determined by comparing the mean AI to zero with the one-sample t-test (two-tailed). The significance level was adjusted with the Bonferroni correction; p-value$=6.17\times10^{-4}$.

	Region	AI		p-Value (mean AI compared to zero)	
		DTI	DKI	DTI	DKI
Leftward	Parstriangularis	0.42 (0.55)	0.33 (0.40)	1.47×10^{-5}	4.40×10^{-6}
	Parsopercularis	0.53 (0.43)	0.33 (0.34)	9.36×10^{-10}	2.29×10^{-7}
	Precentral	0.31 (0.31)	0.24 (0.26)	8.23×10^{-8}	4.74×10^{-7}
	Postcentral	0.30 (0.34)	0.25 (0.29)	1.63×10^{-6}	3.01×10^{-6}
	Supramarginal	0.33 (0.31)	0.38 (0.31)	2.53×10^{-8}	6.68×10^{-10}
	Inferiorparietal	0.23 (0.35)	0.29 (0.31)	7.79×10^{-5}	3.24×10^{-7}
	Middletemporal	0.40 (0.28)	0.34 (0.22)	1.30×10^{-11}	1.24×10^{-12}
	Superiortemporal	0.28 (0.25)	0.16 (0.24)	4.82×10^{-9}	8.44×10^{-5}
	Transversetemporal	0.69 (0.49)	0.60 (0.55)	2.56×10^{-11}	1.17×10^{-8}
	Insula	0.36 (0.29)	0.26 (0.29)	6.42×10^{-10}	5.81×10^{-7}
	Lateralorbitofrontal		0.29 (0.32)		7.05×10^{-7}
	Inferiortemporal		0.18 (0.29)		2.16×10^{-4}
Rightward	Superiorfrontal	−0.25 (0.21)	−0.24 (0.17)	2.37×10^{-9}	1.34×10^{-11}
	Rostralanteriorcingulate	−0.46 (0.61)	−0.28 (0.48)	1.47×10^{-5}	4.00×10^{-4}
	Fusiform	−0.27 (0.40)	−0.31 (0.28)	1.00×10^{-4}	8.08×10^{-9}
	Putamen	−0.19 (0.25)	−0.20 (0.28)	1.34×10^{-5}	3.47×10^{-5}
	Parahippocampal		−0.37 (0.50)		2.66×10^{-5}