Morphological Analysis of Cerebral Cortex based on Magnetic Resonance Imaging in the Elderly

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by

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CERTIFICATE OF AUTHORSHIP/ORIGINALITY

I certify that the work in this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree except as fully acknowledged with the text.

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ABSTRACT

Aging is generally associated with cognitive decline and the increased probability of a specific disease, such as Alzheimer's disease (AD). Despite intensive research into the aging brain, the mechanisms underpinning cognitive aging and the risk factors for AD still remain unknown. Magnetic resonance imaging (MRI) has been used as a valuable non-invasive technique for detecting changes within the brain in vivo. Several researchers have already applied computer-based brain morphometry techniques based on MRI. Most previous studies focus on measuring cortical thickness or brain volume, while few studies examine features of the cortical sulci, which embed at least two distinct sources of genetic influences. The goals of this dissertation are to use novel computer-based brain morphometry techniques in T1-weighted scans in the elderly to reveal cortical sulcal variability with aging, cognitive decline, and earlier-stage AD, in order to assist with the prevention of cognitive disorders. There are three sub-projects within this dissertation. Firstly, using automated methods, we measured the global sulcal indices (g-SIs) of both cerebral hemispheres and the average sulcal span in five prominent sulci from a large community cohort of 319 non-demented individuals aged 70–90 years. Our findings suggest that both age and sex contribute to significant cortical gyrification differences and variations in the elderly. The first study establishes a reference for future studies of age-related brain changes and neurodegenerative diseases in the elderly. Secondly, we examined the relationship between cortical features and cognitive function in the same sample. To our knowledge, this is the first study to examine three-dimensional cortical sulcal patterns in community-dwelling elderly with

multiple cognitive domains. The results showed the cognitive performances were correlated with sulcal features but not with cortical thickness. The findings suggest that regionally specific sulcal morphology is associated with cognitive function in elderly individuals. In the third study, we investigated sulcal morphology and cortical thickness in earlier-stage AD. The results suggest that abnormalities of the cortical sulci are characteristic of patients with even very mild AD, and could facilitate early diagnosis of this condition. In summary, we found changes in brain structure, especially the cortical surface, are associated with aging, cognitive decline, and AD. The novel sulci features may contribute to building biomarkers of cognitive decline and AD, and ultimately to assisting with the prevention of cognitive disorders.

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THESIS-RELATED PUBLICATIONS

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Journal

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Tao Liu; Wen Wei; Wanlin Zhu; Nicole A Kochan; Julian N Trollor; Simone Reppermund; Jesse S Jin; Suhuai Luo; Henry Brodaty; Perminder S Sachdev. The relationship between cortical sulcal variability and cognitive performance in the elderly. *NeuroImage* 2011; 56(3):865-873

Tao Liu; Wei Wen; Wanlin Zhu; Julian Trollor; Simone Reppermund; John Crawford; Jesse S Jin; Suhuai Luo; Henry Brodaty; Perminder Sachdev. The effects of age and sex on cortical sulci in the elderly. *NeuroImage* 2010;51(1):19-27

Conference

Tao Liu; Wei Wen; Wanlin Zhu; Jesse S Jin; Suhuai Luo; Perminder Sachdev. The influence of memory on cortical correlations in the elderly. *15th Annual Conference of the Organization for Human Brain Mapping,* June, 2009, San Francisco, USA.

Tao Liu; Feng Shi; Yuan Zhou; Wanlin Zhu; Lei Lin; Jesse Sheng Jin; Tianzi Jiang, Suhuai Luo; Mira Park; Paul Rasser; Ulrich Andreas Schall. Morphological abnormalities of the cerebral cortical thickness in schizophrenia. *14th Annual Conference of the Organization for Human Brain Mapping,* June, 2008, Melbourne, Australia.

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LIST OF ABBREVIATIONS

AC	Anterior Commissure
AD	Alzheimer's disease
ADNI	Alzheimer's Disease Neuroimaging Initiative
APOE	Apolipoprotein E
ANOVA	Analysis of Variance
BET	Brain Extraction Tool
CDR	Clinical Dementia Rating Scale
CSF	Cerebral Spinal Fluid
DTI	Diffusion tensor imaging
FDR	False discovery rate
fMRI	Functional Magnetic Resonance Imaging
GSI	Global Sulcal Index
GM	Gray Matter
ICV	Intracranial Volume
LH	Left Hemisphere
MANOVA	Multivariate Analysis of Variance
MCI	Mild Cognitive Impairment
MMSE	Mini Mental Status Exam
MRI	Magnetic Resonance Imaging
NC	Normal Control
OASIS	Open Access Serier of Imaging Studies
PC	Posterior Commissure
PET	Positron Emission Topography
RH	Right Hemisphere
ROI	Region of Interest
SD	Standard deviation
SI	Sulcal Index
sMRI	Structural Magnetic Resonance Imaging
SPM	Statistical parametric mapping
SS	Sulcal Span
VBM	Voxel Based Morphometry
WM	White Matter