



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

James V. Nguyen, Alissa M. Rothman, Cassie Cummings,  
Laura J. Balcer, Elliot M. Frohman, Peter A. Calabresi, Shiv Saidha

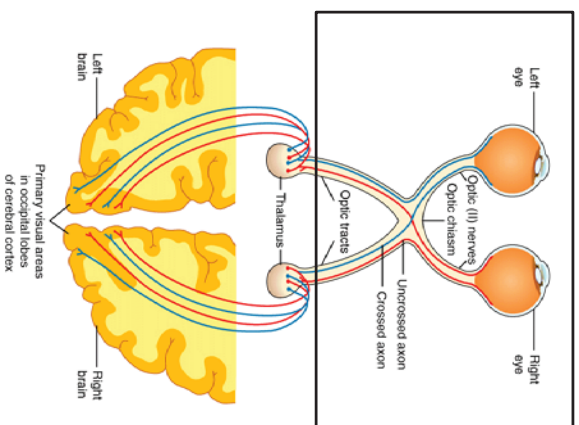
Research Coordinator  
Johns Hopkins School of Medicine  
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### Disclosures

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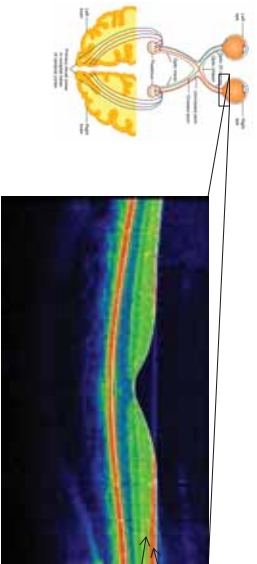
## Anterior Visual Pathway (AVP)

- 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



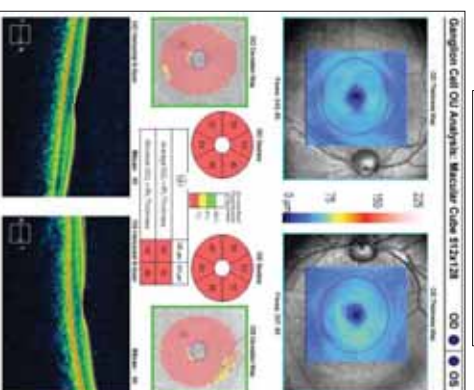
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4196746/>

## Optical Coherence Tomography (OCT)



Retinal Nerve Fiber Layer (RNFL)

Ganglion Cell + Inner Plexiform Layer (GCIP)



- 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 (BVM-T-R) Total Recall	Visuospatial and working memory
Brief Visuospatial Memory Test-Revised (BVM-T-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

	<b>Overall n=131</b>	<b>RRMS n=95</b>	<b>Progressive MS n=36</b>	<b><i>p</i>-value RRMS vs PMS</b>
<b>Mean age, years (SD)</b>	45 (12.3)	41 (11.5)	55 (8.1)	< 0.001
<b>Mean disease duration, years (SD)</b>	11 (8.8)	8.6 (6.6)	18.3 (9.9)	< 0.001
<b>Females (%)</b>	66	65	67	0.8317
<b>Race</b> <ul style="list-style-type: none"><li>• Caucasian</li><li>• African American</li><li>• Other</li></ul>	112 11 8	79 9 7	33 2 1	0.1260
<b>Eyes with ON History</b>	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 <sup>2</sup>	p-value	R <sup>2</sup>	p-value	R <sup>2</sup>	p-value	R <sup>2</sup>
MSFC (n=131) <sup>a</sup>	0.263	0.1045	0.797	0.0314	<b>0.047</b>	<b>0.0624</b>	0.14	0.066
SDMT (n=99) <sup>b</sup>	0.369	0.1479	0.408	0.1649	<b>0.047</b>	<b>0.1905</b>	<b>0.004</b>	<b>0.1408</b>
BVMT-R 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>	<b>0.001</b>	<b>0.1889</b>
BVMT-R Delayed recall (n=92) <sup>c</sup>	0.469	0.1739	0.215	0.264	0.47	0.0967	<b>0.068</b>	<b>0.1278</b>
JLO (n=56) <sup>a</sup>	0.975	0.0626	0.19	0.3384	0.975	0.3157	0.143	0.1881
DKEFS (n=39) <sup>a</sup>	0.681	0.0651	0.458	0.3738	0.454	0.454	0.365	0.4149
COWAT (n=55) <sup>b</sup>	0.784	0.0616	0.212	0.3529	0.31	0.1603	0.152	0.1186
BDI (n=48) <sup>d</sup>	0.628	0.0398	0.459	0.2579	0.162	0.3856	0.487	0.2573
MEFS (n=9) <sup>d</sup>	<b>0.026</b>	<b>0.1467</b>	<b>0.029</b>	<b>0.1513</b>	0.163	0.0403	0.467	0.0712

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

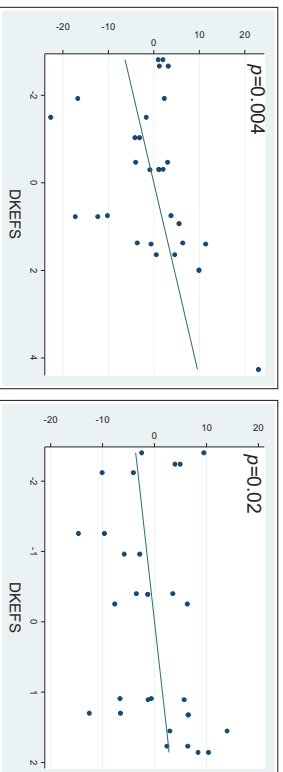
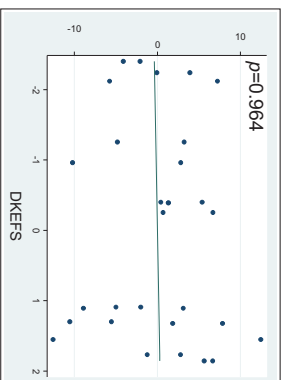
## AVP measures are associated with cognitive & fatigue scores in RRMS

Scores	Anterior Visual Pathway Measures							
	Average GCIP Thickness		100%-VA		2.5%-VA		1.25%-VA	
	p-value	R <sup>2</sup>	p-value	R <sup>2</sup>	p-value	R <sup>2</sup>	p-value	R <sup>2</sup>
MSFC (n=95) <sup>a</sup>	0.616	0.114	0.511	0.114	<b>0.048</b>	<b>0.056</b>	0.107	0.052
SDMT (n=76) <sup>b</sup>	0.47	0.237	0.689	0.287	<b>0.055</b>	<b>0.118</b>	<b>0.002</b>	<b>0.161</b>
BVMT-R Total Recall (n=71) <sup>c</sup>	0.978	0.244	<b>0.025</b>	<b>0.348</b>	<b>0.092</b>	<b>0.125</b>	<b>0.001</b>	<b>0.205</b>
BVMT-R Delayed Recall (n=71) <sup>c</sup>	0.206	0.259	0.364	0.318	0.361	0.098	<b>0.024</b>	<b>0.149</b>
JLO (n=30) <sup>a</sup>	0.277	0.232	<b>0.097</b>	<b>0.387</b>	0.47	0.306	0.166	0.209
DKEFS (n=24) <sup>a</sup>	0.386	0.217	0.964	0.449	<b>0.004</b>	<b>0.617</b>	<b>0.02</b>	<b>0.572</b>
COWAT (n=45) <sup>b</sup>	0.706	0.154	0.689	0.249	<b>0.027</b>	<b>0.368</b>	0.139	0.201
BDI (n=39) <sup>d</sup>	0.446	0.149	0.325	0.372	<b>0.015</b>	<b>0.480</b>	0.12	0.295
MEFS (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	0.811	0.021

p-value 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

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>	<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	0.732	0.0929
SDMT (n=23) <sup>b</sup>	0.638	0.1048	0.893	0.1152	0.765	0.0919	0.908	0.1488
BVMT-R								
Total Recall (n=21) <sup>c</sup>	0.889	0.1877	<b>0.049</b>	<b>0.2136</b>	0.483	0.1248	0.558	0.1438
BVMT-R								
Delayed Recall (n=21) <sup>c</sup>	0.45	0.2046	0.541	0.1428	0.471	0.1225	0.754	0.1347
JLO (n=11) <sup>a</sup>	0.213	0.8159	0.807	0.2156	0.545	0.4576	0.151	0.3157
DKFS (n=8) <sup>a</sup>	0.728	0.9253	0.398	0.8933	0.399	0.6916	0.205	0.5733
COVAT (n=10) <sup>b</sup>	0.369	0.6859	0.349	0.4469	0.99	0.4745	<b>0.054</b>	<b>0.3444</b>
BDI (n=9) <sup>d</sup>	0.54	0.7364	0.111	0.5802	<b>0.033</b>	<b>0.5736</b>	0.747	0.1961
MFIS (n=22) <sup>d</sup>	0.143	0.1349	0.999	0.1298	0.134	0.2433	0.119	0.2804

<sup>a</sup> *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

# 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?

