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## 2 BRAIN DIFFUSIVITY PATTERN IS INDIVIDUAL-SPECIFIC INFORMATION

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9 Abstract-The human brain is composed of complex networks of 100 billion neurons that underlie its higher functions. The set of neural connections in the brain has recently attracted growing interest from the scientific community. It is important to identify individual differences in these neural connections to study the background of individual differences in brain function and performance. In the present study, we investigated whether the pattern of brain diffusion, reflecting neural connections, is discernibly different among individuals; i.e., whether brain diffusivity is personally identifiable information. Using diffusion tensor imaging data from 224 healthy subjects scanned twice at an interval of about 1 year, we performed brain recognition by spatial normalization of fractional anisotropy maps, feature extraction based on Principal Component Analysis, and calculation of the Euclidean distances between image pairs projected into the subspace. Even with only 16 dimensions used for projection, the rank-one identification rate was 99.1%. The rank-one identification rate was 100% with  $\geq$  32 dimensions used for projection. The genuine accept rates were 95.1% and 100% at a false accept rate of 0.001%, with 16 and  $\geq$  32 dimensions used for projection, respectively. There were no large differences in the Euclidean distance among different combinations of scanners used or between image pairs with and without scanner upgrade. The results indicate that brain diffusivity can identify a specific individual; i.e., the pattern of brain diffusion is personally identifiable information. Individual differences in brain diffusivity will form the basis of individual differences in personality and brain function. © 2015 Published by Elsevier Ltd. on behalf of IBRO.

Key words: biometrics, diffusion tensor imaging, eigenbrain, magnetic resonance imaging, recognition, white matter.

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#### INTRODUCTION

The human brain is composed of networks of 100 billion neurons, each of which has thousands of synaptic connections to other neurons. This complex network underlies the higher functions of the human brain. Mapping and characterizing brain structural connectivity is important to improve our understanding of the complex functions of the human brain. The set of neural connections in the brain, now termed the connectome (Sporns et al., 2005), has been the focus of neuroanatomy and has recently attracted growing interest from the scientific community (Smith, 2013). The connectome is a complete map of neural connections in the brain: however, brain networks can be defined and examined at different levels of scale that correspond to the level of spatial resolution. Although all scales of resolution are closely related, each provides a unique perspective on the connectome. Mapping brain networks at a macroscopic scale provides the systems-level understanding of neural processing (Behrens and Sporns, 2012). Recent advances in MRI have enabled the structural connectome to be explored in vivo at the level of macroscopic connectivity through diffusion-weighed MRI and tractography. At a macroscopic scale, diffusion-weighted MRI is the main imaging technique employed for mapping the structural connectivity of the human connectome.

Diffusion-weighted imaging is sensitive to the random 37 motions of water molecules (Basser et al., 1994; Basser 38 and Pierpaoli, 1996). Diffusion tensor imaging (DTI), one 39 of the most widely used forms of this technique, measures 40 the direction and extent of microscopic water diffusion, 41 which is affected by microstructure and is greatest in the 42 direction of least restriction. Anisotropy in neural fibers 43 is mainly due to the dense packing of axons and their 44 intact cell membranes, and myelination modulates the 45 degree of anisotropy (Beaulieu, 2002). Measuring aniso-46 tropy using DTI is a useful method for noninvasively 47 detecting subtle white matter changes, even if the brain 48 tissue appears normal on conventional MRI (Werring 49 et al., 2000; Rovaris et al., 2002). DTI has been widely 50 applied to study white matter tracts in normal brains 51 (Rilling et al., 2008; Takao et al., 2011a, 2011g), in devel-52 oping and aging brains (Sullivan and Pfefferbaum, 2006; 53 Inano et al., 2011; Lebel et al., 2012), and in a variety of 54 neurological and neuropsychiatric disorders (Takao 55 et al., 2010b; Thomason and Thompson, 2011; Gold 56 et al., 2012). The changes in brain diffusivity that occur 57 during brain development, maturation, and aging are 58 related to changes in brain function and performance; 59 and a variety of neurological and neuropsychiatric 60

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Abbreviations: ADNI, Alzheimer's Disease Neuroimaging Initiative; DTI, diffusion tensor imaging; FA, fractional anisotropy; FDT, FMRIB's Diffusion Toolbox; PCA, Principal Component Analysis.

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disorders cause and/or are related to changes in brain dif-61 fusivity. In addition, there is a relation between brain diffu-62 sivity and various types of specialized individual 63 performance, such as in musicians (Bengtsson et al., 64 2005; Imfeld et al., 2009; Steele et al., 2013). 65 Longitudinal studies have shown that even learning and 66 training cause changes in brain diffusivity (Scholz et al., 67 68 2009: Zatorre et al., 2012).

Large-scale brain imaging studies, such as the 69 Human Connectome Project (Van Essen et al., 2013), 70 which aims to construct a map of the complete macro-71 scopic structural and functional neural connections of 72 73 the human brain in vivo within and across healthy individ-74 uals, and the Alzheimer's Disease Neuroimaging Initiative (ADNI) study (Jack et al., 2010), which is a longitudinal 75 multi-center observational study of healthy elders and 76 patients with mild cognitive impairment and Alzheimer's 77 disease, have recently been conducted to overcome the 78 limited power of smaller studies and to increase the sen-79 sitivity and reliability of the findings. These studies include 80 diffusion-weighted MRI as part of the imaging protocol to 81 map the macroscopic structural connections of the brain 82 83 and their variability, and to identify disease-related alterations in the white matter. These large-scale brain imag-84 85 ing studies have made anonymized data, including 86 imaging and clinical information and DNA sequences, 87 widely available to the scientific community for examina-88 tion and exploration.

Brain function and performance differ individually. The 89 identification of individual differences in neural 90 connections (white matter diffusivity) of the brain is 91 important to study the background of individual 92 differences in brain function and performance. In the 93 present study, we investigated whether the pattern of 94 brain diffusion is discernibly different among individuals; 95 i.e., whether brain diffusivity is personally identifiable 96 97 information. Using DTI data from 224 healthy subjects 98 scanned twice, for this purpose, we performed brain recognition by spatial normalization of fractional 99 anisotropy (FA) maps, feature extraction based on 100 Principal Component Analysis (PCA), and calculation of 101 the Euclidean distances between image pairs projected 102 into the subspace. To our knowledge, there have been 103 no previous studies that examined whether diffusion-104 weighted MRI can be used to identify a specific person 105 and that have evaluated inter-individual differences in 106 brain diffusivity from the point of view of biometrics. 107

### EXPERIMENTAL PROCEDURES

#### 109 Subjects and imaging data acquisition

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110 The present study included data from 224 healthy subjects (161 males and 63 females; mean age, 111 57 ± 10 years; age range, 40-83 years) (Takao et al., 112 2011c, 2012). None of the subjects had a history of neu-113 ropsychiatric disorders including serious head trauma, 114 psychiatric disorder, or alcohol/substance abuse or 115 dependence. The mean Mini-Mental State Examination 116 score was 29.6  $\pm$  0.7 (range, 27–30). A board-certified 117 radiologist reviewed all scans (including T1-weighted 118 T2-weighted images) and found no gross and 119

abnormalities such as infarct, hemorrhage, or brain tumor in any of the subjects. The Fazekas score (range, 0–3), which is a four-point rating scale of white matter hyperintensities, was 0 (absence) or 1 (caps, pencil-thin lining and/or punctate foci) (Fazekas et al., 1987). The ethics committee of the University of Tokyo Hospital approved this study. After a complete explanation of the study to each subject, written informed consent was obtained.

MR data were obtained on two 3.0-T Signa scanners (GE Medical Systems, Milwaukee, WI, USA with an 8channel brain phased-array coil. Both scanners were the exact same model, and were simultaneously upgraded from HDx to HDxt during the scan period. Each subject was scanned twice at an interval of about 1 year (mean interval,  $1.0 \pm 0.1$  years; range, 0.6-1.3 years) (Takao et al., 2011c, 2012). Table 1 shows the number of subjects for the different scanner combinations, and those of subjects with and without scanner upgrade between the two scans.

Diffusion tensor images were acquired using a singleshot spin-echo echo-planar sequence in 50 axial slices (repetition time = 13,200 ms; echo time = 62 ms; field of view = 288 mm; slice thickness = 3 mm with no gap; acquisition matrix =  $96 \times 96$ ; number of excitations = 1; image matrix =  $256 \times 256$ ). Diffusion weighting was applied along 13 non-collinear directions with a b-value of 1000 s/mm<sup>2</sup> and a single volume was collected with no diffusion gradients applied  $(b_0)$ . Parallel imaging (ASSET; Array Spatial Sensitivity Encoding Technique) was used with an acceleration factor of 2.0. The acquired and reconstructed voxel dimensions were  $1.125 \times 1.125 \times 3.0$  mm.  $3.0 \times 3.0 \times 3.0$  mm and respectively.

The raw diffusion tensor images were corrected for eddy current distortion and head motion using FMRIB's Diffusion Toolbox (FDT) 2.0 (Smith et al., 2004), and corrected for spatial distortion due to gradient non-linearity using grad\_unwarp (Jovicich et al., 2006; Takao et al., 2010a). Following brain extraction using Brain Extraction Tool (BET) 2.1 (Smith, 2002), FA maps were created by fitting a tensor model to the diffusion data using FDT.

#### PCA-based brain recognition

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Image processing was performed mainly using MATLAB1627.13 (Mathworks, Sherborn, MA, USA) and FSL (FMRIB163Software Library)4.1 software (http://www.fmrib.ox.ac.164uk/fsl)developed at the Oxford Centre for Functional165

Table 1. Combinations of scanners used for image pairs and the	
presence or absence of scanner upgrade between the two scans	

	First scan	Second scan	
Scanner combination			
A ( <i>n</i> = 70)	Scanner 1	Scanner 1	
B ( <i>n</i> = 45)	Scanner 1	Scanner 2	
C ( <i>n</i> = 56)	Scanner 2	Scanner 1	
D ( <i>n</i> = 53)	Scanner 2	Scanner 2	
With or without scanner upgrade			
Upgrade $-(n = 159)$	Before upgrade	Before upgrade	
Upgrade + $(n = 65)$	Before upgrade	After upgrade	

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