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Language, aging, and cognition: Frontal aslant tract and superior longitudinal fasciculus contribute to working memory performance in older adults

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Abstract

Previous research has documented change in white matter tract integrity with increasing age. Both inter- and intra-hemispheric tracts that underlie language processing are susceptible to these age-related changes. The objective of the current study was to explore age and white matter integrity in language-related tracts as predictors of cognitive task performance in younger and older adults. To this end, we conducted principal component analyses of white matter tracts and confirmatory factor analysis of neuropsychological measures. We next conducted a series of regression analyses that used white matter components to predict scores on each of the neuropsychological components. For both younger and older adults, age was a significant predictor of processing speed and working memory. However, white matter integrity did not independently contribute to these models. In older adults only, both age and a white matter component that included the bilateral frontal aslant tract and left superior longitudinal fasciculus were significant predictors of working memory. Taken together, these results extend our understanding of the contributions of language-related white-matter structure to cognitive processing, and highlight the effects of age-related differences in both frontal and dorsal tracts.

Keywords

Language; Aging; Cognition; White Matter; Diffusion Tensor Imaging

Aging is often associated with cognitive and behavioral change, and these changes are assumed to correspond to changes in brain structure, though the complex relations between these cognitive and neural variables is not fully explicated. Certain aspects of language, particularly language production, experience age-related decline [1]. Moreover, many aspects of language are intimately tied to other cognitive functions that change with age, such as working memory and executive function [2]. Considering this relationship, it is plausible that the neural infrastructure that supports language function in older adults may also support other aspects of cognition. While white matter tracts have been identified for their role in supporting language function, their role supporting other aspects of cognition is less well understood, particularly with respect to older adults.

Language processing in healthy adults relies on a distributed network of brain regions [3, 4]. According to the dual stream model of language, the dorsal stream supports speech perception and production [3, 4], and includes white matter tracts such as the superior longitudinal fasciculus (SLF) [5] and frontal aslant tract (FAT) [6, 7]. The ventral stream supports speech comprehension and general semantic processes [3], and includes tracts such as the inferior longitudinal fasciculus (ILF) [8], the middle longitudinal fasciculus (MdLF) [9], and the uncinate fasciculus (UF) [10]. Though not linked directly to either the dorsal or ventral language processing streams, white matter tracts of the anterior (genu) and posterior (splenium) corpus callosum have a prominent role in interhemispheric communication and have been implicated in language function [11], as well as other cognitive domains [12].

Previous studies have shown that white matter microstructure, particularly in the frontal lobe, is reduced with age [13]. Moreover, lateral tracts in dorsal regions, such as the SLF, are more strongly affected by age than those in inferior regions [14]. As such, degradation of frontal and dorsal tracts may have significant consequences for behavioral functioning, particularly language production. Specifically, white matter fractional anisotropy (FA) in the prefrontal cortex has been shown to predict both processing speed and working memory in older adults [12]. Considering this, it is important to investigate the possibility that the integrity of the frontal tracts most typically associated with language function, such as the SLF and FAT, may also influence these other aspects of cognition, particularly in older adults whose performance may be more sensitive to neural variability.

The current study addresses the extent to which language-related white matter structures contribute more generally to cognitive performance in older adults. We explored the ways in which age and the integrity of language-associated white matter tracts predicted behavioral outcomes on measures of working memory, language, speed, and memory. This approach allowed us to test how structures that support language may also contribute to task performance in other related cognitive domains.

Method

Participants

Thirty-five younger adults ($M = 24.11$; $SD = 4.08$; range = 19 – 35) and 25 older adults ($M = 66.97$; $SD = 4.75$; range = 59 – 78) participated in this study. All participants were healthy native English speakers. No participant scored below 27 on the Mini-Mental State Examination (MMSE), indicating that none were cognitively impaired [15]. All participants provided written informed consent, and all experimental procedures were approved by the Institutional Review Board of the Duke Medical Center.

Procedure

Participants completed two sessions: a behavioral session and a magnetic resonance imaging (MRI) session. During the behavioral session, 11 neuropsychological tasks measuring functioning across five domains of cognition were collected. Measures of language included verbal fluency and the vocabulary test subset of the Wechsler Adult Intelligence Scale (WAIS-III); working memory included nonverbal/spatial working memory [adapted from

16], and both forward and backward digit span [17]. Episodic memory was evaluated through both short and long term memory tasks [18]. Speed was measured on three dimensions, including (1) simple speed, in which participants pressed a single key whenever a symbol appeared on the screen, (2) complex speed, in which participants pressed a key that corresponded to the direction of an arrow, and (3) a computerized version of the digit symbol subtest of the WAIS-III [17]. Finally, inhibitory control was measured with the Stroop task [19]. MRI data were collected on a separate day, no more than two weeks later.

Imaging Acquisition and Diffusion Tensor Imaging (DTI) processing

High-resolution T1-weighted structural images were acquired using a 3D fSPGR pulse sequence (Repetition Time (TR) = 8.14 ms; Echo Time (TE) = 3.22 ms; flip angle = 12°; Field of View (FOV) = 24 cm²; 256×256 matrix; voxel size = 0.9375×0.9375×1mm; 162 contiguous oblique-axial slices). Diffusion MR scans were acquired for each participant (TR = 10,000 ms; TE = 82.3 ms; flip angle = 90°; FOV = 24cm²; matrix = 128×128; voxel size = 2 mm³; 68 contiguous oblique-axial slices; 35 to 55 diffusion-weighted directions¹; b = 1000s/mm²; 1 non-diffusion-weighted reference image).

Following visual inspection of the raw diffusion-weighted and b0 images, we conducted an extensive quality control procedure with DTIPrep [20]. Eddy-current and head motion artifacts were corrected with linear registration to the averaged b0 image, and rotation of the diffusion vectors. All other DTI preprocessing steps and probabilistic tractography were conducted with FSL 5.0 tools (BEDPOSTX, DTIFIT [21]). We targeted 12 tracts (see Figure 1): the genu and splenium of the corpus callosum, and six bilateral pathways: SLF (branch III) and arcuate fasciculus (SLF/AF), ILF, MdLF, FAT, and UF (see Figure 1). We label the SLF/AF pathway as such because these fasciculi are not easily differentiated from each other with DTI-based tractography. Cortical region masks, thresholded at 50%, taken from the Harvard-Oxford Cortical Atlas were used as seeds and targets, with the exception of white matter seeds for the genu and splenium, and the SLF/AF. All seeds and targets began in standard Montreal Neurological Institute (MNI) space and were deprojected into native diffusion space prior to tractography (see supplemental material for additional details).

Statistical Analyses

A confirmatory factor analysis (CFA) was conducted on the 11 neuropsychological measures. Goodness of fit indices were assessed in accordance with previous studies [22]. Because we did not make a-priori hypotheses regarding the underlying organization of the white matter tracts, we employed an exploratory approach based on principal components analysis (PCA). This data reduction method computes orthogonal principal components (linear combinations of optimally weighted variables) from the covariance matrix of the data across the 12 white matter tracts. After the DTI and neuropsychological factors were created, a series of regression analyses were performed. In the first set, predictor variables were age as a discrete variable (younger adults; older adults), and each of the DTI component variables, while neuropsychological factors were used as outcome variables. In

¹Thirty four participants (16 younger adults and 18 older adults) had 55 diffusion-weighted directions, and 36 participants (19 younger adults and 17 older adults) had 35 directions, for an average of 45.2 directions across the sample (younger adult average = 44.7; older adult average = 45.7).

the second set of analyses, only data from older adult participants were used. This model was similar to the previous model except that age was modeled as a continuous variable, and the DTI factors were obtained through from a PCA factor structure using only older adult data.

Results

CFA: Neuropsychological Measures

A model was built that divided the measures into four factors: speed, working memory, episodic memory, and language. The inhibition factor, comprised of Stroop task, was excluded because it could not be fit into the overall model. This model provided a good fit for the data, $\chi^2(29, N = 60) = 26.12, p > 0.005$. Additional indices confirmed the goodness of fit, as Root Mean Square Error of Approximation (RMSEA) = 0.00, Comparative Fit Index (CFI) = 1.00, and Adjusted Goodness of Fit Index (AGFI) = 0.856. While the AGFI value was slightly smaller than 0.90, no additional changes to the model improved its fit.

PCA: White Matter FA

The PCA that included both older and younger participants revealed a two factor solution, explaining 64.65% of the total variance in white matter integrity. The first component included the genu, splenium, bilateral ILF, SLF/AF, MdLF, and FAT. The second component included only the bilateral UF. The second PCA revealed that older adults' white matter integrity was best characterized by a three factor solution, explaining 62.08% of the total variance. The first component included the bilateral MdLF, the bilateral ILF, the genu, and the splenium. The second component included the bilateral FAT and the left SLF. The third component included the bilateral UF and the right SLF/AF.

Multiple Regression: Younger and Older Adults

Four regression analyses were conducted, one for each of the neuropsychological components, using age and DTI factors as predictors. The models to predict language [$F(3, 66) = 0.225, p > 0.05$] and episodic memory [$F(3, 66) = 0.938, p > 0.05$] were not significant. The next analysis was significant, predicting 43% of the total variance in processing speed [$F(3, 66) = 16.48, p < 0.001$]. Age was the only significant predictor of processing speed ($\beta = 0.565, t = 4.381, p < 0.001$), indicating that as age increased, so too did scores on this factor, such that participants generally became slower. Additional tests indicated that the degree of collinearity observed was not problematic, as tolerance values were greater than 0.10, and variance inflation factors were less than 10.00. The final analysis was also significant, predicting 8% of the total variance in working memory [$F(3, 66) = 3.031, p < 0.05$]. Age ($\beta = -0.395, t = -2.474, p < 0.05$) was the only significant predictor of working memory, such that as age increased, working memory decreased. Additional tests indicated that the degree of collinearity observed was not problematic.

Multiple Regression: Older Adults

To further explore the relationship between age, white matter integrity, and cognition, additional regression analyses were conducted with only the older adult subset of participants (see Table 1). Predictor variables for all regressions were age and DTI factors.

Analyses revealed that language [$F(4, 30) = 0.94, p > 0.05$], processing speed [$F(4, 30) = 0.89, p > 0.05$], and episodic memory could not be significantly predicted [$F(4, 30) = 1.06, p > 0.05$]. The model that predicted working memory was significant, and explained 30% of the total variance in working memory ability [$F(4, 30) = 3.176, p < 0.05$]. Age was a significant predictor of working memory ($\beta = -0.489, t = -3.081, p < 0.01$), and the DTI factor comprised of the bilateral FAT and left SLF/AF was also a marginally significant predictor ($\beta = -0.41, t = -2.2, p < 0.059$).

Discussion

The goal of the current study was to explore the ways in which white matter structures that support language function may also contribute to other cognitive processes that are related to language processes. This approach had the benefit of incorporating several neuropsychological measures, which allowed us to explore the ways in which white matter and age may differentially contribute to behavioral performance on a variety of different cognitive processes. The primary finding of our analyses suggests that in older adults, both age and an FA component variable that included the bilateral FAT and left SLF/AF predicted scores on working memory. As our results indicate, the white matter integrity of the bilateral FAT and left SLF/AF are particularly important for the working memory performance of older adults. This finding is consistent with age-related trajectories of white matter decline, such that dorsal regions decline more than ventral regions [14], and anterior regions decline more than posterior regions [13]. The current results thus indicate that older adults who experience the least white matter decline are able to maintain the best working memory performance.

Our primary finding is largely consistent with models of age-related change to brain structure, but also lends new insight to the roles of both the FAT and SLF and their relation to cognition. The FAT has recently been identified as a white matter structure that contributes to language processing, though its exact function remains unclear [7]. While some research links the FAT specifically to speech production [6], Dick, Bernal [23] suggest that the tract could also support aspects of cognitive control that are required for speech, such as selection, inhibition, and ordering. Because the FAT was clustered together with the left SLF/AF, which has been implicated in language articulation and speech perception, our results suggest that these tracts support the ability to maintain and attend to specific aspects of language-related information, as would be required by working memory tasks. Consistent with this theory, previous work has indicated that lesions to the left dorsolateral prefrontal cortex are associated with deficits in the manipulation of verbal knowledge in working memory [24]. Importantly, these lesions were not contained within the grey matter structure, but also extended to the white matter of the SLF and FAT [24]. Taken together, it appears as though these frontal and dorsal tracts play an important role not only in speech production itself, but also in other aspects of cognition, such as working memory, that may require the manipulation of verbal information. Age-related development of dorsal stream white matter integrity has been linked to increased behavioral performance on complex sentence processing tasks in children and young adults [25]. Our results complement these findings, illustrating that degeneration of dorsal and frontal tracts in older adulthood affects aspects of cognition that rely on language processing.

Despite the need for continued investigation, the current study provides information regarding the ways in which both age and language-related white matter tracts contribute to behavioral performance. Specifically, we demonstrate that both frontal (FAT) and fronto-temporal (SLF/AF) white matter integrity are particularly important for maintaining working memory performance in older adults. This information lends clarity to the role of both the frontal aslant tracts and the superior longitudinal fasciculus, while also contributing to the current literature regarding age-related changes to brain structure.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. White matter tracts investigated in the study included five bilateral intrahemispheric pathways and two interhemispheric pathways.

Table 1

Regression analyses including only older adults

Outcome Variable	Predictor Variables	R ²	F	p	Standardized β	t	p
Language	Age	0.11	0.94	ns			
	DTI Component 1				0.04	0.23	ns
	DTI Component 2				0.02	0.13	ns
	DTI Component 3				0.00		
Working Memory	Age	0.30	3.18	0.03	0.31	1.80	ns
	DTI Component 1				-0.49	-3.31	0.01
	DTI Component 2				-0.22	-1.41	ns
	DTI Component 3				0.30	1.96	0.06
Processing Speed	Age	0.11	0.90	ns	0.07	0.47	ns
	DTI Component 1				0.23	1.26	ns
	DTI Component 2				-0.01	-0.03	ns
	DTI Component 3				-0.25	-1.44	ns
Memory	Age	0.12	1.06	ns	-0.14	-0.79	ns
	DTI Component 1				0.13	0.75	ns
	DTI Component 2				0.12	0.71	ns
	DTI Component 3				0.15	0.85	ns
					-0.28	-1.64	ns

DTI Component 1 = bilateral MdLF, ILF, genu, and splenium; DTI Component 2 = bilateral FAT and left SLF/AF; DTI Component 3 = bilateral UF and right SLF