Improving the differential diagnosis of multiple sclerosis using MRI

Neuromyelitis spectrum disorders Imaging

Jackie Palace

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Definitions of NMO/SD

NMOSD

NMO ~ 60% AQP4-Abs

ON + TM
and
2 of 3:
- **LETM**
- **NMO abs**
- **Non MS brain MRI**

2006
Wingerchuk

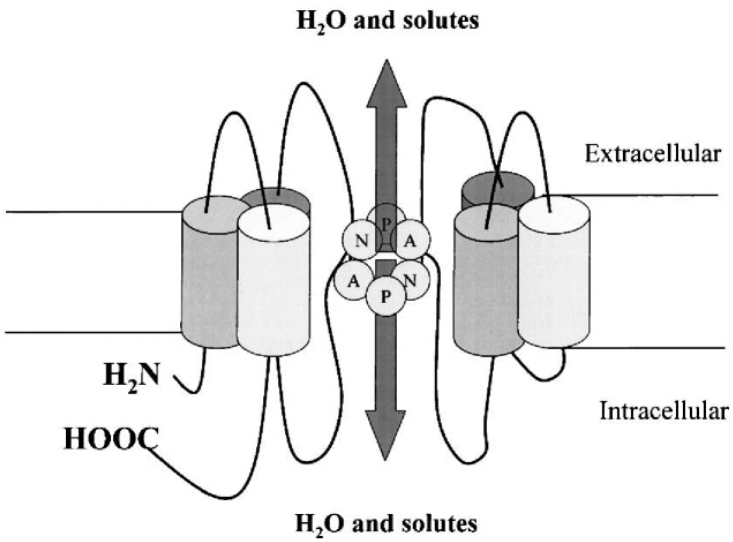
LETM ~ 60% AQP4-Abs

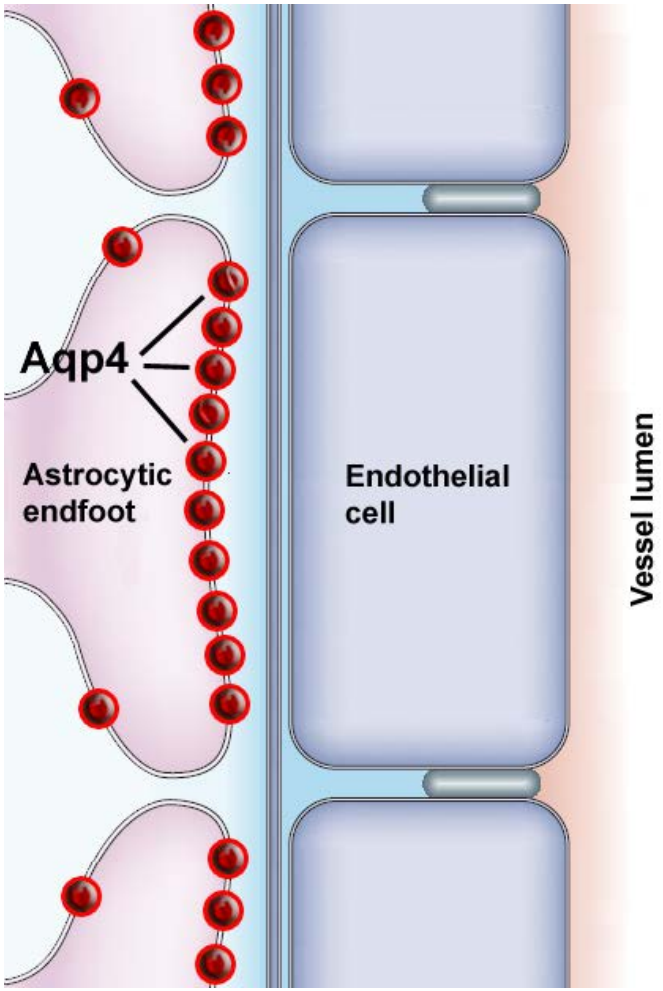
ON: ~ 50% AQP4-Abs
recurrent
simultaneous bilateral
w auto-immune disease
w NMO typical brain lesions
poor visual outcome

Inflammatory brain lesions with NMO abs
eg area postrema (~1/3**)**
100% AQP4-Abs

2007
Wingerchuk

Aquaporin-4



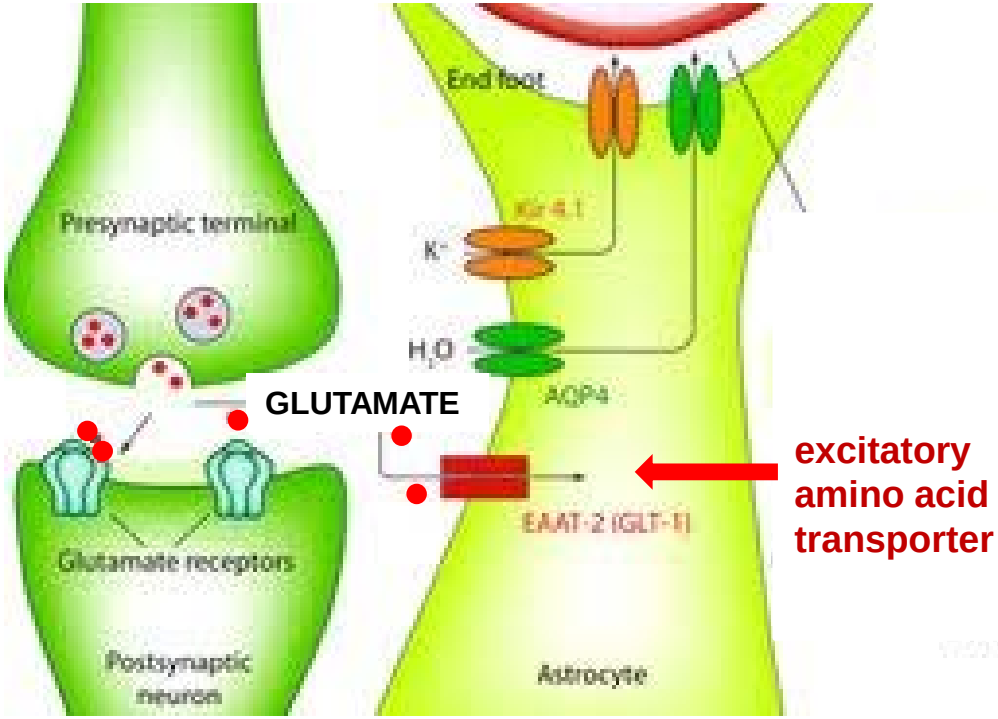


most abundant water channel in CNS
concentrated in astrocytic foot processes

Lennon et al Lancet 2004; J Ex Med 2005

Antibodies to AQP4 → astrocytopathy

reduced glutamate uptake → secondary myelin damage

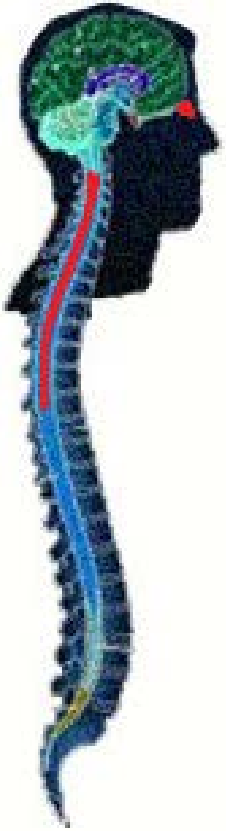


excitatory amino acid transporter

AQP4-Ab disease

- Female > 80%
- Non-Caucasian predominance
- Relapsing if untreated
- Severe disability and high mortality
- Associated with other auto-immunity
- Onset with both ON + TM uncommon

Definitions of NMO/SD 2015



NMOSD

AQP4-Ab positive disease

AQP4-Ab negative

MS

~25%

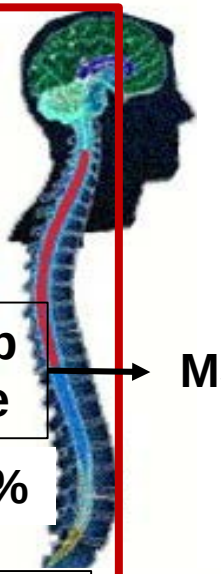
Ab negative diseases

MOG-Ab

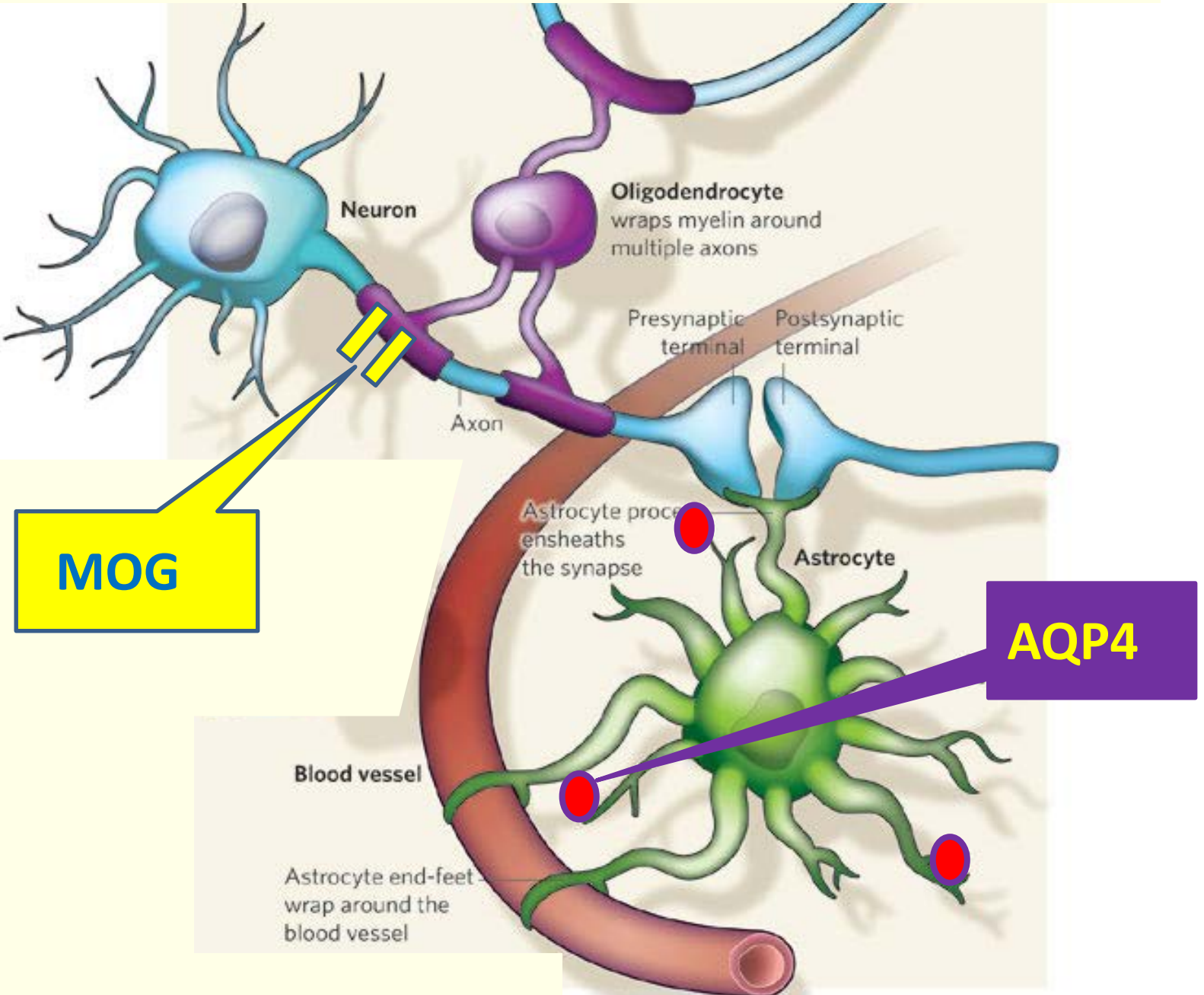
Attack(s) involves ≥ 2 sites:
≥ 1 from ON, SC, *area postrema,*

includes monophasic & relapsing conditions

1 site
ON or LETM
relapsing or monophasic



Wingerchuk *et al* 2015 Neurology 85:1


Neuron
Oligodendrocyte
wraps myelin around
multiple axons
Presynaptic
terminal
Postsynaptic
terminal
Axon
MOG
Astrocyte proce
ensheaths
the synapse
Astrocyte
AQP4
Blood vessel
Astrocyte end-feet
wrap around the
blood vessel

MOG

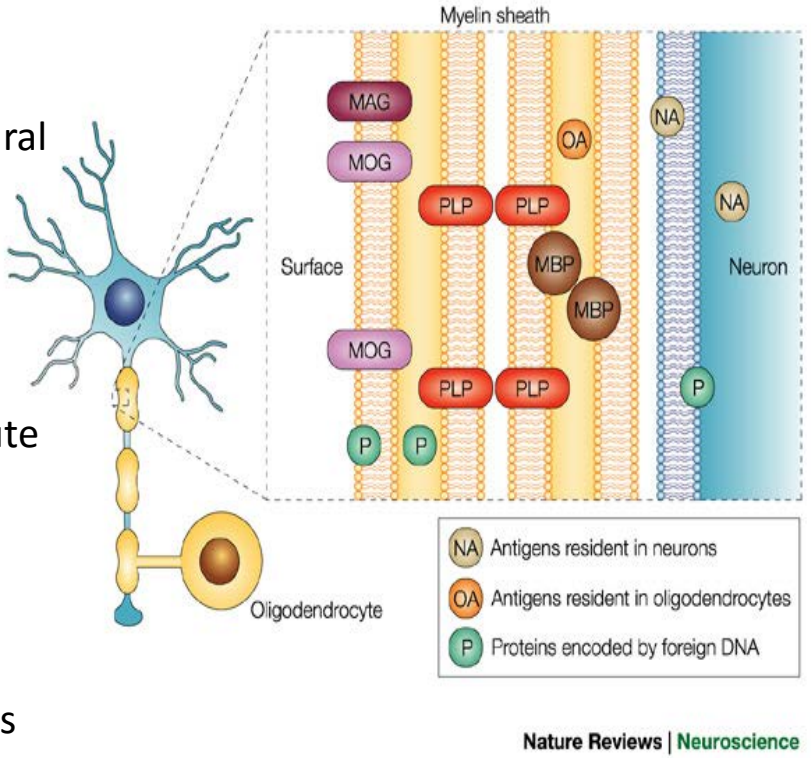
- glycoprotein: myelin sheath surface important for structural integrity
- exclusively expressed in CNS
- accessible

- MOG used in EAE: MOG-Abs shown to induce or contribute to demyelination

- early studies used assay detecting antibodies against denatured MOG (linear epitopes)

  reported MOG antibodies in MS and other controls
- current cell-based assays can detect binding to conformational MOG epitopes

- predict MOG-Ab disease to be 1ry demyelinating disease

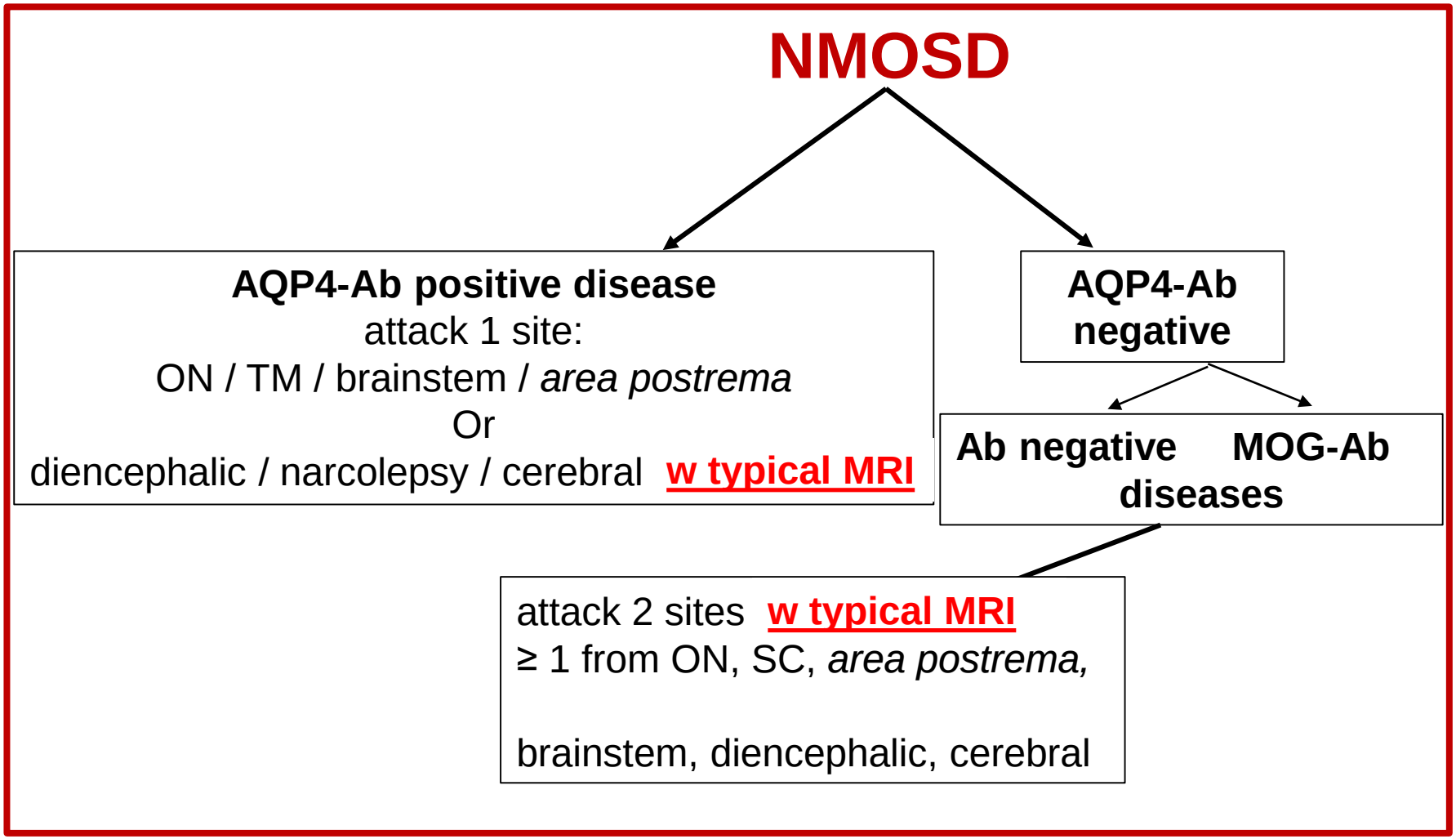


Hemmer B. et al. Nature Reviews Neuroscience 2002; 3:291-301

MOG-Ab disease

- Female : Male equal
- No non-caucasian predominance
- ~ 50% monophasic
- Better outcome than AQP4-Ab disease
- Not associated with other auto-immunity
- Onset with both ON + TM common
- Overlap with ADEM (monophasic & relapsing)

Definitions of NMO/SD 2015



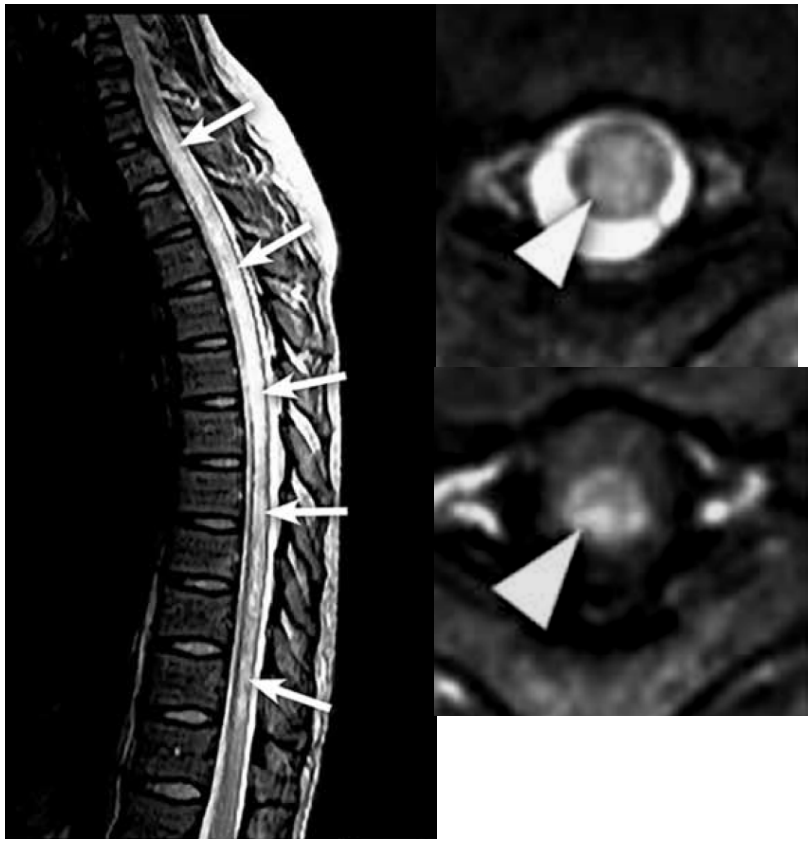
Wingerchuk *et al* 2015 Neurology 85:1

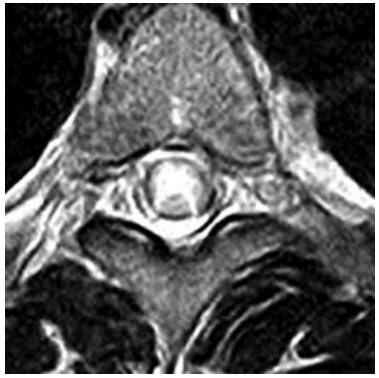
TRANSVERSE MYELITIS

LETM ≥ 3 vertebral segments

Wingerchuk *et al* 2015 Neurology 85:1

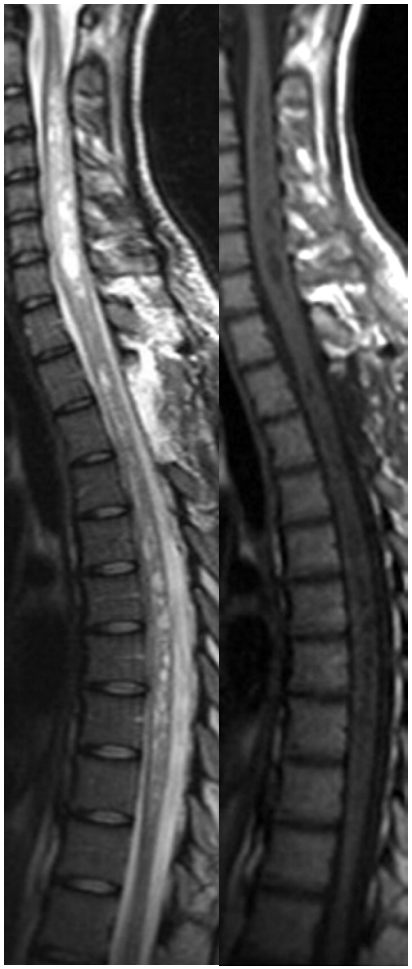
Spinal Cord: central, extend medulla





Wingerchuk *et al* 2015 Neurology 85:1

Spinal cord:
T1 hypointensity acute lesions



Wingerchuk *et al* 2015 Neurology 85:1
Muchison *et al* J Neurol Sci, 355, 49

Original Investigation

Short Myelitis Lesions in Aquaporin-4-IgG–Positive Neuromyelitis Optica Spectrum Disorders

Eoin P. Flanagan, MBBCh; Brian G. Weinshenker, MD; Karl N. Krecke, MD; Vanda A. Lennon, MD, PhD; Claudia F. Lucchinetti, MD; Andrew McKeon, MBBCh; Dean M. Wingerchuk, MD; Elizabeth A. Shuster, MD; Yujuan Jiao, MD; Erika S. Horta, MD; Sean J. Pittock, MD

JAMA Neurol.2015;72(1):

RESULTS Twenty-five patients who were AQP4-IgG seropositive with an initial STM represented 14% of initial myelitis episodes among patients with NMOSD. The STM episode was defined as the first manifestation of NMOSD in 10 patients (40%) preceded by optic

OPTIC NEURITIS

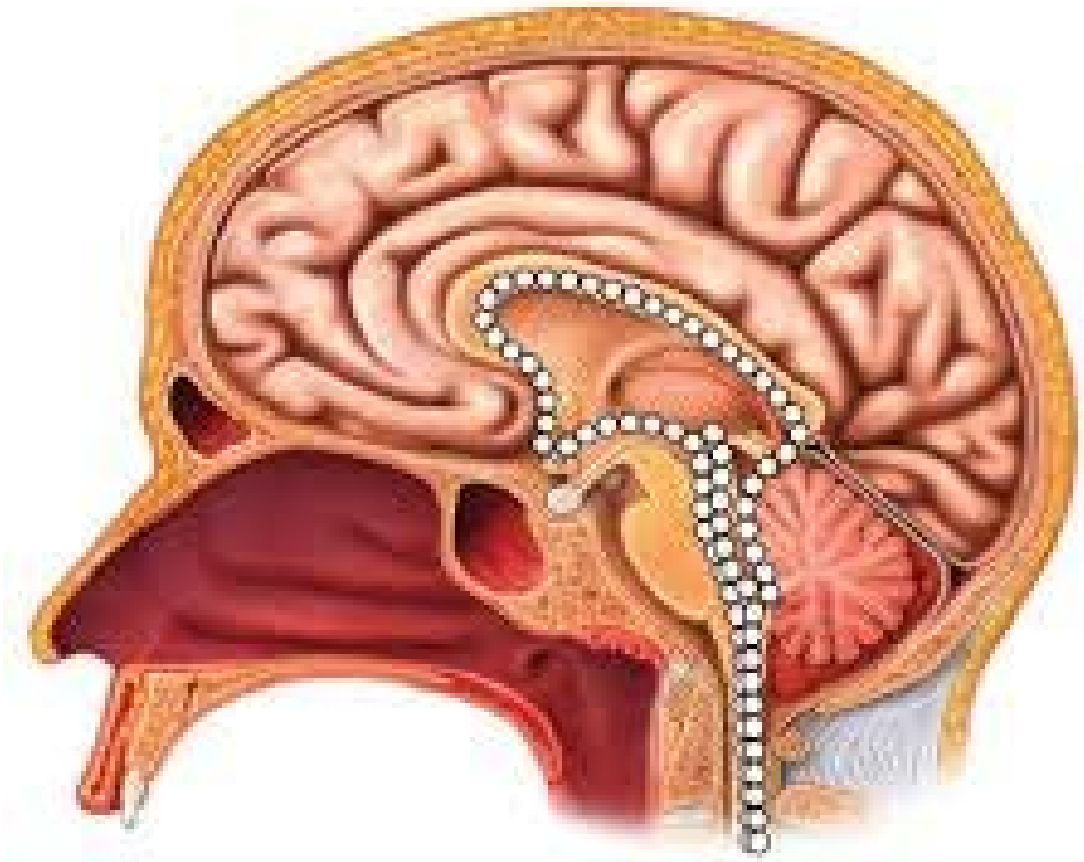
> ½ ON length or chiasmatic involvement

OR

BRAIN MRI: normal or non-specific WMLs

Wingerchuk *et al* 2015 Neurology 85:1

Periependymal expression AQP4



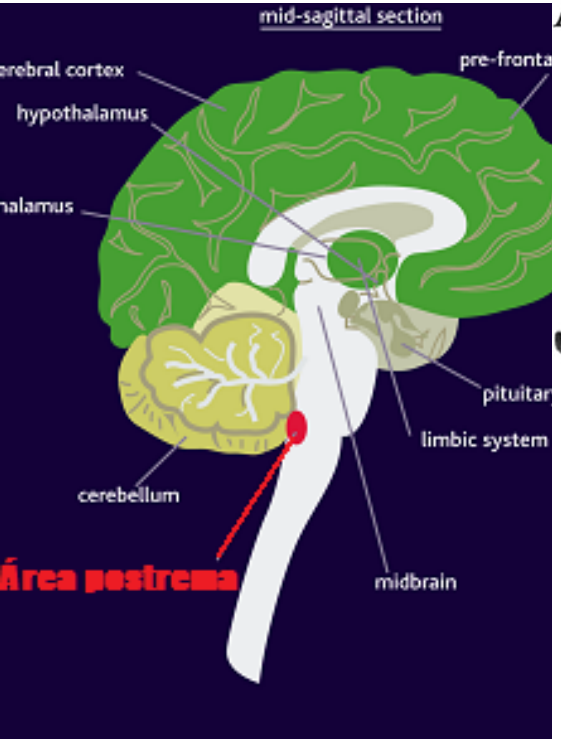
The spectrum of neuromyelitis optica

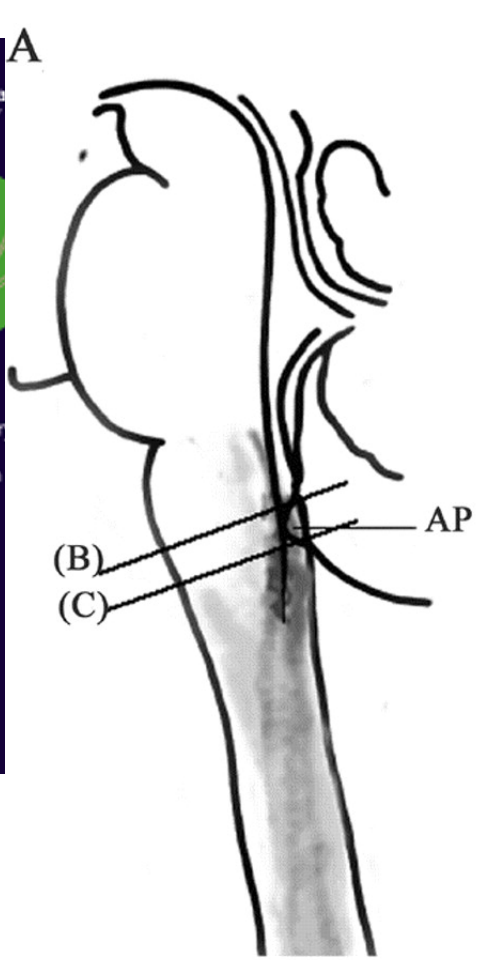
Dean M Wingerchuk, Vanda A Lennon, Claudia F Lucchinetti, Sean J Pittock, Brian G Weinshenker

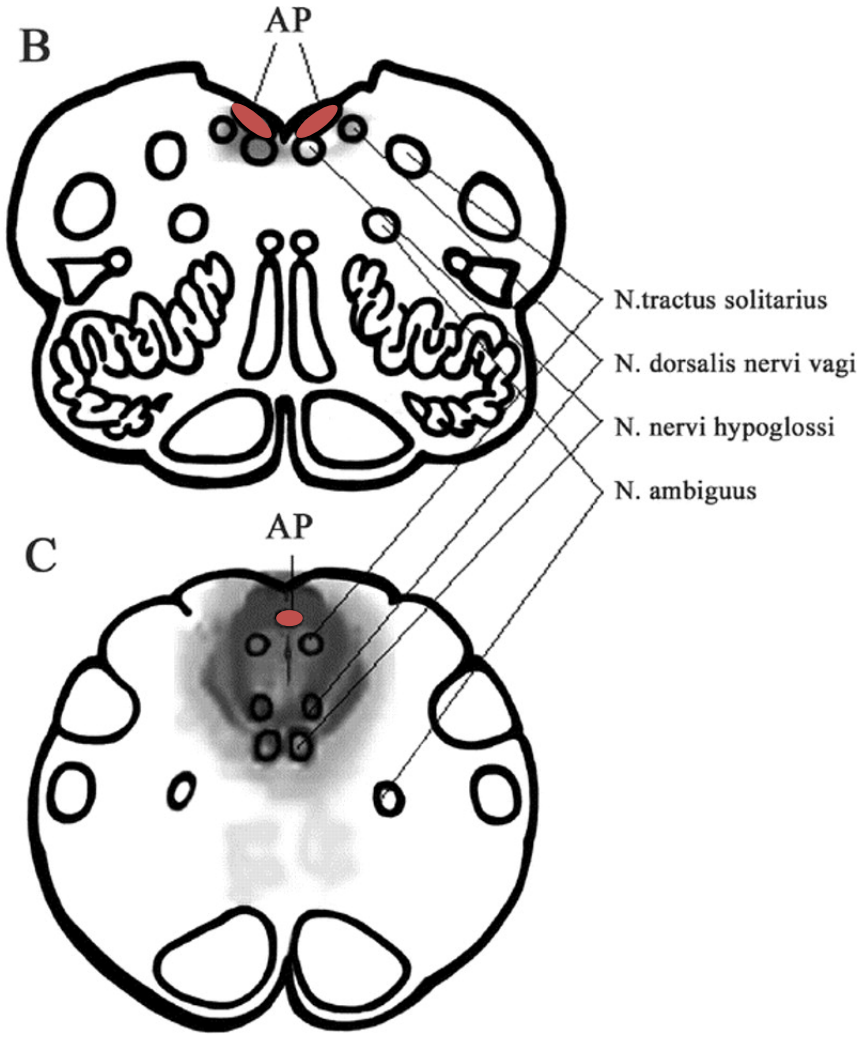
Lancet Neurol 2007; 6: 805–15

Area Postrema

A small, rounded eminence on each side of the 4th ventricle, in medulla.
Lies outside the BBB



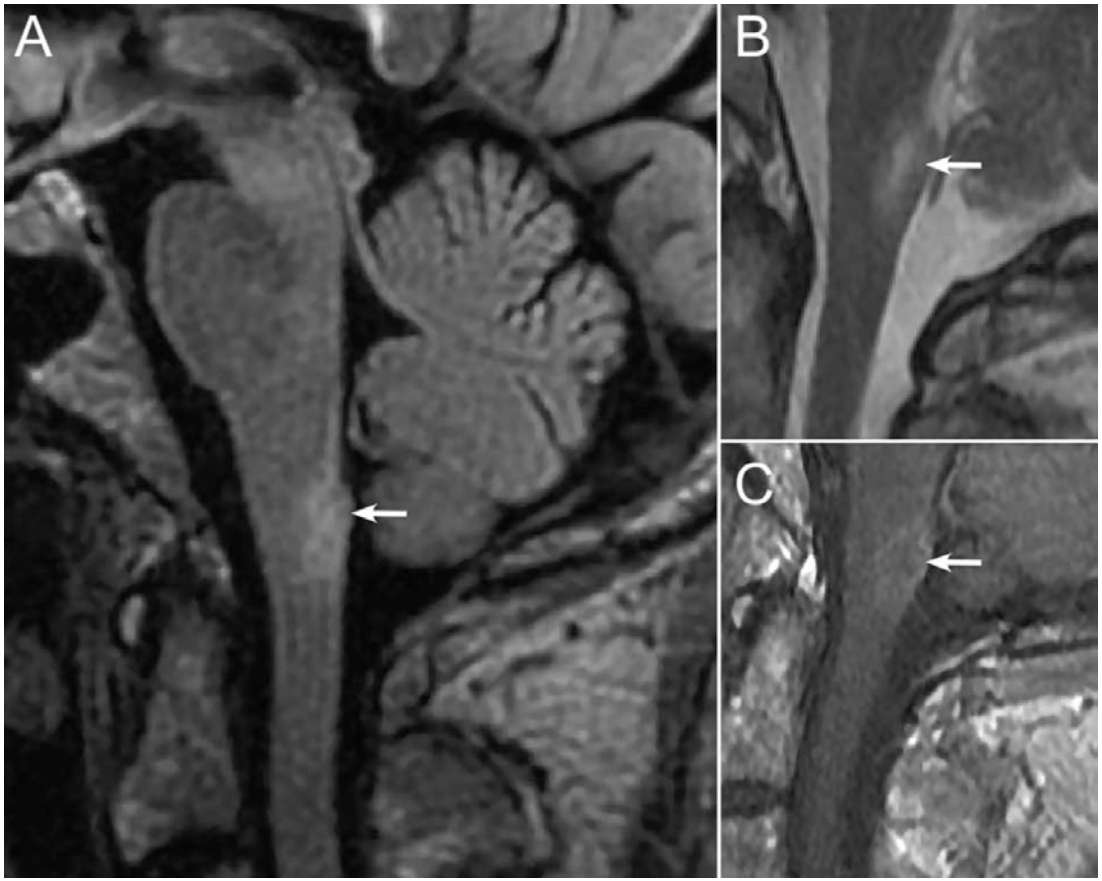


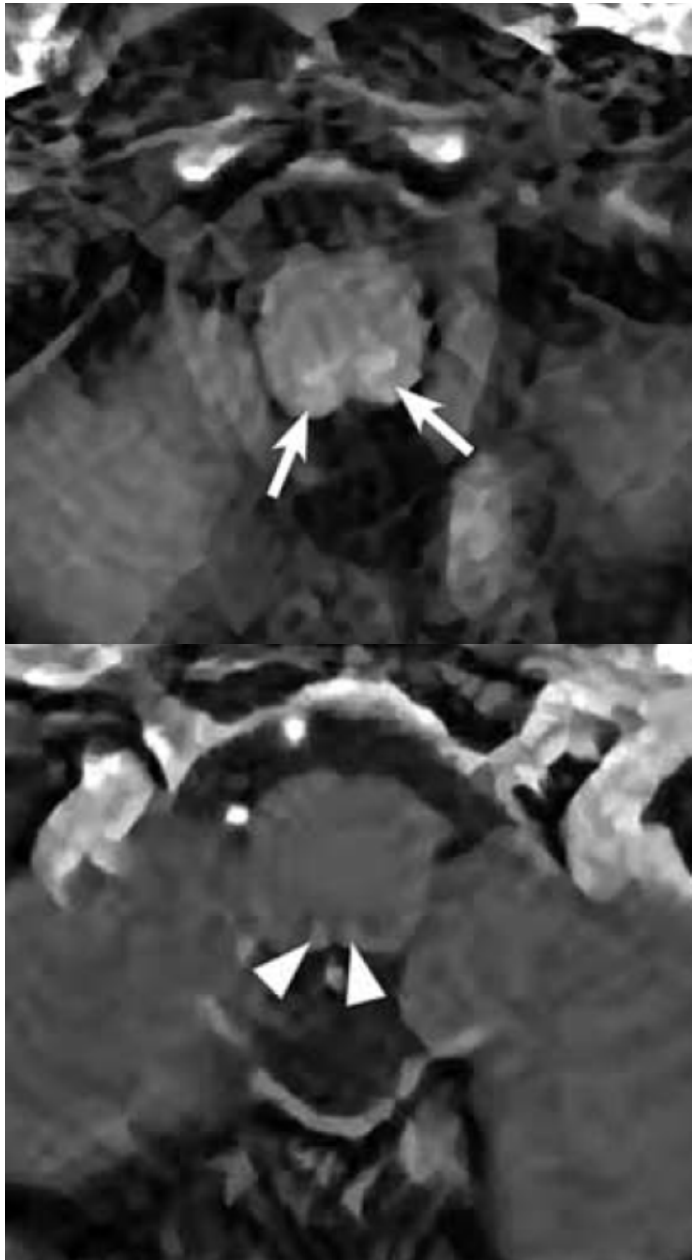


T. Misu et al. Neurology 2005;65:1479-1482

AREA POSTREMA ATTACK

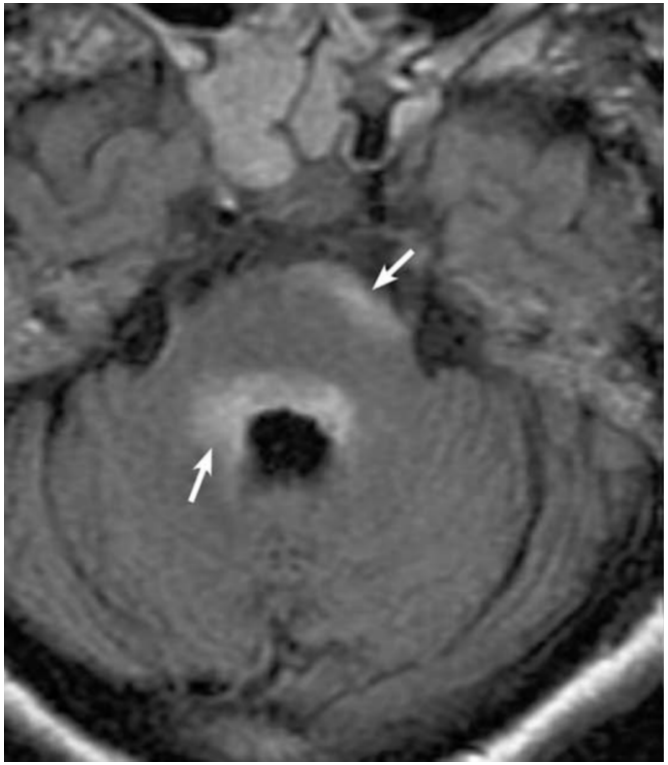
Area postrema / dorsal medulla

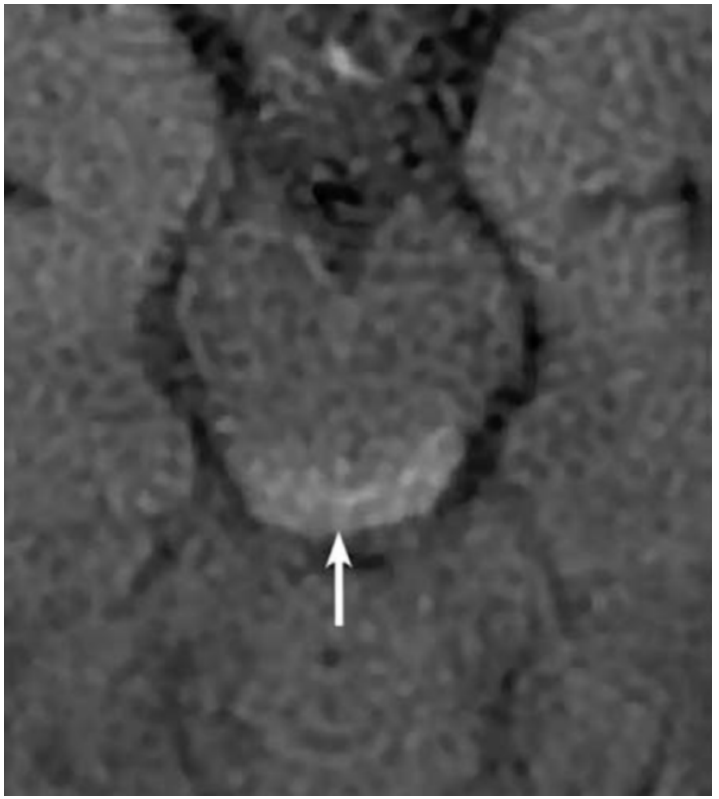




BRAINSTEM ATTACK

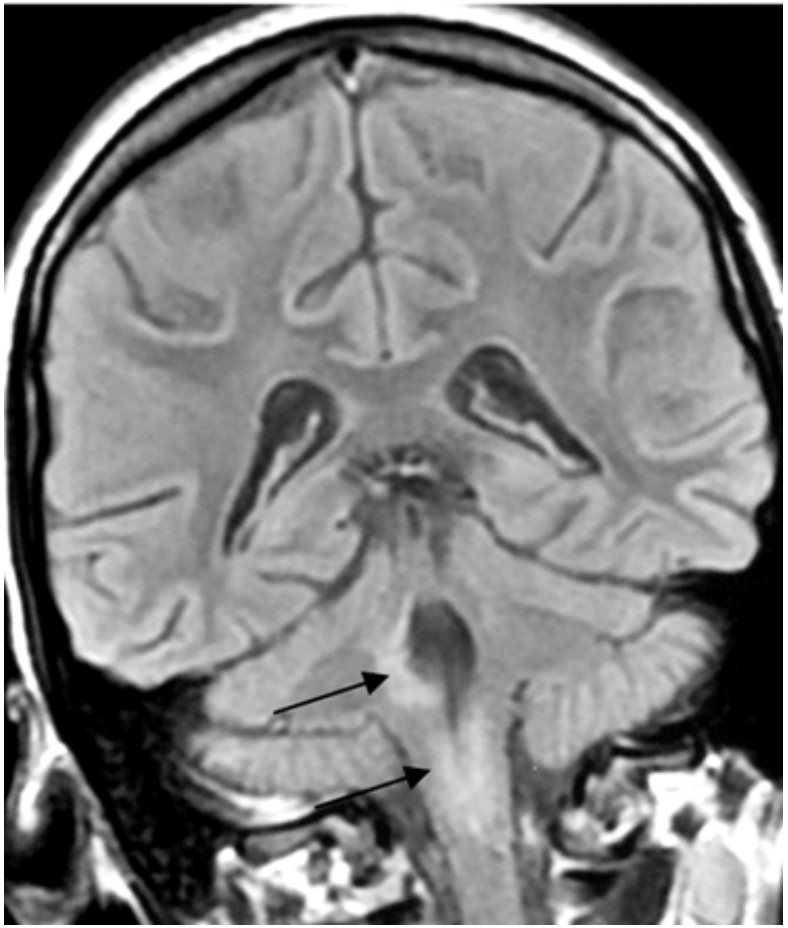
Periependymal lesions





Wingerchuk *et al* 2015 Neurology 85:1

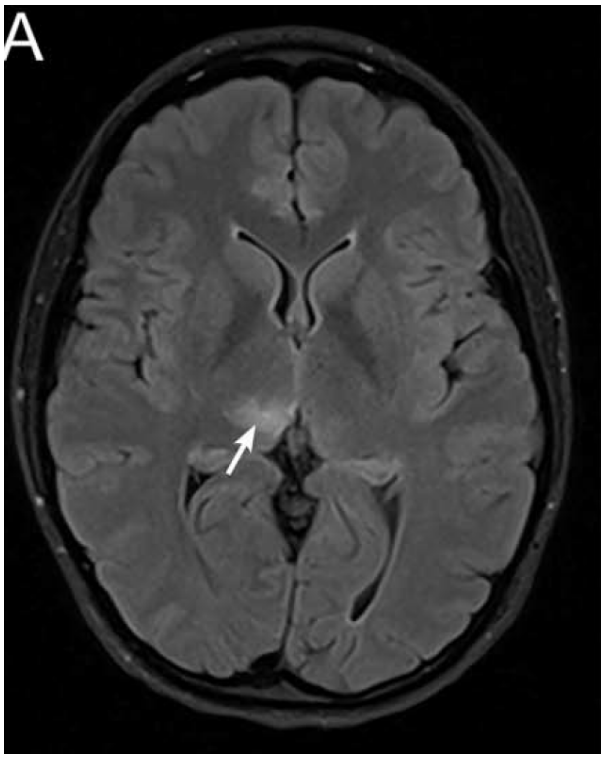
4th ventricle

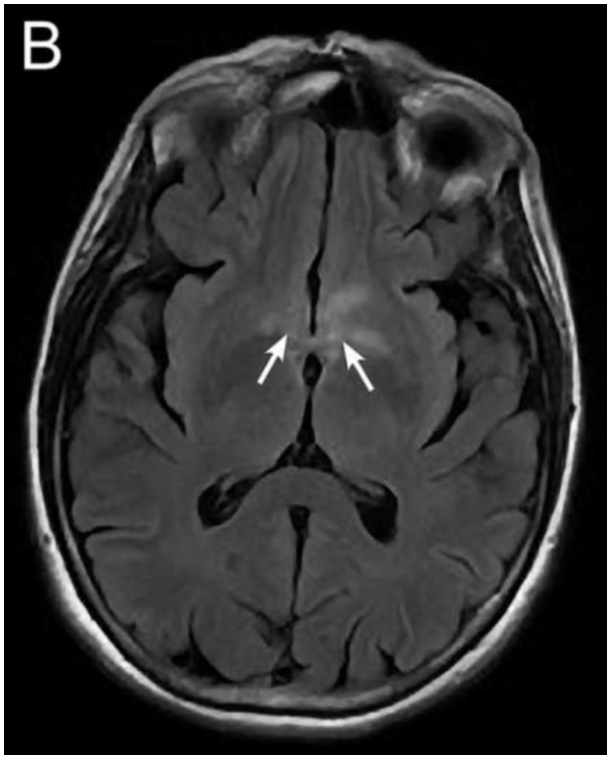


Viegas *et al,* 2009 JNNP 80:679
Wingerchuk *et al* 2015 Neurology 85:1

NARCOLEPSY OR DIENCEPHALIC ATTACK

NMOSD typical Diencephalic lesions





thalamus

hypothalamus

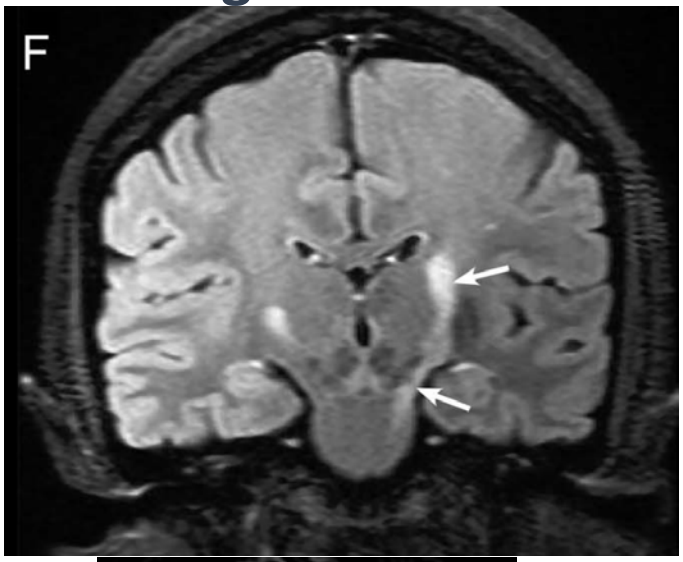
Viegas *et al,* 2009 JNNP 80:679

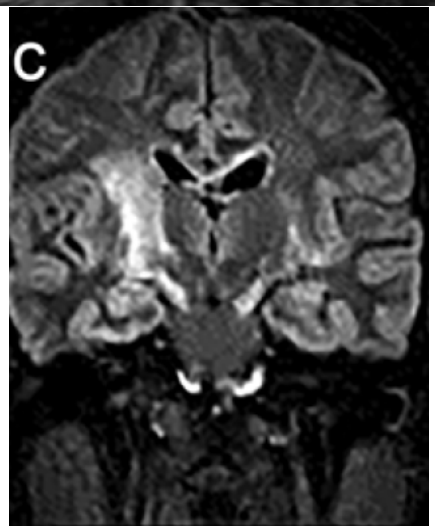
Wingerchuk *et al* 2015 Neurology 85:1

CEREBRAL ATTACK

NMOSD typical brain lesions

Long CS tract lesion

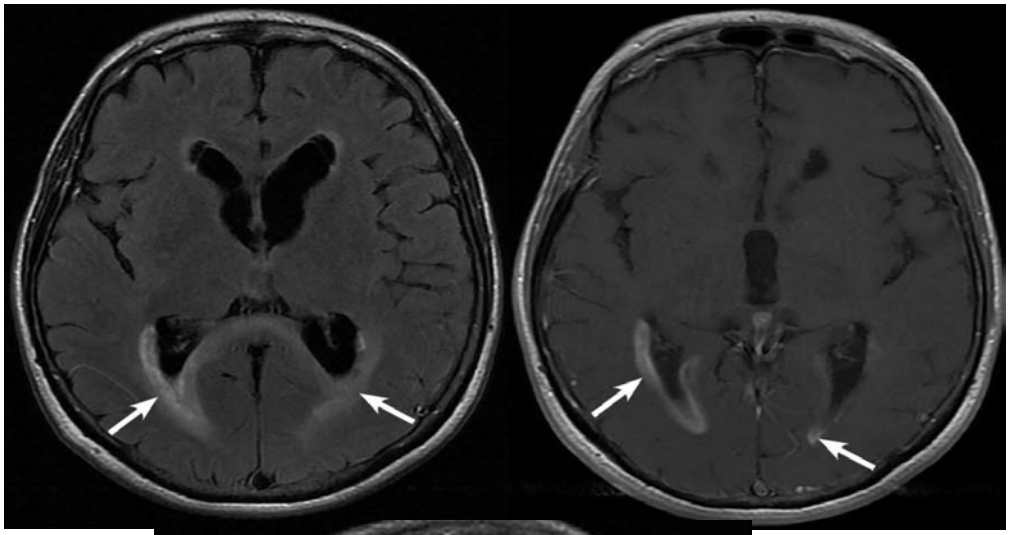


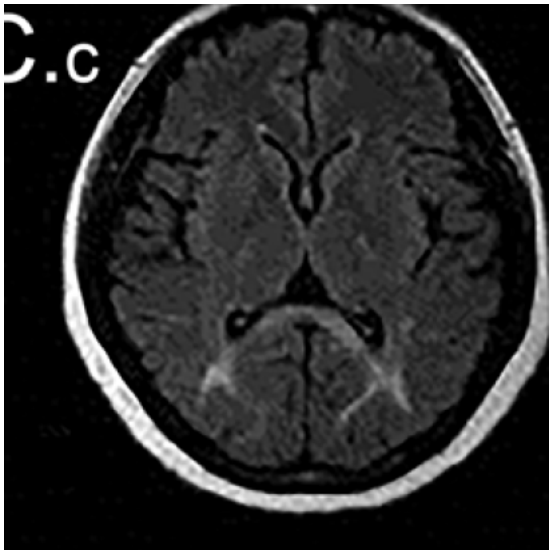


Wingerchuk *et al* 2015 Neurology 85:1

CEREBRAL ATTACK

Peri ependymal / ventricular lesions/CC

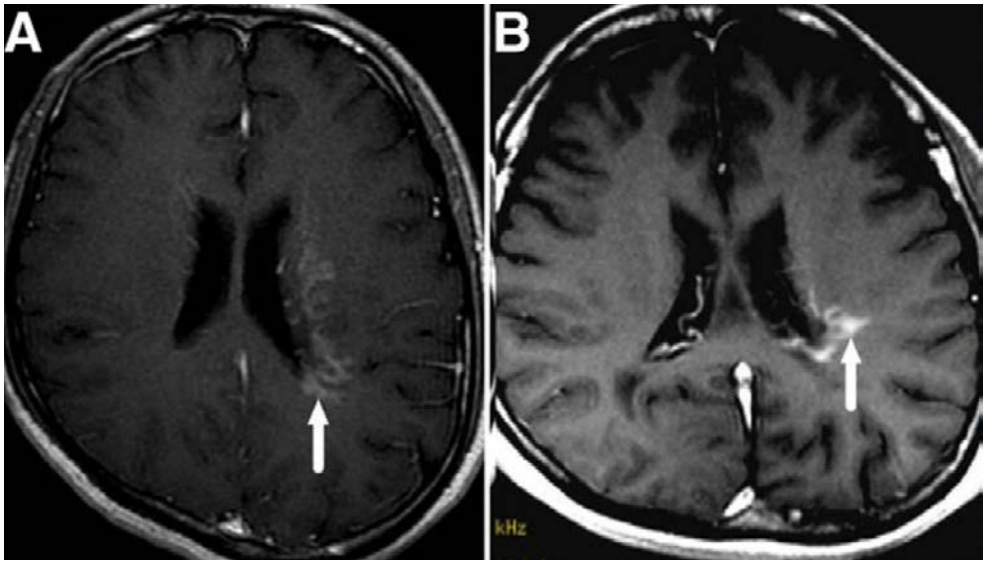


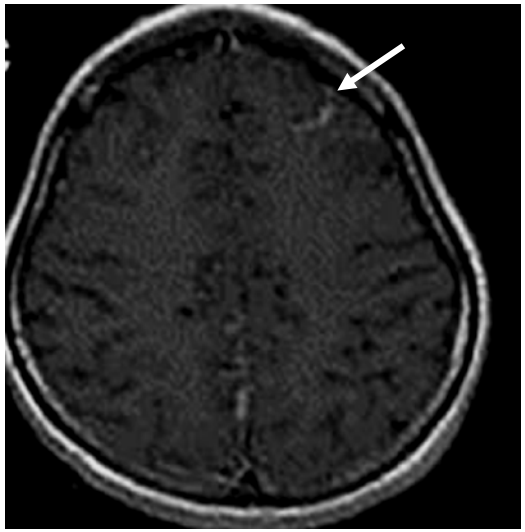


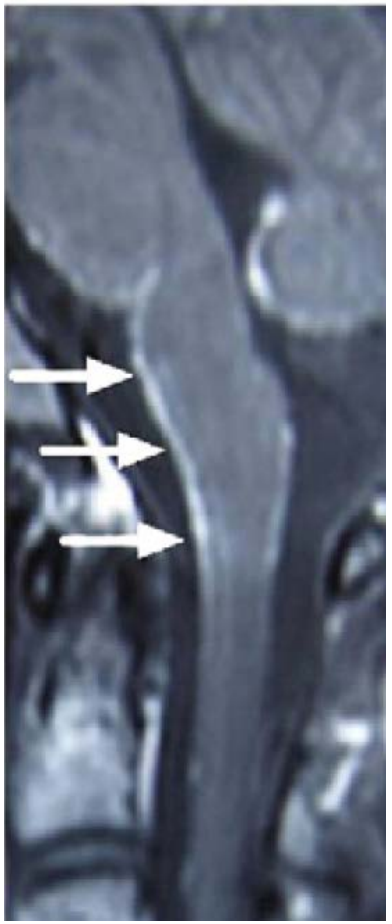
Wingerchuk *et al* 2015 Neurology 85:1

CEREBRAL ATTACK

Patterns of enhancement





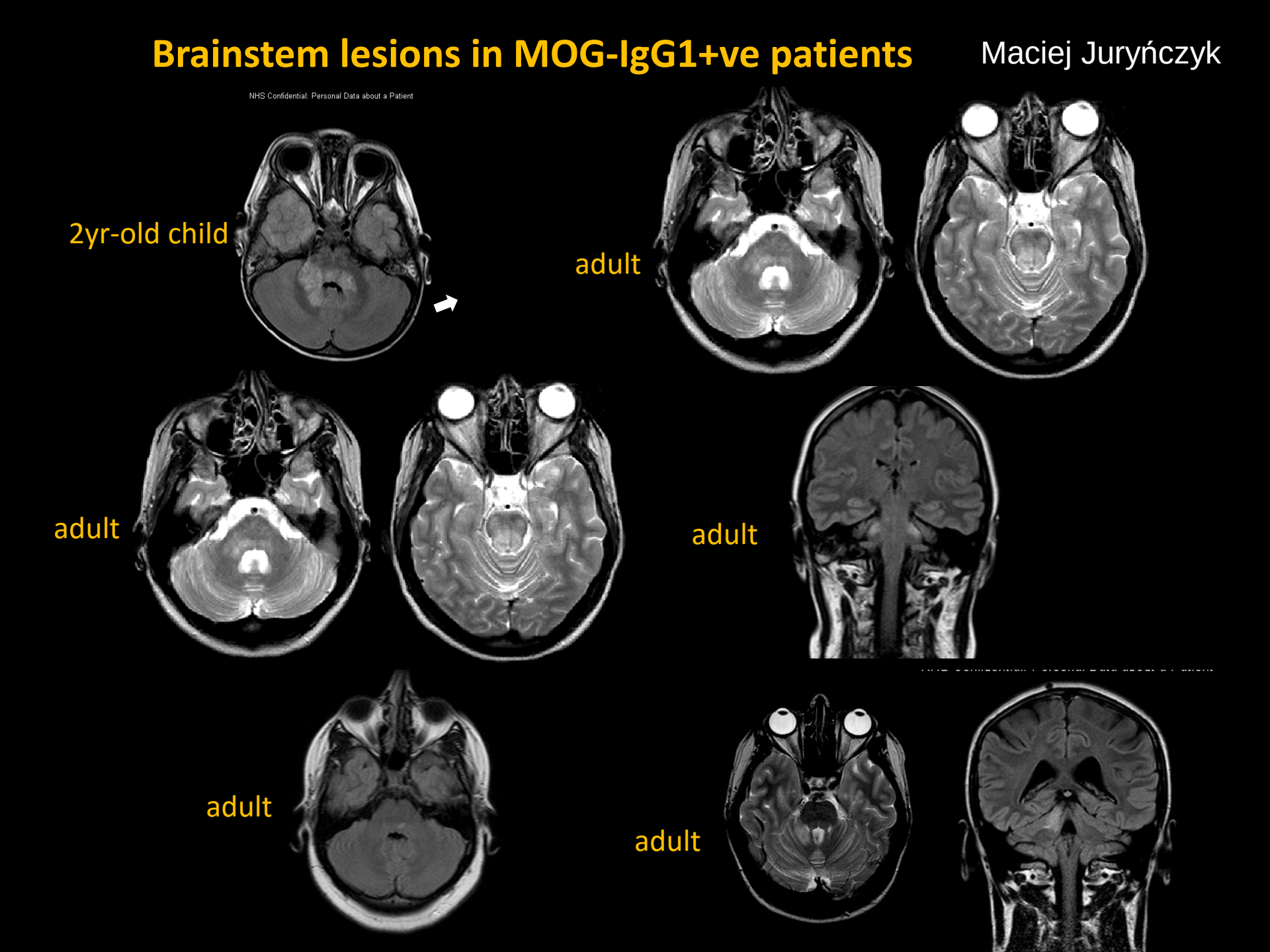


Ito et al Ann Neurol 2009;66:425

MRI examples of MOG-Ab disease:

Brainstem lesions in MOG-IgG1+ve patients

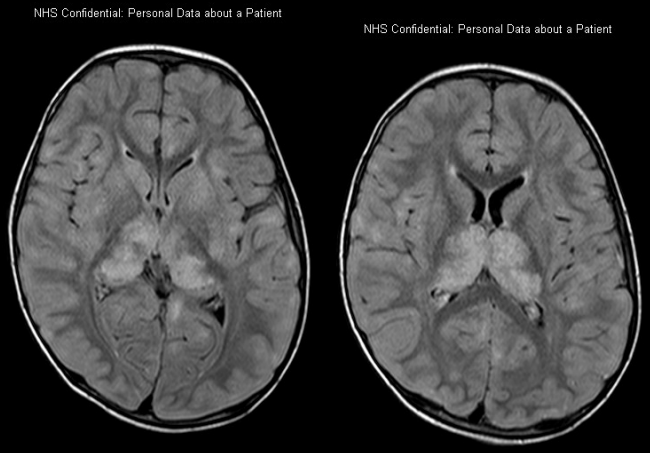
Maciej Juryńczyk



Basal ganglia/thalamic lesions in MOG-IgG1+ve patients

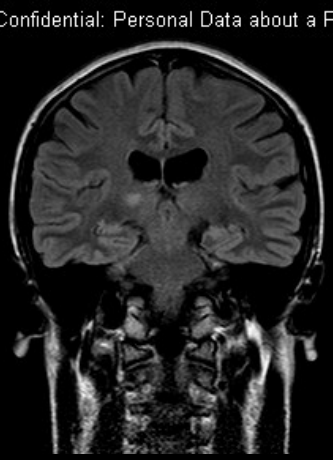
Maciej Juryńczyk

2yr child

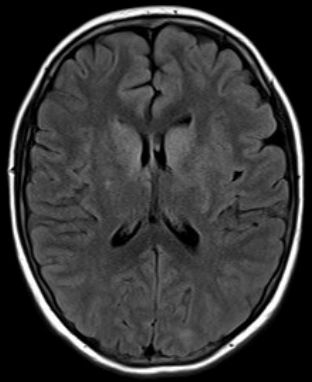


11yr child

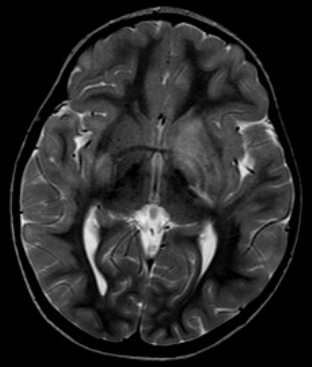
adult



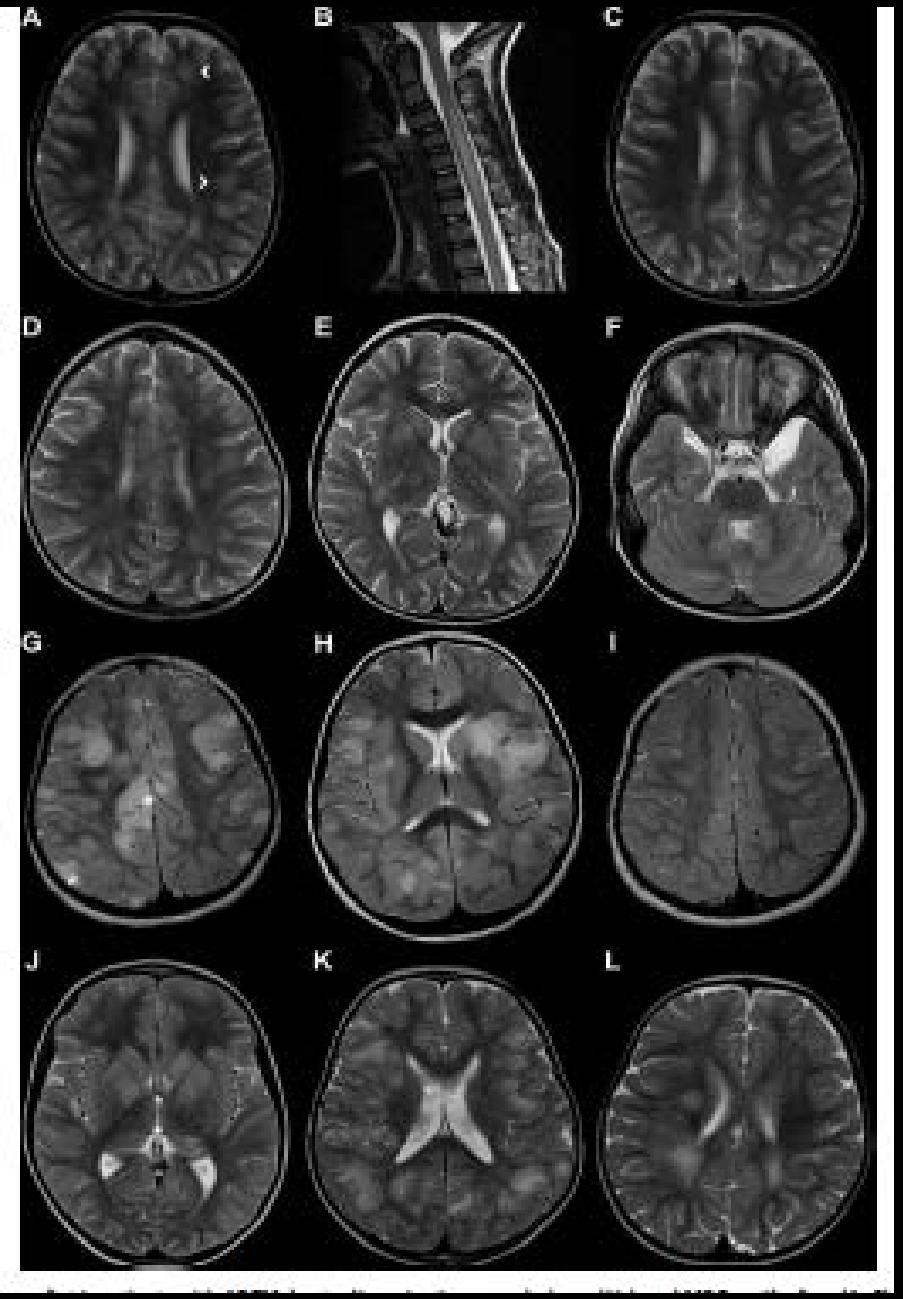
14yr child

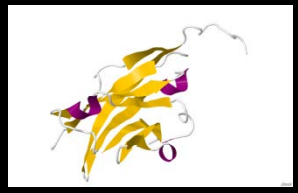


3yr child



MOG-Ab with ADEM





A-C 6yrs C 2/52 on
headache, lethargy, Lt sensory, paraparesis, sphincter,

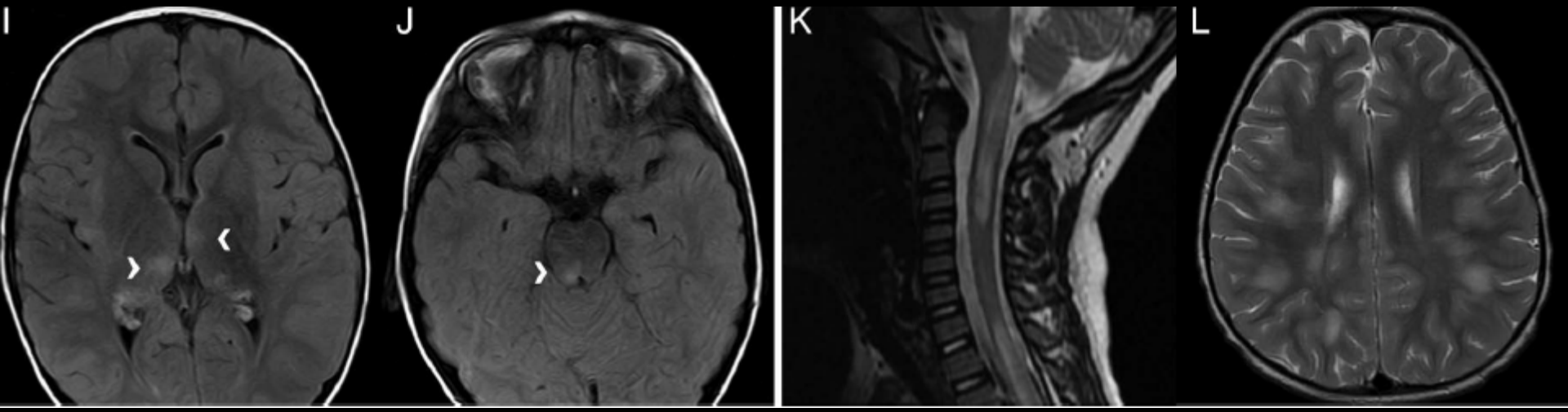
D-F 4yrs
Lethargy, headaches, paraparesis (cord LETM)

G-I 2yr I 5/12 later
Somnolence, opisthotonus, bulbar and resp

J 5yr headache, ataxia lethargy
K 3yr fever, headache, dysarthria, rt hemi, gait
L 1yr ataxia, strabismus, lethargy,

Baumann M et al., J Neurol Neurosurg Psychiatry. 2015

Lechner et al JNNP 2015
Paediatric MOG ab

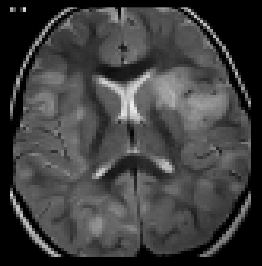


MRI MOG-Ab vs AQP4-Ab disease

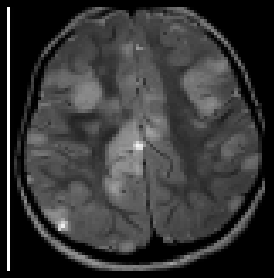
Similar to AQP4-Ab disease

More:
conus involvement (left w isolated sphincter and erectile dysfunction)

fluffy lesions (adults, or ADEM attacks childhood)



bilateral cerebellar peduncle lesions
thalamic lesions



Maciej Juryńczyk
Friday 17.30

NMOSD from MS

Imaging criteria: MS and NMO

17% OS MS had LETM

Revised diagnostic criteria for neuromyelitis optica

D.M. Wingerchuk, MD, FRCP(C); V.A. Lennon, MD, PhD; S.J. Pittock, MD; C.F. Lucchinetti, MD; and B.G. Weinshenker, MD, FRCP(C)

'Barkof criteria for MS' positive in 16% AQP4-Ab +ve patients

Lucy Matthews

Distinction of seropositive NMO spectrum disorder and MS brain lesion distribution

Lucy Matthews, MRCP

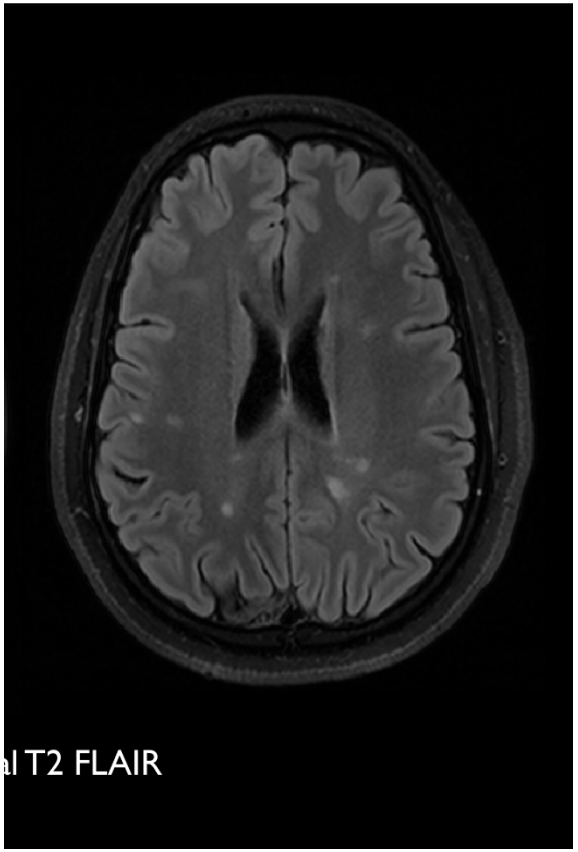
ABSTRACT

AQP4-Ab Brain MRI

~ 9% have characteristic peri-ependymal or diencephalic

Normal in around 1/3

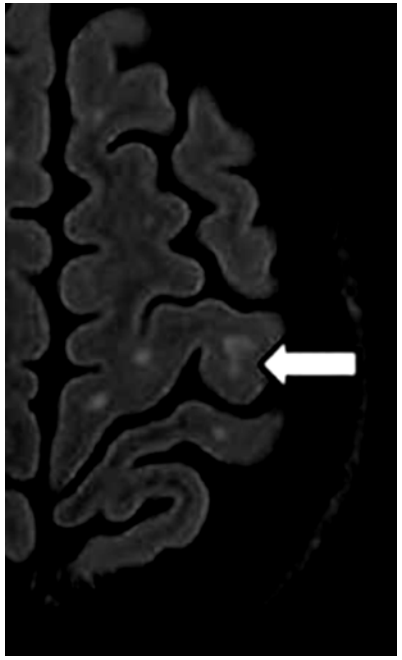
Non-specific WML commonest ab^{n}



MS and NMO w abn brain MRIs – can be differentiated

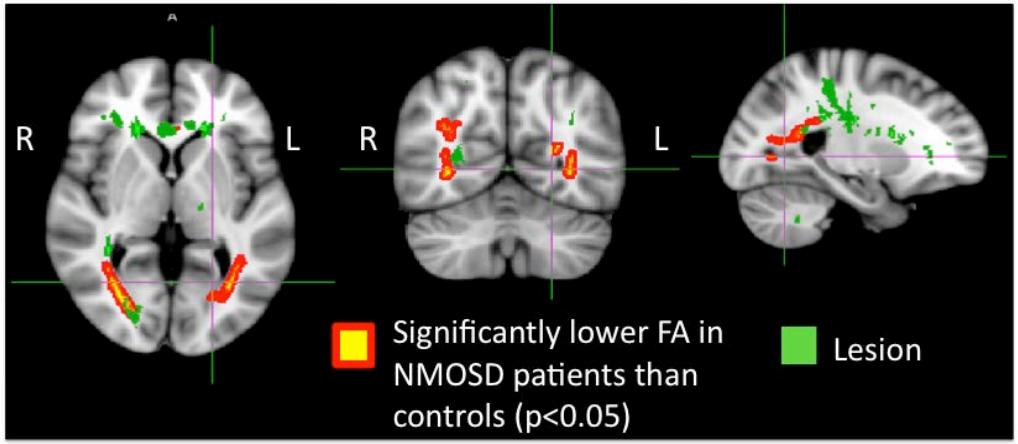
	Number	Lesions adjacent to lateral ventricle and in the inferior temporal lobe, or Dawson's finger or S-shaped U fibre lesion
AQP4+ve w abn brain MRIs	26	1
RRMS	50	46
Sensitivity	-	92 %
Specificity	-	96 %

Lucy Matthews



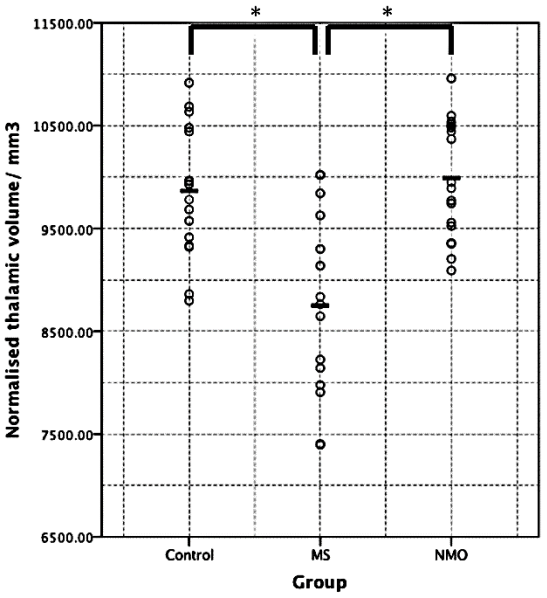
Non-conventional imaging

- Normal appearing brain tissue:
  abnormal in MS,
  prob normal NMOSD (outside of connected tracts)



Lucy Matthews

PLOS ONE | DOI:10.1371/journal.pone.0137715 September 18, 2015



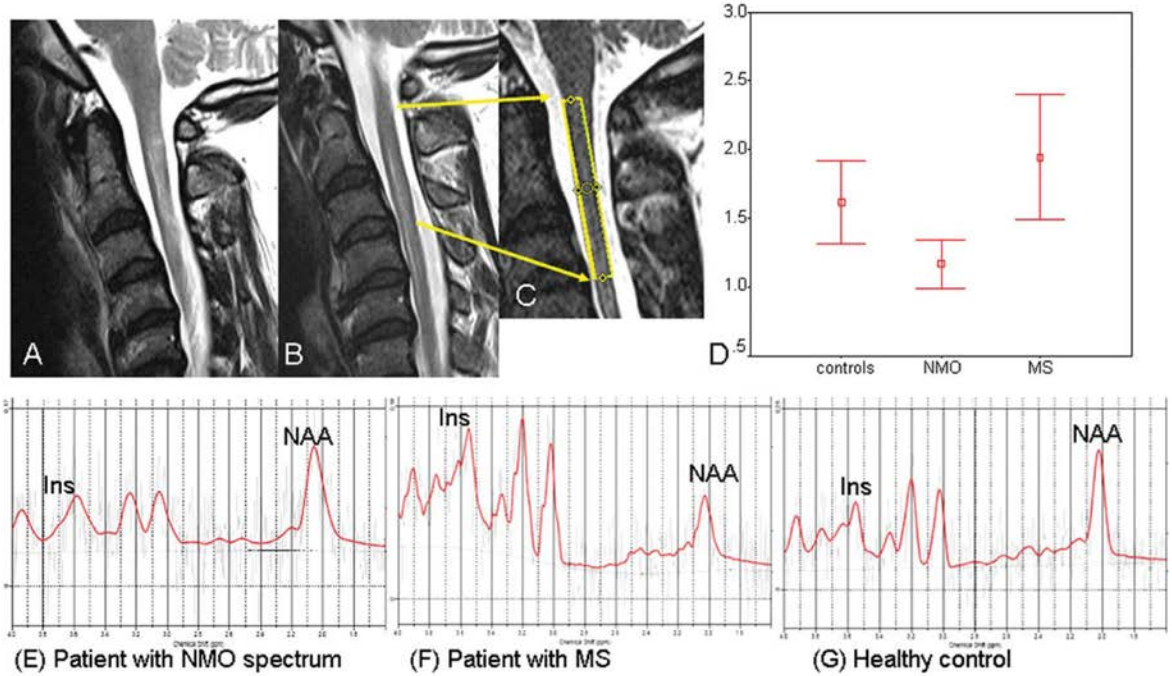
- Cortical lesions in MS, not NMO

Sinnecker et al
Calebrese et al

- Thalamic (& Caudate) atrophy in MS

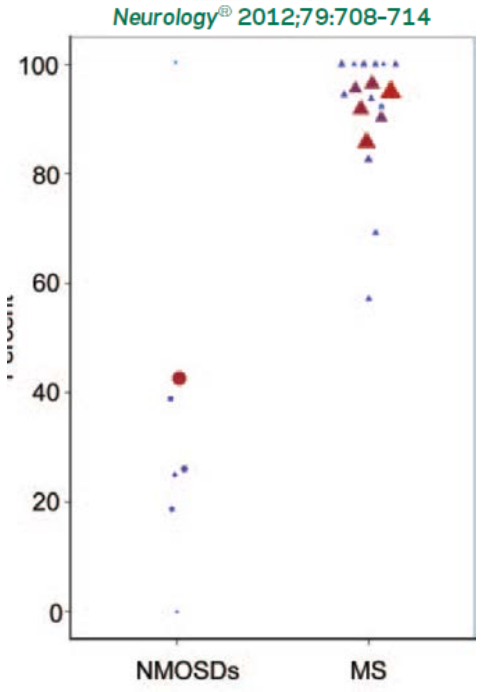
Non-conventional imaging

- Astrocyte damage (myo-inositol) reduced in NMOSD

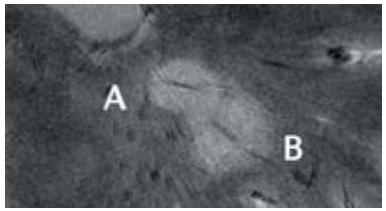


Ciccarelli et al
Ann Neurol 2013;74:301

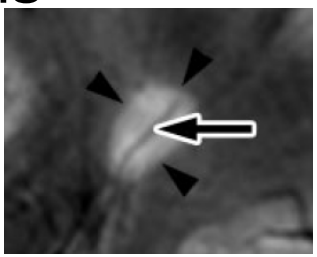
Sinnecker et al
Neurology® 2012;79:708-714



- Lesions with central veins



Absinta et al, Nat Rev Neurol 2016;12:358



Conclusion: NMOSD vs MS

long lesions

typical NMOSD brain MRI features (minority)

ns wml or normal brain MRI common

can fulfil MS brain MRI criteria

NMO 2015 diagnostic criteria more reliant on MRI if no AQP4-Abs

AQP4-Ab contrast to MS less/absence of:

Dawsons fingers, S-shaped U fibre cortical lesions,
lesional central veins, cortical lesions, NAWM ab^{n,}
thalamic atrophy, lesional myo-inositol ,

MOG-Ab disease: similar to AQP4-Abs, more lesions:

fluffy, conus, (bilateral cerebellar peduncles, thalamus)