Neuropädiatrie Kinderspital Luzern

Institut für Sozial- und Präventivmedizin, Universität Bern

Vogelflug: Neuroinflammation

PD Dr. med. Sandra Bigi, MSc

Leitende Ärztin und Abteilungsleitung Neuropädiatrie

RESEARCH ARTICLE   OPEN ACCESS

Retrospective Pediatric Cohort Study Validates NEOS Score and Demonstrates Applicability in Children With Anti-NMDAR Encephalitis

Marc Nikolaus, MD,* Philipp Rausch, PhD,* Kevin Rostásy, MD, Annikki Bertolini, MD, Ronny Wickström, MD,
Jessika Johannsen, MD, Jonas Denecke, MD, Markus Breu, MD, Mareike Schimmel, MD,
Katharina Diepold, MD, Martin Haeusler, MD, Annegret Quade, MD, Andrea Berger, MD,
Hendrik Rosewich, MD, Claudia Steen, MD, Katja von Au, MD, Mona Dreesmann, MD, Carsten Finke, MD,
Frederik Bartels, MD, Angela M. Kaindl, MD, PhD, Markus Schuelke, MD, and Ellen Knierim, MD

Correspondence
Dr. Knierim
ellen.knierim@charite.de

Neurol Neuroimmunol Neuroinflamm 2023;10:e200102. doi:10.1212/NXI.0000000000200102

NEOS: anti-**N**MDAR **E**ncephalitis **O**ne-Year Functional **S**tatus
         Estimates patient outcomes

Design: Retrospective observational study
   59 patients, median age 8y
         Median follow up 20 months

Table 2 Adapted NEOS Score Compiled by Adjusting the Population-Specific Cutoff Median Values of the 5 NEOS Items

NEOS	Original	Adapted
Disease onset to treatment	>28 d	>16 d
Treatment to improvement	>28 d	>15 d
Admission to ICU	Yes/No	Yes/No
MRT pathology	Yes/No	Yes/No
CSF cell count	>20/μL	>13/μL

Figure 1 Validation of the NEOS Score in Children

A. Association of NEOS and mRS
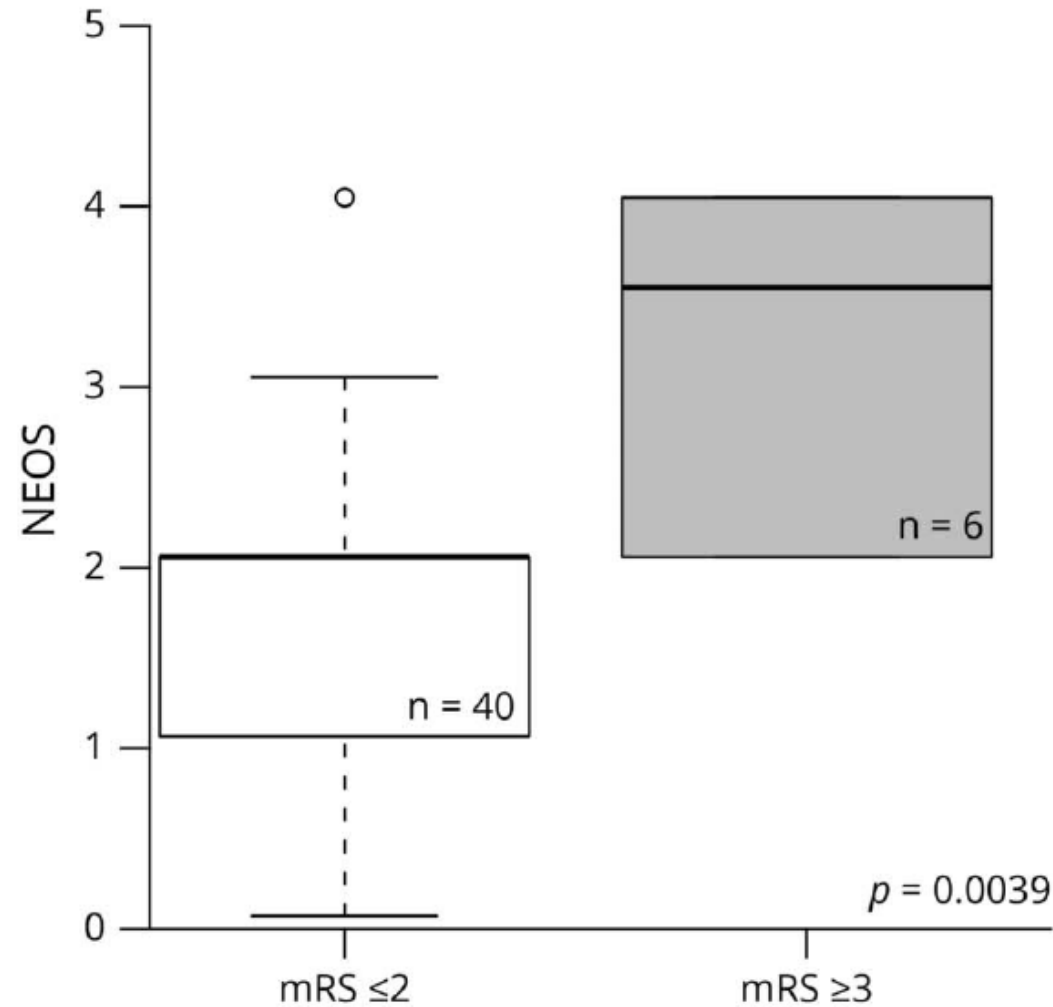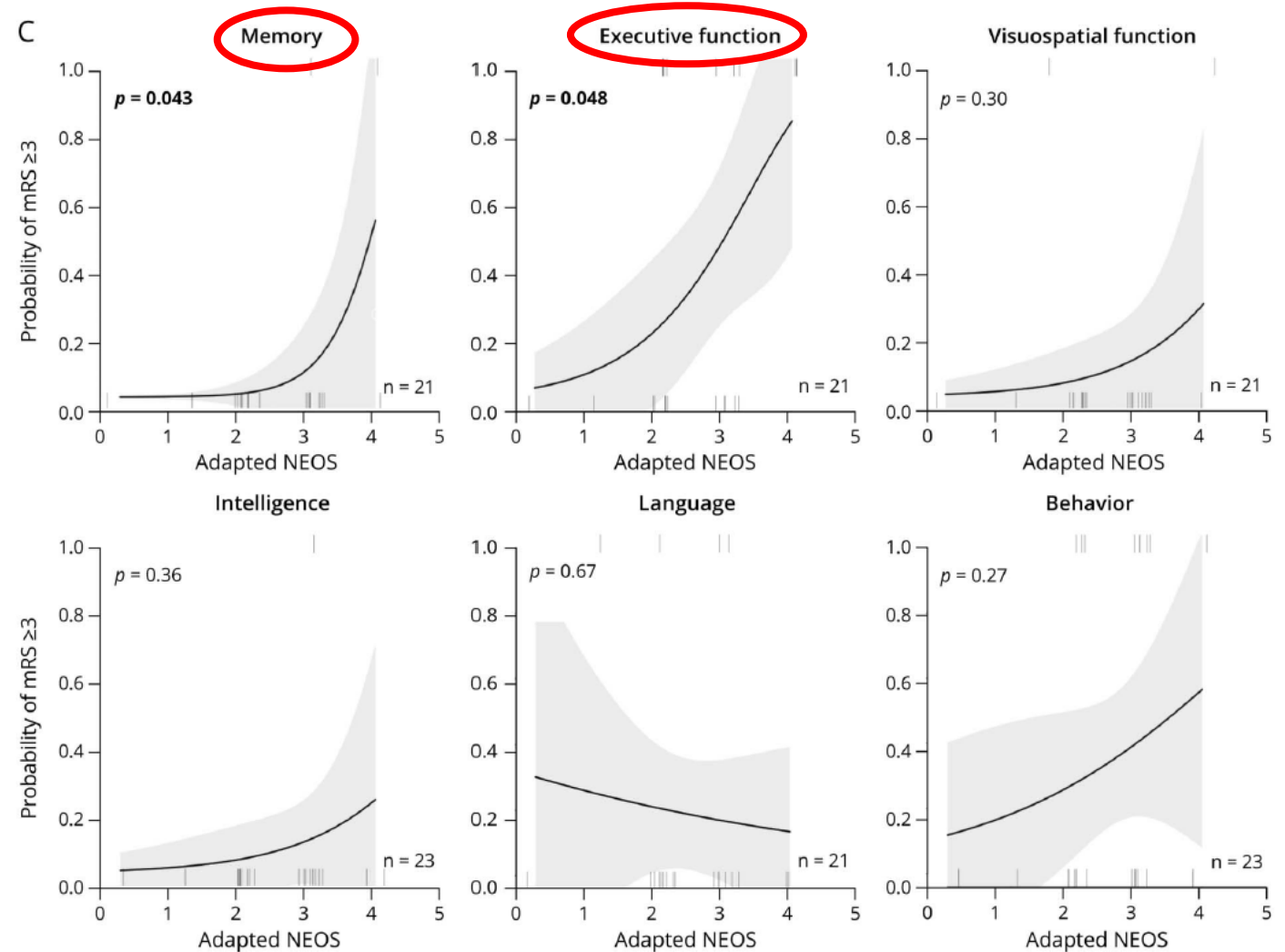
B. Outcome prediction
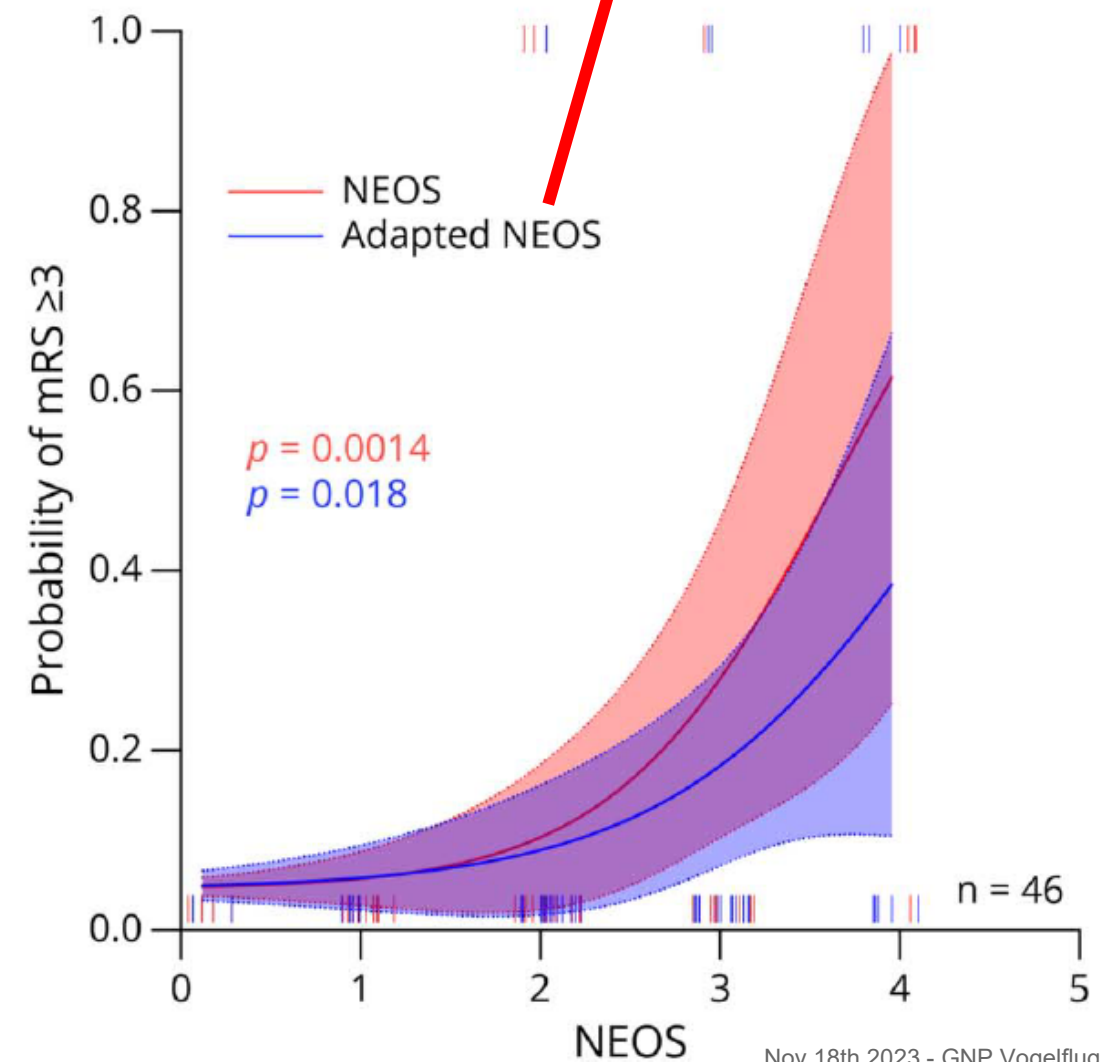
Summary

- Additional influence on predictability

  - Age at disease onset

  - HSE Status

- Supports applicability in children
  - Early identification of patients at risk
- Requires prospective validation

JAMA Neurology | Original Investigation

Use and Safety of Immunotherapeutic Management of *N*-Methyl-D-Aspartate Receptor Antibody Encephalitis
# A Meta-analysis

Margherita Nosadini, MD, PhD; Michael Eyre, MD; Erika Molteni, PhD; Terrence Thomas, MD;
Sarosh R. Irani, MD, PhD; Josep Dalmau, MD, PhD; Russell C. Dale, MD, PhD; Ming Lim, MD, PhD;
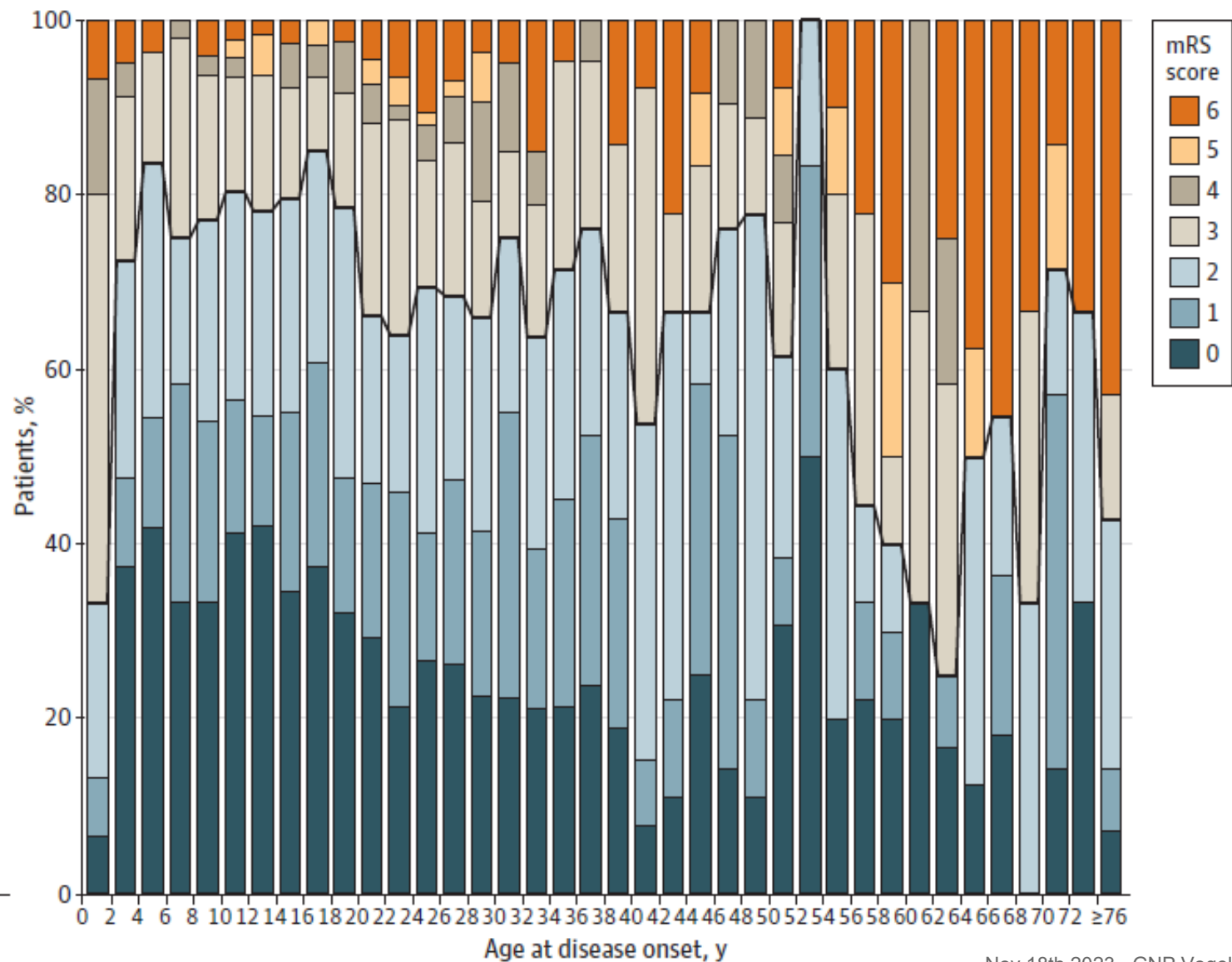and the International NMDAR Antibody Encephalitis Consensus Group

1550 cases

Almost 50% <18y at disease onset

Figure 1. Associations Between Age at Onset and Sex and Modified Rankin Scale (mRS) score
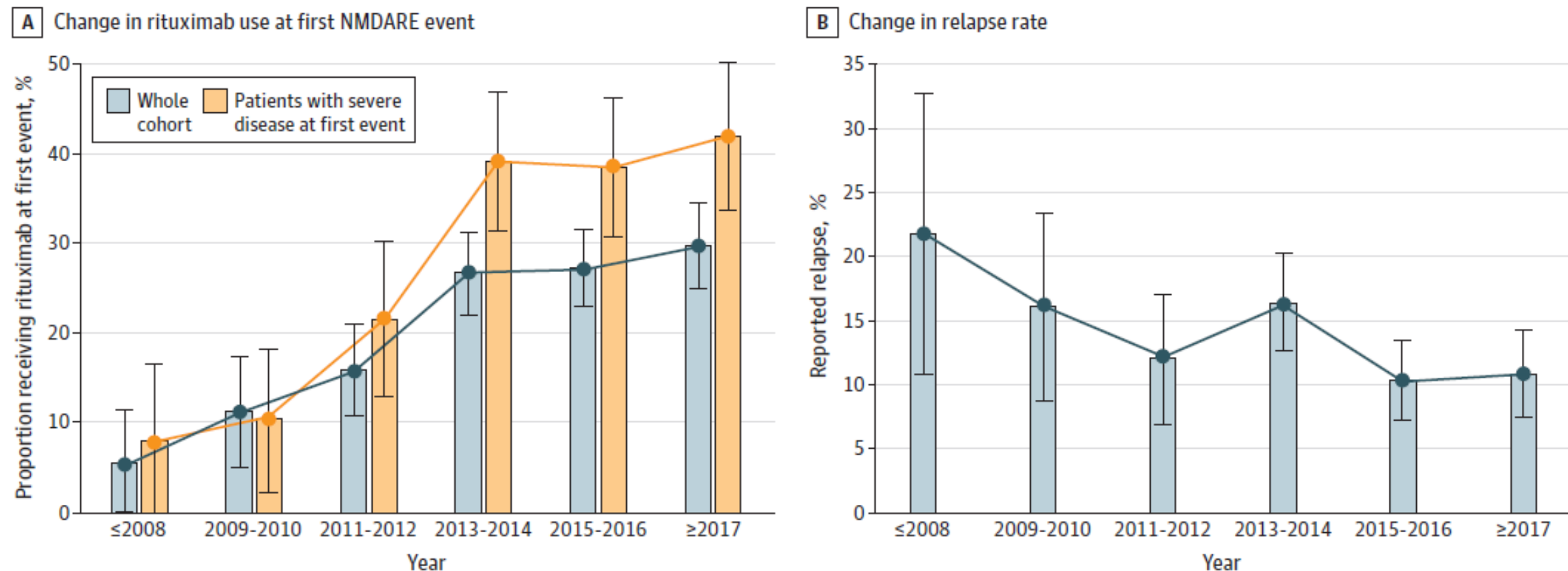

A Age at disease onset by sex
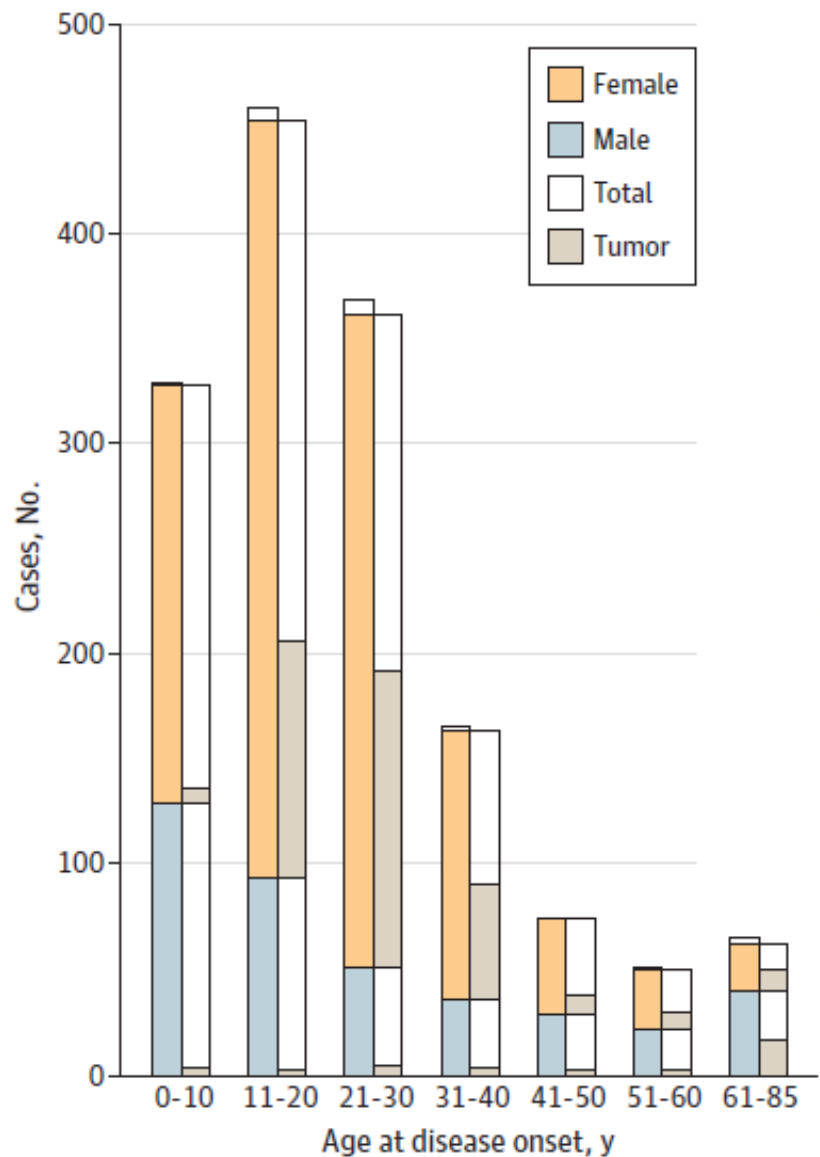
B mRS score by age at disease onset

Figure 3. Changes in Rituximab Use at First *N*-Methyl-D-Aspartate Receptor Antibody Encephalitis (NMDARE) Event and Changes in Relapse Rate Over Time

A Change in rituximab use at first NMDARE event

B Change in relapse rate

Data are displayed over 6 temporal epochs, defined by the year of disease onset, if reported; otherwise, the year of publication was used. A, Proportion of patients receiving rituximab at first event over 6 temporal epochs in the whole cohort (363 of 1484 patients [24.5%]) and in the subset of patients with severe disease (modified Rankin Scale score of 5) at first event (205 of 627 [32.7%]), showing a greater increase in the proportion of rituximab use in patients with severe disease. B, Proportion of patients with reported relapse over 6 temporal epochs (182 of 1380 patients [13.2%]). Error bars represent 95% CIs.

Figure 4. Association Between Modified Anti-NMDAR Encephalitis One-Year Functional Status (NEOS) Score and 1-Year Functional Status
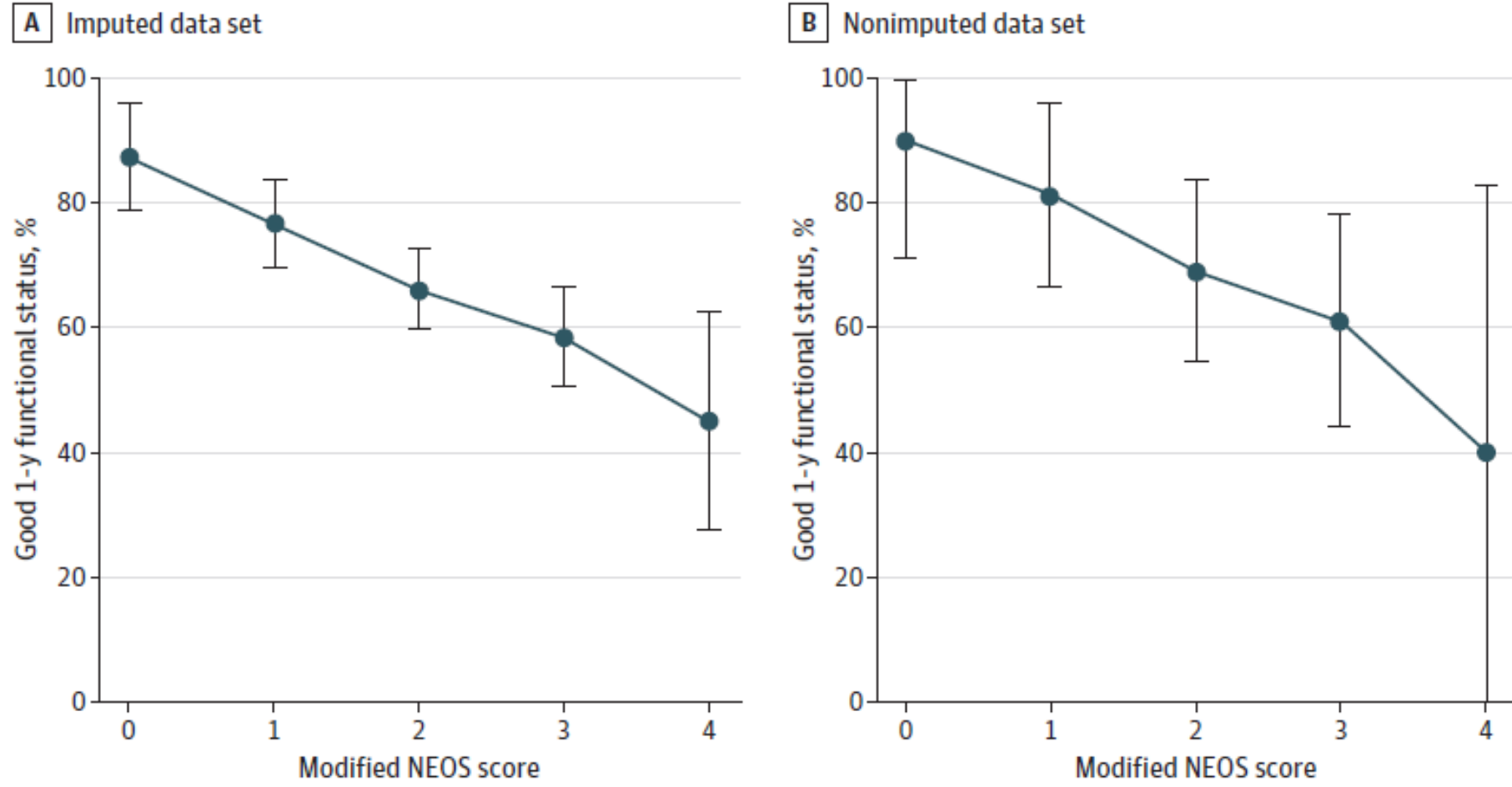
Probability of good functional status (modified Rankin Scale score of 0 to 2) at 1 year after disease onset according to the modified NEOS score for all patients with available data in the imputed (n = 582) and nonimputed (n = 112) data sets. Error bars represent 95% CIs.

Nov 18th 2023 - GNP Vogelflug

Key Points

Question What are the most effective treatments for *N*-methyl-D-aspartate receptor (NMDAR) antibody encephalitis?

Findings In this meta-analysis of individual patient data including 1550 cases, treatment factors at first event that were significantly associated with good functional outcome 12 months from disease onset included first-line treatment with therapeutic apheresis alone, corticosteroids in combination with intravenous immunoglobulin (IVIG), or corticosteroids in combination with IVIG and therapeutic apheresis, while lack of immunotherapy within 30 days of disease onset was significantly associated with poor outcome. Rituximab and long-term IVIG use were significantly associated with nonrelapsing disease course.

Meaning Separate treatment factors are associated with functional outcomes and relapsing disease biology in those with NMDAR antibody encephalitis.

No evidence of disease activity including cognition (NEDA-3 plus) in naïve pediatric multiple sclerosis patients treated with natalizumab

Monica Margoni[1,2] · Francesca Rinaldi[1] · Alice Riccardi[1] · Silvia Franciotta[1] · Paola Perini[1] · Paolo Gallo[1,3]

Table 1 Baseline demographic and clinical features of the 20 pediatric-onset multiple sclerosis patients included in the study

	Mean (SD)
Age at MS onset (years)	13.8 (2.7)
Pre-NTZ disease duration (months)	6.0 (4.0)
Age ad NTZ initiation (years)	14.2 (2.5)
Number of relapses prior NTZ initiation	2.1 (0.3)
Number of Gd+ MRI lesions prior NTZ initiation	1.2 (0.4)
EDSS at NTZ initiation	2.6 (0.7)

NTZ natalizumab, *EDSS* Expanded Disability Status Scale, *Gd* gadolinium, *MRI* magnetic resonance imaging

NEDA-3 plus:
- no clinical relapses
- no increase in disability
- no MRI activity and
- no cognitive decline

Giovannoni G et al; Mult Scler Relat Disord; 2015, 4(4):329–333

No evidence of disease activity including cognition (NEDA-3 plus) in naïve pediatric multiple sclerosis patients treated with natalizumab

Monica Margoni[1,2] · Francesca Rinaldi[1] · Alice Riccardi[1] · Silvia Franciotta[1] · Paola Perini[1] · Paolo Gallo[1,3]
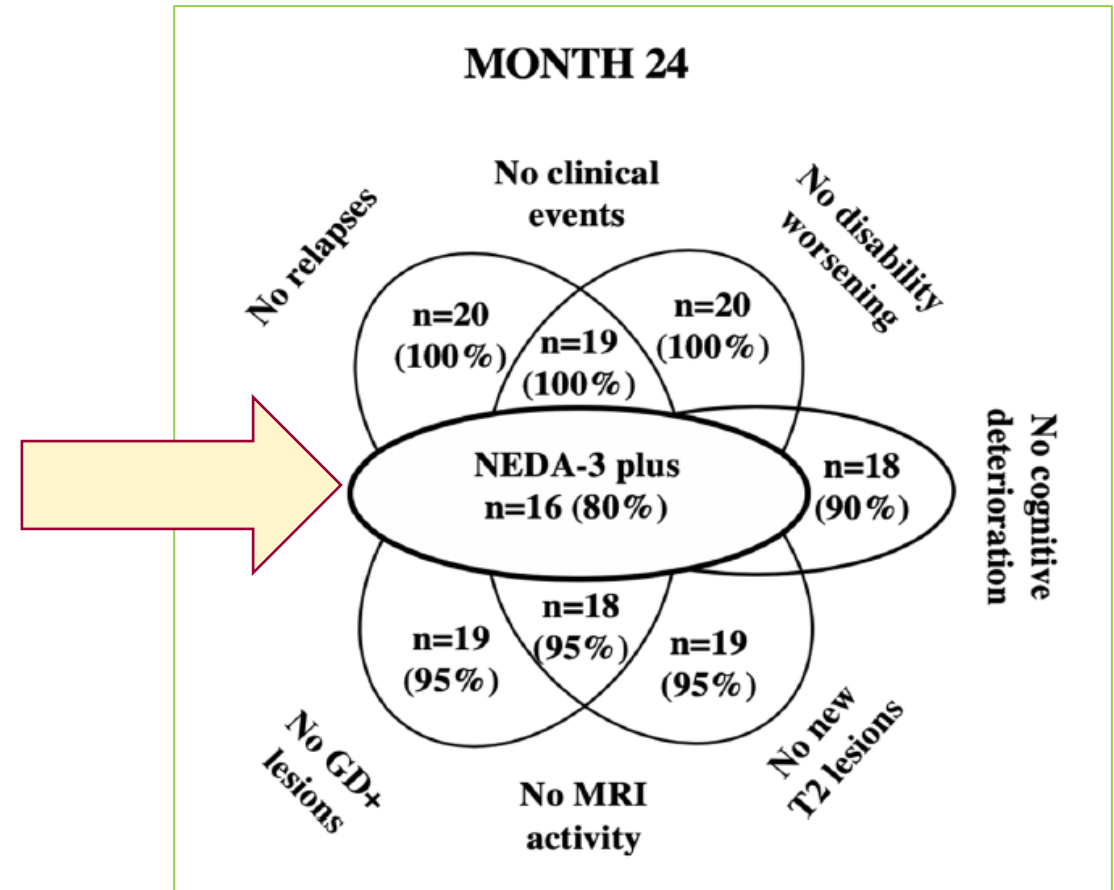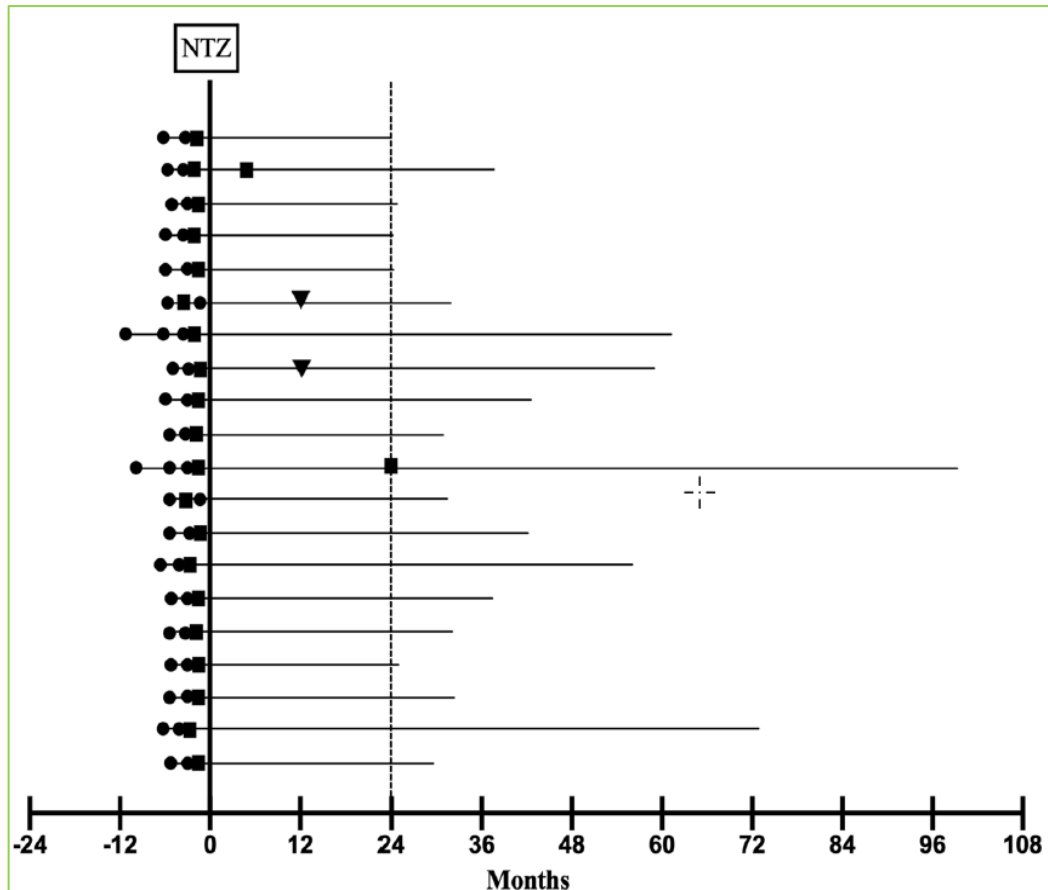
Early effective treatment may protect from cognitive decline in paediatric multiple sclerosis

A. Johnen [a,*,1], C. Elpers [b,1], E. Riepl [a], N.C. Landmeyer [a], J. Krämer [a], P. Polzer [c], H. Lohmann [d], H. Omran [b], H. Wiendl [a], K. Göbel [a,2], S.G. Meuth [a,2]

**Table 1 – Baseline sample characteristics of the n = 19 paediatric MS patients.**

Demographics	Mean (SD)	
Age (years)	15.05 (2.01)	
Sex (f/m)	14/5	
Education (years)	9.73 (1.52)	
Clinical and Paraclinical Measures	**Mean (SD)**	**Median (IQR)**
Disease Duration (months)	12.95 (23.52)	4.00 (9.00)
EDSS	0.50 (0.61)	0.00 (1.00)
Total Number of Relapses	2.68 (1.88)	2.00 (1.00)
Number of Lesions on MRI	21.44 (17.52)	15.50 (27.75)
Treatment		
Naïve, n	3	
Interferon beta-1a, n	16	

Note. EDSS = Expanded Disability Status Scale; Disease Duration = time since first symptoms; IQR=Interquartile range.
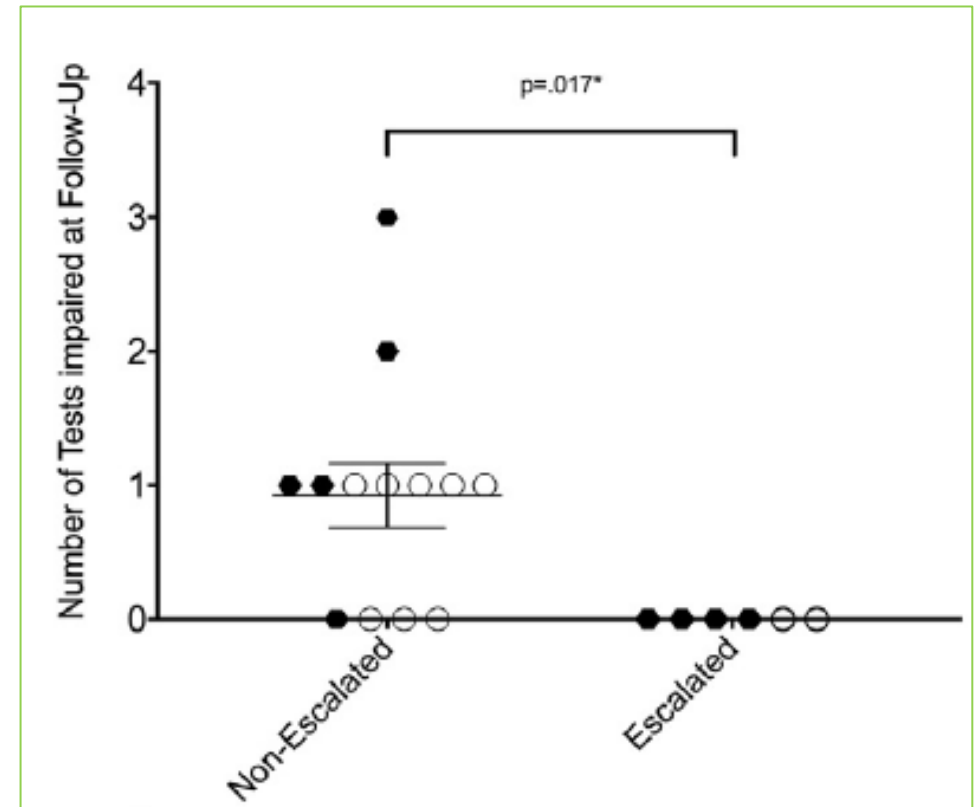
Vielen Dank für die Aufmerksamkeit
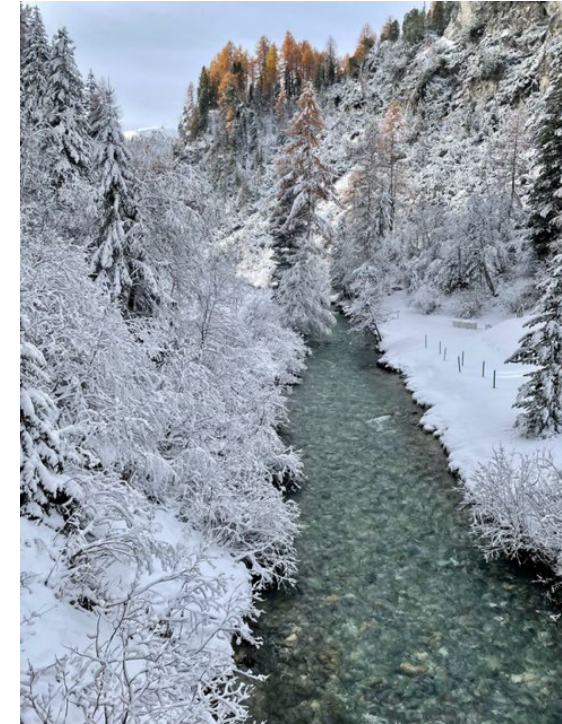
Sandra.Bigi@luks.ch

Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria

Brenda Banwell*, Jeffrey L Bennett*, Romain Marignier*, Ho Jin Kim*, Fabienne Brilot, Eoin P Flanagan, Sudarshini Ramanathan, Patrick Waters, Silvia Tenembaum, Jennifer S Graves, Tanuja Chitnis, Alexander U Brandt, Cheryl Hemingway, Rinze Neuteboom, Lekha Pandit, Markus Reindl, Albert Saiz, Douglas Kazutoshi Sato, Kevin Rostasy*, Friedemann Paul*, Sean J Pittock*, Kazuo Fujihara*, Jacqueline Palace*

Diagnosis of MOGAD (requires fulfilment of A, B, and C)

(A) Core clinical demyelinating event	Optic neuritis* Myelitis† ADEM‡ Cerebral monofocal or polyfocal deficits§ Brainstem or cerebellar deficits¶ Cerebral cortical encephalitis often with seizures‖		
(B) Positive MOG-IgG test	Cell-based assay: serum**	Clear positive††	No additional supporting features required
		Low positive‡‡	• AQP4-IgG seronegative AND • ≥1 supporting clinical or MRI feature
		Positive without reported titre	
		Negative but CSF positive§§	
Supporting clinical or MRI features	Optic neuritis		• Bilateral simultaneous clinical involvement • Longitudinal optic nerve involvement (> 50% length of the optic nerve) • Perineural optic sheath enhancement • Optic disc oedema
	Myelitis		• Longitudinally extensive myelitis • Central cord lesion or H-sign • Conus lesion
	Brain, brainstem, or cerebral syndrome		• Multiple ill-defined T2 hyperintense lesions in supratentorial and often infratentorial white matter • Deep grey matter involvement • Ill-defined T2-hyperintensity involving pons, middle cerebellar peduncle, or medulla • Cortical lesion with or without lesional and overlying meningeal enhancement
(C) Exclusion of better diagnoses including multiple sclerosis¶¶			

Nov 18th 2023 - GNP Vogelflug

# Clinical Guidelines for the Diagnosis of Pediatric Autoimmune Encephalitis

Diagnosis of autoimmune encephalitis (AE) in a developing child is challenging because of

- **Overlapping clinical presentation with other diseases**
- **Complexity of normal behaviour changes**
- **Limited capacity of very young children to describe symptoms**

Adult guidelines are not applicable in children due to differences in

- **Clinical presentations and paraclinical findings**
- **Autoantibody profiles**

Psychiatric disorders?

Infections?
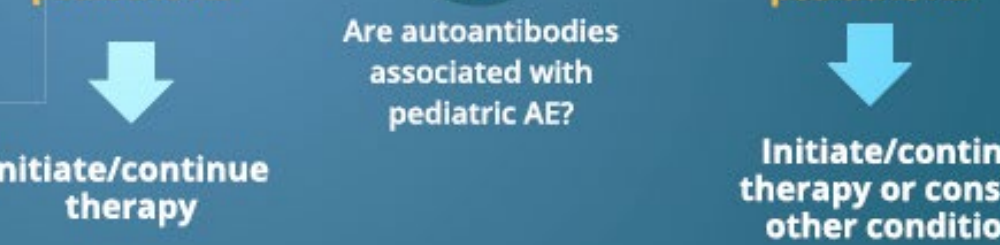
Metabolic diseases?

Inflammation?
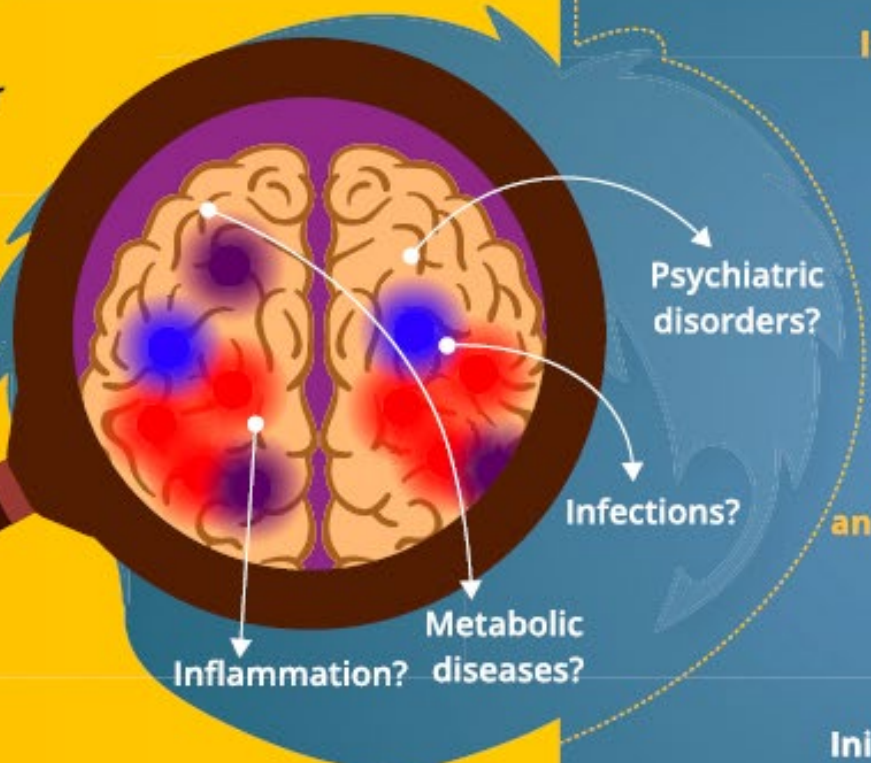
International Autoimmune Encephalitis Working Group has modified existing criteria for adult AE to propose new criteria and an algorithm to guide early diagnosis of pediatric AE

Patient with clinical presentation of pediatric AE

YES / NO — No → **Consider other conditions**

Is paraclinical and antibody testing consistent with AE?

Blood   MRI   CSF   Urine

Initiate/continue immune therapy ← YES / NO ⟶ **Consider other conditions**

Definite antibody-positive pediatric AE ← Yes — **Are autoantibodies associated with pediatric AE?** — No → **Probable antibody-negative pediatric AE**

Initiate/continue therapy

Initiate/continue therapy or consider other conditions

Pediatric AE should be diagnosed based on clinical history as well as paraclinical and autoantibody testing

Nov 18th 2023 - GNP Vogelflug