学位論文内容の要旨

博士の専攻分野の名称　　博士（医理工学）　　　　氏 名　 李　忻南

学 位 論 文 題 名

Exploring the brain's microstructure by using diffusion spectrum imaging and double diffusion encoding magnetic resonance imaging

（拡散スペクトラムイメージングとダブル拡散エンコーディング磁気共鳴画像を用いた脳の微細構造の評価）

Chapter 1. Normative values of diffusion spectrum imaging indices of the brain in adults

Background and Objectives: Interpreting pathological states requires the knowledge of the normal distribution of normative values. This study aimed to determine the normative values of the major diffusion spectrum imaging (DSI) indices across the brain in adults and their variation with anatomical locations, age, and gender.

Materials and Methods: Thirty-six healthy volunteers underwent DSI of the brain. Generalized fractional anisotropy (GFA), normalized quantitative anisotropy (NQA), fractional anisotropy (FA), and mean diffusivity (MD) maps were generated from the DSI data. Normalized diffusion indices maps were then generated, and the regional values in GFA, NQA, FA, and MD were extracted for 14 anatomical regions of interest (ROIs). Variations in anatomical locations and gender were evaluated using repeated-measures analysis of variance (ANOVA) and two-sample t-tests. The correlation of regional diffusion indices with age was evaluated by using Pearson's product-moment correlation analyses.

Results: Widespread regional variations, such as higher GFA, NQA, and FA in the pons, were observed across the brain. Women had lower GFA, higher FA, and higher MD in several anatomical locations than men. GFA, NQA, and FA decreased with age in the majority of anatomical locations, whereas age-dependent GFA and FA increase and MD decrease were observed in the lentiform nucleus.

Discussion: The observed variations are thought to be related to alterations in fiber density, brain volume, and myelination.

Conclusions: GFA, NQA, FA, and MD values derived from DSI are influenced by anatomical location, gender, and age. Interpretation of these values would require normative reference values specific for anatomical location, age, and gender.

Chapter 2. Microstructural Attributes of Hemispheric Lateralization: A Combined Evaluation of Diffusion Spectrum Imaging and MR Spectroscopic Imaging

Background and Objectives: The application of diffusion magnetic resonance imaging (MRI) with other MRI techniques may acquire a better understanding of the alterations of brain tissues. This study aimed to identify the extent of lateralization of the diffusion indices derived from DSI and test the association of lateralization of these indices with lateralization in the essential neurometabolite concentrations estimated with whole-brain magnetic resonance spectroscopic imaging (WB-MRSI).

Materials and Methods: Twenty-nine healthy right-handed volunteers underwent DSI and WB-MRSI of the brain. GFA, NQA, FA, and MD maps were generated from DSI data and N-acetyl aspartate (NAA), choline (Cho), creatine (Cr), glutamate+glutamine (Glx), and myoinositol (mI) maps from WB-MRSI data. Normalized and smoothed diffusion indices maps and metabolite ratio (NAA/Cr,

Cho/Cr, Glx/Cr, and mI/Cr) maps were then generated. Voxels with significant lateralization were identified from the GFA, NQA, and FA maps by using paired t-tests. Mean values in these voxels were extracted on normalized DSI and WB-MRSI maps and corresponding flipped maps to calculate laterality index (LI). LI in voxels with leftward or rightward asymmetry derived from voxel-based analyses were evaluated by using one-sample t-tests.

Results: Voxels with leftward asymmetry were mainly observed in the thalamus and posterior cingulate cortex, whereas rightward asymmetry was mainly in the superior temporal gyrus, sublobar white matter, and frontal lobe white matter. NAA/Cr has similar leftward and rightward patterns of lateralization of GFA, NQA, and FA. Cho/Cr, Glx/Cr, and mI/Cr were independent of GFA, NQA, and FA lateralization, which showed rightward, leftward, and no lateralization, respectively.

Discussion: Anatomical locations with leftward and rightward asymmetry were associated with hemispheric brain functions. Different patterns of lateralization of NAA/Cr, Cho/Cr, and Glx/Cr in voxels with leftward and rightward GFA, NQA, and FA lateralization may be influenced by the neuronal and axonal configuration and myelin content. Lack of laterality in mI/Cr may imply that the contribution of glial cells in lateralization of tissue microstructure is small.

Conclusions: The knowledge about the normal hemispheric asymmetry of diffusion and WB-MRSI indices is required in interpreting their changes in pathological states. Combined evaluation of these indices provides insights into neural underpinnings associated with lateralization.

Chapter 3. Tissue Microstructural Changes following Four-Week Cognitive Training: Observations of Double Diffusion Encoding MRI

Background and Objectives: Cognitive training-derived neuroplastic brain changes have been reported in DTI studies. This prospective study aimed to compare the performance of microscopic fractional anisotropy (μFA) derived from double diffusion encoding (DDE) MRI to FA and MD derived from DTI in identifying cognitive training-derived microstructural brain changes.

Materials and Methods: Twenty-one healthy participants were recruited to undergo a 4-week cognitive training consisting of attention network training (ANT) and dual N-back training (DBT). Another eight age, sex, and education level-matched healthy participants were recruited as the control group. All participants underwent neuropsychological tests and brain MRI including DDE MRI, repeated after 4 to 6 weeks. μFA, FA, and MD maps were generated from DDE MRI data. The training and time-related μFA, FA, and MD changes, and response time (RT) in ANT and error rate in DBT were evaluated using mixed-design ANOVA. Correlations of μFA, FA, and MD changes with changes in RT in ANT and error rate in DBT were tested using Pearson's product-moment correlation analyses.

Results: μFA in the left middle frontal gyrus decreased upon the training, accompanied by a decrease in RT in the executive control component of ANT and the error rate of DBT. No significant changes were observed in FA and MD. The change in μFA had a moderate negative correlation with the RT change for the orienting component of ANT ($r = -0.521$, uncorrected $P = 0.032$).

Discussion: Cognitive training and time-related μFA changes were observed in the left middle frontal gyrus that plays an important role in the modulation of attention, which is thought to be due to axonal and dendritic pruning. Lack of change in FA and MD may imply that these indices are not as sensitive as μFA to detect these minute changes.

Conclusions: The observations of training and time-related μFA change and its correlation with RT change for ANT, but not the FA and MD, suggesting μFA is more sensitive than FA and MD in evaluating cognitive training-derived microstructural brain changes.