GEAI 2016

Anticorps anti-MOG: applications cliniques

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Ann Neurol. 2000 Jun;47(6):707-17.

Heterogeneity of multiple sclerosis lesions: implications for the pathogenesis of demyelination.

Lucchinetti C, Brück W, Parisi J, Scheithauer B, Rodriguez M, Lassmann H.
Department of Neurology, Mayo Clinic, Rochester, MN, USA

➔ 4 types de lesions anatomopathologiques

Groupe II ➔ dépôts Ig + C'
➔ efficacité des plasmaphérèses

➔ Rôle pathogène probable des anticorps

➔ Mais quelle cible antigénique ??

The NEW ENGLAND JOURNAL of MEDICINE

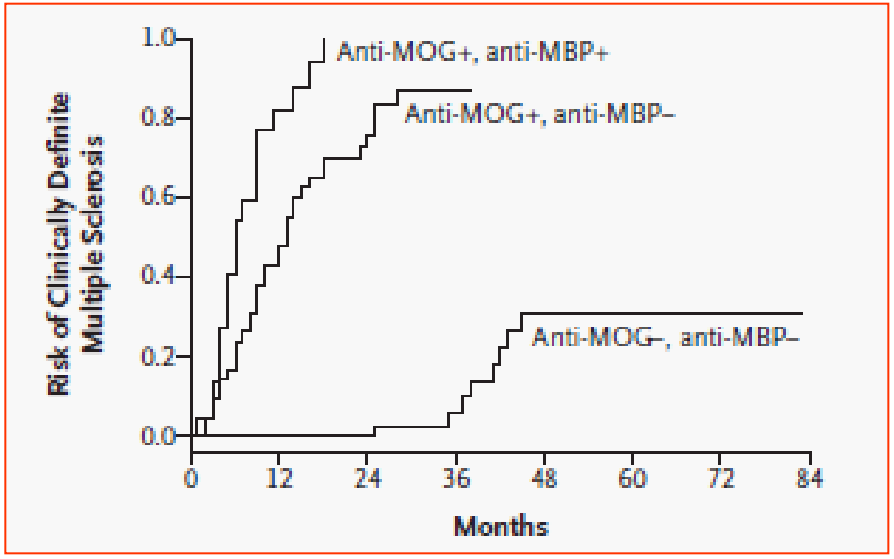
ORIGINAL ARTICLE

Antimyelin Antibodies as a Predictor of Clinically Definite Multiple Sclerosis after a First Demyelinating Event

Thomas Berger, M.D., Paul Rubner, M.D., Franz Schautzer, M.D., Robert Egg, M.D., Hanno Ulmer, Ph.D., Irmgard Mayringer, M.D., Erika Dilitz, M.D., Florian Deisenhammer, M.D., and Markus Reindl, Ph.D.

N Engl J Med. 2003; 349: 139-145

Fig 1. Risk of Clinically Definite MS, According to Ab Status.



Anti-MOG- / anti-MBP- ➔ 23%

Anti-MOG+ / anti-MBP- ➔ 83%

Anti-MOG+ / anti-MBP+ ➔ 95%

Anti-MOG and anti-MBP IgM identification / western blot

Mais résultats non confirmés:

Similar low frequency of anti-MOG IgG and IgM in MS patients and healthy subjects.
Lampasona V, Franciotta D, Furlan R, Zanaboni S, Fazio R, Bonifacio E, Comi G, Martino G.
Neurology. 2004 Jun 8;62(11):2092-4.

Ni même par l'équipe initiale…

Anti-myelin antibodies do not allow earlier diagnosis of multiple sclerosis.
Lim ET, Berger T, Reindl M, Dalton CM, Fernando K, Keir G, Thompson EJ, Miller DH, Giovannoni G.
Mult Scler. 2005 Aug;11(4):492-4.

Epitopes conformationnels

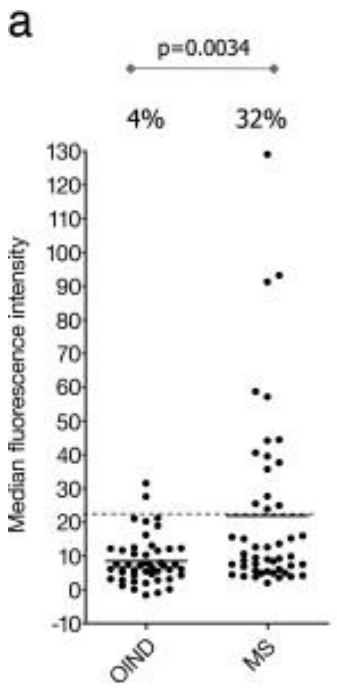
PNAS

Identification of a pathogenic antibody response to native myelin oligodendrocyte glycoprotein in multiple sclerosis

Dun Zhou*, Rajneesh Srivastava*, Stefan Nessler*, Verena Grummel*, Norbert Sommer†, Wolfgang Brück‡, Hans-Peter Hartung*, Christine Stadelmann‡, and Bernhard Hemmer*§

*Department of Neurology, Heinrich Heine University, 40225 Dusseldorf, Germany; †Department of Neurology, Philipps University, 35033 Marburg, Germany; and ‡Institute of Neuropathology, Georg August University, 37099 Gottingen, Germany

➔ **Cell based assay expressing natively folded MOG**

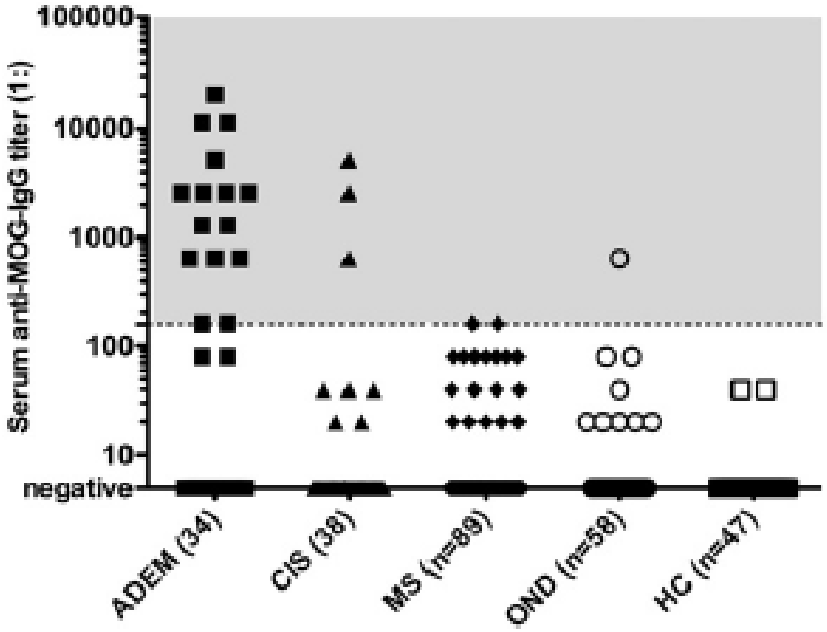


Détection d'Ac dirigés contre les épitopes conformationnels de la MOG augmente la spécificité

Proc Natl Acad Sci U S A. 2006 Dec 12;103(50):19057-62

Formes cliniques associées aux Ac anti-MOG

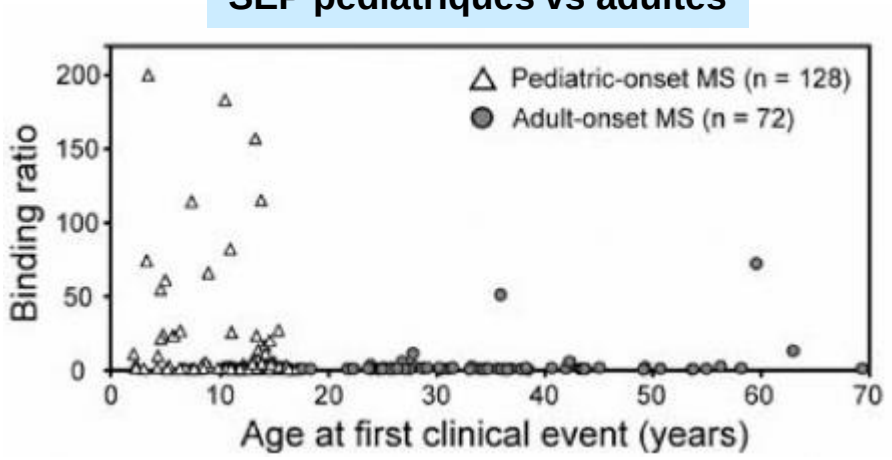
Maladies démyélinisantes du SNC



Anti-MOG sont plus fréquents au cours d'une ADEM (40%) que d'une SEP

(Di Pauli t al. Clinical Immunology (2011) 138, 247–254)

SEP pédiatriques vs adultes



Anti-MOG sont plus fréquents lors de SEP à début pédiatrique vs adulte

(McLaughlin et al J Immunol 2009 Sep 15;183(6):4067-76)

Les Ac anti-MOG sont plus fréquents chez l'enfant

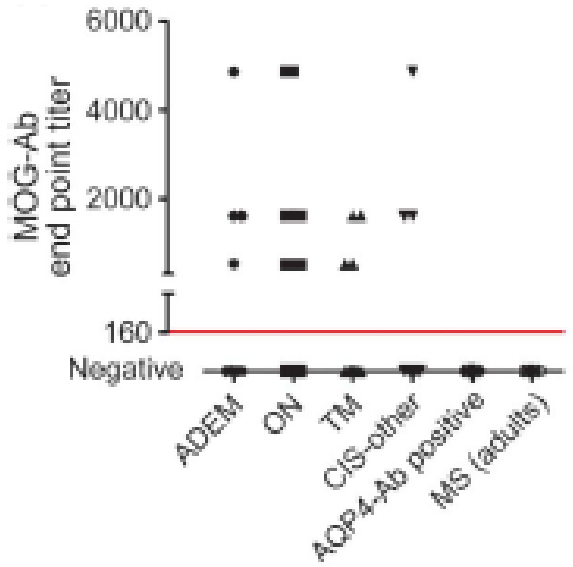
Ketelslegers IA, Mult Scler. 2015 Oct;21(12):1513-20.
Hacohen Y; Neurol Neuroimmunol Neuroinflamm. 2015 Mar 12;2(2):e81

Myelin oligodendrocyte glycoprotein antibodies are associated with a non-MS course in children

Hacohen Y, Neurol Neuroimmunol Neuroinflamm. 2015 Mar 12;2(2):e81.

65 enfants avec un 1er événement démyélinisant

- **12 ADEM**
- **24 névrites optiques**
- **18 myélites transverses**
- **11 autres CIS**



23/65 (35%) = anti-MOG+

9% des anti-MOG+ → SEP (2/23)

38% des anti-MOG- → SEP (16/42)

Ac anti-MOG = transitoires dans l'ADEM / persistants dans la SEP

Seule une minorité (2-9%) des enfants MOG+ vont développer une SEP

Mader et al. Journal of Neuroinflammation 2011, 8:184
http://www.jneuroinflammation.com/content/8/1/184

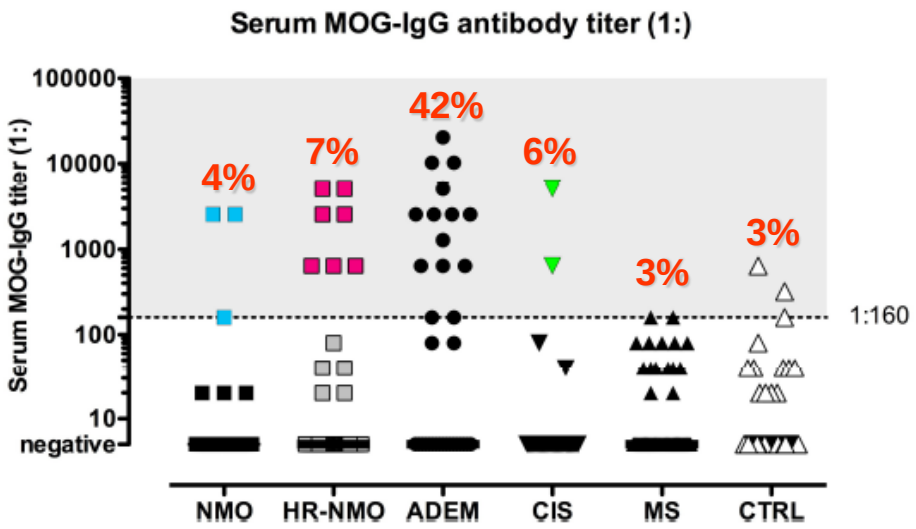
JNI JOURNAL OF NEUROINFLAMMATION

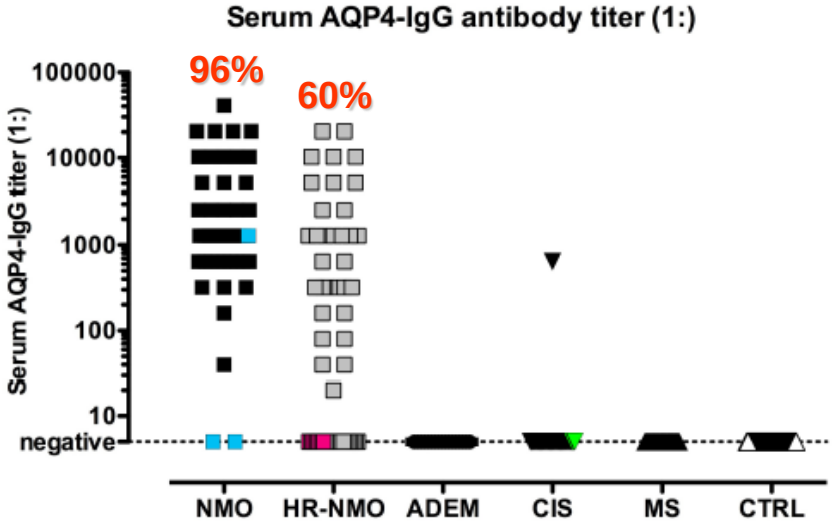
RESEARCH Open Access

Complement activating antibodies to myelin oligodendrocyte glycoprotein in neuromyelitis optica and related disorders

Simone Mader[1], Viktoria Gredler[1], Kathrin Schanda[1], Kevin Rostasy[2], Irena Dujmovic[3], Kristian Pfaller[4], Andreas Lutterotti[1], Sven Jarius[5], Franziska Di Pauli[1], Bettina Kuenz[1], Rainer Ehling[1], Harald Hegen[1], Florian Deisenhammer[1], Fahmy Aboul-Enein[6], Maria K Storch[7], Peter Koson[8,9], Jelena Drulovic[3,10], Wolfgang Kristoferitsch[11], Thomas Berger[1] and Markus Reindl[1*]

MOG-IgG and AQP4-IgG et maladies démyélinisantes du SNC





➔ Anti-MOG présents chez 4-7% des NMOSD

➔ Anti-MOG et anti-AQP4 Abs sont mutuellement exclusifs

Mader S, J Neuroinflammation. 2011 Dec 28;8:184.

OPEN

Distinction between MOG antibody-positive and AQP4 antibody-positive NMO spectrum disorders

Presence of anti-MOG IgG (16/215 NMOSD= 7.4%)

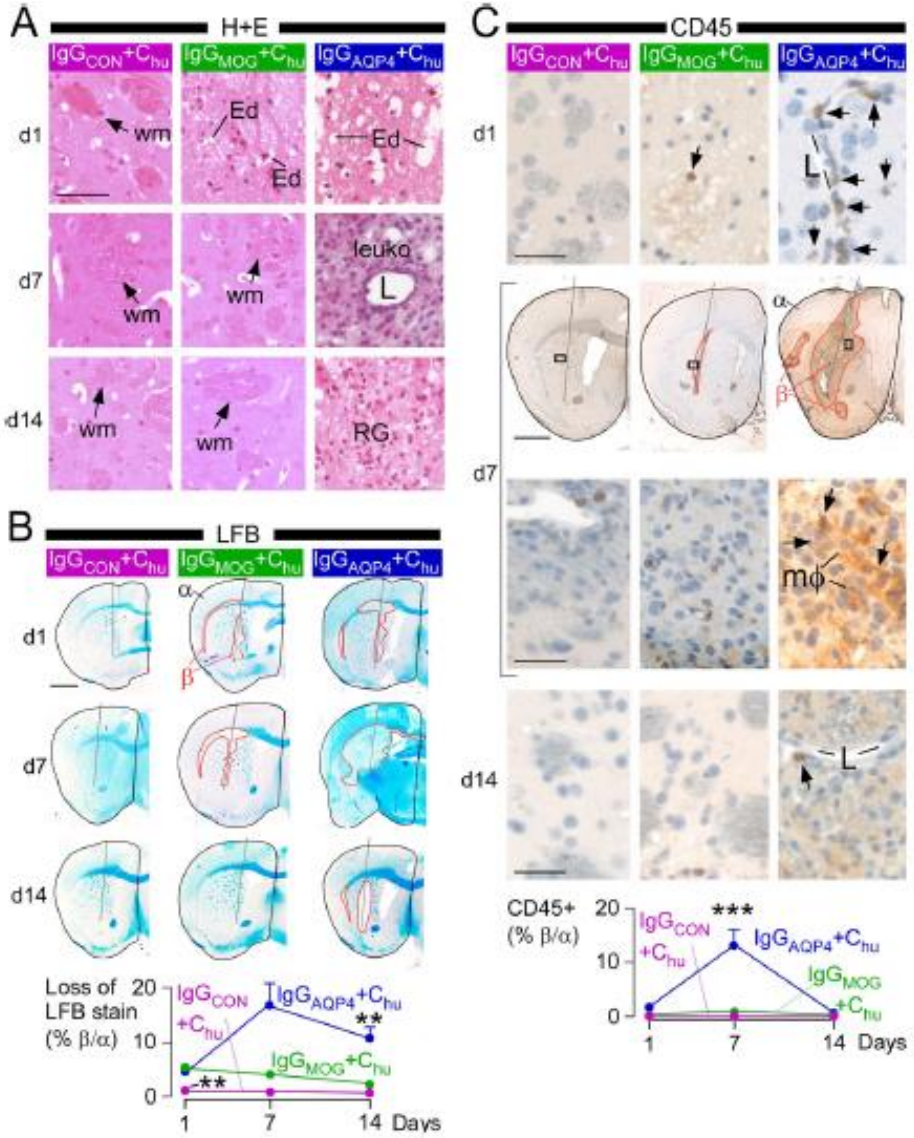
- **Homme > Femme**
- **Âge de début plus précoce**
- **Phénotype plus restreint** (NO > myélite)
- **Plus souvent NO bilatérale**
- **Nombre de poussées plus faible**
- **Meilleure récupération fonctionnelle** (pas toujours)

(Sato DK, Neurology. 2014 Feb 11;82(6):474-81)

RESEARCH Open Access

Neuromyelitis optica MOG-IgG causes reversible lesions in mouse brain

Samira Saadoun[1], Patrick Waters[2], Gregory P Owens[3], Jeffrey L Bennett[3,4], Angela Vincent[2] and Marios C Papadopoulos[1*]



Anti-AQP4

- **Myelin loss** (C' mediated)
- **inflammation**
- **neuronal and astrocyte death**
- **limited recovery at 2 weeks**

Anti-MOG

- **Myelin loss** (independant of C')
- **no inflammation**
- **no neuronal or astrocyte death**
- **recovery within 2 weeks**

Explanation for better outcome of anti-MOG patients ?

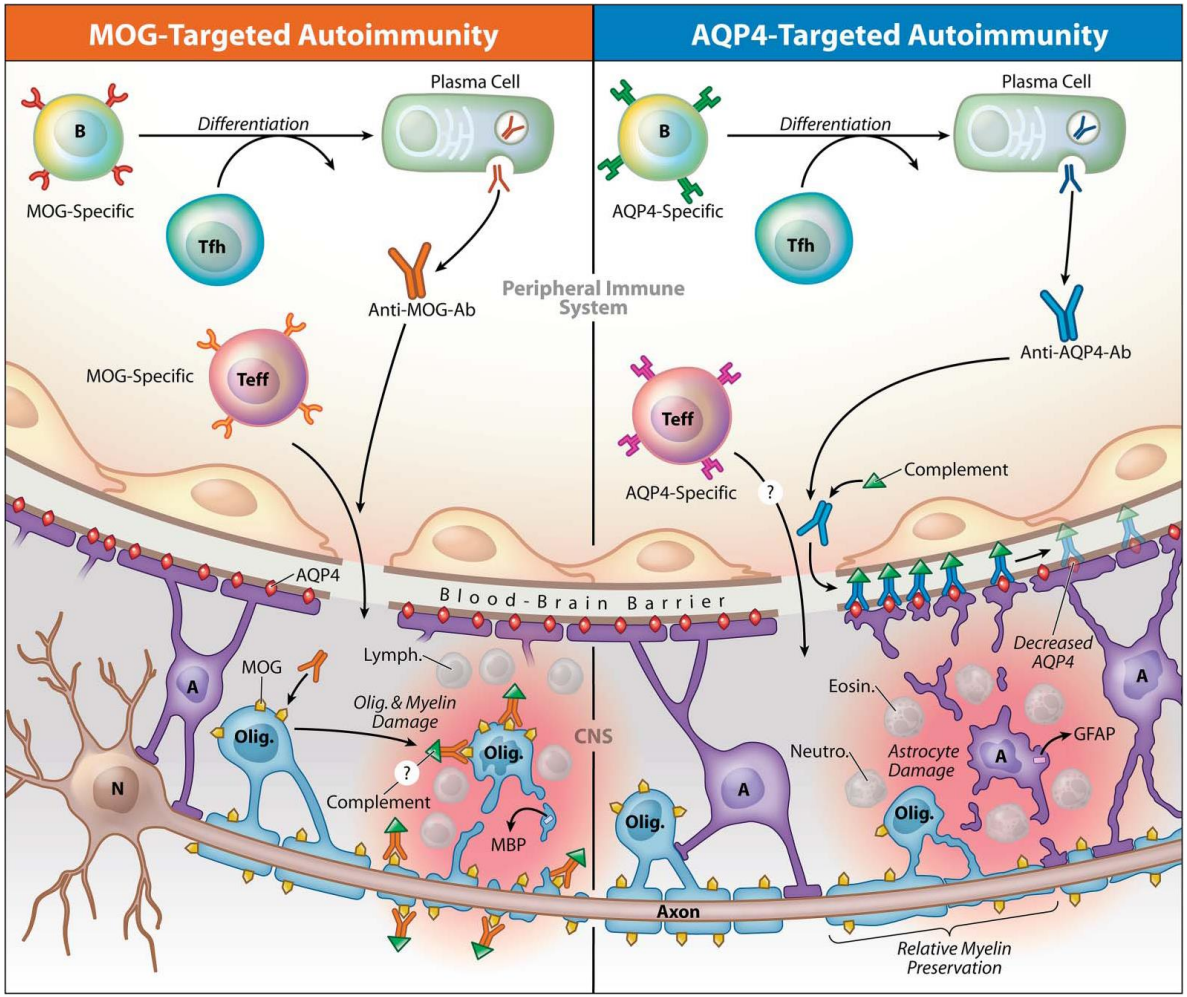
Acta Neuropathologica Communications 2014, 2:35

Does MOG Ig-positive AQP4-seronegative opticospinal inflammatory disease justify a diagnosis of NMO spectrum disorder?

Scott S. Zamvil, MD, PhD
Anthony J. Slavin, PhD

Neurol Neuroimmunol Neuroinflamm 2015;2:e62;

Anti-MOG



Anti-AQP4

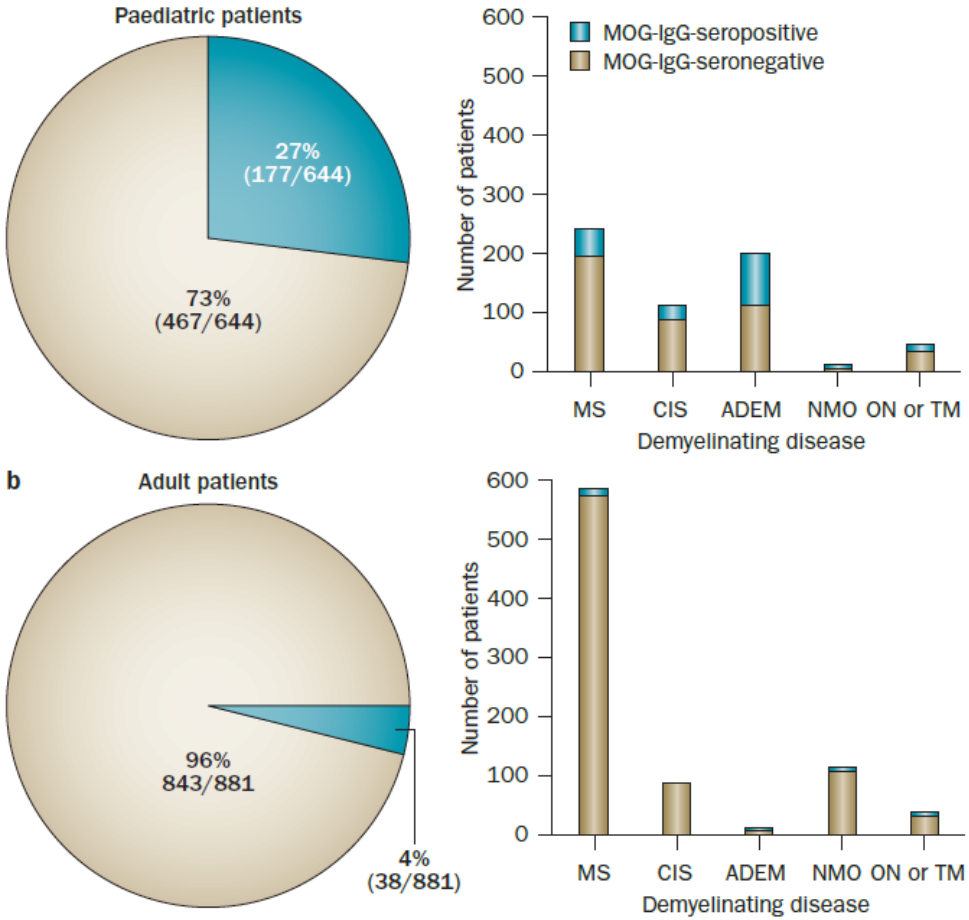
Atteinte primitive de la myéline

Atteinte primitive de l'astrocyte

Nat. Rev. Neurol. 9, 455–461 (2013);

The spectrum of MOG autoantibody-associated demyelinating diseases

Markus Reindl, Franziska Di Pauli, Kevin Rostásy and Thomas Berger



Enfants (27%)

MS	**➔ 4-21%**
ADEM	**➔ 27-47%**
NMOSD	➔ 17-56% (= rare)

Adultes (4%)

MS	**➔ 0-9%**
ADEM	➔ 37-43% (= rare)
NMOSD	**➔ 5-12%**

En résumé…

Les anticorps anti-(native) MOG sont très spécifiques (96-100%) des atteintes inflammatoires démyélinisantes du SNC

Chez l'enfant:

➔ **ADEM (30-50%)**

- ➔ Le plus souvent monophasique
- ➔ Parfois récurrente (MDEM)
- ➔ Évolue rarement vers une SEP

➔ Moins fréquents dans la SEP (4-21%)

Chez l'adulte:

➔ **NMOSD (5-10%)**

- ➔ formes sans anti-AQP4 (20-30%)
- ➔ Meilleur pronostic

➔ Rare dans la SEP (0-9%)

MAAD
=
MOG Ab Associated Demyelination