

035 **COGNITIVE IMPAIRMENTS IN ALS RELATE TO WHITE MATTER INTEGRITY IN SPECIFIC REGIONS OF INTEREST**

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Objective Cognitive impairment in amyotrophic lateral sclerosis is characterized primarily by deficits in executive functioning, and structural and functional imaging studies have revealed changes in extra-motor areas which are consistent with a continuum of multi-system involvement. More recently investigations into white matter in ALS have demonstrated reduced volume and integrity in multiple structures, with a preponderance for frontotemporal involvement. However, the contribution of white matter pathology to cognitive impairment in ALS remains largely unknown. The current study sought to investigate the relationship between white matter integrity and cognitive impairments in tasks assessing executive functioning, memory, and processing speed.

Method The current investigation employed a cross-sectional design comparing 30 ALS patients to 30 age and education matched healthy controls. Several experimental tests were specifically developed to be sensitive to executive dysfunction and processing speed deficits in populations with motor impairments. In addition, diffusion tensor magnetic resonance imaging was employed to investigate the neural correlates of any observed cognitive impairments.

Results ALS patients showed impairments in verbal fluency and dual task measures which correlated with reduced white matter integrity in specific and discrete regions of the prefrontal lobes. Verbal fluency performance was associated with integrity reductions in the white matter adjacent to Broca's area and Brodmann's Area 10. Dual task performance was associated with reduced integrity of the frontal white matter and white matter adjacent to dorsolateral prefrontal cortex. In addition, ALS patients showed impairments in a working memory task which correlated with reduced integrity in the posterior cingulum, and in verbal memory which correlated with reduced integrity in the inferior longitudinal fasciculus.

Conclusion The current study demonstrates that specific white matter pathology may underpin impairments in specific cognitive functions and further highlights the heterogeneity that exists in this disorder.