A Cross Sectional Study on The Relationship between Age, White Matter Lesion, Brain Atrophy and Cognitive Function

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Submitted to the School of Psychology, in fulfilment of the requirement for the Doctor of Clinical and Health Psychology degree

The University of Newcastle

February, 2014
Statement of Originality

The thesis contains no material which has been accepted for award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to this copy of my thesis, when deposited in the University Library, being made available for loan and photocopying subject to the provisions of the Copyright Act 1968.

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Acknowledgements

I would like to express my gratitude to my supervisors Dr Karen Drysdale and Assoc. Prof Frini Karayanidis for supervising my research project and for the completion of my thesis. I thank them for their knowledge, support and precious experience that guide me through this learning process. My sincerest appreciation goes to Todd Jolly for welcoming me to be part of his PhD research project. I will never forget his utmost patience in sharing his knowledge, his supportive attitude and great teamwork. Special thanks to the Hunter Medical Research Institute (HMRI) and School of Psychology University of Newcastle for funding the research project; to the Ministry of Education Malaysia and the International Islamic University Malaysia (IIUM) for sponsoring my doctorate program. I also thank my lecturers/ clinical supervisors and supportive colleagues from the professional doctorate program, co- researchers from the Honours program, and colleagues at the Functional and Neuroimaging Lab. My deepest gratitude especially for my dearest husband Zack, my parents and families, for their love, support and prayers, understanding, and sacrifice throughout my doctorate journey. My exceptional acknowledgement for my two little angels, my antidepressant, the apple of my eyes Zayd and Deena for their comfort and unconditional love that helped me maintain my sanity over the past few years. Also to all my friends who made our stay in Australia feels like home and made this life- time experience a wonderful journey.
ABSTRACT

Scope: The present study was designed to examine the relationship between structural brain changes, involving macrostructural and microstructural white matter changes, brain atrophy and cognitive function.

Purpose: Cognitive deterioration is generally thought to be due to structural brain changes as part of the aging process. The present study sought to determine how age-related structural brain changes at the macrostructural and microstructural levels correlate with cognitive function among a cohort of reasonably healthy elderly. The study also explored the possible link between white matter damage and cognitive dysfunction, and examined whether this relationship was also influenced by age-associated loss of brain volume i.e. brain atrophy. Last but not least, the study examined the level of the usefulness of a global cognitive measure in comparison to specific neuropsychological subtests assessing executive function, working memory and episodic memory domains.

Methodology: The volumetric measures were utilised to account for brain macrostructural changes, while the Diffusion Tensor Imaging (DTI)-based measures were used to examine microstructural properties of white matter disruptions among seventy reasonably healthy elderly recruited from Hunter Medical Research Institute (HMRI) Volunteer Register and specialised neurovascular clinic. The Montreal Cognitive Assessment (MoCA) was used to assess global cognition and twelve neuropsychological subtests were administered to measure specific deficit associated with subtle cognitive dysfunction in white matter pathology. The Pearson correlation coefficient and hierarchical multiple regression were utilised for data analyses.
Results: The MoCA has captured variation associated with brain volumes and DTI-based changes, not fully accounted by specific cognitive tests administered in this study. Even after adjusting for age, FSIQ, and brain atrophy separately, the independent association between the MoCA and radial diffusivity remained stable. Interestingly, the MoCA is a brief, yet powerful tool that even accounts for global cognitive deficit for which white matter pathology and brain atrophy are not sensitive markers. White matter macrostructural and microstructural changes are associated with age-related cognitive dysfunction, characterised as subtle, varied and diffuse in nature. Brain atrophy not only linked to age, but also influenced the association between global cognition and white matter pathology on the volumetric measure; and partially explained the relationship between white matter microstructural disruption and specific deficit in visual working memory and visual episodic memory. In addition, the hierarchical regression analysis revealed that the MoCA was the strongest predictor of radial diffusivity ($R^2 = .476, \rho<.01$) even after controlling for age ($R^2 = .392, \rho<.01$), and cerebral atrophy was not a significant predictor of radial diffusivity.

Conclusions and Implications: Age-related white matter macrostructural and microstructural changes are not benign, even among reasonably healthy elderly by which their future functioning may be compromised. The so-called ‘healthy’ elderly appear to be a more vulnerable population, as the nature of the dysfunction can be very subtle and diffuse. Early detection thus, serves as a main preventative measure for this population. Since our findings strongly point to the MoCA as a beneficial screening tool for cognitive dysfunction at the early stage of white matter disease, we therefore recommend this brief,
easily accessible tool for frontline clinicians to incorporate into their investigation protocol.