Anti-MOG Associated Disorder: Insights Into Neuroplasticity and Opportunities for Repair

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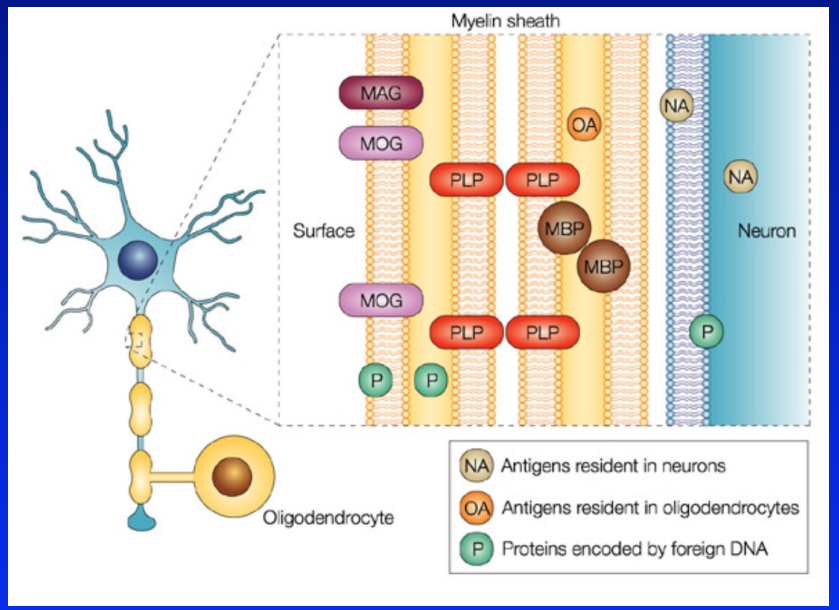
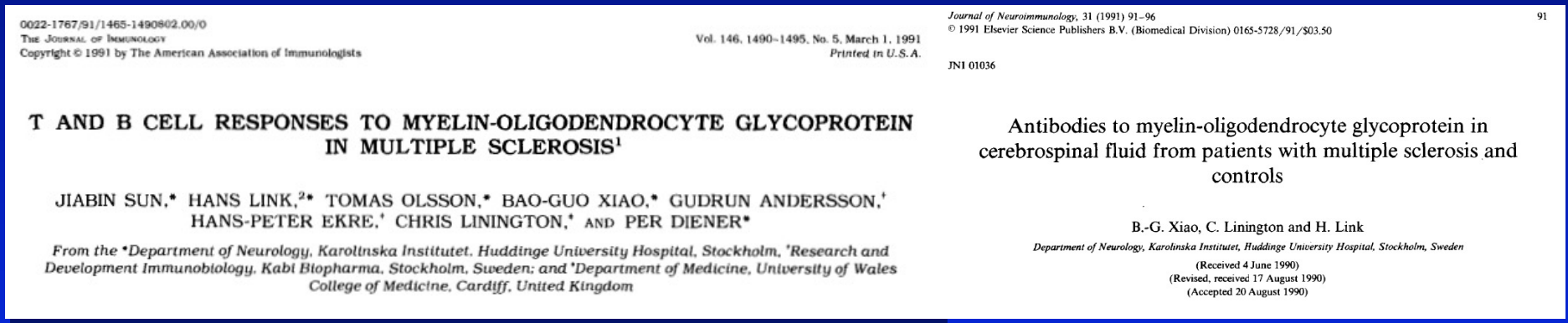
Myelin Oligodendrocyte Glycoprotein

- CNS restricted myelin protein
- Minor component of myelin
- Produced by oligodendrocytes late in myelination
- First identified in 1984 using a mouse monoclonal antibody
- Surface based glycoproteins are through to mediate glial-glial or glial-neuronal interactions
- Two isoforms form dimers on cell surface
- DNA sequence determined it was in the immunoglobulin superchain family and encoded within HLA portion of genome



History of anti-MOG Antibodies: Human Detection



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T AND B CELL RESPONSES TO MYELIN-OLIGODENDROCYTE GLYCOPROTEIN IN MULTIPLE SCLEROSIS[1]

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Antibodies to myelin-oligodendrocyte glycoprotein in cerebrospinal fluid from patients with multiple sclerosis and controls

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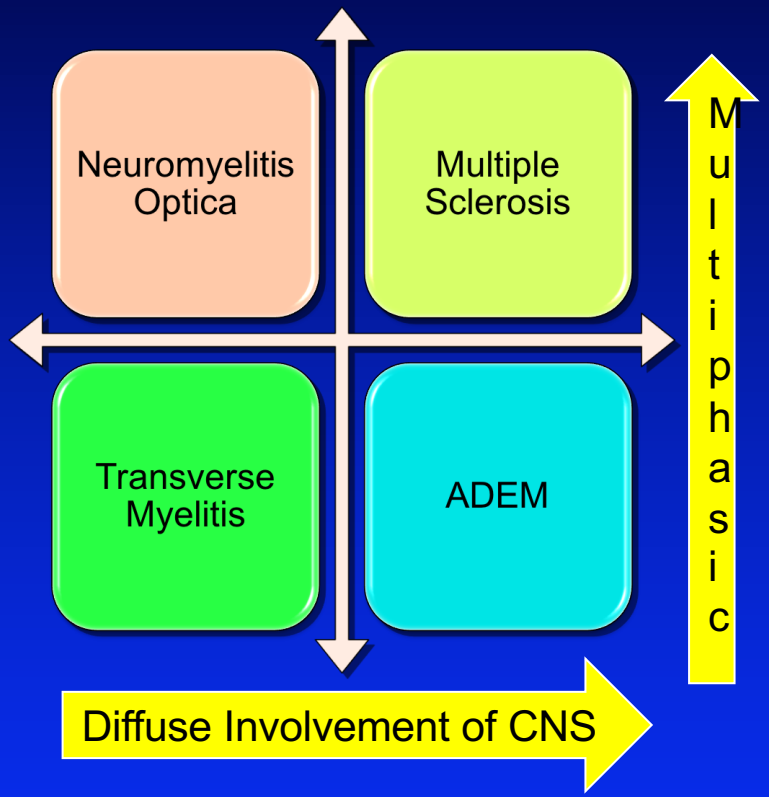
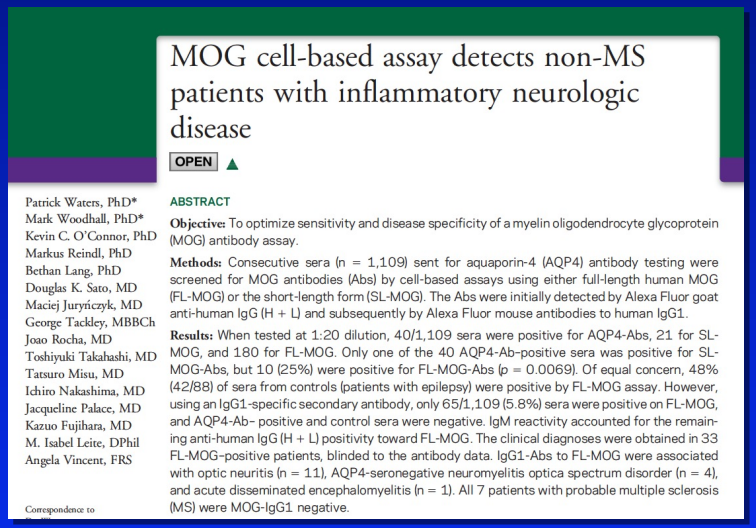
ELISA using MOG from human brain (purified as 4 bands on SDS Page Gel, using a specific antibody (the one from EAE) as a positive control



- Antibodies to MOG first described by ELISA or western blot in patients with MS, but also bacterial CNS infections, viral CNS infections and NMO
- Findings not reproducible
- Assay that used soluble MOG tetramers detected Ab in ADEM but not MS patients
- Some assays using truncated MOG found Ab in AQP4 seronegative patients, but not MS
- Some assays using full length MOG finds Ab in AQP4 seronegative patients, but also positive in MS and healthy controls.

Assay Research Clarified the Molecular Biomarker



MOG cell-based assay detects non-MS patients with inflammatory neurologic disease

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ABSTRACT

Objective: To optimize sensitivity and disease specificity of a myelin oligodendrocyte glycoprotein (MOG) antibody assay.

Methods: Consecutive sera (n = 1,109) sent for aquaporin-4 (AQP4) antibody testing were screened for MOG antibodies (Abs) by cell-based assays using either full-length human MOG (FL-MOG) or the short-length form (SL-MOG). The Abs were initially detected by Alexa Fluor goat anti-human IgG (H + L) and subsequently by Alexa Fluor mouse antibodies to human IgG1.

Results: When tested at 1:20 dilution, 40/1,109 sera were positive for AQP4-Abs, 21 for SL-MOG, and 180 for FL-MOG. Only one of the 40 AQP4-Ab-positive sera was positive for SL-MOG-Abs, but 10 (25%) were positive for FL-MOG-Abs ($p = 0.0069$). Of equal concern, 48% (42/88) of sera from controls (patients with epilepsy) were positive by FL-MOG assay. However, using an IgG1-specific secondary antibody, only 65/1,109 (5.8%) sera were positive on FL-MOG, and AQP4-Ab– positive and control sera were negative. IgM reactivity accounted for the remaining anti-human IgG (H + L) positivity toward FL-MOG. The clinical diagnoses were obtained in 33 FL-MOG–positive patients, blinded to the antibody data. IgG1-Abs to FL-MOG were associated with optic neuritis (n = 11), AQP4-seronegative neuromyelitis optica spectrum disorder (n = 4), and acute disseminated encephalomyelitis (n = 1). All 7 patients with probable multiple sclerosis (MS) were MOG-IgG1 negative.

Neurol Neuroimmunol Neuroinflamm 2015

Age Distribution Relative to First Symptom for anti-MOG Ab Disease

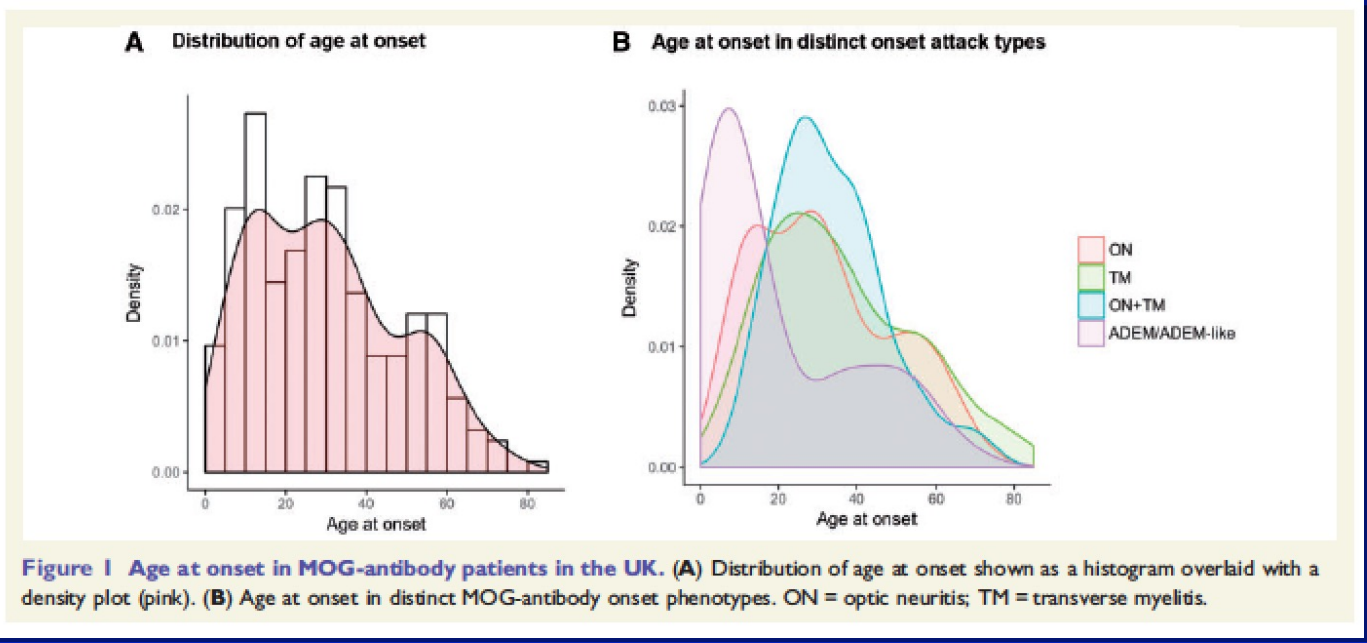
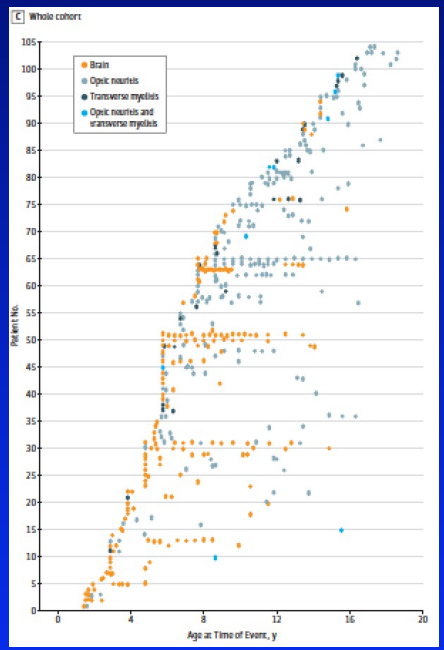


Figure 1 Age at onset in MOG-antibody patients in the UK. (**A**) Distribution of age at onset shown as a histogram overlaid with a density plot (pink). (**B**) Age at onset in distinct MOG-antibody onset phenotypes. ON = optic neuritis; TM = transverse myelitis.



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Jurynczyk, et al, Brain, 2017

Relapse Risks for anti-MOG

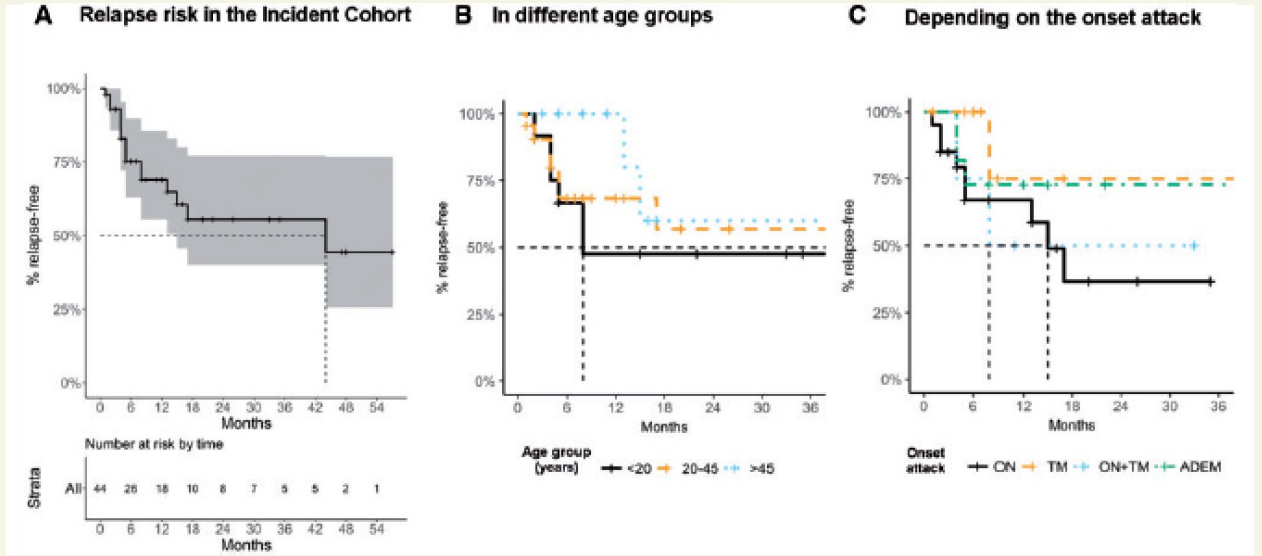
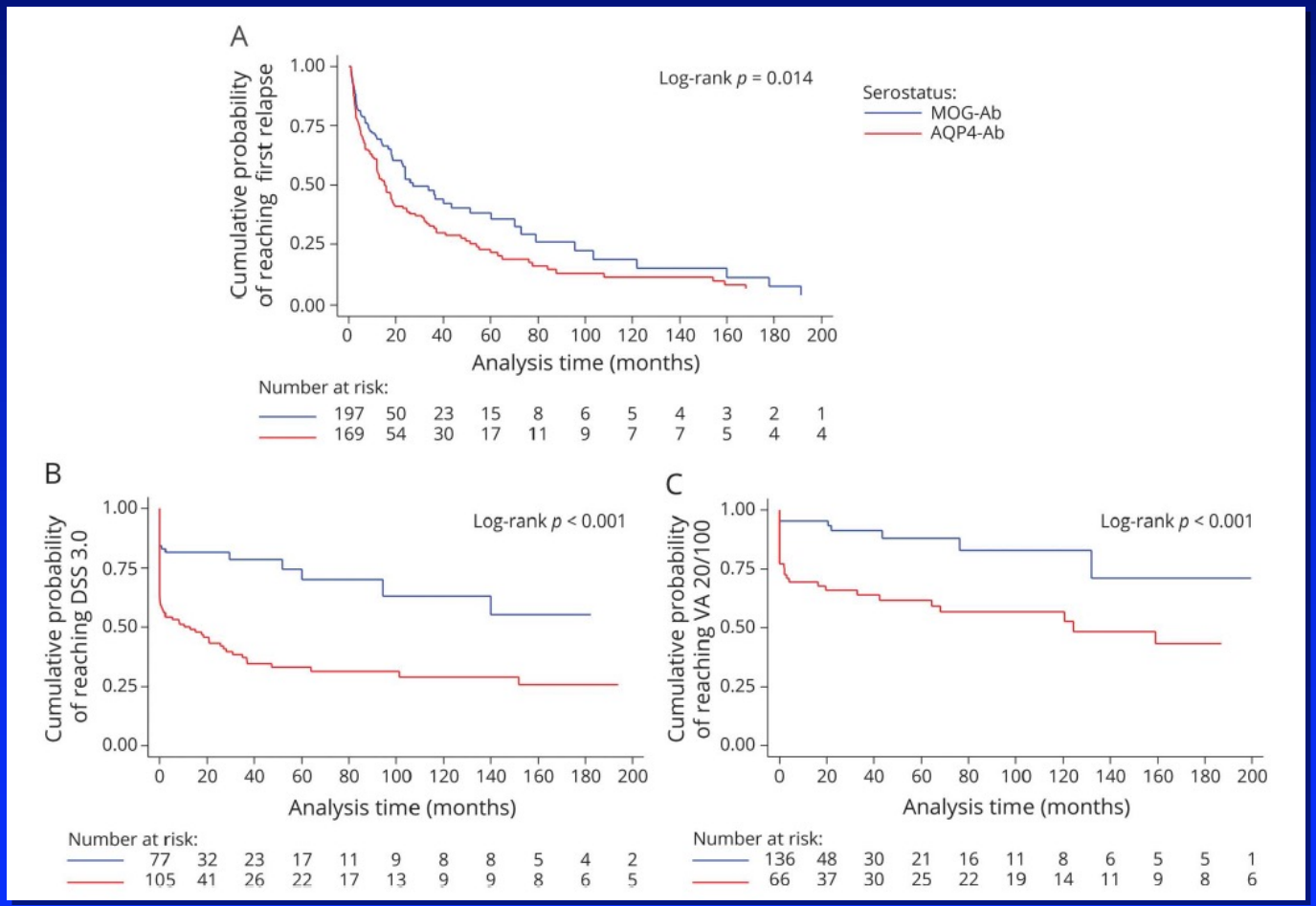


Figure 3 Kaplan-Meier curves showing cumulative probability over time of remaining relapse free in the Oxford incident cohort. (**A**) All patients in the Oxford incident cohort are included. The 95% confidence interval is shown in grey. The dashed line represents the number of months until 50% patients relapsed. The risk table shows the number of patients at risk of the relapse at each time point, (**B**) depending on the age at onset; (**C**) depending on the onset phenotype. ON = optic neuritis; TM = transverse myelitis.

Jurynczyk, et al, Brain, 2017

Time to Event and Outcomes of MOGAD vs. AQP4 mediated disease



Neurology® 2018;0:e1-e12. doi:10.1212/WNL.0000000000005560

MRI Findings in MOGAD

Table 2 Radiologic features in MOG-Ab–positive patients with an initial abnormal brain MRI

	MOG-Ab group (n = 49)	AQP4-Ab group (n = 22)	*p* Value
Radiologic features, n (%)			
Predominantly cortical gray matter	8 (16.33)	1 (4.55)	0.257
Confined to brainstem and/or basal ganglia	14 (28.57)	8 (36.36)	0.511
Hazy/poorly demarcated lesions	10 (20.41)	3 (13.64)	0.741
Tumefactive lesions	5 (10.20)	2 (9.09)	0.884
Nonspecific white matter lesions	7 (14.29)	3 (13.64)	0.942
Gadolinium enhancement	6 (12.24)	5 (22.73)	0.298
Lesion location at onset, n (%)			
Bilateral	22 (44.90)	11 (54.54)	0.563
Leptomeningeal enhancement[a]	3 (6.12)	0 (0)	0.236
Juxtacortical	20 (40.82)	7 (31.82)	0.599
Deep white matter	24 (48.98)	13 (59.09)	0.455
Periventricular	13 (26.53)	6 (27.27)	0.948
U or S shape	5 (10.20)	1 (4.55)	0.658
Dawson finger	4 (8.16)	0 (0)	0.303
Corpus callosum	5 (10.20)	2 (9.09)	0.884
Thalamus[b]	9 (18.37)	0	0.031
Brainstem	18 (36.73)	13 (59.09)	0.079
Midbrain	5 (10.2)	3 (13.64)	0.672
Pons	17 (34.69)	1 (4.55)	0.007
Medulla oblongata	7 (14.29)	10 (45.45)	0.004
Area postrema	1 (2.04)	7 (31.82)	<0.001
Adjacent to 4th ventricle	11 (22.45)	3 (13.64)	0.388
Cerebellar peduncles	9 (18.37)	4 (18.18)	0.985
Cerebellum	2 (4.08)	2 (9.09)	0.397

Periventricular	13 (26.53)
Dawson finger	4 (8.16)
Corpus callosum	5 (10.20)

Neurology® 2018;0:e1-e12. doi:10.1212/WNL.0000000000005560

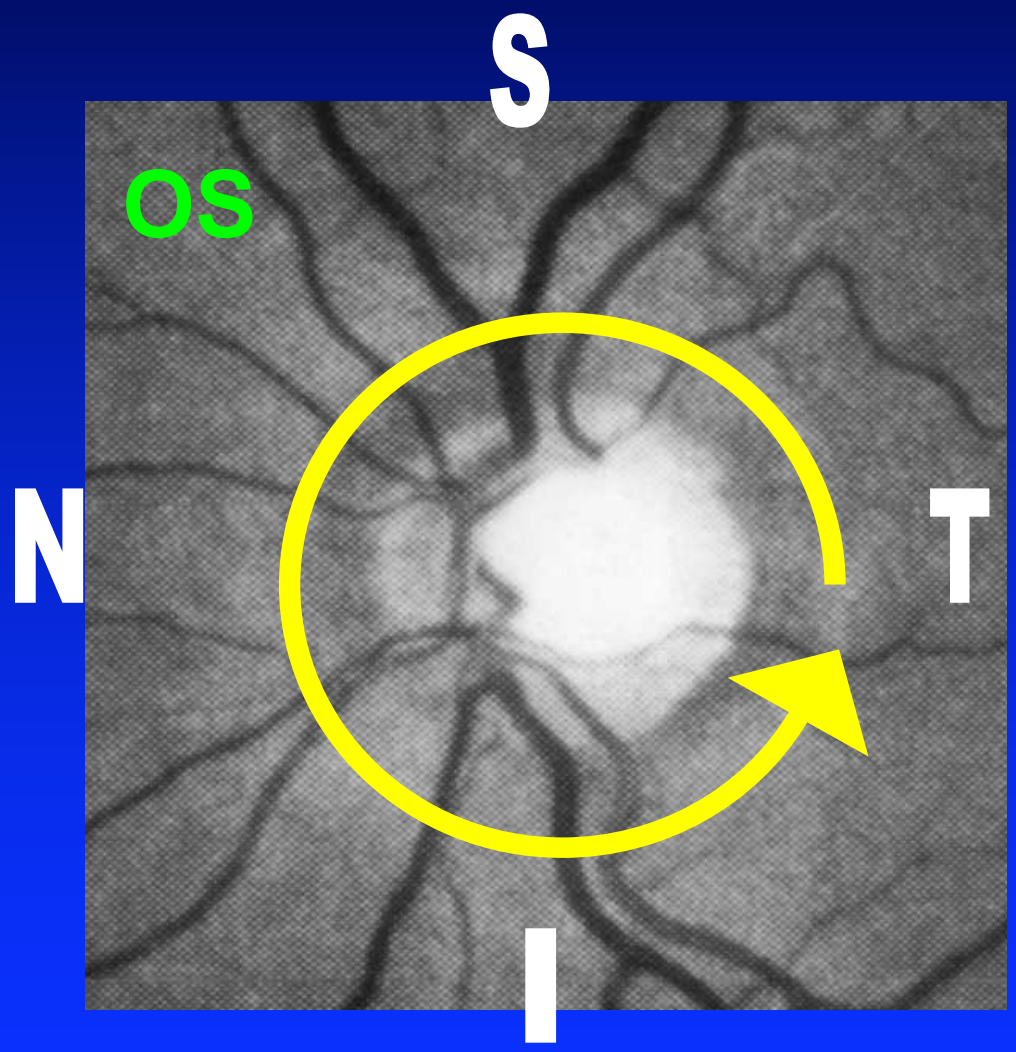
Unique Features of MOG

Preserved Vision in MOG

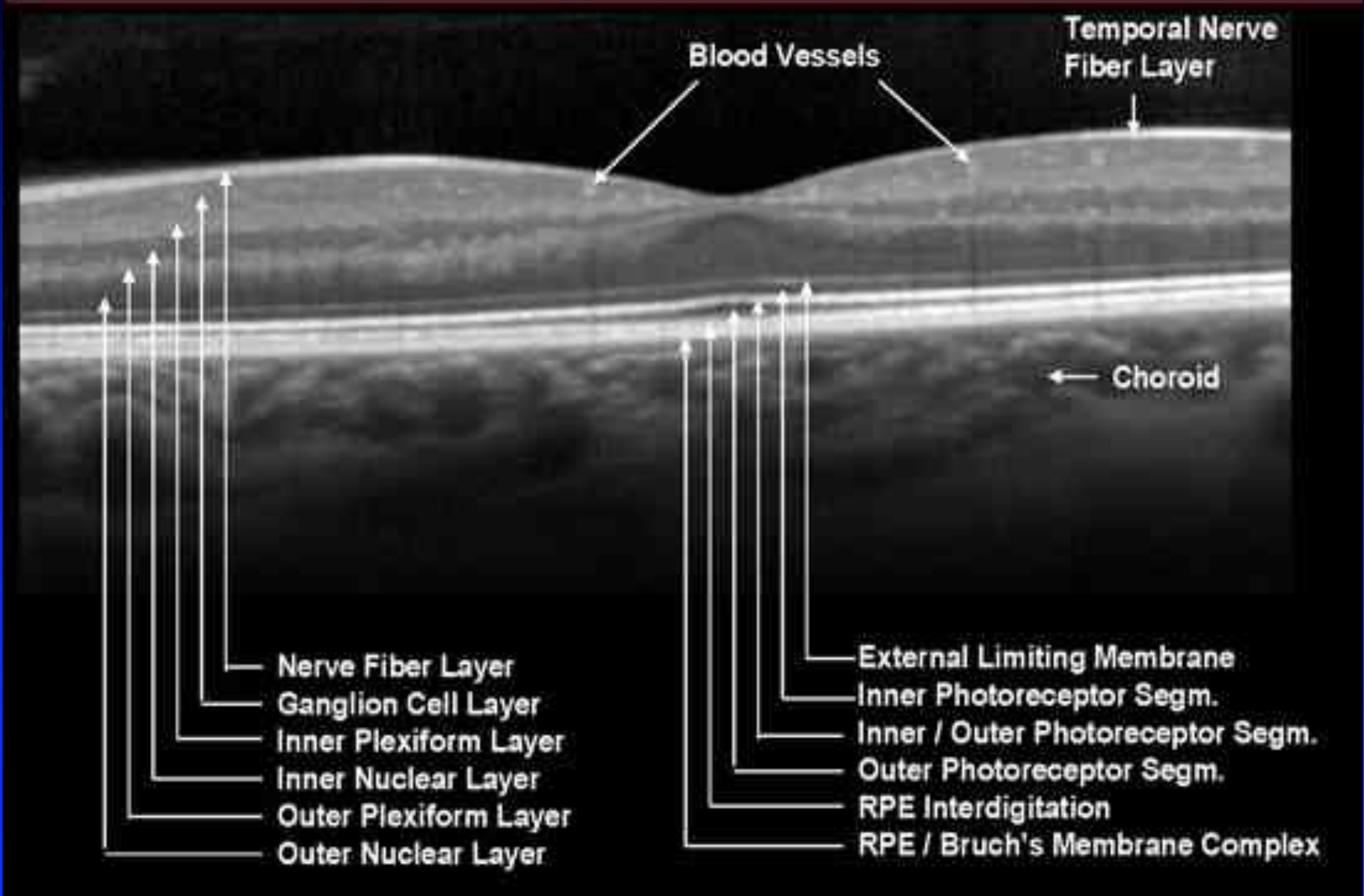

R
A

RNFL scans

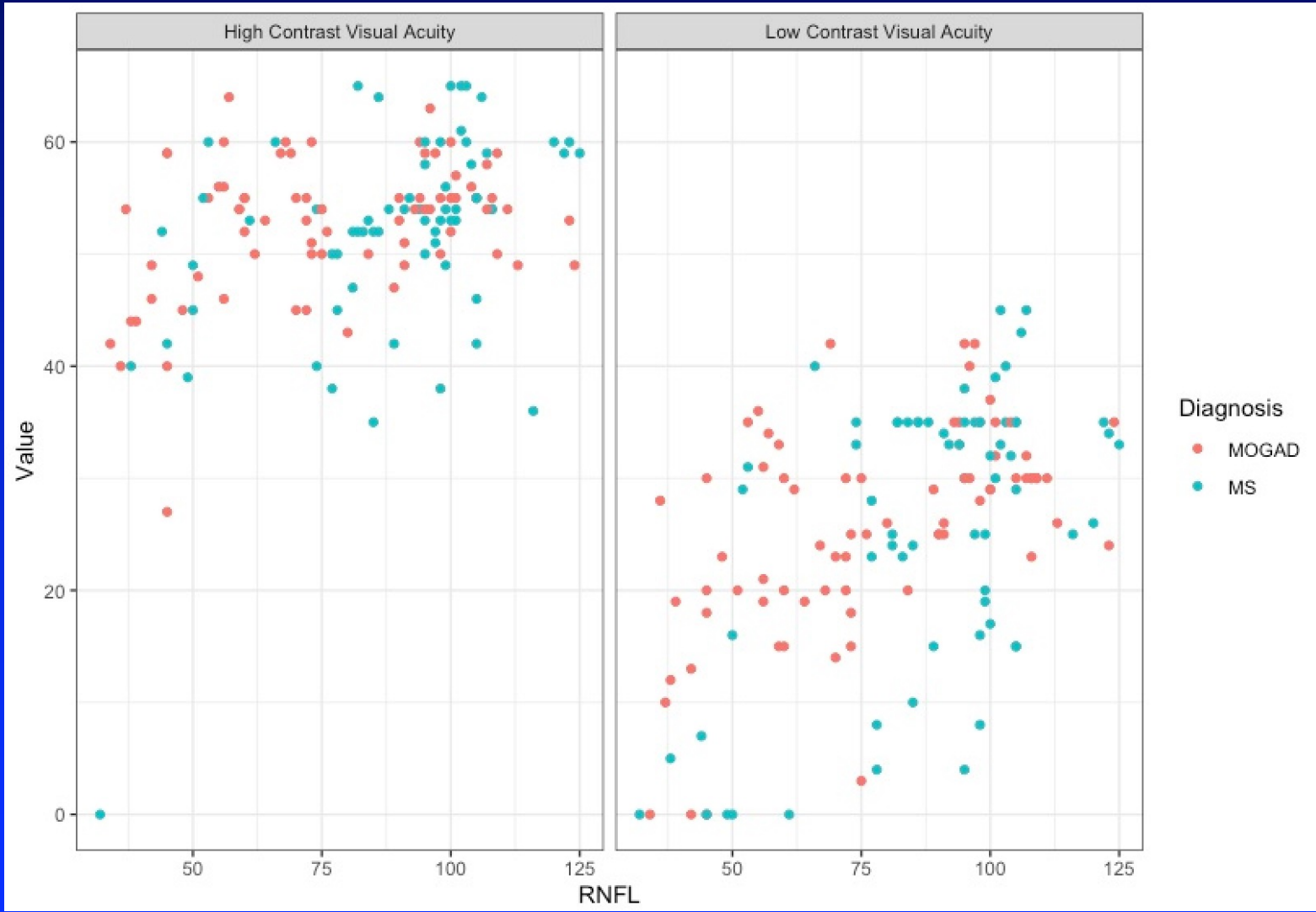
- Circular scans around ONH at a radius of 1. 73mm
- Scan begins temporally
- Three scans are acquired and data are averaged



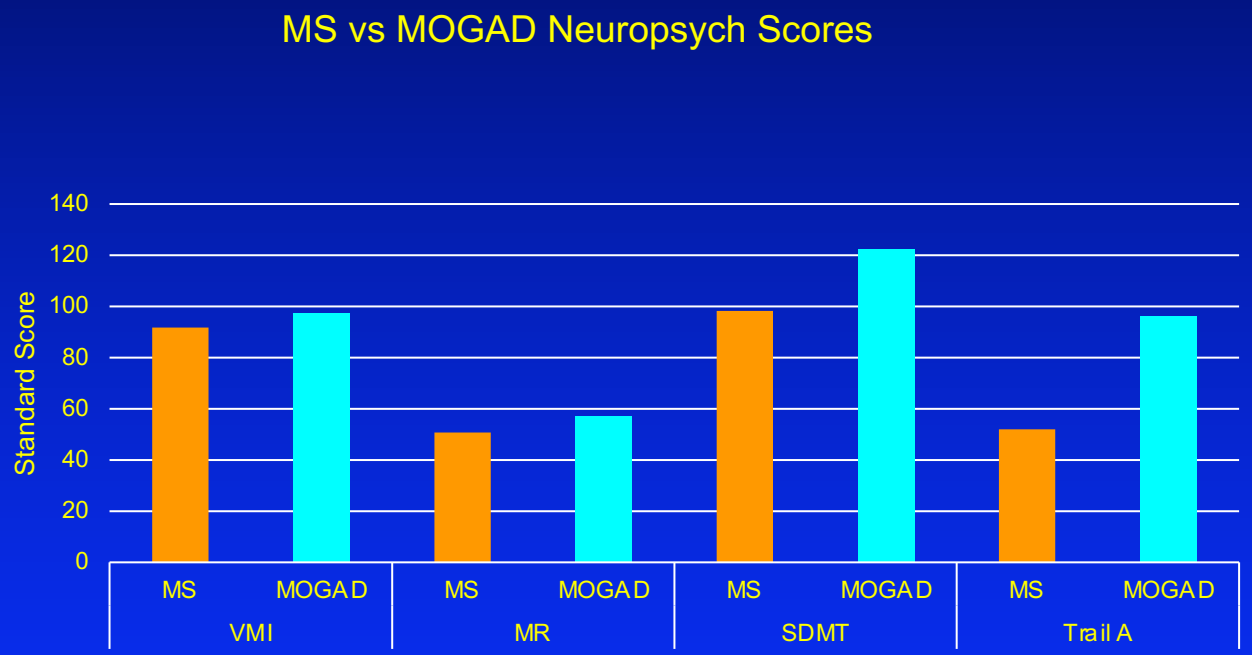
Retinal Labeled Layers (Image zoomed to ~15°)



Preserved Vision in MOG



Cognition in MOG Patients



Future Studies

- MRI imaging of plasticity correlated to vision and cognition
- Opportunity to learn about repair and plasticity