Microstructural white matter changes mediate age-related cognitive decline on the Montreal Cognitive Assessment (MoCA)

TODD A. D. JOLLY,[a,b,c] PATRICK S. COOPER,[a,b,c] SYARIFAH AZIZAH WAN AHMADUL BADWI,[a,d]
NATALIE A. PHILLIPS,[e,f] JAIME L. RENNIE,[a,b,c] CHRISTOPHER R. LEVI,[b,c,g] KAREN A. DRYSDALE,[a,b,c]
MARK W. PARSONS,[b,c,g] PATRICIA T. MICHIE,[a,b,c] AND FRINI KARAYANIDIS[a,b,c]

[a]Functional Neuroimaging Laboratory, School of Psychology, Faculty of Science & IT, University of Newcastle, Newcastle, Australia
[b]Centre for Brain and Mental Health Research, University of Newcastle, Newcastle, Australia
[c]Hunter Medical Research Institute, Newcastle, Australia
[d]Department of Psychology, Kulliyyah of IRKHS, International Islamic University Malaysia, Kuala Lumpur, Malaysia
[e]Centre for Research in Human Development, Department of Psychology, Concordia University, Montreal, Quebec, Canada
[f]Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, Quebec, Canada
[g]School of Medicine and Public Health, Faculty of Health and Medicine, University of Newcastle, Newcastle, Australia

Abstract

Although the relationship between aging and cognitive decline is well established, there is substantial individual variability in the degree of cognitive decline in older adults. The present study investigates whether variability in cognitive performance in community-dwelling older adults is related to the presence of whole brain or tract-specific changes in white matter microstructure. Specifically, we examine whether age-related decline in performance on the Montreal Cognitive Assessment (MoCA), a cognitive screening tool, is mediated by the white matter microstructural decline. We also examine if this relationship is driven by the presence of cardiovascular risk factors or variability in cerebral arterial pulsatility, an index of cardiovascular risk. Sixty-nine participants (aged 43–87) completed behavioral and MRI testing including T1 structural, T2-weighted FLAIR, and diffusion-weighted imaging (DWI) sequences. Measures of white matter microstructure were calculated using diffusion tensor imaging analyses on the DWI sequence. Multiple linear regression revealed that MoCA scores were predicted by radial diffusivity (RaD) of white matter beyond age or other cerebral measures. While increasing age and arterial pulsatility were associated with increasing RaD, these factors did not mediate the relationship between total white matter RaD and MoCA. Further, the relationship between MoCA and RaD was specific to participants who reported at least one cardiovascular risk factor. These findings highlight the importance of cardiovascular risk factors in the presentation of cognitive decline in old age. Further work is needed to establish whether medical or lifestyle management of these risk factors can prevent or reverse cognitive decline in old age.

Descriptors: Aging, Executive function, Older adults, Anatomical (e.g, sMRI, DTI)

White matter disease or leukoaraiosis is believed to result from hardening and restriction of the small arteries that supply deep cerebral white matter and to produce reduced efficiency of neural communication (e.g., Pantoni & Garcia, 1997). These changes in cerebral tissue appear as white matter hyperintensities (WMH) on T2-weighted MRIs. WMH are typically detected as an incidental finding during clinical investigations for transient ischemic attack, stroke, or dementia and are associated with increased risk of stroke and dementia (e.g., Gerdes et al., 2006; Imaizumi, Inamura, & Nomura, 2014; Young, Halliday, & Krill, 2008). However, cerebral white matter changes are also common in healthy older adults who show no clinical signs of dementia (e.g., Madden, Spaniol et al, 2009; Salat, 2011; Sullivan & Pfefferbaum, 2006), especially in the presence of cardiovascular risk factors, such as hypertension and high blood cholesterol (e.g., Liao et al. 1996; Yamauchi, Fukuda, & Oyanagi, 2002; Wong et al., 2002). Despite differences in the methods used to quantify white matter changes and to assess cognitive functioning (Frisoni, Galluzzi, Pantoni, & Filippi, 2007), early studies using volumetric measures or visual ratings of WMH mostly concur that increasing severity of WMH is associated with cognitive decline in otherwise healthy older adults (e.g., De Groot et al., 2000; Gunning-Dixon & Raz, 2003; Prins et al., 2005; Söderlund et al., 2006).