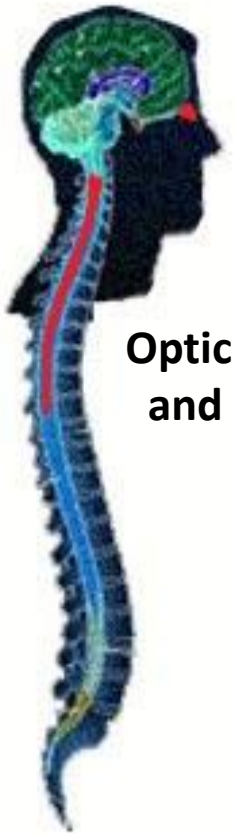
Definitions

NMO

~ 60% AQP4-Abs



Optic Neuritis + Transverse Myelitis and 2 of 3:

LETM
NMO antibodies
Non MS like brain MRI

2006
Wingerchuk

NMOSD

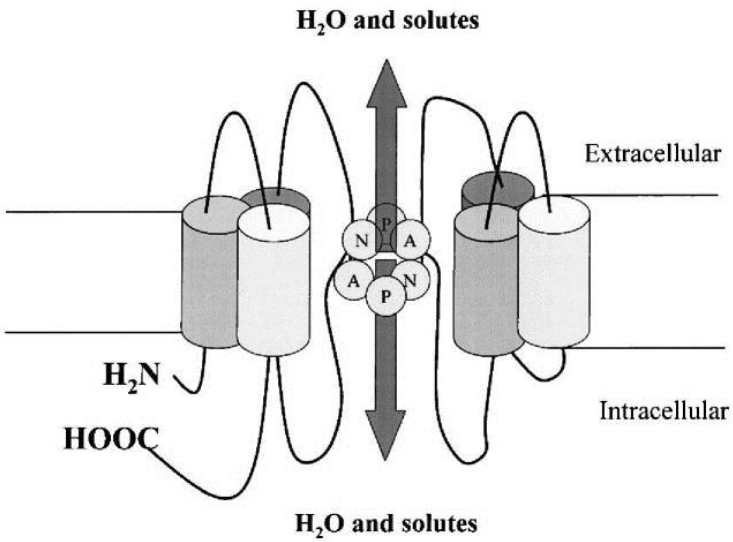
Longitudinally extensive TM
~ 60% AQP4-Abs

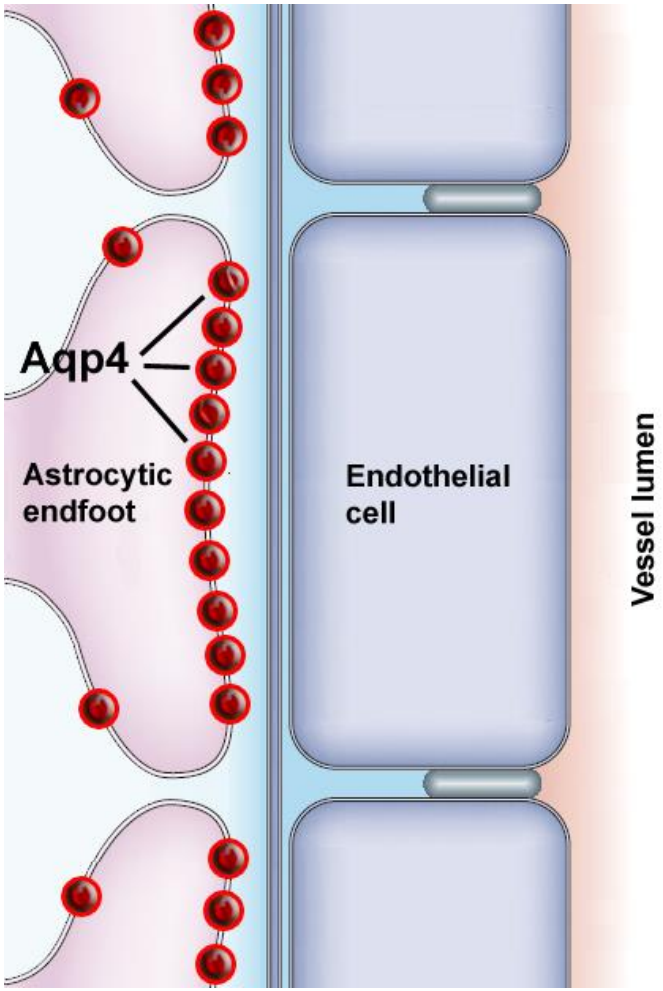
ON: ~ 50% AQP4-Abs
recurrent
simultaneous bilateral
w auto-immune disease
w NMO typical brain lesions
poor visual outcome

Inflammatory brain lesions with NMO abs
100% AQP4-Abs

2007
Wingerchuk

Aquaporin-4



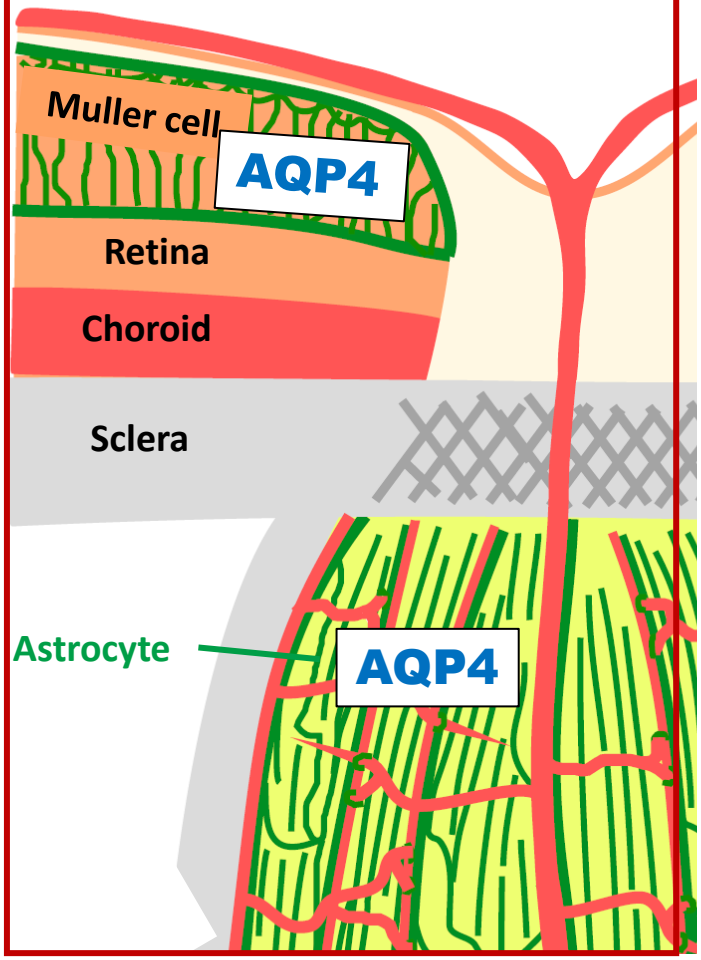


most abundant water channel in CNS
concentrated in astrocytic foot processes

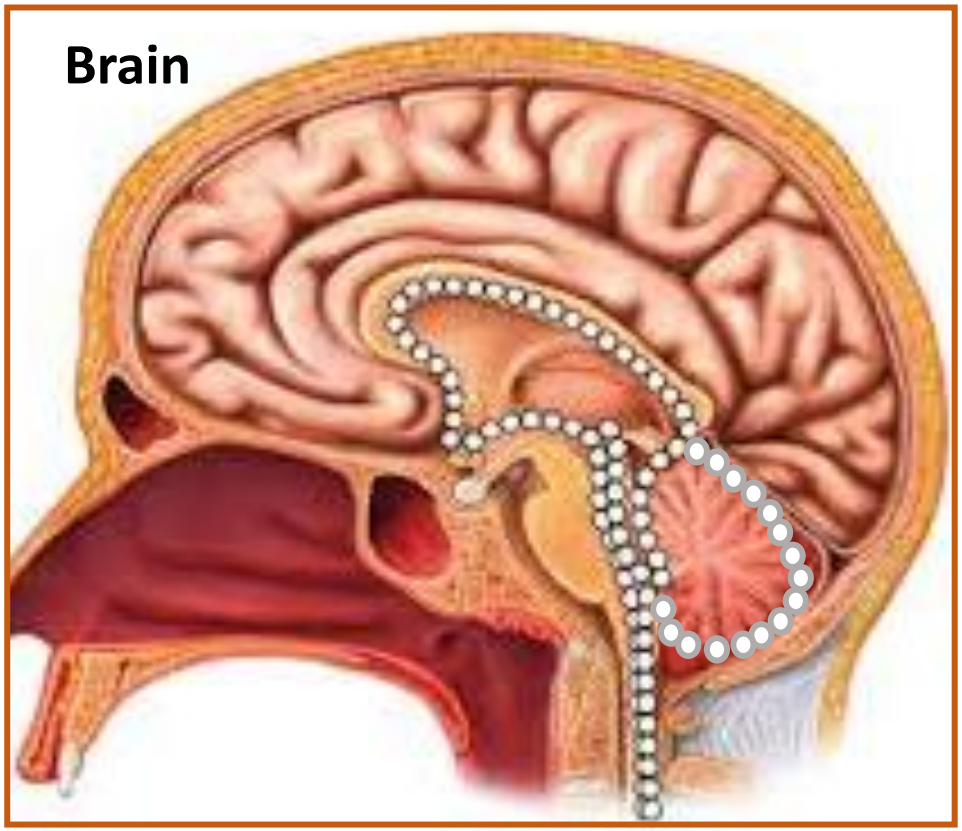
Lennon et al Lancet 2004; J Ex Med 2005

AQP4 expression

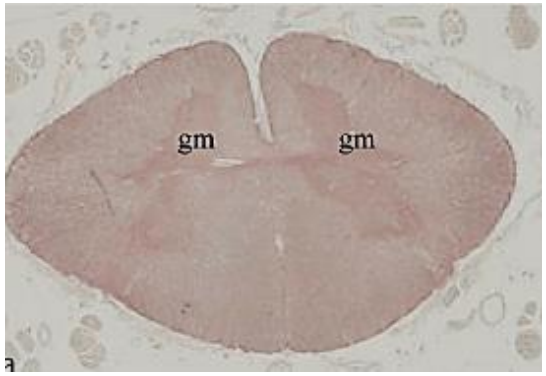
ON + Retina

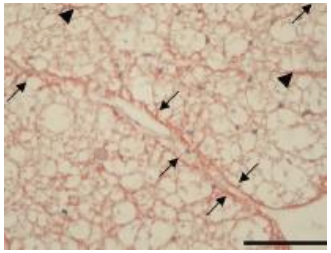


Brain



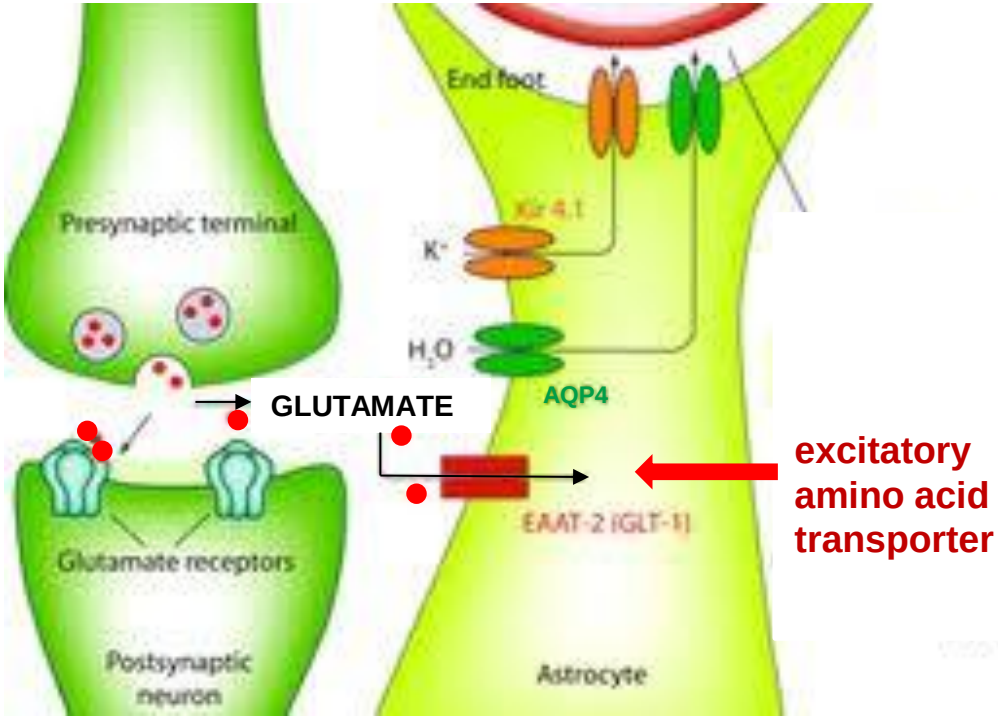
Spinal Cord





Antibodies to AQP4 → astrocytopathy

reduced glutamate uptake → secondary myelin damage



2015 Definition

NMOSD

female,
non-Caucasian,
severe disability
auto-immune diseases
relapsing

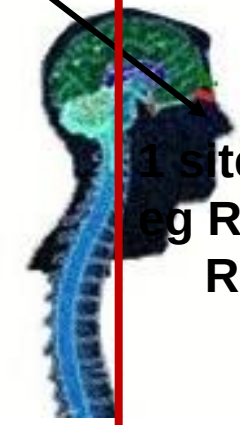
AQP4-Ab positive disease

AQP4-Ab negative

attacks from 2 sites:
≥ 1 from ON, SC, *area postrema,*

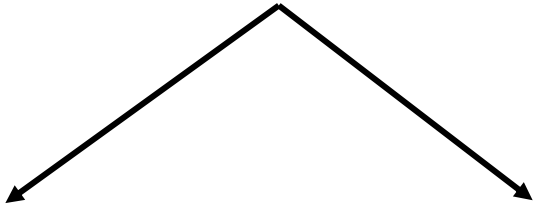
brainstem, diencephalic, cerebral

1 site
eg R ON
R LETM



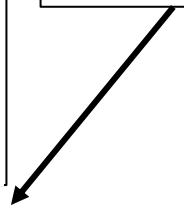
2015 Definition

NMOSD



AQP4-Ab positive disease
attack 1 site:
ON / TM / *area postrema* / brainstem
or
narcolepsy / diencephalic / cerebral w typical MRI

AQP4-Ab negative



attack 2 sites w typical MRI
≥ 1 from ON, SC, *area postrema,*

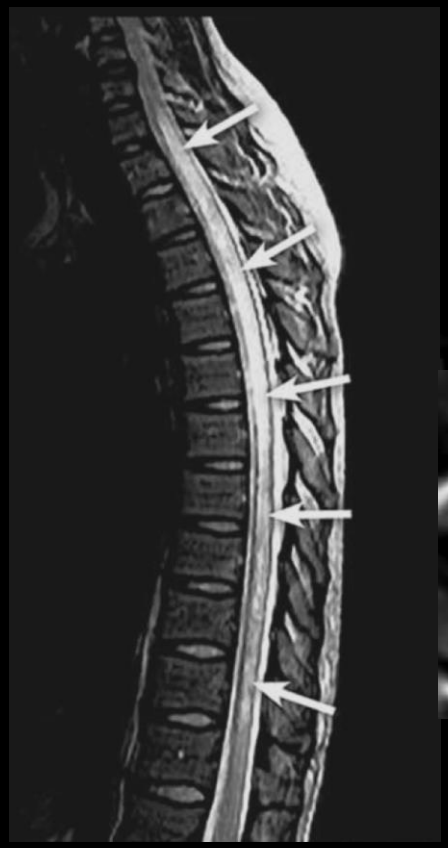
brainstem, diencephalic, cerebral

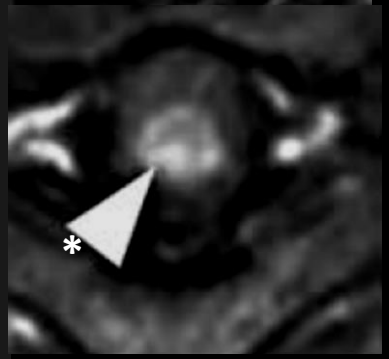
ACUTE MYELITIS

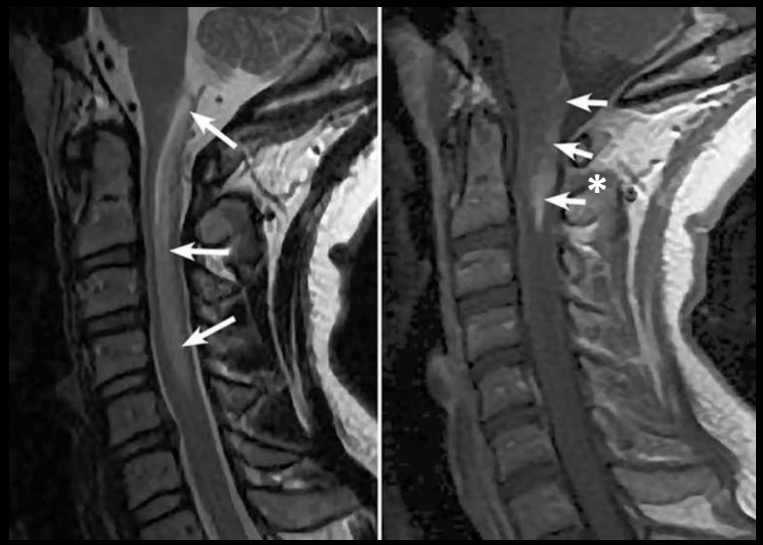
LETM ≥ 3 vertebral segments

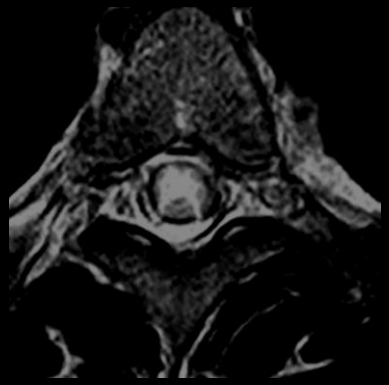
or chronic

Spinal Cord: central, extend medulla



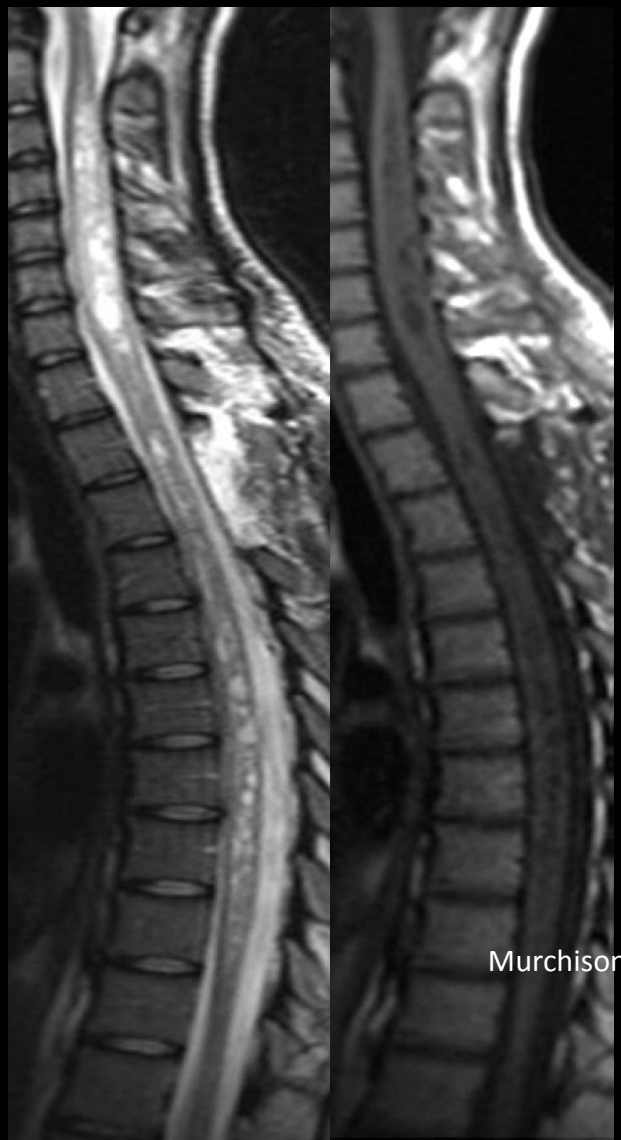






Kim et al Neurology 2015;84:1165

Spinal cord:
T1 hypointensity acute lesions



Murchison et al 2015 355:215

OPTIC NEURITIS

BRAIN MRI: normal or non-specific WMLs

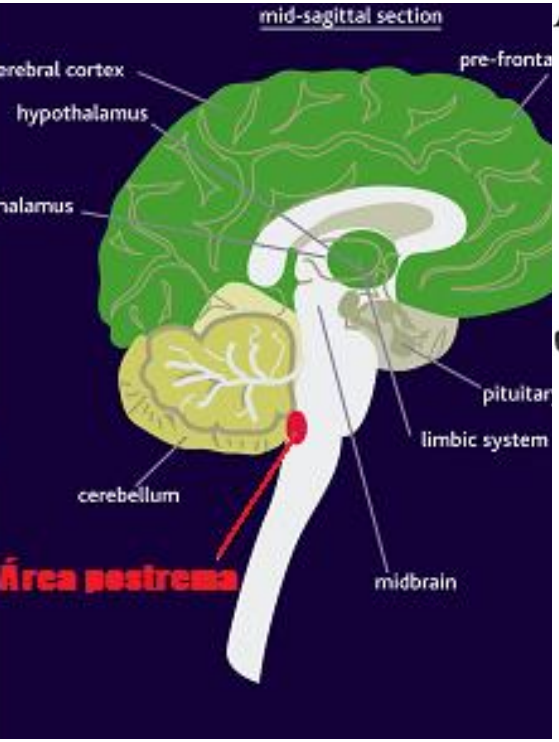
OR

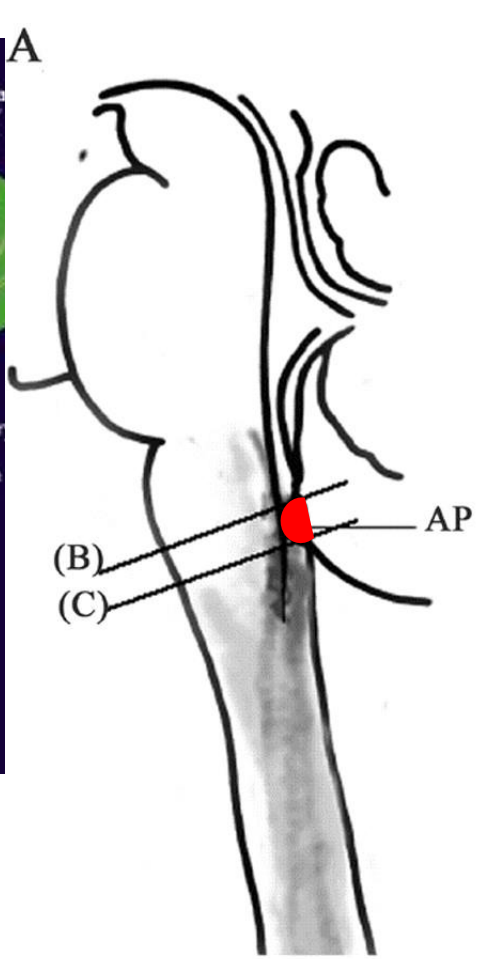
> ½ ON length or chiasmatic involvement (usually posterior)

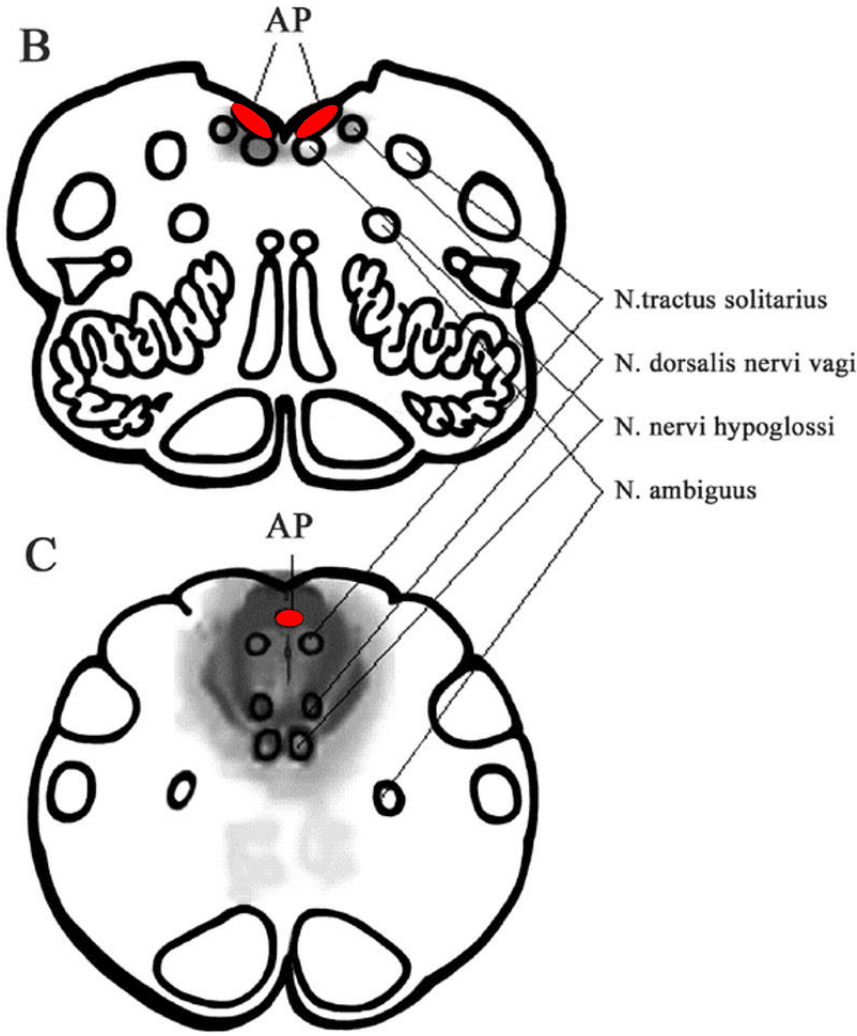
Kim et al Neurology 2015;84:1165

Area Postrema

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



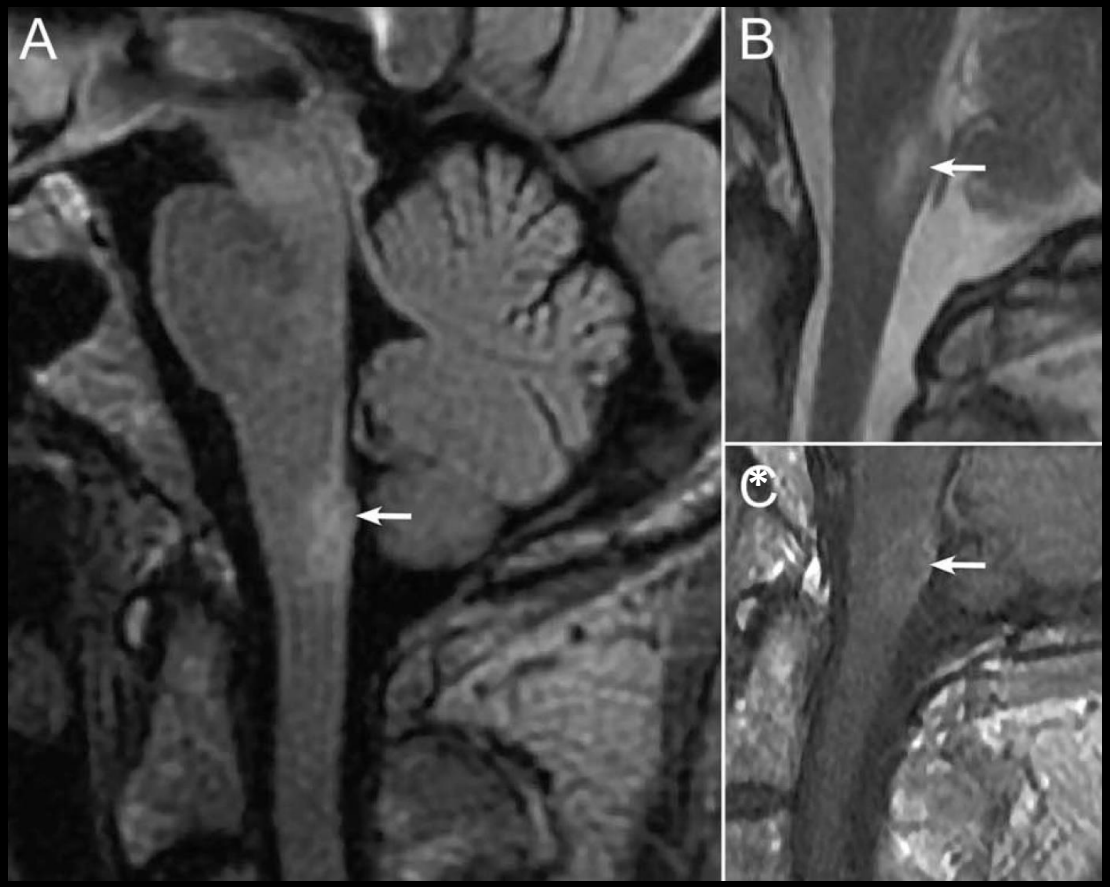


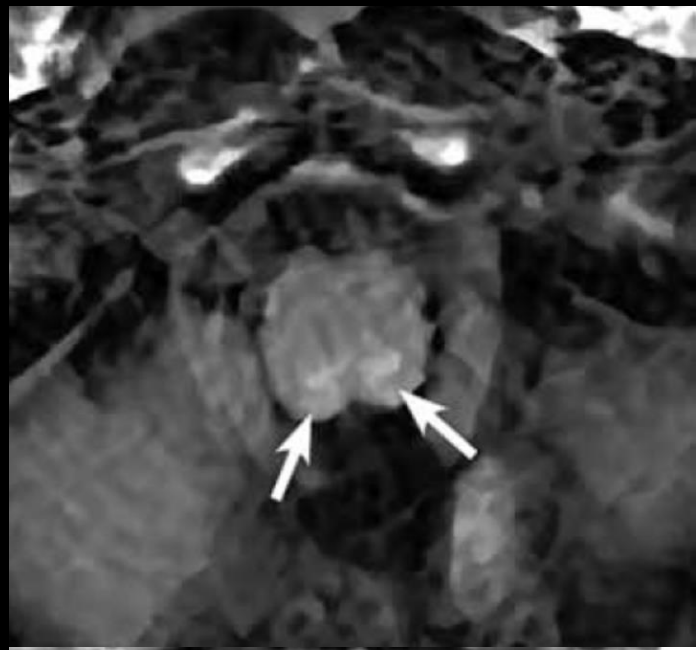


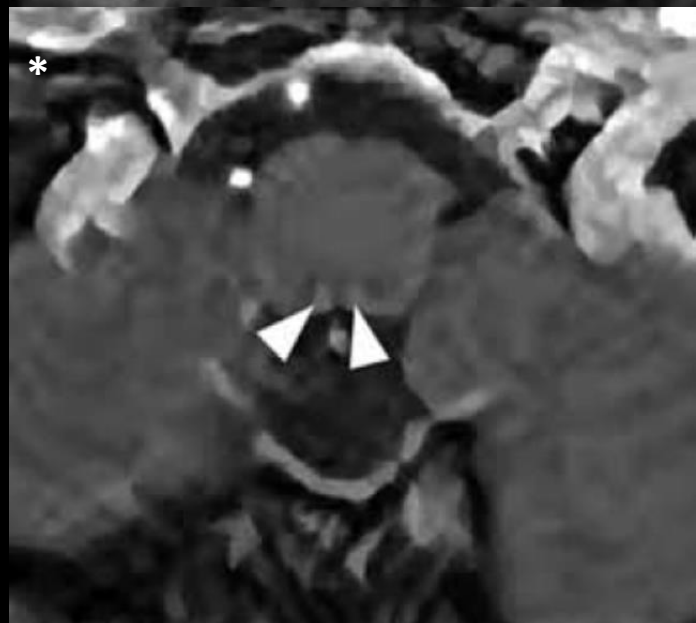
T. Misu et al. Neurology 2005;65:1479-1482

AREA POSTREMA ATTACK

Area postrema / dorsal medulla

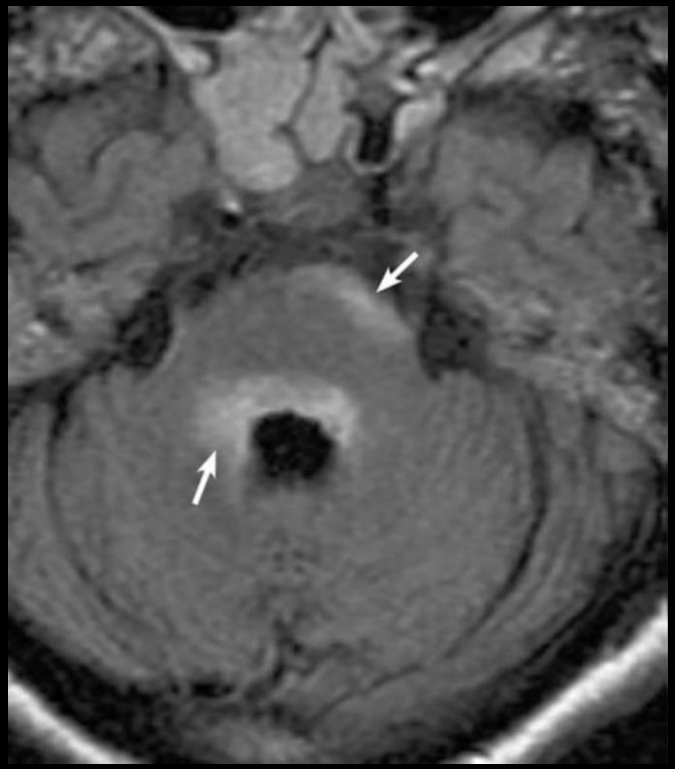


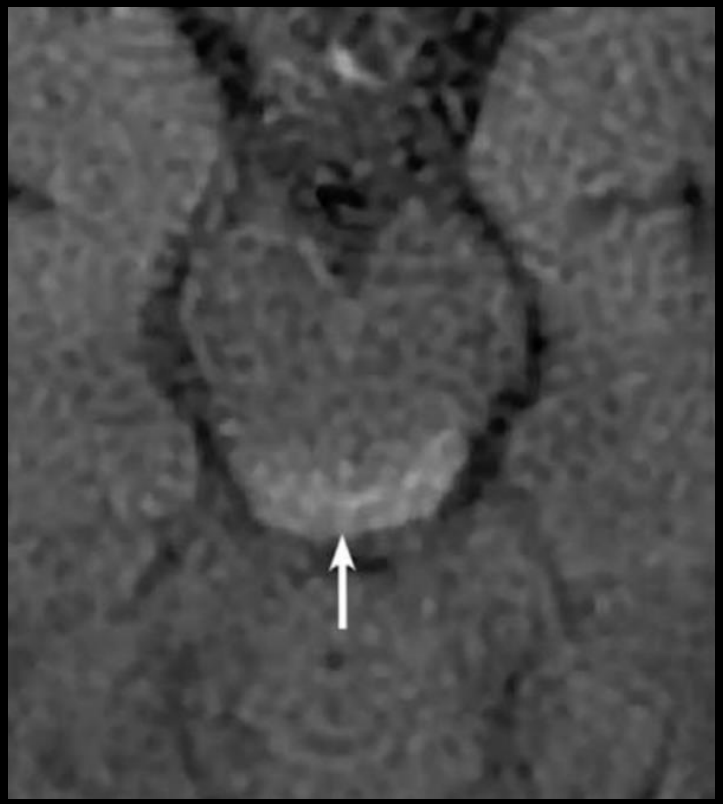




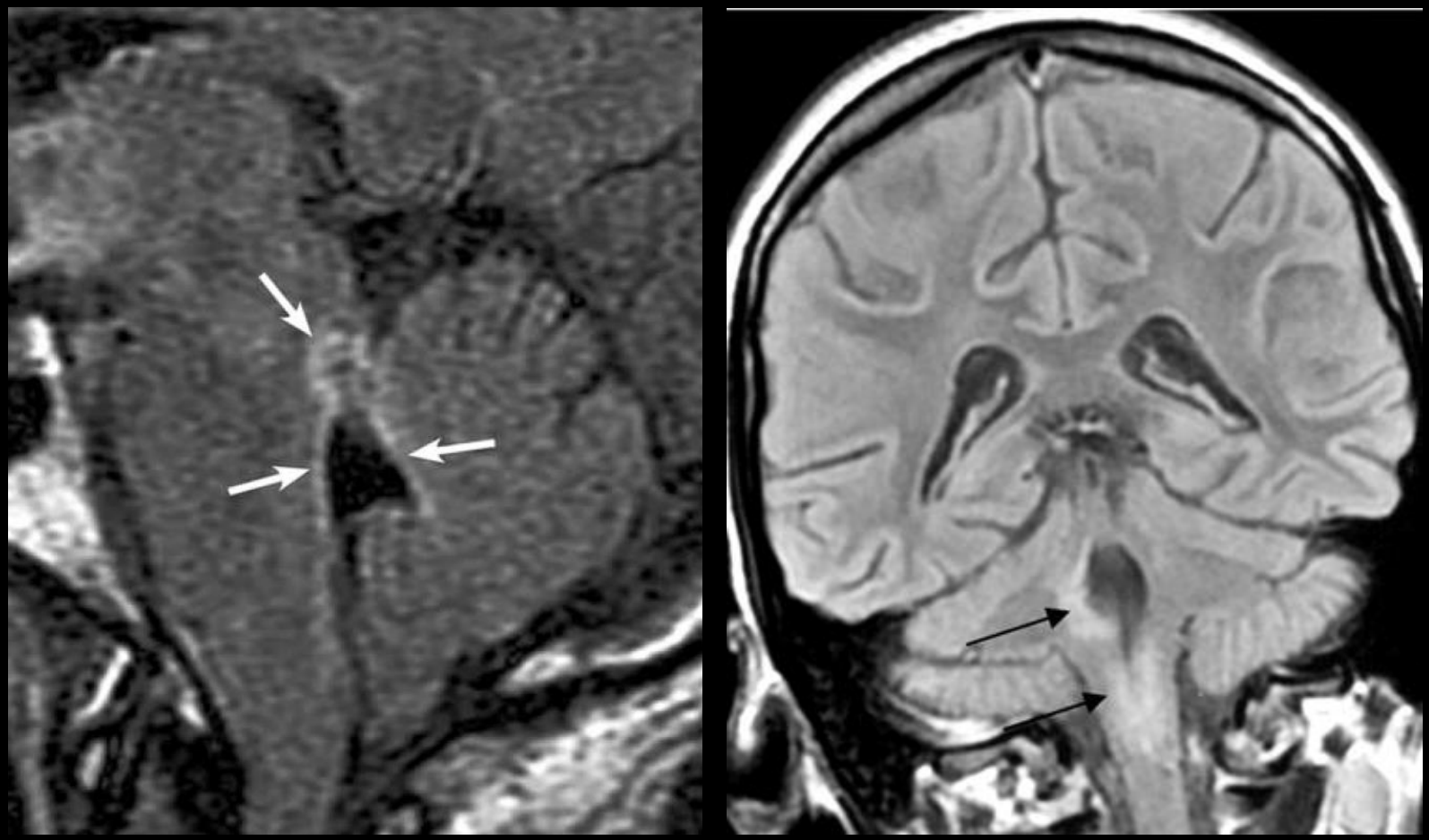
BRAINSTEM ATTACK

Periependymal lesions





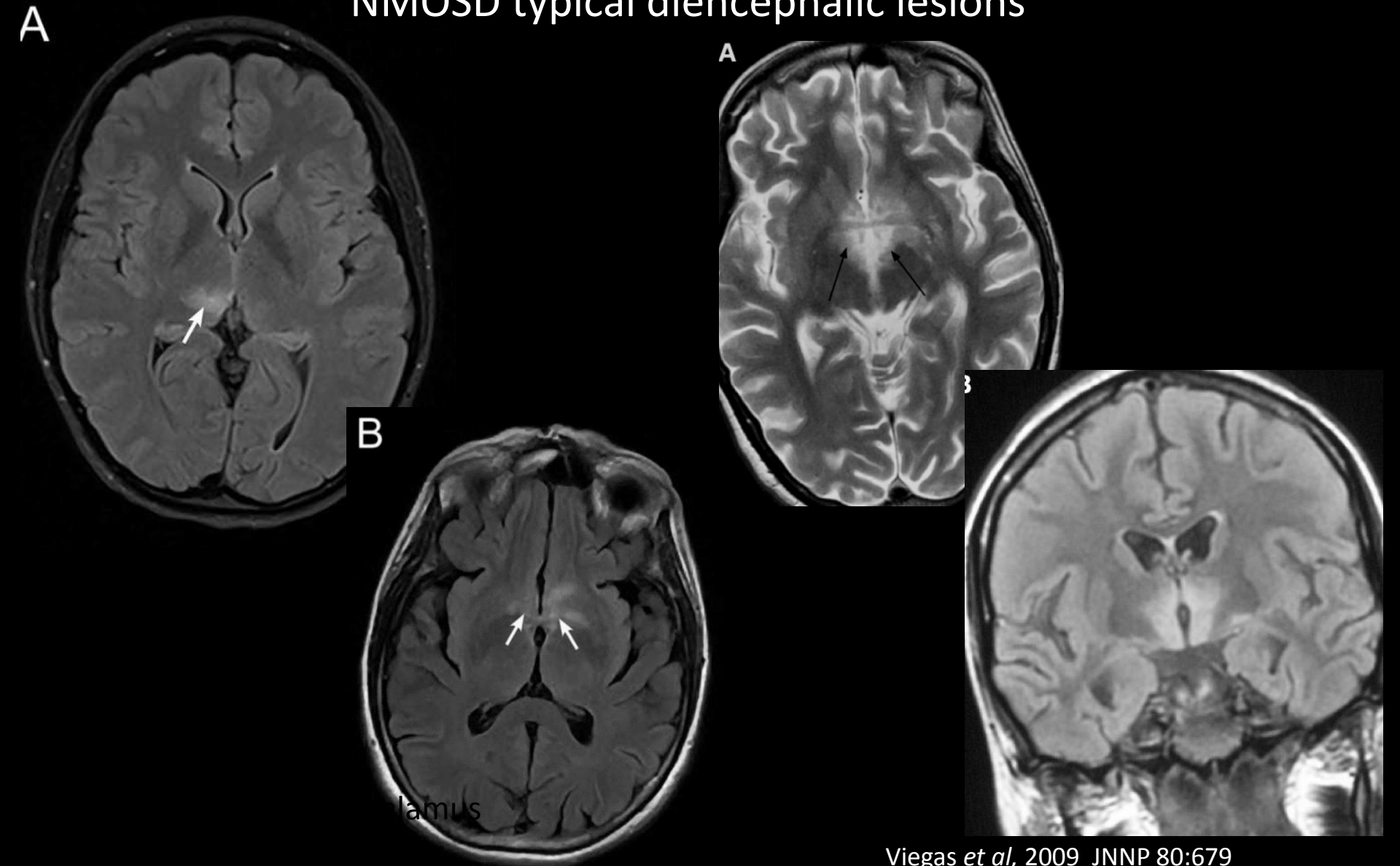
4th ventricle



Viegas *et al,* 2009 JNNP 80:679

NARCOLEPSY OR DIENCEPHALIC ATTACK

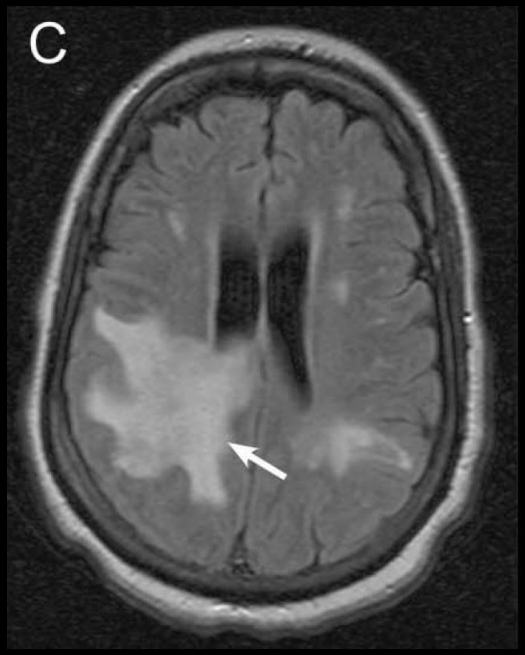
NMOSD typical diencephalic lesions



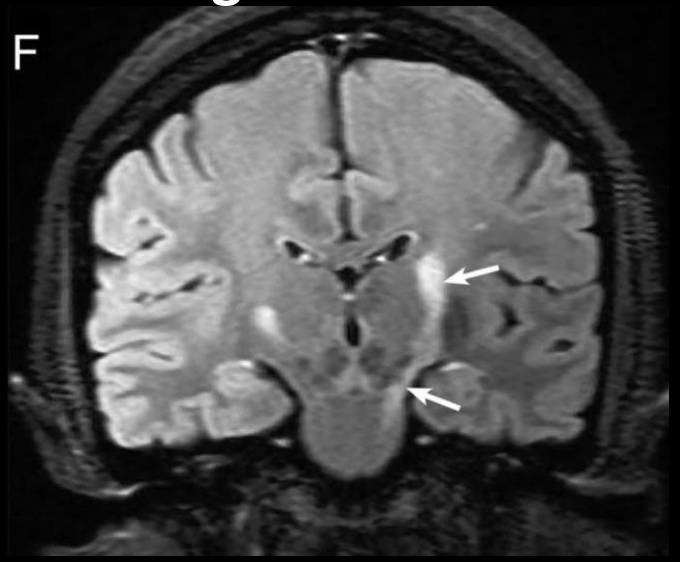
Viegas *et al,* 2009 JNNP 80:679

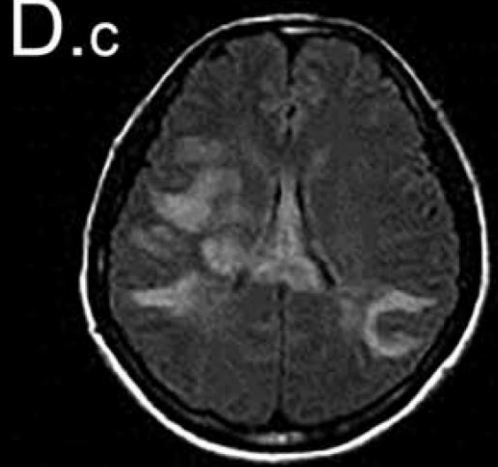
CEREBRAL ATTACK

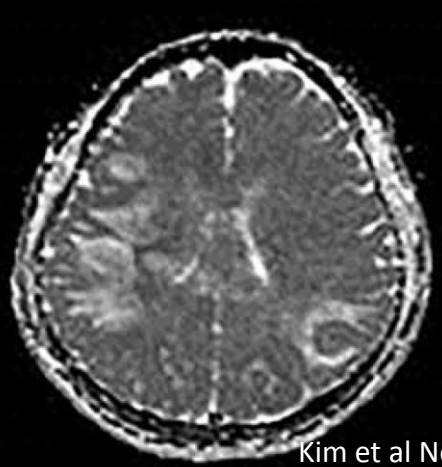
NMOSD ‘typical’ brain lesions



Long CS tract lesion





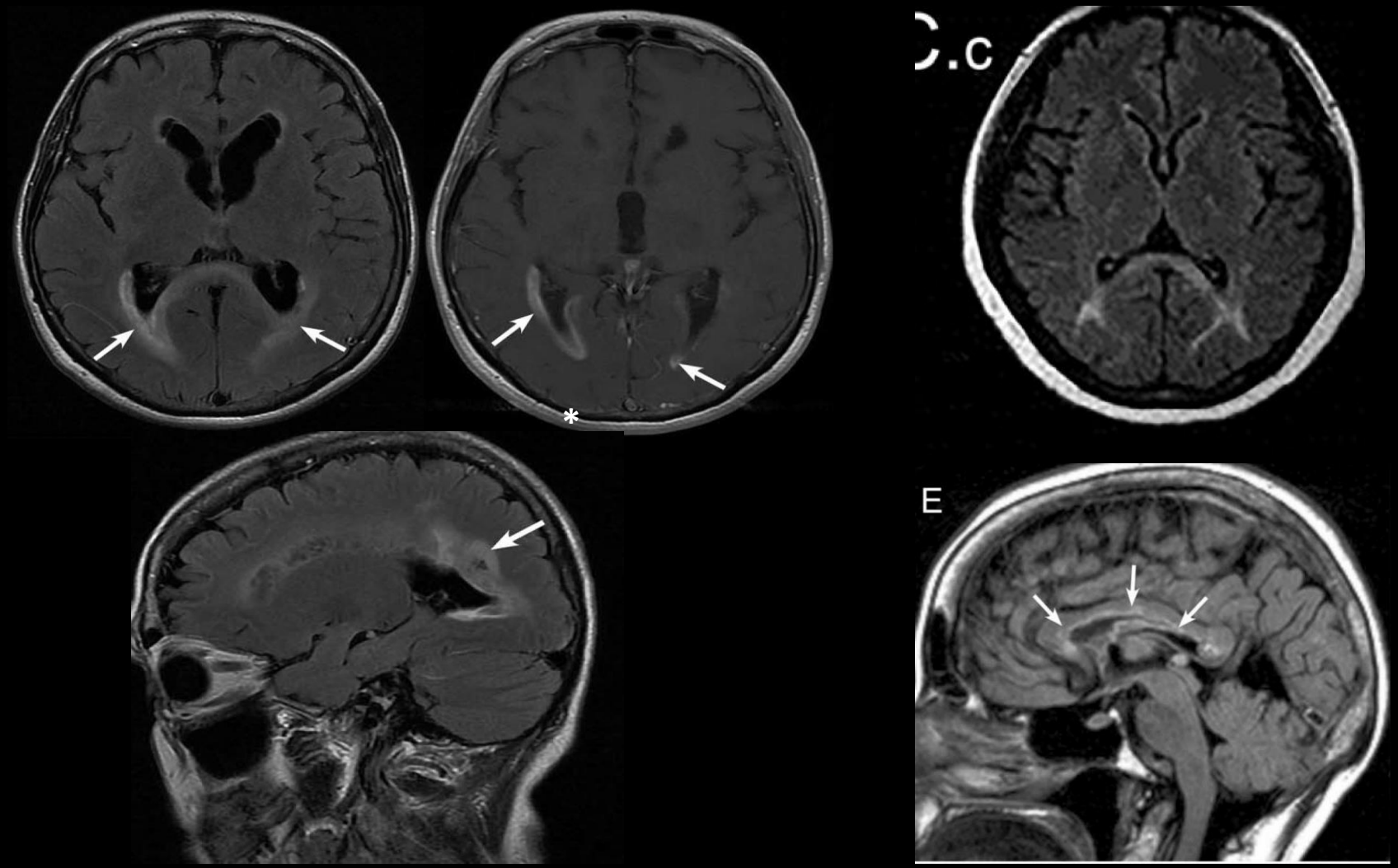


Kim et al Neurology 2015;84:1165

CEREBRAL ATTACK

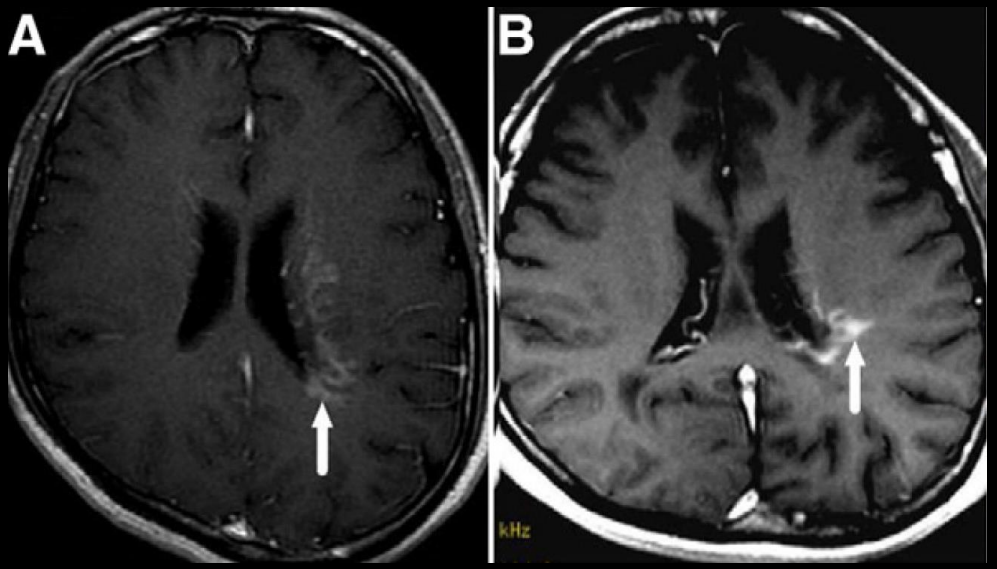
Peri ependymal / ventricular lesions/CC

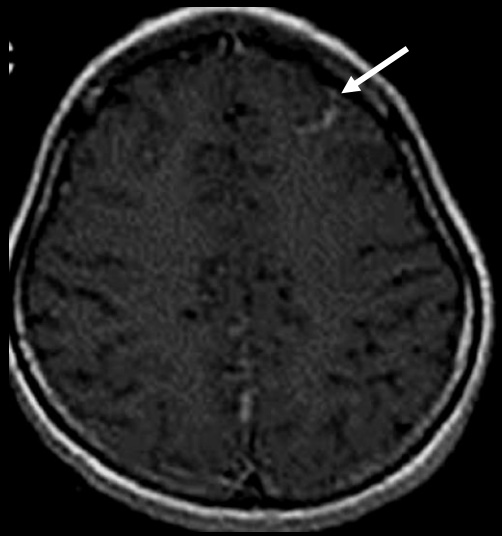
Kim et al Neurology 2015;84:1165



CEREBRAL ATTACK

Patterns of enhancement



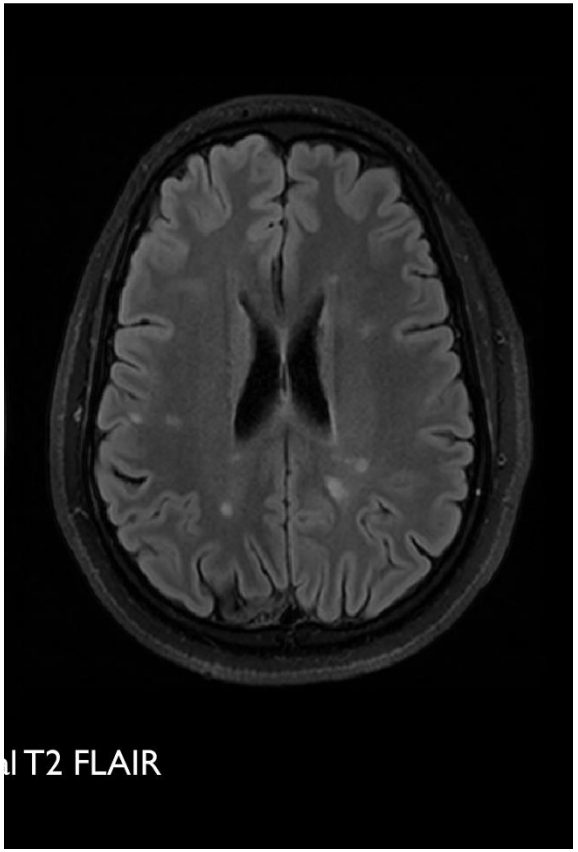


AQP4-Ab Brain MRI

~<10% have characteristic peri-ependymal or diencephalic

Normal in around 1/3

Non-specific WML commonest ab^{n}



Overlap with MS and NMO

MS can present as:

recurrent ON

recurrent TM

sequential ON and TM

short lesions / TM: asymmetrical, post, white matter / MS MRI diagnostic criteria

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)

14% AQP4-Ab TM present with short TM lesions

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;

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

Distinction of seropositive NMO spectrum disorder and MS brain lesion distribution

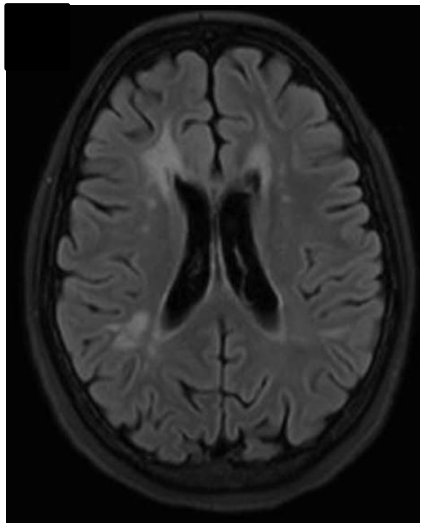
Lucy Matthews

Lucy Matthews, MRCP ABSTRACT

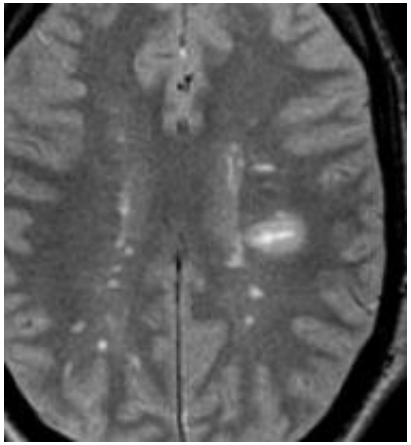
MS and NMO w abn brain MRIs – can be differentiated

Lucy Matthews, Neurology 2013;80:1-8

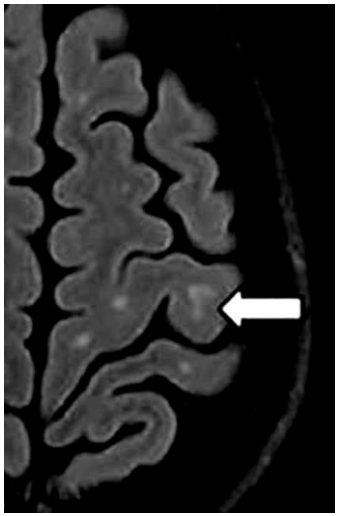
+



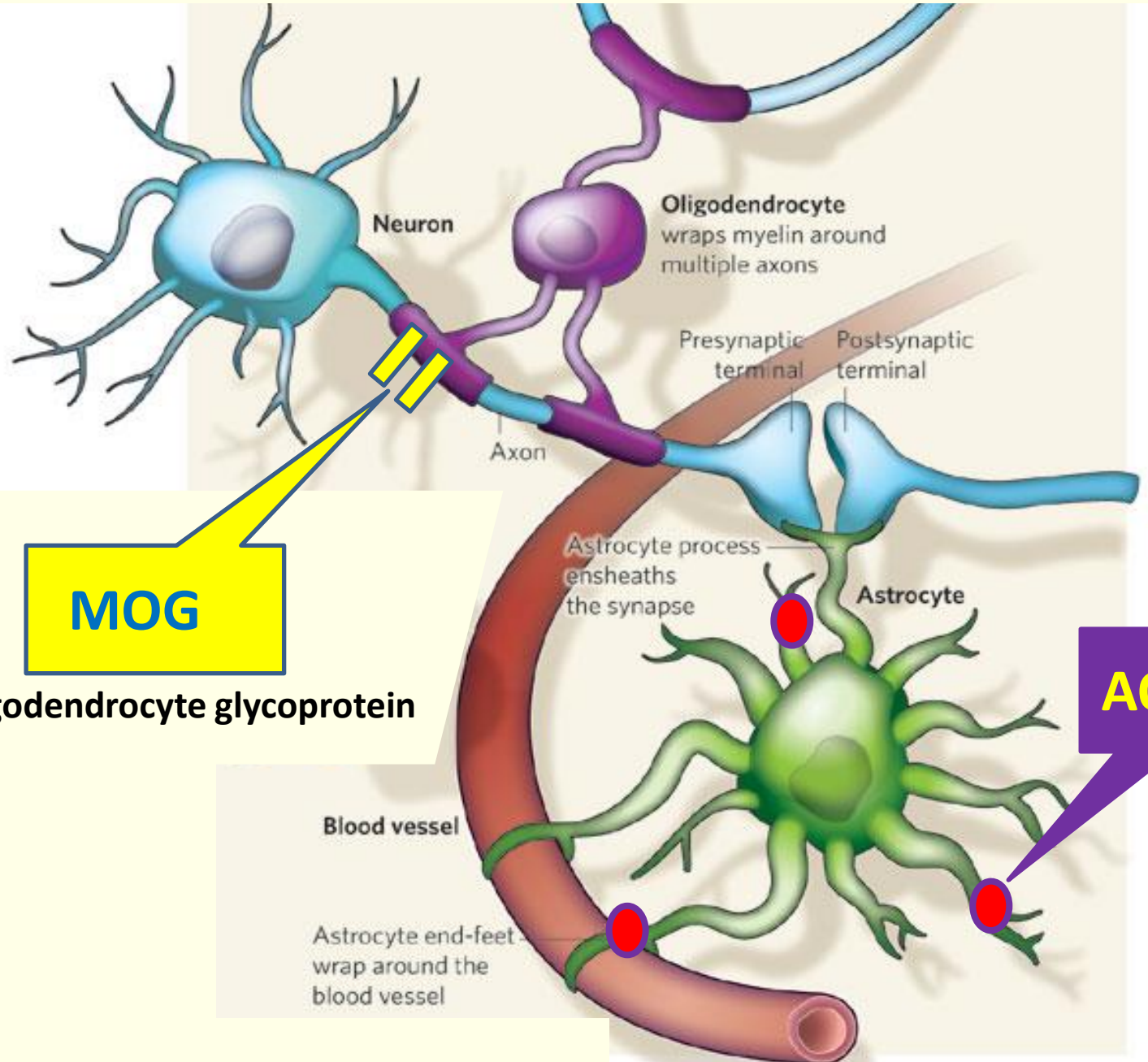
or



or



	n	Lesions adjacent to lateral ventricle & 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 %



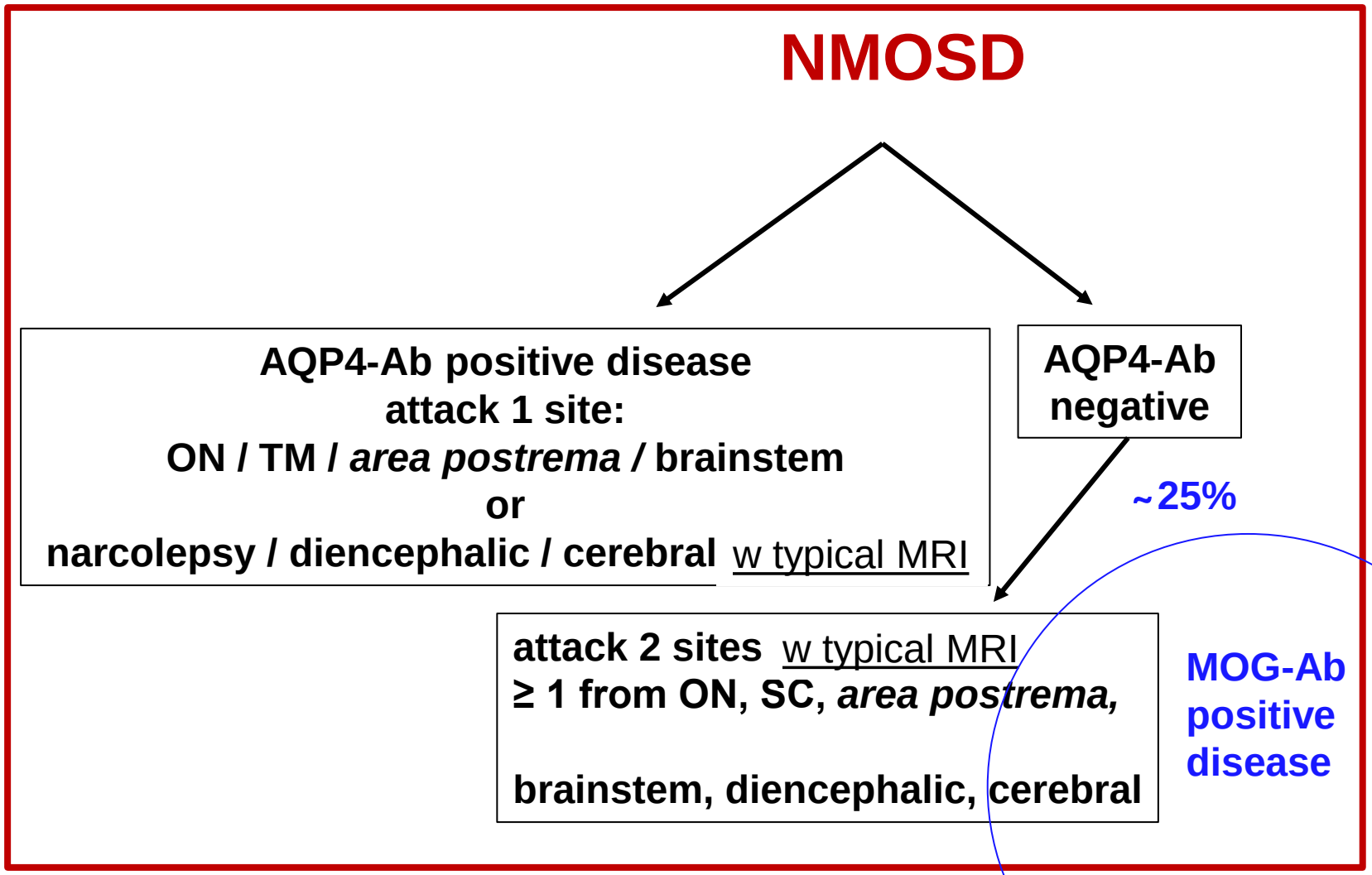
MOG

myelin oligodendrocyte glycoprotein

AQP4

2015 Definition

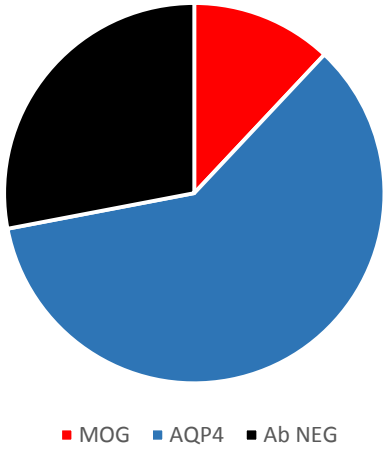
Wingerchuk



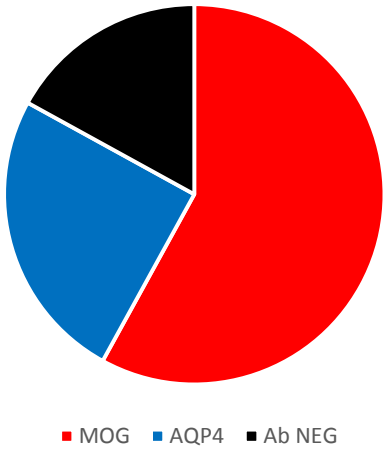
age effect on antibodies

Kitley et al JAMA" neurol 2013
Piccolo et al ~ J Neurol 2016
Lechner et al† JNNP 2015
Baumann et al + JNNP 2015
Hacohen et al* Neurol Neuroimmunol Neuroinflamm 2015

Adult NMO



Paed NMO



MOG-Abs
AQP4-Abs
Neg Abs

MOG-Ab compared to AQP4-Ab NMOSD

Jo Kitley

From: **Neuromyelitis Optica Spectrum Disorders With Aquaporin-4 and Myelin-Oligodendrocyte Glycoprotein Antibodies: A Comparative Study**

JAMA Neurol. 2014;71(3):276-283. doi:10.1001/jamaneurol.2013.5857

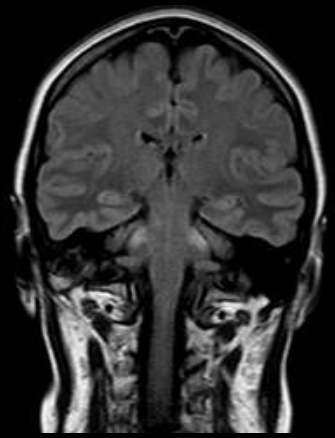
Finding	No. (%) MOG-Ab Positive	No. (%) AQP4-Ab Positive	*P* Value
MRI cord lesions	n = 9	n = 11	
Length of longest lesion, median (IQR)	3 (3-11.5)	5 (3.5-8)	NS
Length of longest lesion, mean (SD)	6.78 (5.5)	6.25 (3.4)	NS
T1 hypointensity	5 of 8 (63)	4 of 10 (40)	NS
Central gray matter involvement	5 of 6 (83)	9 of 11 (82)	NS
Postcontrast enhancement	2 of 6 (33)	7 of 8 (88)	NS
Cord edema	9 (100)	11 (100)	NS
Sagittal location			
Involving cervical cord	6 of 9 (66)	9 of 11 (82)	NS
Involving thoracic cord	8 of 9 (89)	8 of 11 (73)	NS
Involving conus	6 of 8 (75)	2 of 11 (18)	.02
MRI brain classification	n = 9	n = 18	
Normal	3 (33)	7 (39)	NS
Nonspecific	2 (22)	7 (39)	NS
MS-like	0 (0)	2 (11)	NS
NMO-like	0 (0)	2 (11)	NS
ADEM-like	4 (44)	0 (0)	.007
MRI brain lesions	n = 9	n = 18	
Large hemispheric	1 (11)	1 (6)	NS

Brainstem lesions in MOG-IgG1+ve patients

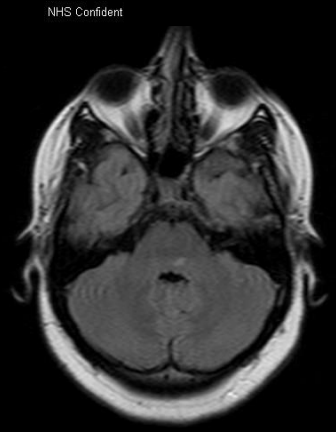
Maciej Juryńczyk

2yr-old child

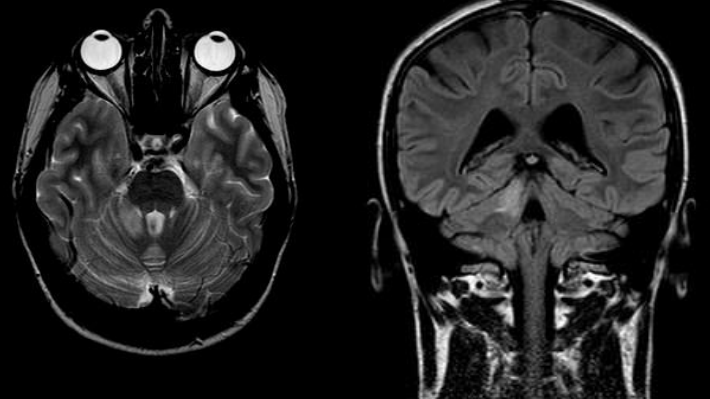
adult



adult



adult

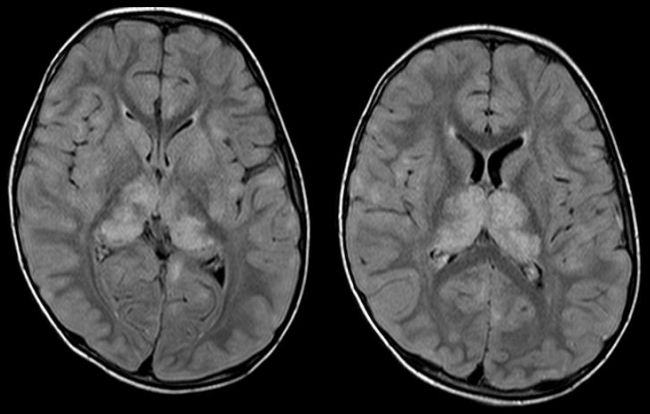


adult

Maciej Juryńczyk

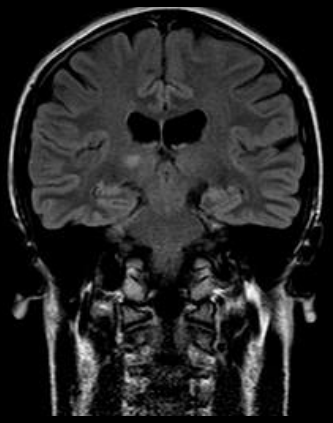
Basal ganglia/thalamic lesions in MOG-IgG1+ve patients

2yr child

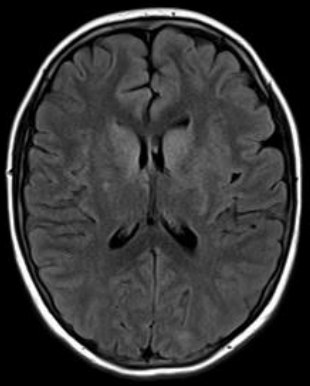


11yr child

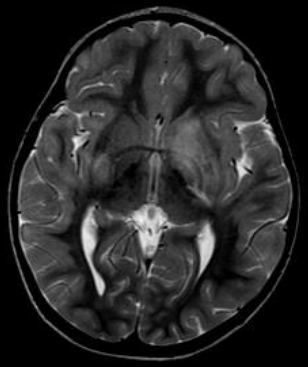
adult



14yr child

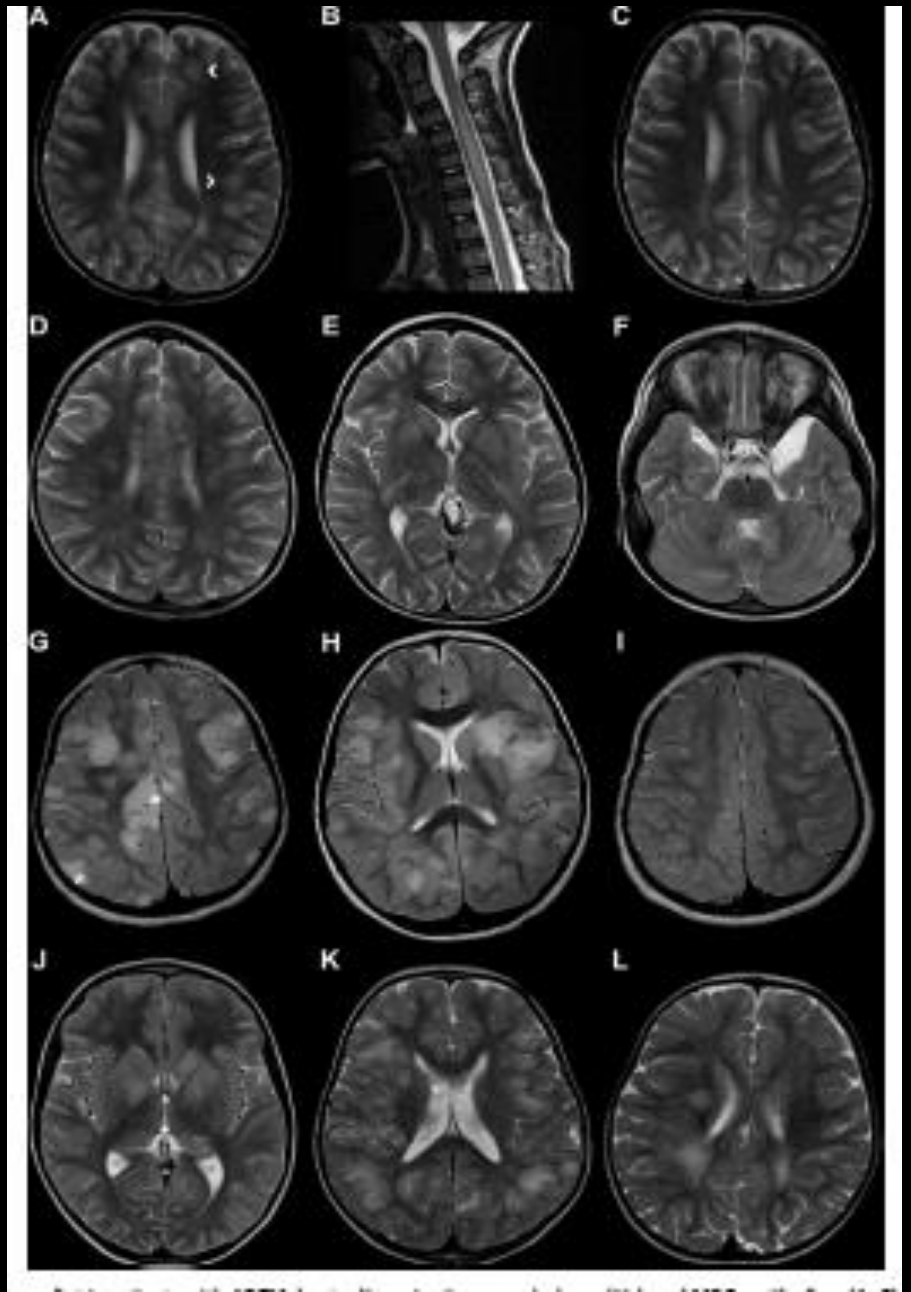


3yr child

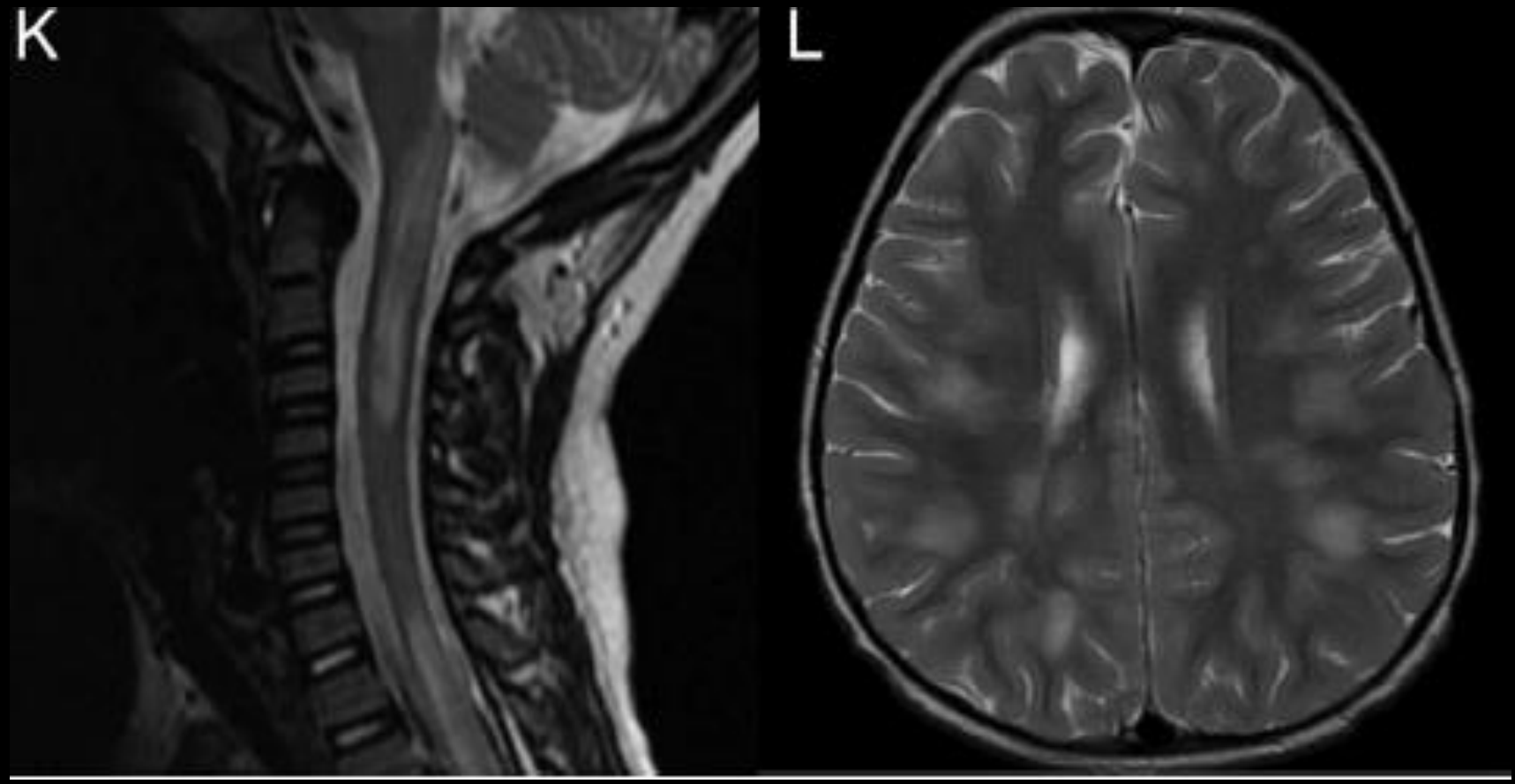


MOG-Ab with ADEM

Baumann M et al, J NNP 2015



Lechner et al JNNP 2015
Paediatric MOG ab



Brain MRI MOG-Ab disease:

fluffy, large, bilateral,
brainstem, cerebellar peduncles,
basal ganglia, thalamus

MRI MOG-Ab vs AQP4-Ab disease

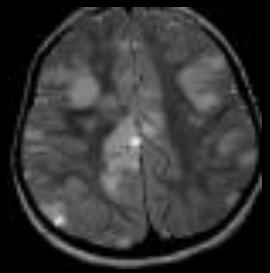
Similar to AQP4-Ab disease

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

fluffy lesions (adults)

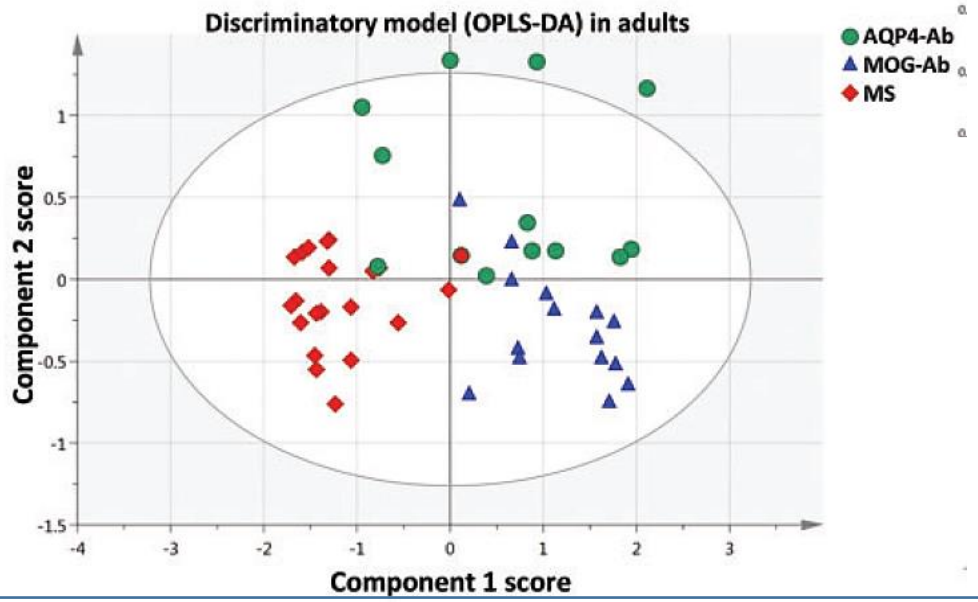
bilateral cerebellar peduncle lesions
thalamic/basal ganglia lesions

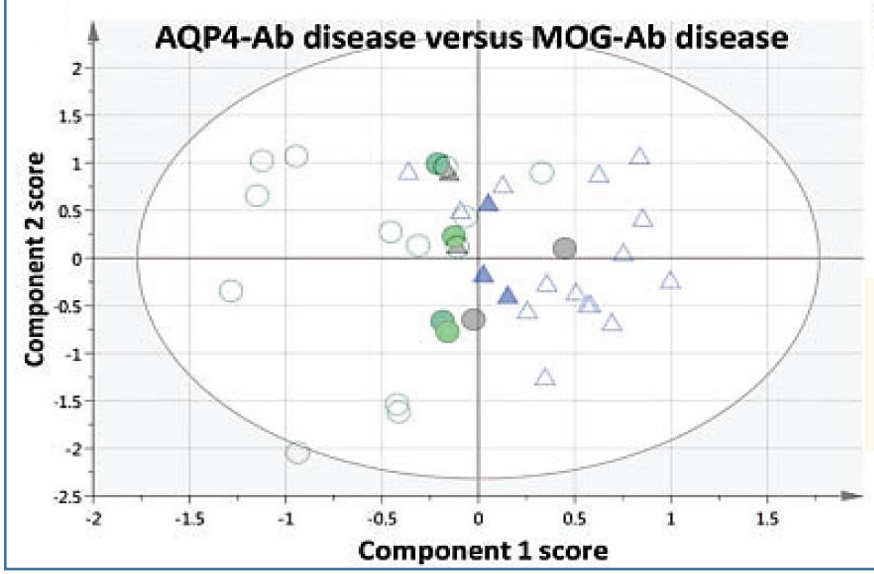
anterior and bilateral ON (papillitis)



Maciej Juryńczyk

Poor differentiation of MOG-Ab from AQP4-Ab disease

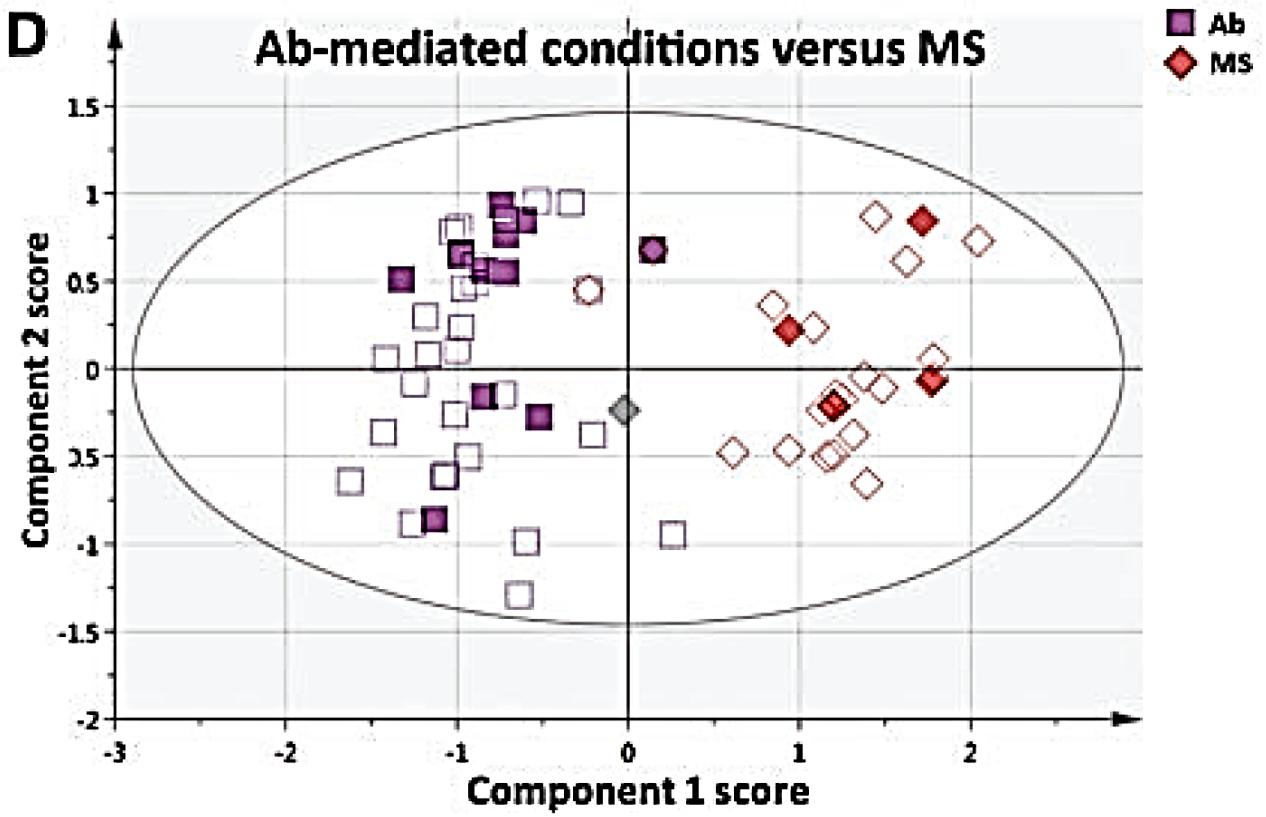




	AQP4-Ab NMOSD	MOG-Ab NMOSD
AQP4-Ab NMOSD	4	2
MOG-Ab NMOSD	2	3

But antibody disease (AQP4 and MOG) differentiates from MS

Jurynczyk Brain 2017;140:617-627



But antibody disease (AQP4 and MOG) differentiates from MS

Jurynczyk Brain 2017;140:617-627

9.6% those w MOG-Ab brain lesions Barkhof criteria

Matthews criteria for MS versus NMOSD

Lesions:

adjacent to lateral ventricle and in the inferior temporal lobe,
or Dawson's finger
or S-shaped U fibre lesion

Vs MS	APQ4-Ab	MOG-Ab
Sensitivity	**91-92%**	**91%**
Specificity	**87-96%**	**95%**
PPV	**91-98%**	**98%**
NPV	**86-87%**	**83%**

MOG-Ab disease	AQP4-Ab disease	MS
Ab mediated	Ab mediated	T cell mediated
myelin	astrocytes	myelin

Conclusion MRI in NMOSD

- NMOSD consists of AQP4-Ab disease, MOG-Ab disease, Ab negative disease

- 2015 diagnostic criteria more reliant on MRI if no AQP4-Abs
- long lesions typical (SC, ON, CC, CST)
- typical lesions: area postrema, brainstem, periependymal, diencephalon,

- non-specific wml or normal brain MRI common

- MS MRI criteria not accurate to distinguish from NMOSD
  but MS likely if: lat ventricle and inf temporal lobe lesions,
  or Dawsons fingers
  or S shaped juxtacortical lesions

- 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, normal lesional myo-inositol

- MOG-Ab disease: similar to AQP4-Abs, more lesions:
  fluffy, conus, cerebellar peduncles, thalamus

- clinically silent lesions uncommon in NMOSD, typical for MS