

## Anterior Visual Pathway Measures are Associated with Cognition in Multiple Sclerosis

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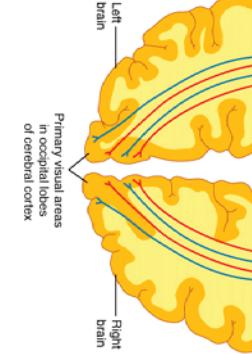
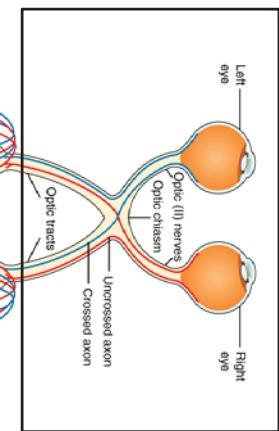
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### Disclosures

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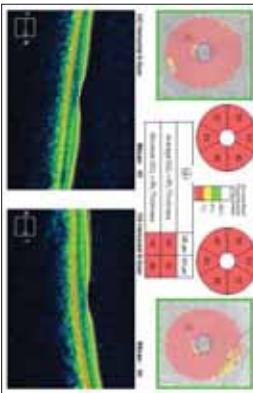
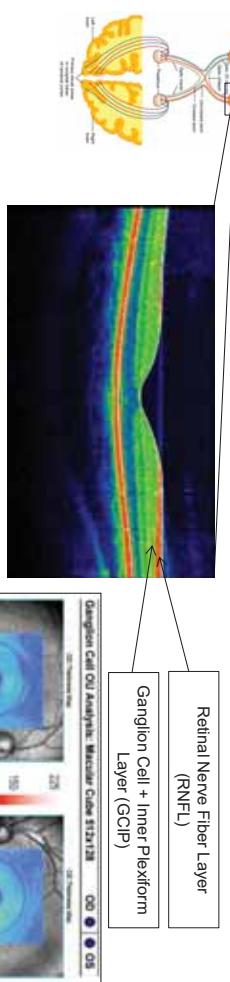
## Anterior Visual Pathway (AVP)

- 94-99% of multiple sclerosis (MS) patients exhibit optic nerve lesions postmortem
- Retrograde neurodegeneration of retinal nerve fiber layer (RNFL) fibers → ganglion cell + inner plexiform (GCIP) layer atrophy



[https://commons.wikimedia.org/wiki/File:Wing\\_James\\_Visual\\_System.pdf](https://commons.wikimedia.org/wiki/File:Wing_James_Visual_System.pdf)

## Optical Coherence Tomography (OCT)



- OCT is a sensitive measure of retinal neurodegeneration, which reflects global atrophy

## Cognition in MS

- 43-70% of MS patients are affected by cognitive impairment
- An established battery of tests is used to measure cognitive function

Common Neuropsychological Tests/Surveys	Domains Tested
Multiple Sclerosis Functional Composite (MSFC)	Working memory, concentration, speed of informational processing, lower extremity and fine motor skills
Symbol Digit Modalities Test (SDMT)	Attention, concentration, speed of informational processing, and working memory
Brief Visuospatial Memory Test-Revised (BVMTR-R)	Visuospatial and working memory
Brief Visuospatial Memory Test-Revised (BVMTR-R) Delayed Recall	Visuospatial and short-term memory
Benton Judgment of Line Orientation (JLO)	Visuospatial functioning
Controlled Oral Word Association Test (COWAT)	Language, abstract thought, and executive functioning
Delis-Kaplan Executive Functioning System (DKEFS)	Abstract thought, executive functioning
Beck Depression Inventory-II (BDI-II)	Self-analyzed depression severity
Modified Fatigue Impact Scale (MFIS)	Self-analyzed fatigue impact

## Goal

The primary objective of this study was to determine the relationships between anterior visual pathway neurodegeneration in MS and global cognitive function

## Methods

- MS patients were recruited by convenience sampling in a single academic MS center
- Study participants were clinically diagnosed with relapsing remitting MS (RRMS), secondary progressive MS (SPMS), or primary progressive MS (PPMS)
- SPMS and PPMS together were designated as progressive MS (PMS)
- History of optic neuritis (ON) was determined
- Patients underwent 100%-, 2.5%-, and 1.25%-contrast visual acuity (VA) testing using Sloan letter charts and cognitive testing within 6 months of OCT scans
- Multilevel mixed-effects linear regression models, accounting for age, sex, disease duration, race, years of education, history of ON, and within-subject inter-eye correlations were utilized

## Demographics and Baseline Characteristics

	Overall n=131	RRMS n=95	Progressive MS n=36	<i>p</i> -value RRMS vs PMS
Mean age, years (SD)	45 (12.3)	41 (11.5)	55 (8.1)	< 0.001
Mean disease duration, years (SD)	11 (8.8)	8.6 (6.6)	18.3 (9.9)	< 0.001
Females (%)	66	65	67	0.8317
Race				
• Caucasian	112	79	33	0.1260
• African American	11	9	2	
• Other	8	7	1	
Eyes with ON History	56	47	9	0.0311

## AVP measures are associated with cognitive & fatigue scores across the cohort

Scores	Anterior Visual Pathway Measures					
	Average GCIP Thickness	$100\%_{-VA}$	$2.5\%_{-VA}$	$1.25\%_{-VA}$	$p$ -value	$R^2$
MSFC (n=131) <sup>a</sup>	0.263	0.1045	0.797	0.0314	<b>0.047</b>	<b>0.0624</b>
SDMT (n=99) <sup>b</sup>	0.369	0.1479	0.408	0.1669	<b>0.047</b>	<b>0.1905</b>
BVMT-R						<b>0.004</b>
Total recall (n=92) <sup>c</sup>	0.877	0.1701	<b>0.002</b>	<b>0.3077</b>	<b>0.025</b>	<b>0.1371</b>
BVMT-R						<b>0.001</b>
Delayed recall (n=92) <sup>c</sup>	0.469	0.1739	0.215	0.264	0.47	0.0967
JLO (n=56) <sup>a</sup>	0.975	0.0626	0.19	0.3384	0.975	0.3157
DKEFS (n=39) <sup>a</sup>	0.681	0.0651	0.458	0.3738	0.454	0.454
COWAT (n=55) <sup>b</sup>	0.784	0.0616	0.212	0.3529	0.31	0.1603
BDI (n=48) <sup>d</sup>	0.628	0.0398	0.459	0.2579	0.162	0.3856
MFIS (n=91) <sup>d</sup>	<b>0.026</b>	<b>0.1467</b>	<b>0.029</b>	<b>0.1513</b>	0.163	0.0403

$p$ -values and coefficients of determination were adjusted for:

<sup>a</sup> age, sex, disease duration, years of education, and ON history

<sup>b</sup> sex, disease duration, and ON history

<sup>c</sup> sex, disease duration, years of education, and ON history

<sup>d</sup> age, sex, disease duration, and ON history

## AVP measures are associated with cognitive & fatigue scores in RRMS

Scores	Anterior Visual Pathway Measures					
	Average GCIP Thickness	$100\%_{-VA}$	$2.5\%_{-VA}$	$1.25\%_{-VA}$	$p$ -value	$R^2$
MSFC (n=95) <sup>a</sup>	0.516	0.114	0.511	0.114	<b>0.048</b>	<b>0.056</b>
SDMT (n=76) <sup>b</sup>	0.47	0.237	0.689	0.287	<b>0.055</b>	<b>0.118</b>
BVMT-R						<b>0.002</b>
Total Recall (n=71) <sup>c</sup>	0.978	0.244	<b>0.025</b>	<b>0.348</b>	0.092	0.125
BVMT-R						<b>0.001</b>
Delayed Recall (n=71) <sup>c</sup>	0.206	0.259	0.364	0.318	0.361	0.098
JLO (n=30) <sup>a</sup>	0.277	0.232	<b>0.097</b>	<b>0.387</b>	0.47	0.306
DKEFS (n=24) <sup>a</sup>	0.386	0.217	0.964	0.449	<b>0.004</b>	<b>0.617</b>
COWAT (n=45) <sup>b</sup>	0.706	0.154	0.689	0.249	<b>0.027</b>	<b>0.368</b>
BDI (n=39) <sup>d</sup>	0.446	0.149	0.325	0.372	<b>0.015</b>	<b>0.480</b>
MFIS (n=68) <sup>d</sup>	<b>0.06</b>	<b>0.187</b>	<b>0.016</b>	<b>0.262</b>	0.305	0.037

$p$ -values and coefficients of determination were adjusted for:

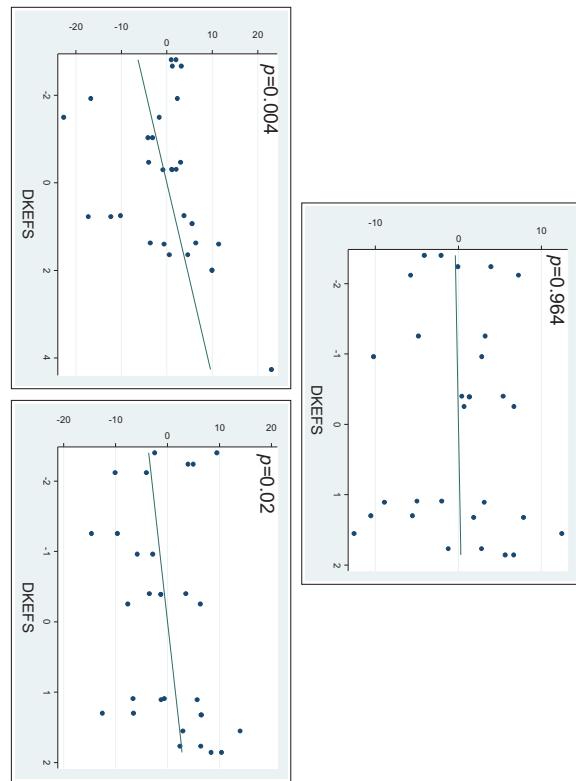
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<sup>c</sup> sex, disease duration, years of education, and ON history

<sup>d</sup> age, sex, disease duration, and ON history

Low contrast VA is more closely associated with cognitive scores than high contrast VA



## AVP measures are weakly associated with cognitive scores in PMS

Scores	Anterior Visual Pathway Measures					
	Average GCIP Thickness	100%-VA	2.5%-VA	1.25%-VA		
	<i>p</i> -value	R <sup>2</sup>	<i>p</i> -value	R <sup>2</sup>	<i>p</i> -value	R <sup>2</sup>
MSFC (n=36) <sup>a</sup>	0.226	0.1702	0.238	0.0956	0.552	0.0908
SDMT (n=23) <sup>b</sup>	0.638	0.1048	0.893	0.1152	0.765	0.0919
BVMT-R						
Total Recall (n=21) <sup>c</sup>	0.889	0.1877	<b>0.049</b>	<b>0.2135</b>	0.483	0.1248
BVMT-R						
Delayed Recall (n=21) <sup>c</sup>	0.45	0.2046	0.541	0.1428	0.471	0.1225
JLO (n=11) <sup>a</sup>	0.233	0.8159	0.807	0.2156	0.545	0.4576
DKEFS (n=8) <sup>a</sup>	0.728	0.9253	0.398	0.8933	0.399	0.6916
COWAT (n=10) <sup>b</sup>	0.369	0.6859	0.349	0.4469	0.99	0.4745
BDI (n=9) <sup>d</sup>	0.54	0.7364	0.111	0.5802	<b>0.033</b>	<b>0.5736</b>
MFIS (n=22) <sup>d</sup>	0.143	0.1349	0.999	0.1298	0.134	0.2433

<sup>a</sup>*p*-values and coefficients of determination were adjusted for:

<sup>b</sup>age, sex, disease duration, years of education, and ON history

<sup>c</sup>sex, disease duration, and ON history

<sup>d</sup>age, sex, disease duration, and ON history

<sup>a</sup>age, sex, disease duration, years of education, and ON history

<sup>b</sup>sex, disease duration, and ON history

<sup>c</sup>sex, disease duration, years of education, and ON history

<sup>d</sup>age, sex, disease duration, and ON history

## Summary

- Anterior visual function reflects cognitive function in MS particularly in RRMS
- GCIP thickness was associated with fatigue scores across the cohort
- AVP measures were weakly associated with cognition in PMS
- AVP measures mirror global aspects of the MS disease process
- Future directions

## Collaborators and Funding

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Thank you.

Questions?

