MRI in MS (MAGNIMS) &OPHTHALMIC IMAGING

OPTIC NERVE MRI

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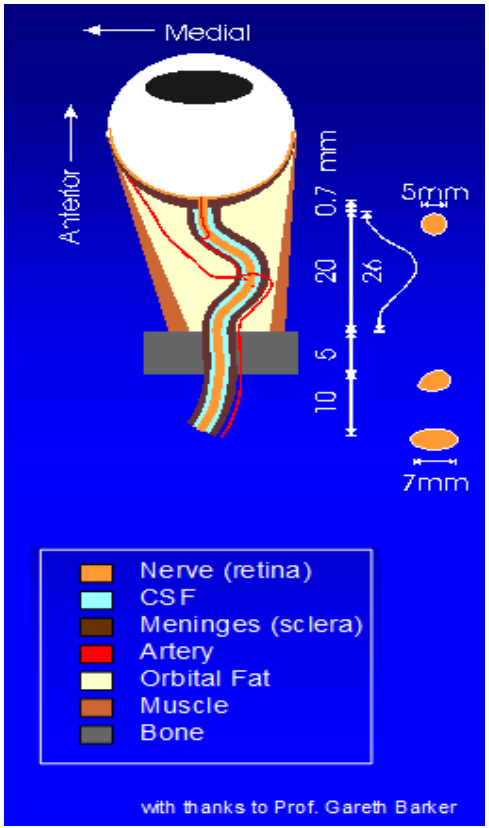
Outline of the presentation

- **Imaging the optic nerve**
- Diagnosis and differential diagnosis
- Understanding disease pathophysiology
- Conclusions

Imaging the optic nerve



Size of nerve

- High in plane resolution
- Thin slices

Surroundings of nerve (fat, CSF, air-bone interfaces)

- Fat-saturated sequences
- Fluid attenuated inversion recovery sequences

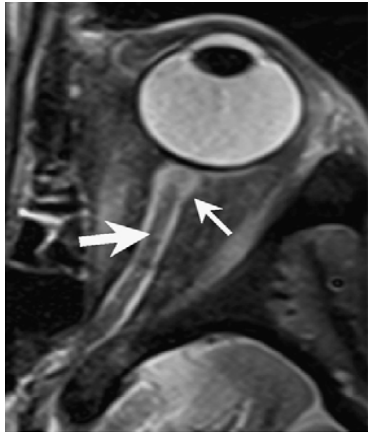
Motion

- Relatively fast sequences

Barker et al., J Neurol Sci 2000

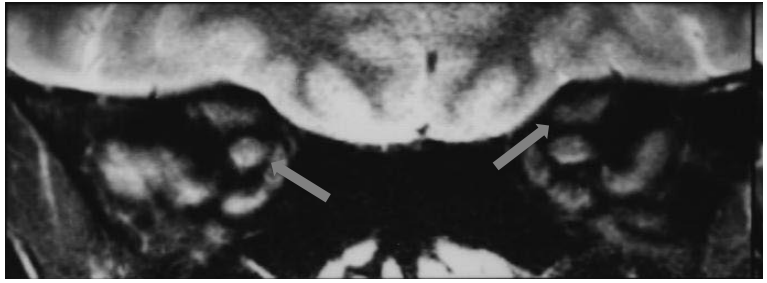
Imaging the optic nerve

STIR sequence



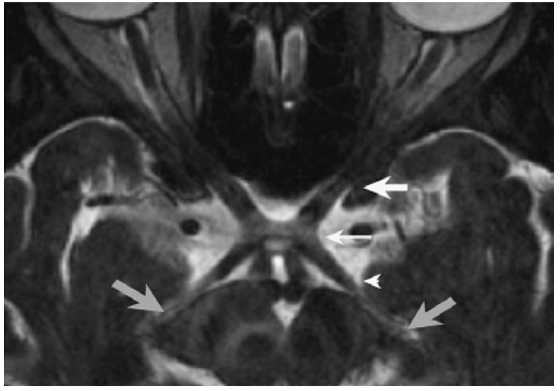
Becker et al., Eur J Radiol 2010

Fat-saturated, T2w, FSE sequence



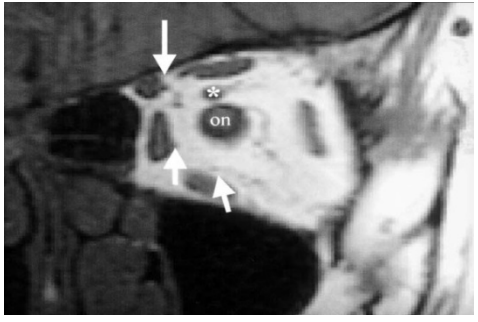
Barker et al., J Neurol Sci 2000

3DFT, T2w sequence



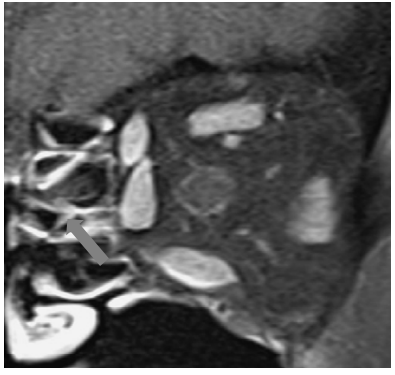
Becker et al., Eur J Radiol 2010

T1w sequence



Aviv et al., Clin Radiol 2005

Fat-saturated, Gd-enhanced, T1w sequence

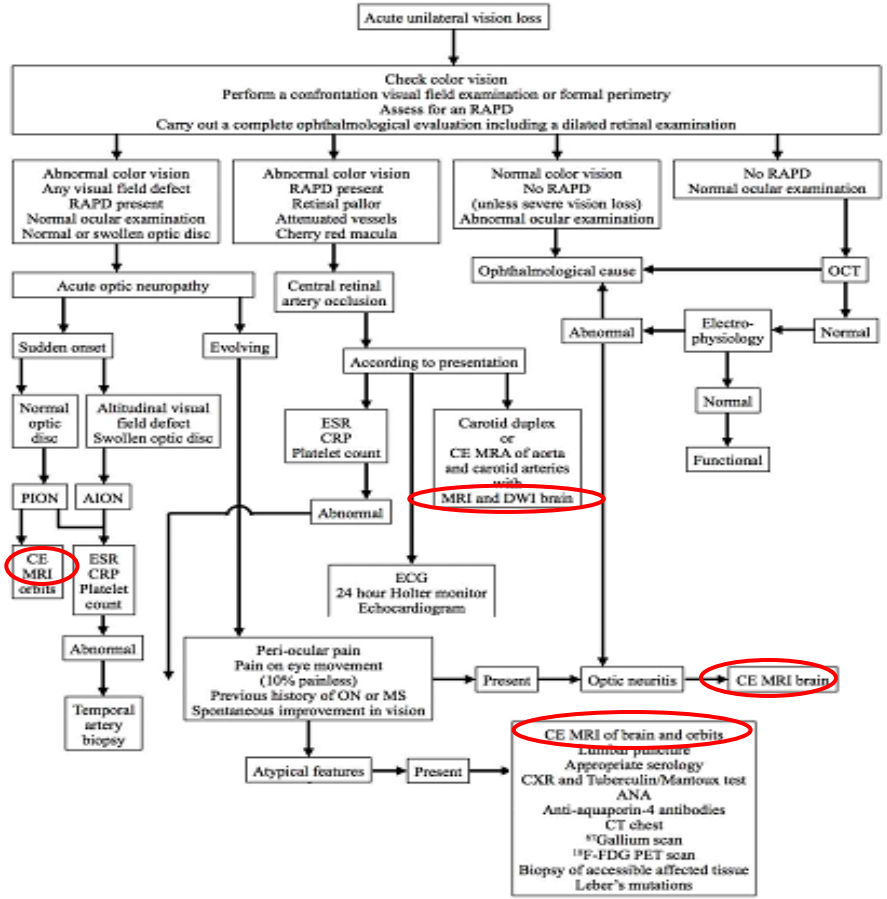


Becker et al., Eur J Radiol 2010

Outline of the presentation

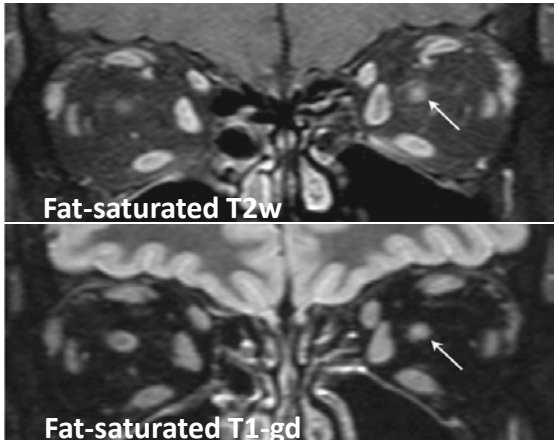
- Imaging the optic nerve
- **Diagnosis and differential diagnosis**
- Understanding disease pathophysiology
- Conclusions

Diagnosis and differential diagnosis



Hickman et al., Imaging of acute neurologic disease 2014

Diagnosis and differential diagnosis



Becker et al., Eur J Radiol 2010

Multiple sclerosis

- **ON lesions are reported in 94–99% of MS autopsy cases** (*Kolappan et al. J Neurol 2009*)
- **Optic neuritis is the presenting symptom of MS in 25% of cases and occurs during the disease in about 70% of cases** (*Toosy et al., Lancet Neurol 2014*)

DIS 2016 MAGNIMS criteria

At least 2 out of 5 areas of the CNS as follows*:

≥ 3 Periventricular lesions

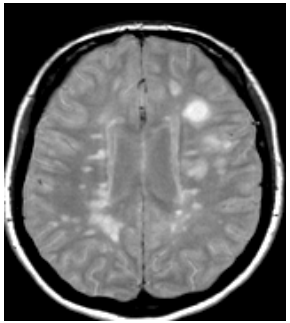
≥ 1 infratentorial lesion

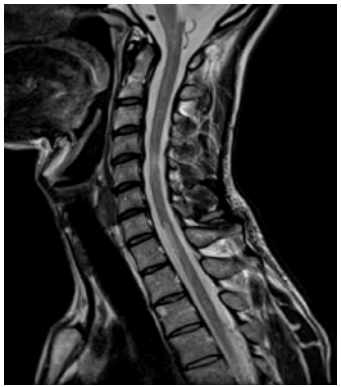
≥ 1 spinal cord lesion

≥ 1 optic nerve lesion

≥ 1 cortical/juxtacortical lesion

* Symptomatic lesion(s) are not excluded from the criteria and contribute to lesion count

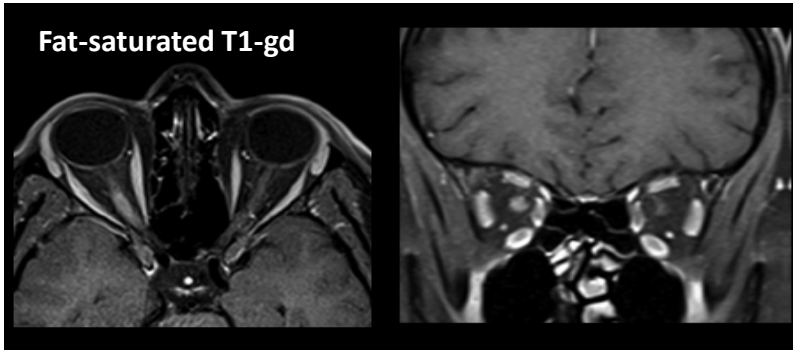




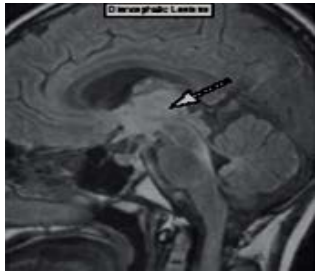
Filippi et al., Lancet Neurol 2016

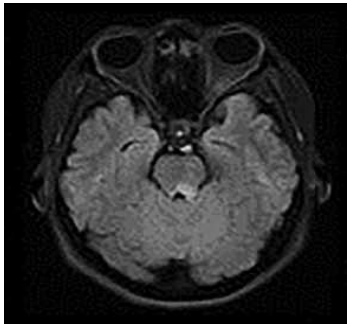
Diagnosis and differential diagnosis

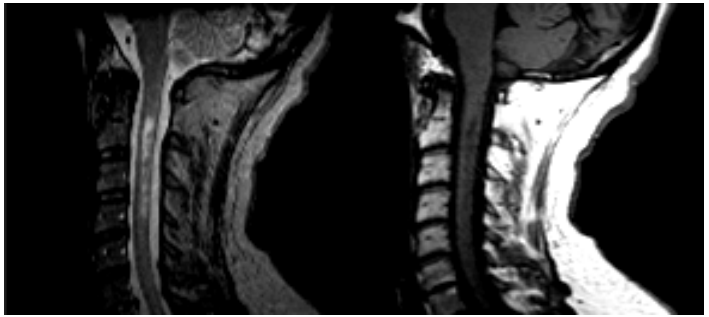
NMO Spectrum Disorders



Barnett et al.,AJNR 2013







Diagnostic criteria for NMOSD with AQP4-IgG

1. At least 1 core clinical characteristic
2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)
3. Exclusion of alternative diagnoses[a]

Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status

1. At least 2 core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:
   a. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome
   b. Dissemination in space (2 or more different core clinical characteristics)
   c. Fulfillment of additional MRI requirements, as applicable
2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable
3. Exclusion of alternative diagnoses[a]

Core clinical characteristics

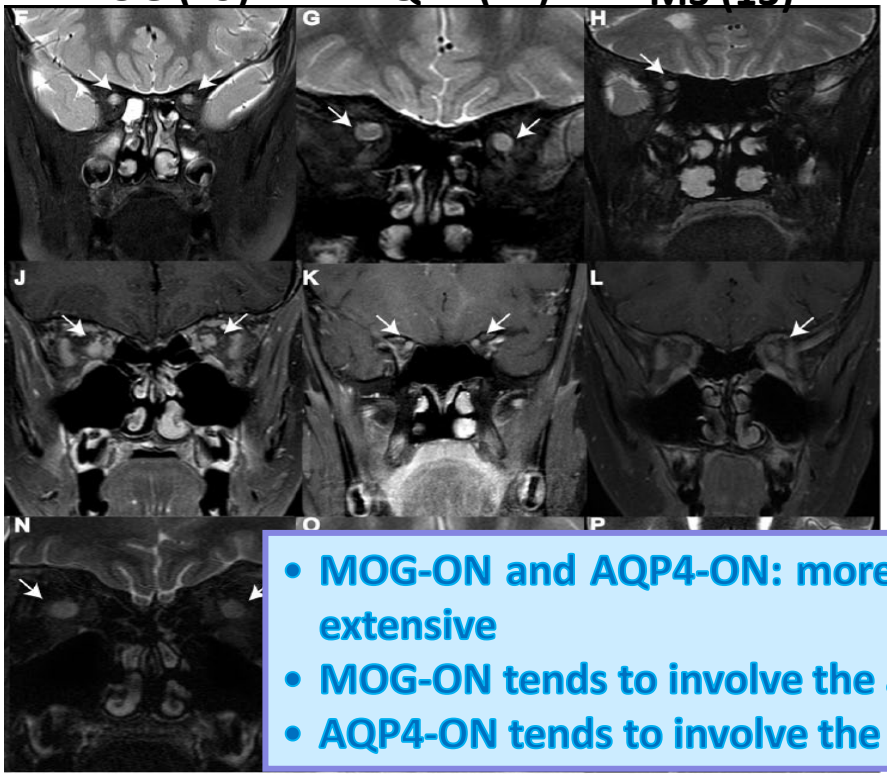
1. Optic neuritis
2. Acute myelitis
3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions (figure 3)
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions (figure 3)

Wingerchuk et al., Neurology 2015

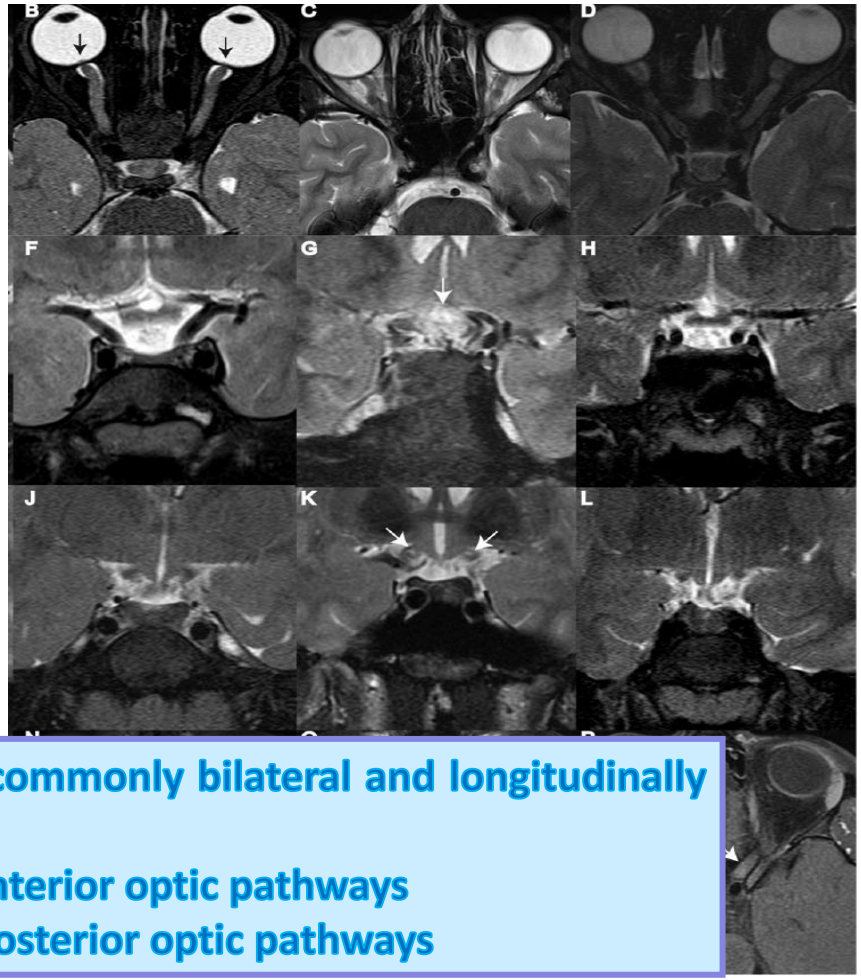
Diagnosis and differential diagnosis

MS *vs* AQP4 *vs* MOG optic neuritis

MOG (19) AQP4 (11) MS (13)



MOG AQP4 MS

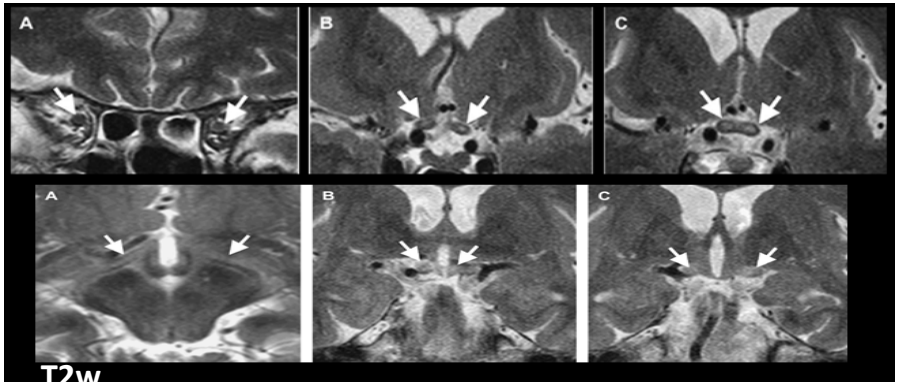


- MOG-ON and AQP4-ON: more commonly bilateral and longitudinally extensive
- MOG-ON tends to involve the anterior optic pathways
- AQP4-ON tends to involve the posterior optic pathways

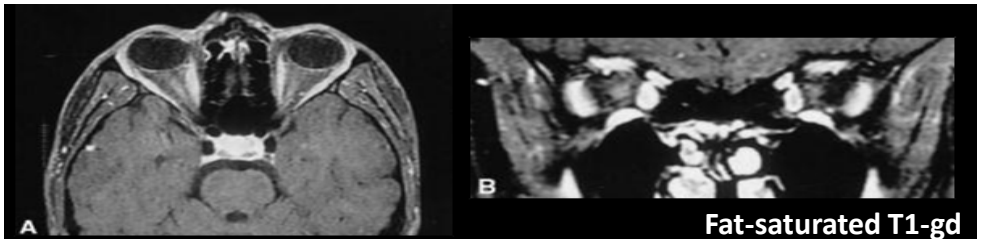
Ramanathan et al., MSJ 2015

Diagnosis and differential diagnosis

LHON

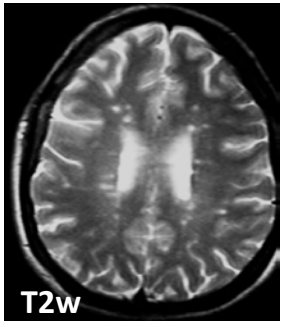


Van Westen et al., J Neuroophthalmol 2011

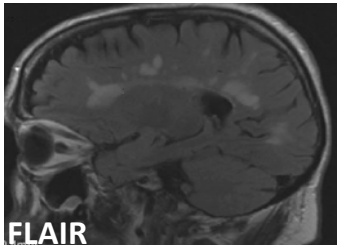


Vaphiades et al., J Neuroophthalmol 2003

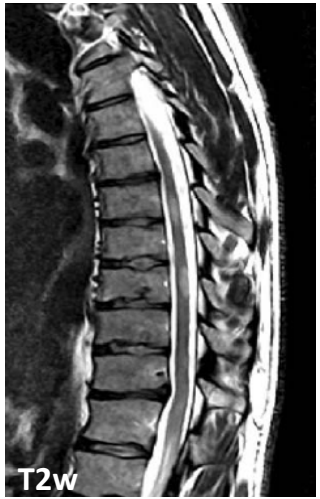
LHON + MS



Kuker et al., Eur J Neurol 2007



Cawley et al., Ir J Med Sci 2010

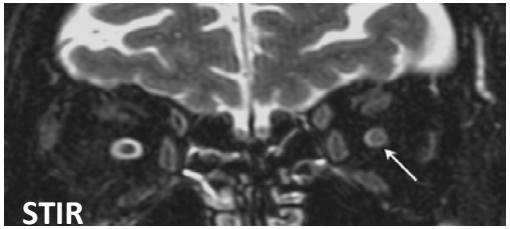


La Russa et al., MSJ 2011

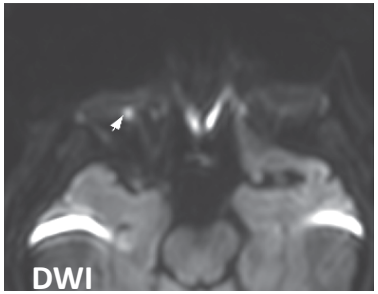
- 27% of LHON patients have aspecific WM lesions
- 25% of LHON patients have MS typical WM lesions (higher risk in females)
- All LMS patients have aspecific and MS typical WM lesions

Diagnosis and differential diagnosis

Ischemic optic neuropathy



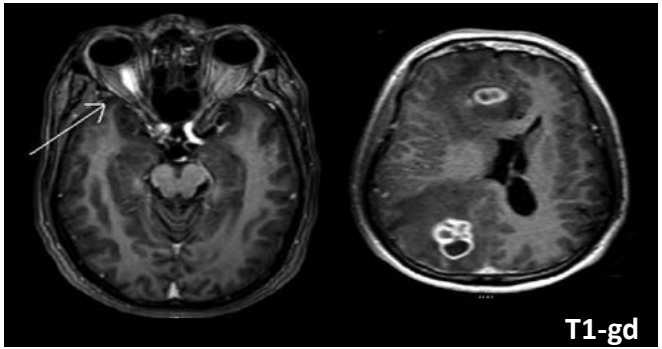
Becker et al.,
Eur J Radiol 2010



He et al.,
Semin Ophthalmol 2010

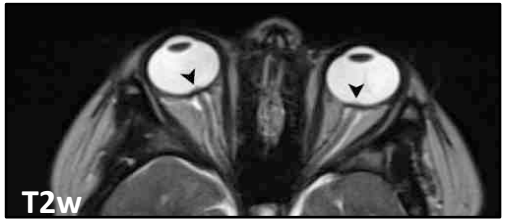
Infectious optic neuropathy

Tuberculosis

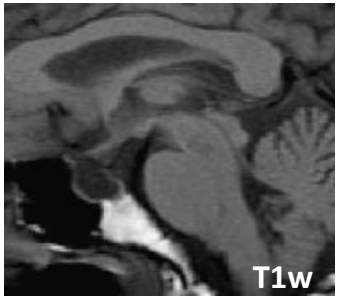


Sivadasan et al.,
Ann Indian Acad Neurol 2013

Idiopathic intracranial hypertension



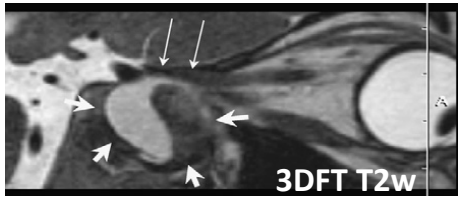
Hickman et al., Imaging of acute neurologic disease 2014

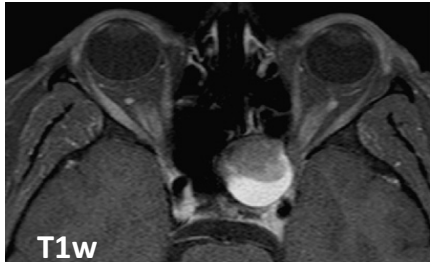


Agid et al.,
Neuroradiology 2006

Optic compressive neuropathy

Mucocele of the sphenoid sinus





Becker et al., Eur J Radiol 2010

Outline of the presentation

- Imaging the optic nerve
- Diagnosis and differential diagnosis
- **Understanding disease pathophysiology**
- Conclusions

Understanding disease pathophysiology

Demyelinating optic neuritis / Lesion features

Visual outcome vs longitudinal extent

	No. of nerves	Mean extent (no. of abnormal coronal slices)
Good recovery	38	1.84* (range, 0-4)
Poor recovery	6	3.50* (range, 2-5)
Fast recovery	26	1.54† (range, 0-3)
Slow recovery	10	2.70† (range, 0-4)

* and † indicate $p < 0.01$ (chi-squared analysis).

Visual outcome vs site

Site	Poor or slow recovery
Anterior	8/18 (44%)
Mid-intraorbital	13/26 (50%)
Intracanalicular	11/15 (73%)

Miller et al., Neurology 1988

Correlation with visual acuity after treatment

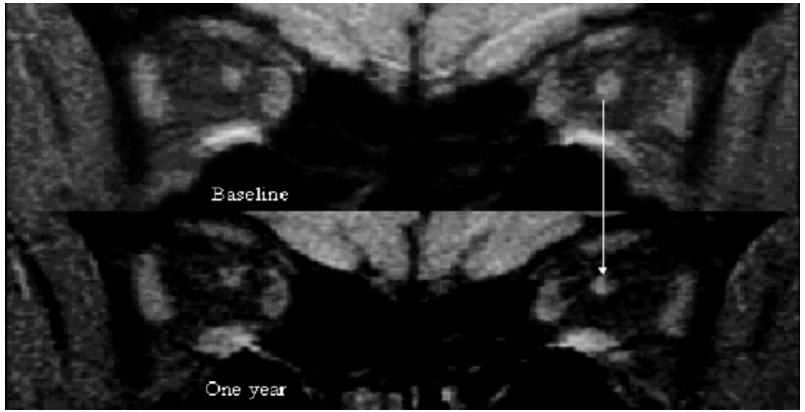
	Length of T2 lesion	Length of Gd enhancing lesion
r	-0,25	-0,3791
p	0,03	0,0012
n	77	70

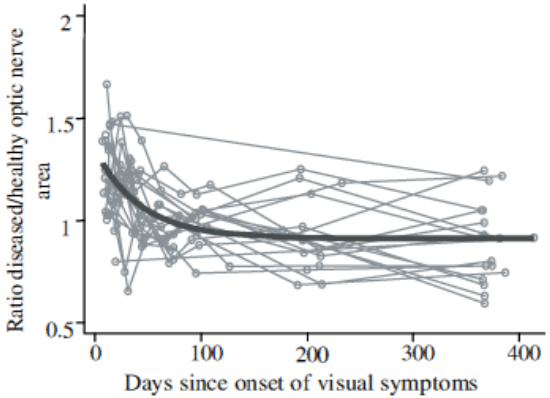
	Gd enhancement of optic nerve				
	n	Mean visual acuity pre treatment	Mean visual acuity post treatment	Mean visual improvement	Median time onset of ON to MRI
Total	77	0.45 ± 0.04 SEM	0.84 ± 0.03 SEM	0.40* ± 0.04 SEM	5 days
lesion localisation					
intraorbital	55	0.46	0.80	0.35*	5 days
canalicular	34	0.47	0.85	0.39	6 days
intracranial	18	0.39	0.81	0.40	6 days
Chiasmal	3	0.57	0.90	0.33	7 days

Berg et al., Plos One 2015

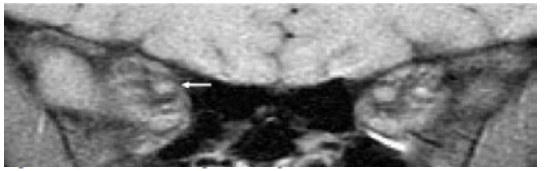
Understanding disease pathophysiology

Demyelinating optic neuritis / Atrophy





Hickman et al., Brain 2004



	Control eyes (n = 15)	Patient unaffected eyes (n = 25)	Patient affected eyes (n = 25)
Optic nerve area (mm^2)	12.7 (2.4)	11.8 (2.0) $P_c = 0.19$	9.0 (1.5) $P_c < 0.001$ $P_f < 0.001$
RNFL thickness (μm)	102.9 (14.6)	94.6 (14.9) $P_c = 0.12$	68.7 (18.8) $P_c < 0.001$ $P_f < 0.001$
Macular volume (mm^3)	6.83 (0.51)	6.71 (0.33) $P_c = 0.49$	6.10 (0.39) $P_c < 0.001$ $P_f < 0.001$

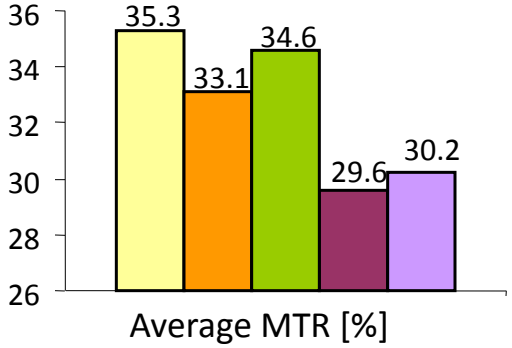
Interocular difference	Optic nerve area
RNFL thickness	$r = 0.66$ $P < 0.001$
Macular volume	$r = 0.59$ $P = 0.002$
Visual acuity (logMAR)	$r = -0.50$ $P = 0.01$
Visual field (mean deviation)	$r = 0.40$ $P = 0.05$
Colour vision (√FM Hue-100 score)	$r = -0.34$ $P = 0.11$

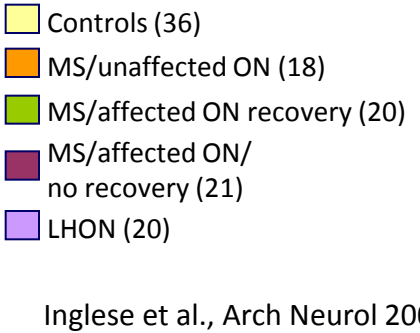
Trip et al., NeuroImage 2006

Understanding disease pathophysiology

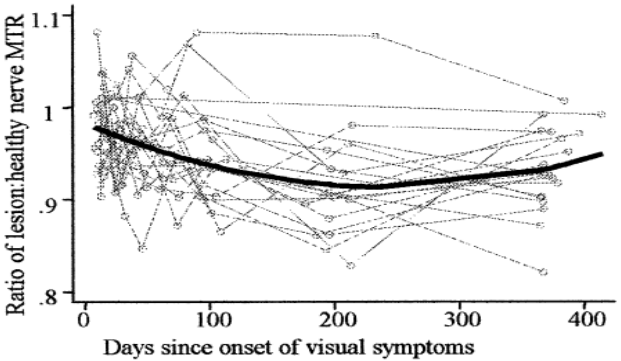
Demyelinating optic neuritis / Microstructural damage

MTR



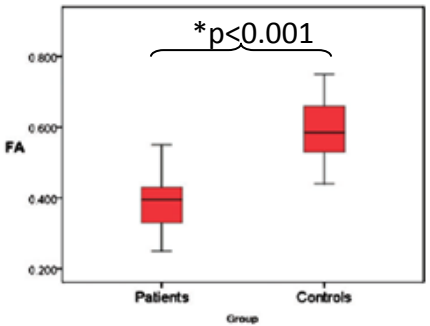


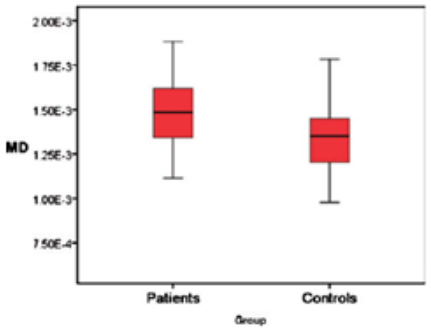
Inglese et al., Arch Neurol 2002

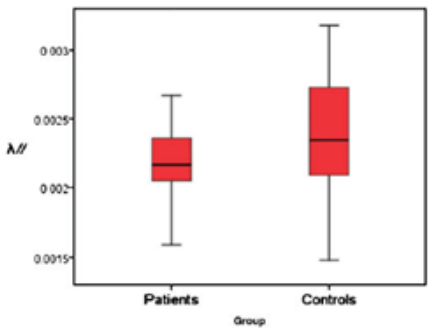


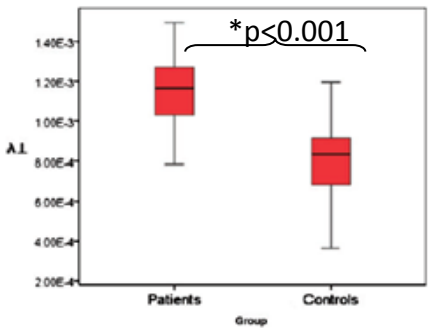
Hickman et al., Brain 2004

DTI









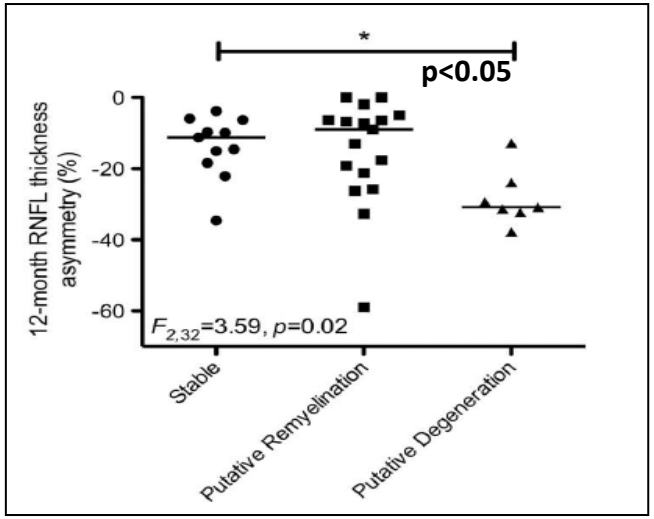
Li et al., Br J Radiol 2011

* first-onset acute ON

Understanding disease pathophysiology

Demyelinating optic neuritis / Prognosis

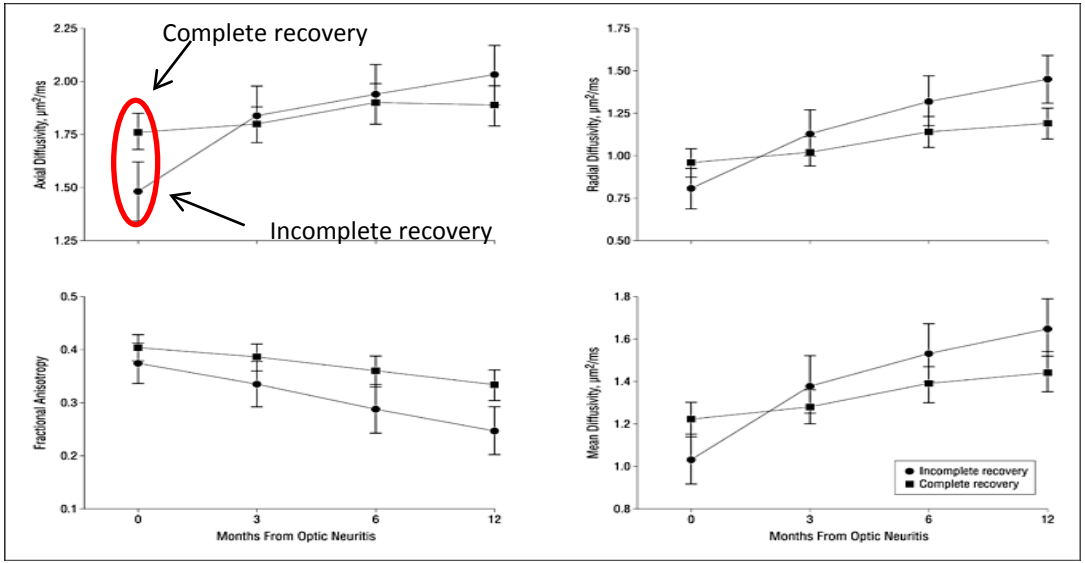
MTR



Association between MTR reduction and worse visual acuity

Wang et al., Plos One 2012

DTI



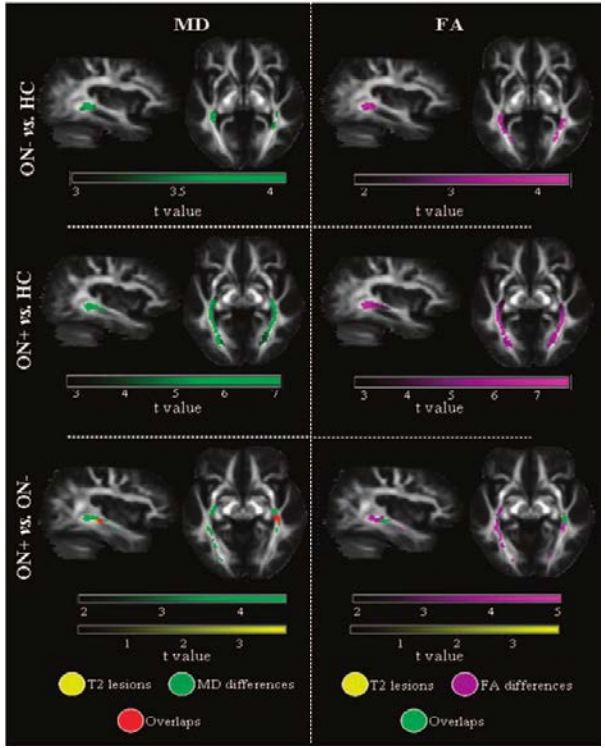
Naismith et al., Arch Neurol 2011

Low baseline AD associated 6 month:

- Worse acuity (r=0.4,p=0.03)
- Worse CS (r=0.5,p=0.03)
- Thinner RNFL (r=0.57,p=0.02)
- Lower VEP amp (r=0.55,p=0.01)
- Longer VEP lat (r=-0.4,p=0.04)

Understanding disease pathophysiology

Demyelinating optic neuritis / Optic radiations and visual cortex

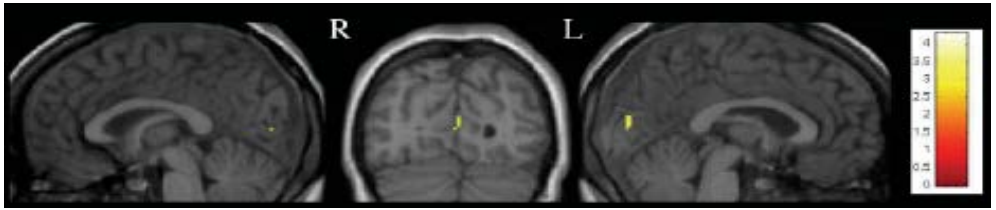


Rocca et al., MSJ 2013

Optic nerve measure[a]	Dependent variables: FA Standardized regression coefficients (95% CI) from multivariate analyses	Dependent variables: RD (mm^2/s) Standardized regression coefficients (95% CI) from multivariate analyses	Joint test *P*-value
Affected optic nerve area at baseline	−0.081 (−0.336, 0.174)	−0.147 (−0.513, 0.219)	0.2569
Affected optic nerve area at 3 months	0.535 (0.207, 0.863)	−0.401 (−0.762, −0.039)	0.0069[b]
Affected optic nerve area at 6 months	0.256 (−0.268, 0.779)	−0.347 (−1.243, 0.549)	0.5996
Lesion length of affected optic nerve at baseline	0.218 (−0.077, 0.513)	−0.469 (−0.874, −0.063)	0.1058
Lesion length of affected optic nerve at 3 months	−0.074 (−0.327, 0.179)	0.048 (−0.288, 0.384)	0.7985
Lesion length of affected optic nerve at 6 months	0.117 (−0.128, 0.361)	−0.096 (−0.502, 0.310)	0.5610
Gd-enhanced lesion length of affected optic nerve at baseline	0.161 (−0.126, 0.449)	−0.276 (−0.663, 0.112)	0.3860

Tur et al., Brain 2016

GM MTR

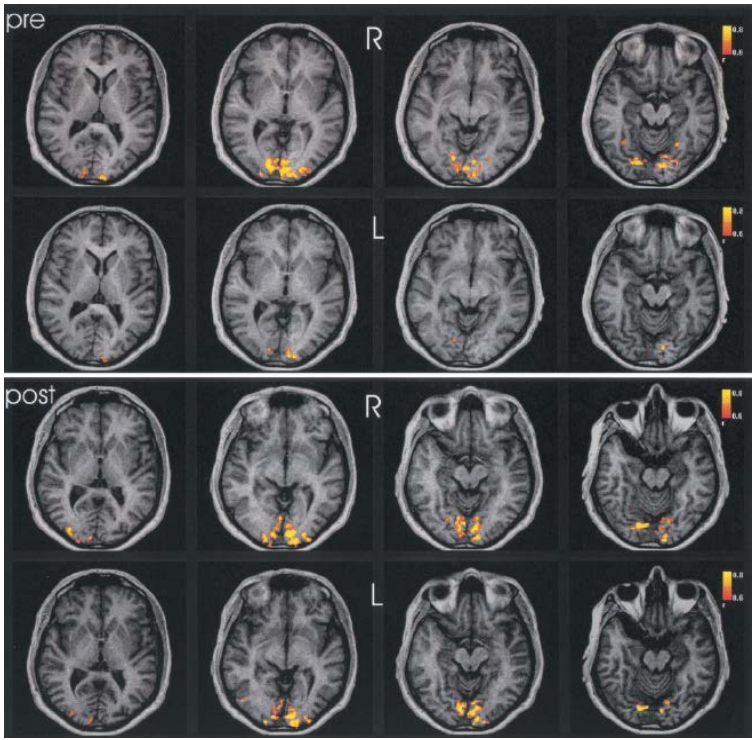


GM MTR in the visual cortex was correlated with the visual acuity at baseline (r = 0.31, p=0.011) and after 3 months (r = 0.30, p=0.011)

Audoin et al., Brain 2006

Understanding disease pathophysiology

Demyelinating optic neuritis / Cortical reorganization (fMRI)



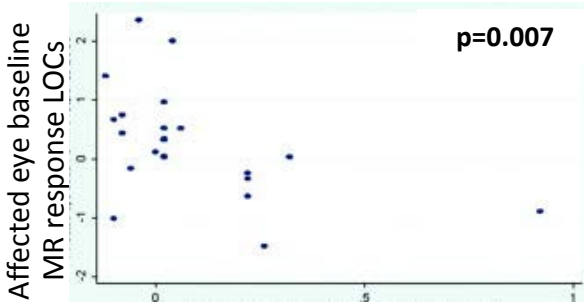
Unaffected eye

Affected eye

Unaffected eye

Affected eye

Russ et al., J Neuroimaging 2002

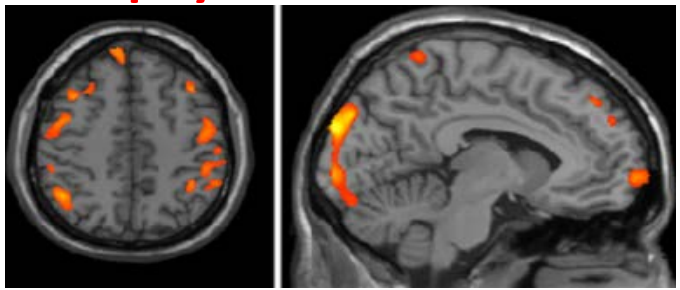


Jenkins et al., Ann Neurol 2010

Understanding disease pathophysiology

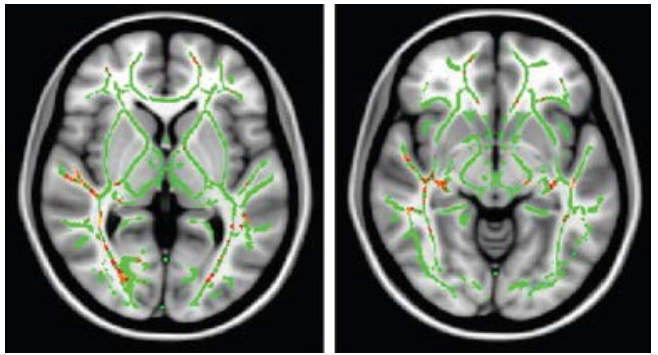
NMO

Atrophy



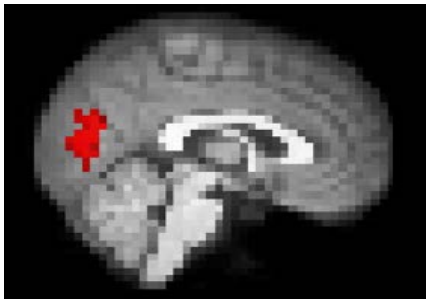
Pichiecchio et al., MSJ 2011

DTI



Pichiecchio et al., MSJ 2011

fMRI



Rueda Lopes et al.,
J Neuroimaging 2015

Visual cortex RS FC *vs* FA of the right ON:
r−0.36 ,p = 0.08

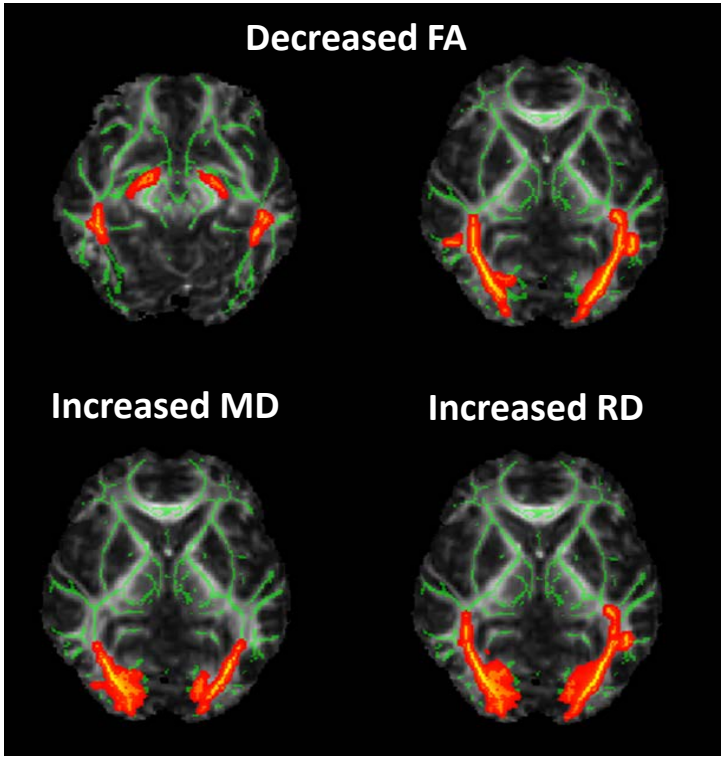
Diffusion Index	OR Visual KFS Score *r* Value	*P* Value
Mean diffusivity ($\times 10^{-4}$ mm^2/sec)	0.523	.022*
FA	0.106	.666
λ_1 ($\times 10^{-4}$ mm^2/sec)	0.504	.027*
λ_{23} ($\times 10^{-4}$ mm^2/sec)	0.285	.236

Yu et al., Radiology 2008

Understanding disease pathophysiology

LHON

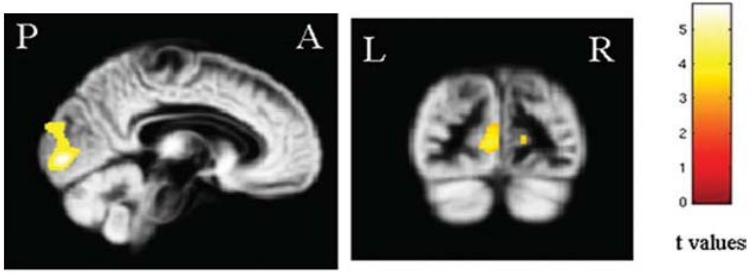
DTI



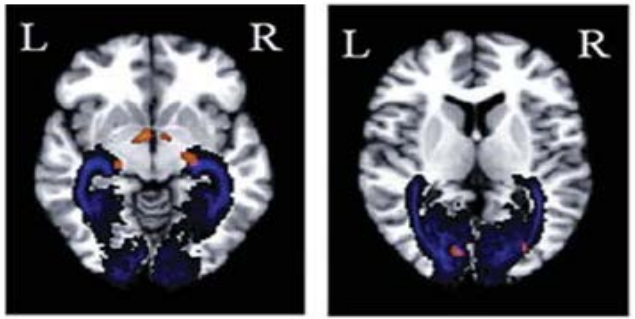
Milesi et al., J Neurol 2012

Atrophy

GM



WM

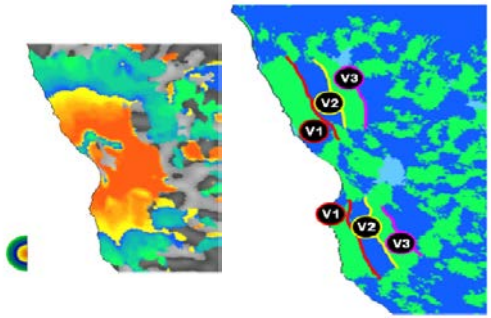


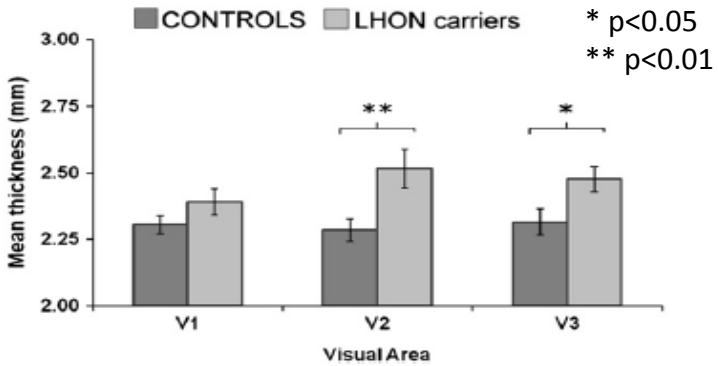
Barcella et al., HBM 2010

Understanding disease pathophysiology

LHON / Cortical reorganization

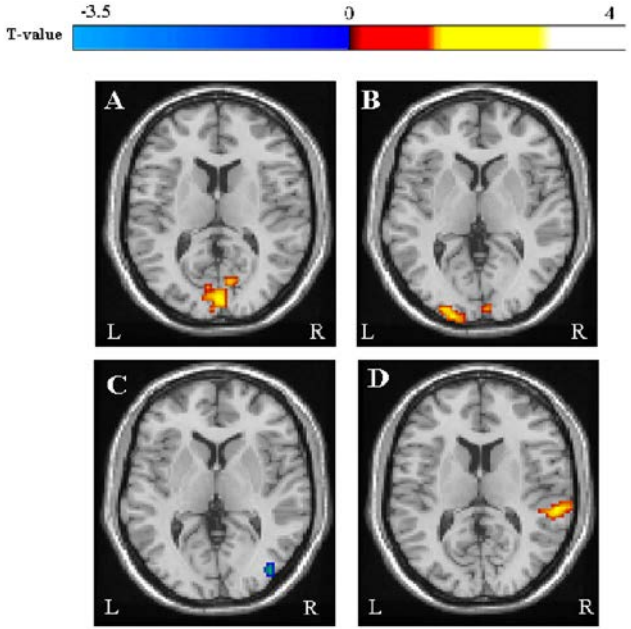
Cortical thickness in LHON carriers





D'Almedia et al., NeuroImage 2013

RS fMRI

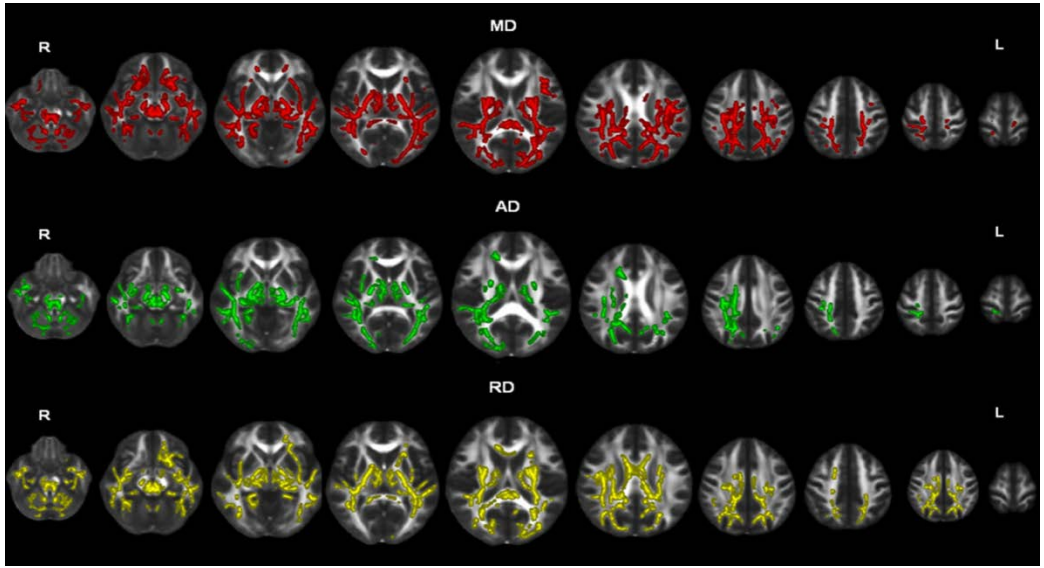


Rocca et al., Plos One 2011

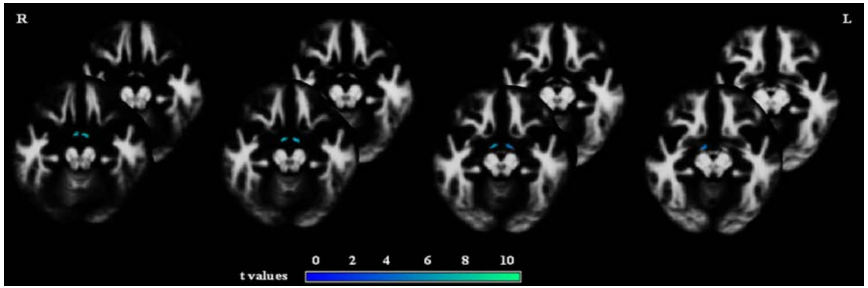
Understanding disease pathophysiology

Dominant optic atrophy and OPA1 mutations

DTI



Atrophy

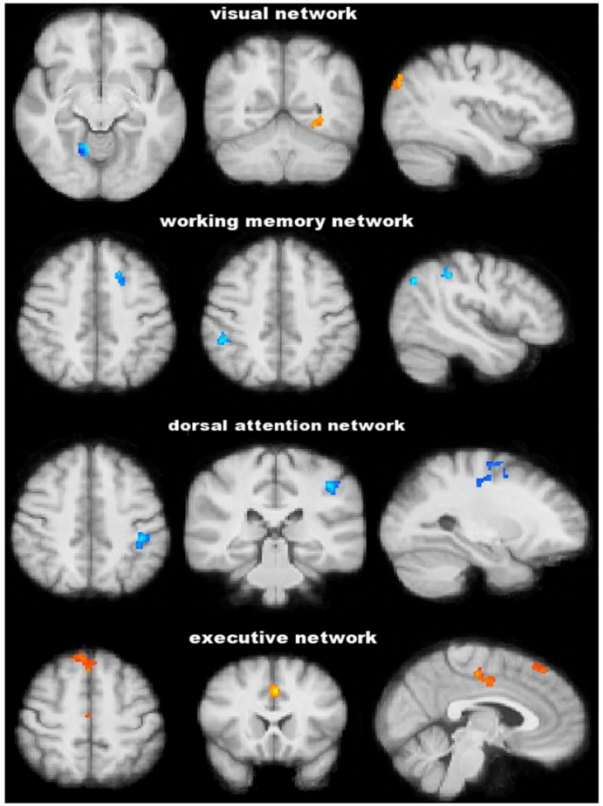


Rocca et al., J Neurol 2015

Understanding disease pathophysiology

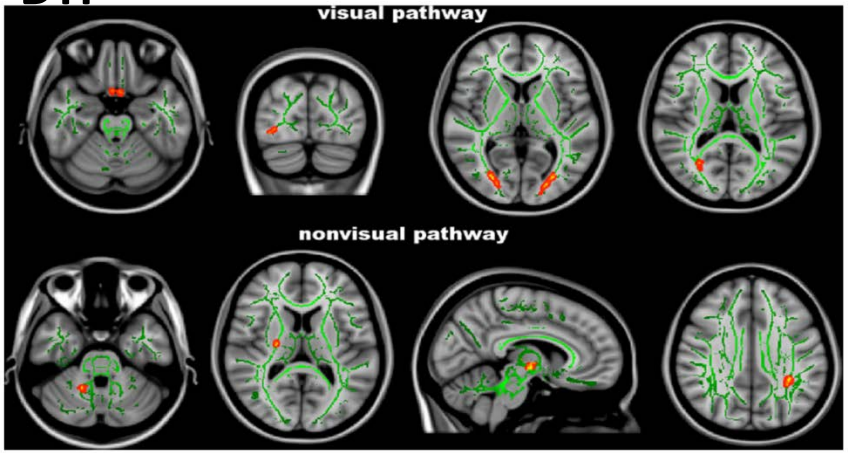
Glaucoma

RS fMRI

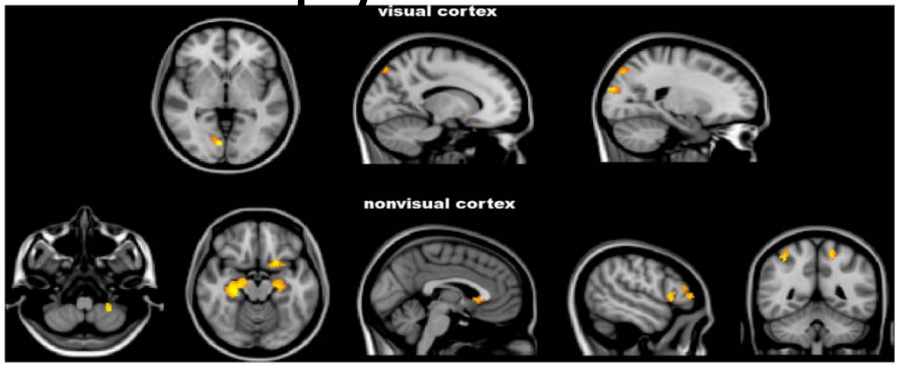


Frezzotti, Giorgio et al., Plos One 2014

DTI



Cortical atrophy



Frezzotti, Giorgio et al., Plos One 2014

Outline of the presentation

- Imaging the optic nerve
- Diagnosis and differential diagnosis
- Understanding disease pathophysiology
- **Conclusions**

Conclusions

- **Although MRI of optic nerve is technically challenging, it is feasible to obtain high quality images of this structure in clinically acceptable scan times**
- **MRI provides useful pieces of information in the diagnostic work up of patients with acute visual loss**
- **The contribution of different MR modalities is offering new insights into the pathophysiology of acute optic neuropathies**
- **It is likely that in the near future novel MR metrics to assess treatment response in clinical trials of acute optic neuropathies will be proposed, validated and used, and possibly enter in daily-life clinical practice**