White Matter Integrity as a Mediator between Age and Memory Retrieval: Implications for Disconnection Theories of Cognitive Aging

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INTRODUCTION

Diffusion tensor imaging can provide detailed delineation of white matter (WM) pathways based on rates of microscopic water diffusion. A higher degree of white matter integrity is reflected in a greater degree of fractional anisotropy (FA) of diffusion. Previous research suggests an age-related decline in FA, particularly in prefrontal regions. Further, there is some evidence that WM integrity is related to cognitive function, especially speed-based measures. Behavioral studies have demonstrated that a substantial portion of age-related variance in episodic memory retrieval is shared with measures of elementary perceptual-motor speed. Thus, it is possible that age-related WM decline may contribute to the well established age-related decline in episodic memory retrieval.

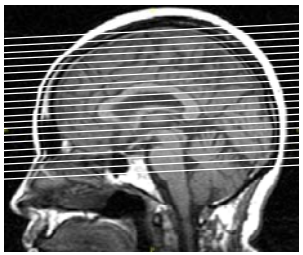
The goal of this study was to confirm, as demonstrated by other research, that speed is a mediator of age-related slowing of episodic retrieval, and secondly, to test the hypothesis that age-related changes in WM integrity mediate speed.

METHOD

Participants

Nineteen younger (20-28 years, *M* = 23.90 years) and 19 older (63-78 years, *M* = 69.58 years) neurologically intact adults participated in this experiment.

Diffusion Tensor Imaging:



Magnetic resonance imaging was conducted at 4T. In the diffusion tensor sequence, we acquired 30 contiguous near-axial slices parallel to the AC-PC, 3.8 mm thick; TR = 30000; per slice, diffusion measured in 6 directions (b = 1000 sec/mm^2) plus one image with no diffusion weighting (b = 0); five signal averages. Diffusion tensor eigenvalues were calculated from custom MATLAB scripts.

Structural Imaging:

3D fast IRP SPGR sequence, 60 contiguous slices, parallel to AC-PC, 1.9 mm thick.

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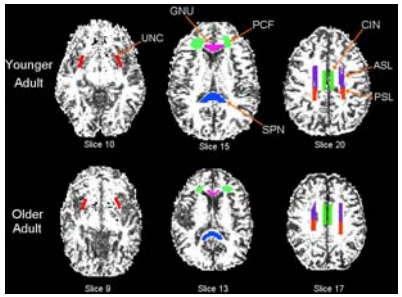
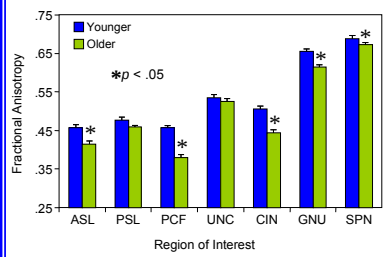
Lab website: http://www.geri.duke.edu/cogpsych/

REGIONS OF INTEREST

ROIs were drawn directly on the diffusion tensor images on a slice-by-slice basis for each participant, using the high-resolution SPGR images as a reference.

ROIs included the genu (GNU) and splenium (SPN) of the corpus callosum, anterior (ASL) and posterior (PSL) regions of the superior longitudinal fasciculus, uncinate fasciculus (UNC), pericallosal frontal (PCF) and the cingulum (CIN).



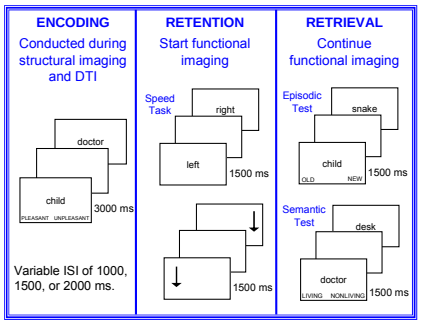


Significant main effects of region, [F (6, 216) = 185.49, p < .0001], age group [F (1, 36) = 19.20, p < .0001], and an Age Group x Region interaction, [F (6, 216) = 2.78, p = .01].

Separate ANOVAs by age group revealed significantly lower mean FA for older adults in ASL, PCF, CIN, GNU, and SPN.

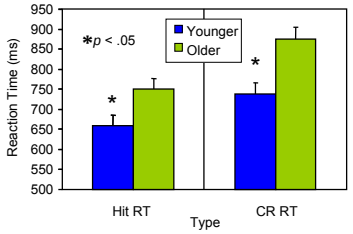
MEMORY RETRIEVAL TASK

- Encoding: pleasantness judgments for 39 words. Participants did not know which type of test they would complete at retrieval.
- Retention: 90 seconds.
- Retrieval: living/nonliving or old/new decisions for the 39 words from encoding along with 39 additional words.
- This sequence was repeated four times.



Accuracy (hit rate – false alarm rate) did not differ between groups for either task [Episodic: older, *M* = .65; younger, *M* = .73] [Semantic: older, *M* = .93; younger, *M* = .91]. For Episodic Reaction Time (RT), younger adults (*M* = 696 ms) were significantly faster compared to older adults (*M* = 804 ms). For Semantic RT, younger adults (*M* = 633 ms) were slightly faster than the older adults (*M* = 725 ms).

ANOVA ON HIT AND CORRECT REJECTION RT



For both hit, [F (1, 36) = 5.32, p = .03] and correct rejection RT, [F (1, 36) = 13.12, p = .0009] younger adults were significantly faster than were the older adults.

For the mediation analyses described below, only perceptual-motor speed, mean FA in the GNU, mean FA in the PCF, episodic RT (hit and correct rejection RT), and age met the criteria established by Baron and Kenny (1986).

MEDIATION ANALYSES

Hit Reaction Time Data

	r^2	Δr^2	F	Attenuation
Speed Mediation of Age Effect				
Model 1				
Age	.129		5.32*	
Model 2				
Speed	.133		5.52*	
Age	.186	.053	2.28	58.91%
GNU Mediation of Speed Effect				
Model 1				
Speed	.133		5.52*	
Model 2				
GNU	.182		8.02*	
Speed	.236	.054	2.46	59.40%
PCF Mediation of Speed Effect				
Model 1				
Speed	.133		5.52*	
Model 2				
PCF	.207		9.37*	
Speed	.278	.071	3.46	46.62%

CR Reaction Time Data

	r^2	Δr^2	F	Attenuation
Speed Mediation of Age Effect				
Model 1				
Age	.267		13.12*	
Model 2				
Speed	.319		16.84*	
Age	.417	.099	5.91*	62.92%
GNU Mediation of Speed Effect				
Model 1				
Speed	.319		16.84*	
Model 2				
GNU	.229		10.72*	
Speed	.410	.181	10.75*	43.26%
PCF Mediation of Speed Effect				
Model 1				
Speed	.319		16.84*	
Model 2				
PCF	.346		19.09*	
Speed	.541	.194	14.82*	39.18%

CONCLUSIONS

- Perceptual-motor speed is a mediator of age-related variance in RT for both hits and correct rejections.
- White matter integrity, in turn, is a mediator of the effects of perceptual-motor speed, especially for hits; additional mechanisms contribute to correct rejections.
- This pattern of age-related deficits may represent a disruption or disconnection of white matter pathways connecting brain regions required for memory retrieval.