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Vogelflug „Varia“

Matthias Baumann

Universitätsklinik Innsbruck

Pädiatrie I, Neuropädiatrie

Update entzündliche ZNS-Erkrankungen

- 2024 Revisionen der McDonald-Kriterien für die Diagnose der Multiplen Sklerose
- MS und MOG-IgG
- MS und EBV
- Neuromyelitis optica Spektrum Erkrankungen (NMOSD)

Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria

Xavier Montalban, Christine Lebrun-Frénay, Jiwon Oh, Georgina Arrambide, Marcello Moccia, Maria Pia Amato, Lilyana Amezcua, Brenda Banwell, Amit Bar-Or, Frederik Barkhof, Helmut Butzkueven, Olga Ciccarelli, Jeremy Chataway, Jeffrey A Cohen, Giancarlo Comi, Jorge Correale, Florian Deisenhammer, Massimo Filippi, Julie Fiol, Mark S Freedman, Kazuo Fujihara, Cristina Granziera, Ari J Green, Hans-Peter Hartung, Kerstin Hellwig, Ludwig Kappos, Dorlan Kimbrough, Joep Killestein, Fred Lublin, Romain Marignier, Ruth Ann Marrie, Aaron Miller, Susana Otero-Romero, Daniel Ontaneda, Sudarshini Ramanathan, Daniel Reich, Maria A Rocca, Àlex Rovira, Shiv Saidha, Amber Salter, Jaume Sastre-Garriga, Deanna Saylor, Andrew J Solomon, Maria Pia Sormani, Bruno Stankoff, Mar Tintore, Helen Tremlett, Anneke Van der Walt, Shanthi Viswanathan, Heinz Wiendl, Brigitte Wildemann, Bassem Yamout, Paola Zaratin, Peter A Calabresi, Timothy Coetzee, Alan J Thompson

Lancet Neurol 2025; 24: 850–65

Montalban X, Lebrun-Frénay C, Oh J, et al. Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria. *Lancet Neurol*. 2025;24(10):850-865.

Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria

- The optic nerve can now serve as a fifth anatomical location within the CNS providing evidence for the dissemination in space.
- Besides clinical manifestation as optic neuritis, optic nerve involvement can be illustrated by optical coherence tomography (OCT), visual evoked potential (VEP) and MRI.
- The central vein sign (CVS), paramagnetic rim lesions (PRL), and kappa free-light chain (kFLC) concentrations in CSF can be used, when available, to provide supportive evidence and confer specificity for a diagnosis of multiple sclerosis in specific situations.
- In certain cases, radiologically isolated syndrome (RIS) or neurological symptoms that do not constitute a clear attack or progression of disability can fulfill the criteria for a multiple sclerosis diagnosis.

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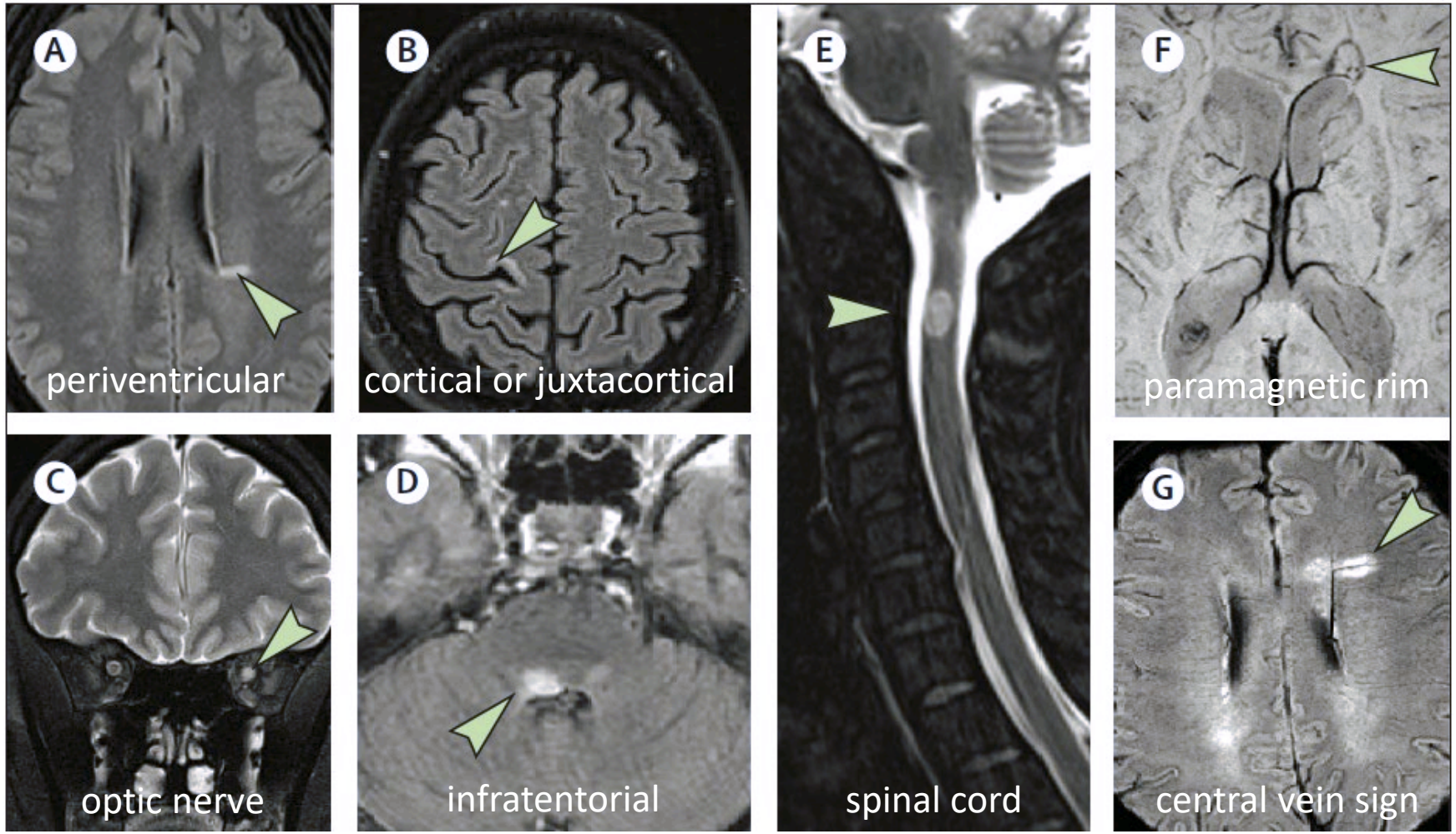
Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria



Dissemination in space (2/5)

- Periventricular
- Cortical/juxtacortical
- Optic nerve
- Infratentorial
- Spinal cord

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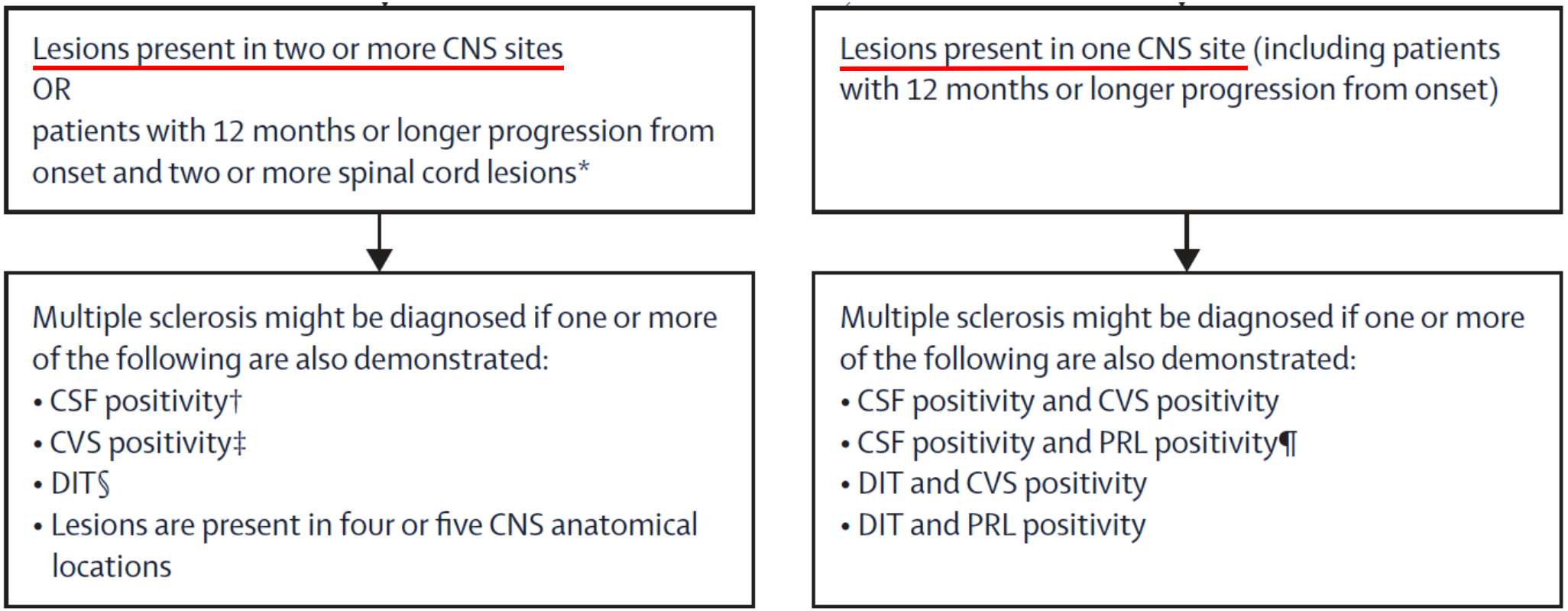
Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria

Diagnostic algorithm for radiologically isolated syndrome and other non-specific presentations



CVS positivity is demonstrated by the presence of six or more lesions with CVS; if fewer than six white matter lesions are seen on MRI, the number of CVS positive lesions should outnumber the CVS negative lesions.

Montalban X, Lebrun-Frénay C, Oh J, et al. Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria. *Lancet Neurol*. 2025;24(10):850-865.

Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria

Paediatric multiple sclerosis

- Paediatric and adult-onset multiple sclerosis can be diagnosed using a single diagnostic criteria framework
- In patients with an acute disseminated encephalomyelitis (ADEM) presentation, a second clinical attack consistent with typical multiple sclerosis attacks or new T2 lesions in typical multiple sclerosis anatomical locations longer than 90 days post-ADEM onset is required before the multiple sclerosis diagnostic criteria can be applied
- In children and adolescents (younger than 18 years), the presence of CVS in more than 50% of T2 lesions strongly supports a diagnosis of multiple sclerosis

Montalban X, Lebrun-Frénay C, Oh J, et al. Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria. *Lancet Neurol*. 2025;24(10):850-865.

Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria

Paediatric multiple sclerosis

- Myelin oligodendrocyte glycoprotein (MOG)-IgG testing using a cell-based assay is strongly recommended in children with incident CNS demyelination younger than 12 years
- In people aged 12 years and older with an incident demyelinating event, MOG-IgG testing using a cell-based assay is recommended in presentations with symptoms not specific to multiple sclerosis or suggestive of myelin oligodendrocyte glycoprotein antibody-associated disease, but not for all people being investigated for multiple sclerosis

Montalban X, Lebrun-Frénay C, Oh J, et al. Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria. *Lancet Neurol*. 2025;24(10):850-865.

Clinical Features of Children With MOG-IgG Who Fulfill Criteria of Multiple Sclerosis and Overlapping Disorders

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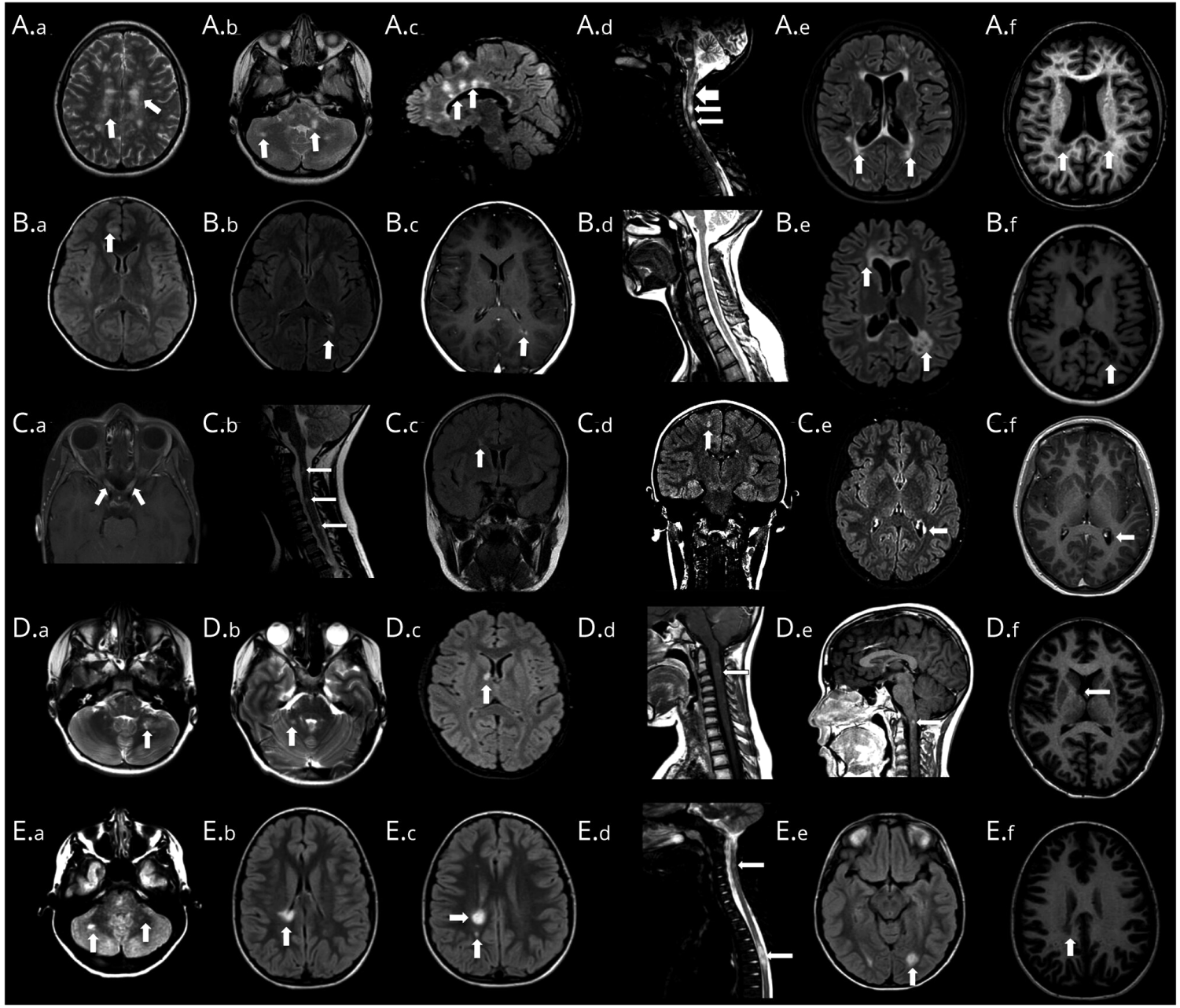
Of 554 children with confirmed ADS (196 with MOG-IgG), 8 (median age 11 years, interquartile range 9–14) harbored MOG-IgG and fulfilled MS criteria: 2 had typical MS and 6 had overlapping MOGAD-MS features at onset, but 5 of the latter group developed an MS-like course during follow-up. Five of 7 patients with assessable samples were Epstein-Barr virus seropositive at disease onset, and all 8 had persistent silent radiologic activity with lesional location and morphology suggestive of MS, leading to initiation of DMT. All initial treatments were well tolerated, but eventually, 7 of 8 children (88%) required high-efficacy DMT.

Of these 8 patients, 7 had CSF-restricted MOG-IgG and one had MOG-IgG in both serum and CSF.



Fonseca EG, Olivé-Cirera G, Chen LW, et al. Clinical Features of Children With MOG-IgG Who Fulfill Criteria of Multiple Sclerosis and Overlapping Disorders.
Neurol Neuroimmunol Neuroinflamm. 2025;12(4):e200400.

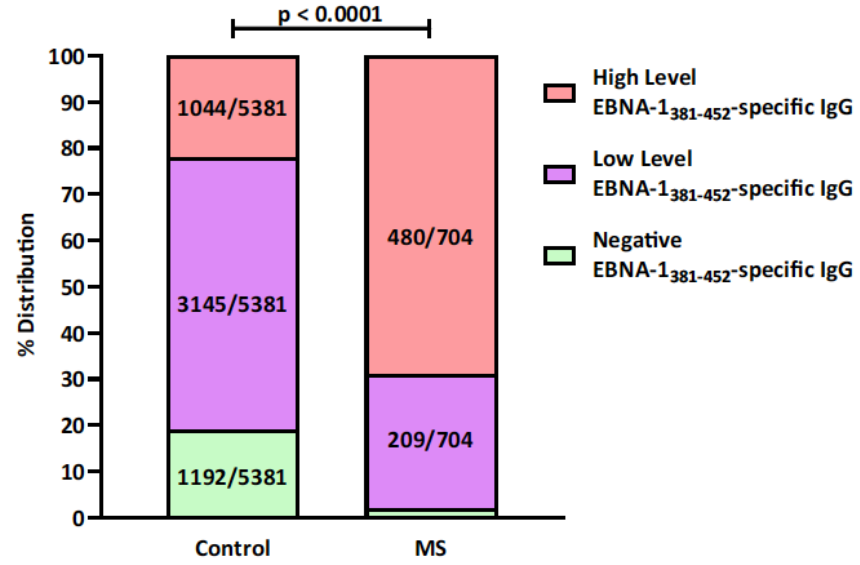
Nature Communications | (2025)16:6416

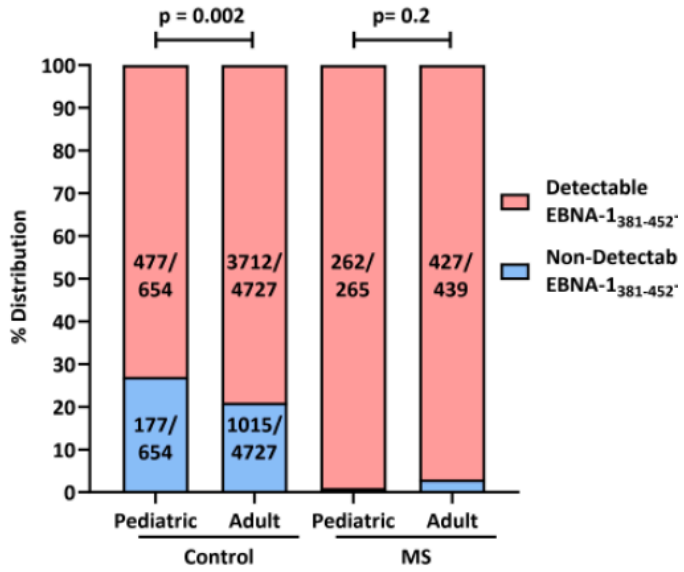
Early identification of individuals at risk for multiple sclerosis by quantification of EBNA-$1_{381-452}$-specific antibody titers

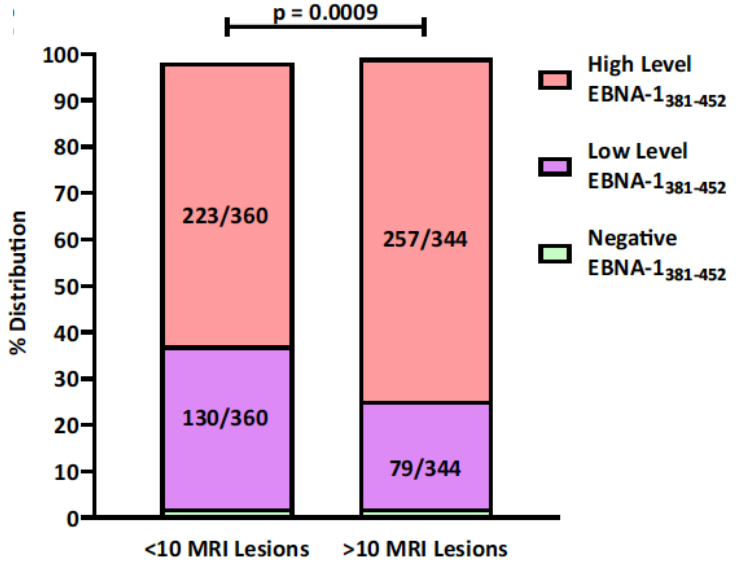
Hannes Vietzen[1], Laura M. Kühner[1], Sarah M. Berger[1], Markus Ponleitner[2,3], Marianne Graninger[1], Charlotte Pistorius[4], Christof Jungbauer[4,5], Markus Reindl[6], Henrieke Saucke[7], Franziska Kauth[7], Eva-Maria Wendel[8], Kevin Rostásy[7], Markus Breu[2,3], Barbara Kornek[2,3], Gabriel Bsteh[2,3], Thomas Berger[2,3], Paulus Rommer[2,3,9] & Elisabeth Puchhammer-Stöckl[1,9]

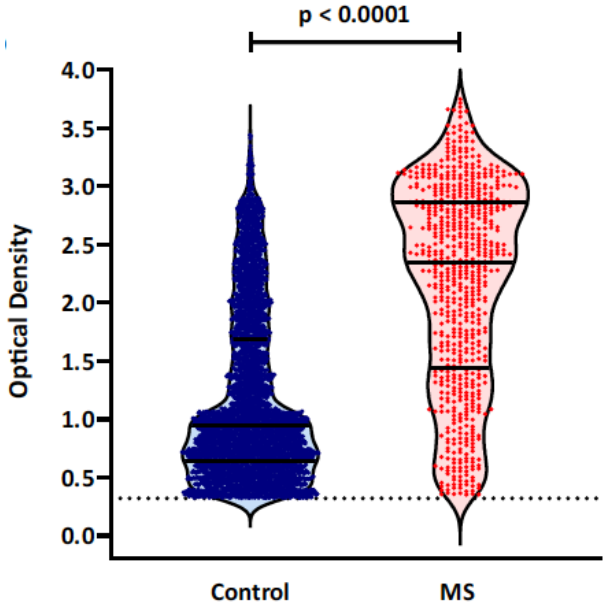
Multiple sclerosis (MS) is an immune-mediated demyelinating disease. Epstein-Barr virus (EBV) encodes for the EBNA-$1_{381-452}$ region that induces autoreactive antibody responses, which are likely critically involved in MS pathogenesis. Here we investigate whether these EBNA-$1_{381-452}$-specific antibodies can serve as a biomarker to identify at-risk individuals for MS. We quantify EBNA-$1_{381-452}$-specific antibody titers from 324 relapsing-remitting MS patients and 324 matched controls in longitudinal follow-up plasma samples, starting from the individual's EBV-seroconversion. In MS patients, significantly elevated EBNA-$1_{381-452}$-specific IgG titers are identified that are increased already as early as nine months after EBV-seroconversion (OR:5.7; 95% CI: 4.1-8.1; $P < 0.0001$) and a median 5.4 years prior to MS diagnosis. Especially, the presence of continuously high EBNA-$1_{381-452}$-specific antibody titers is associated with a more rapid MS diagnosis after EBV-seroconversion ($P < 0.0001$). Thus, the quantification of EBNA-$1_{381-452}$-specific IgG antibody levels may provide a prognostic biomarker to determine the individual's risk for the diagnosis of MS.

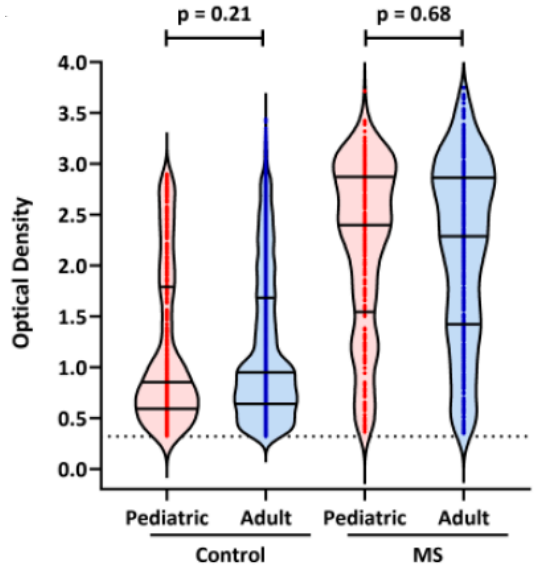
Vietzen H, Kühner LM, Berger SM, et al. Early identification of individuals at risk for multiple sclerosis by quantification of EBNA-$1_{381-452}$-specific antibody titers. *Nat Commun*. 2025;16(1):6416.

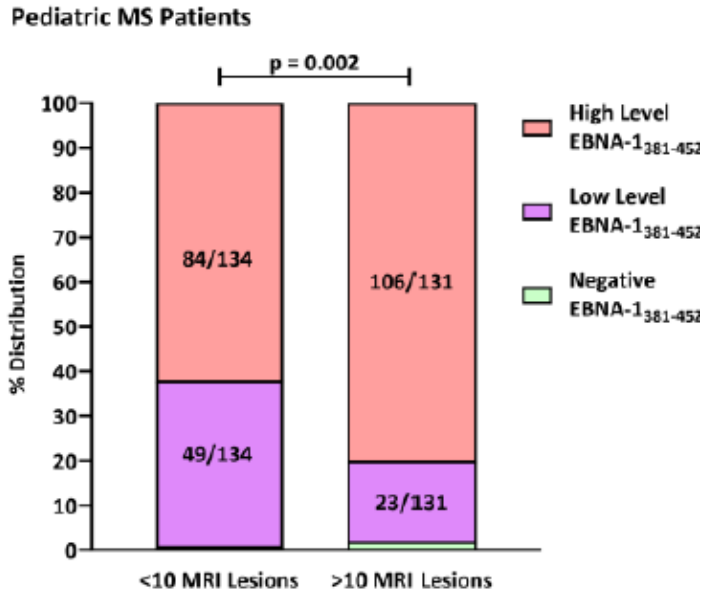








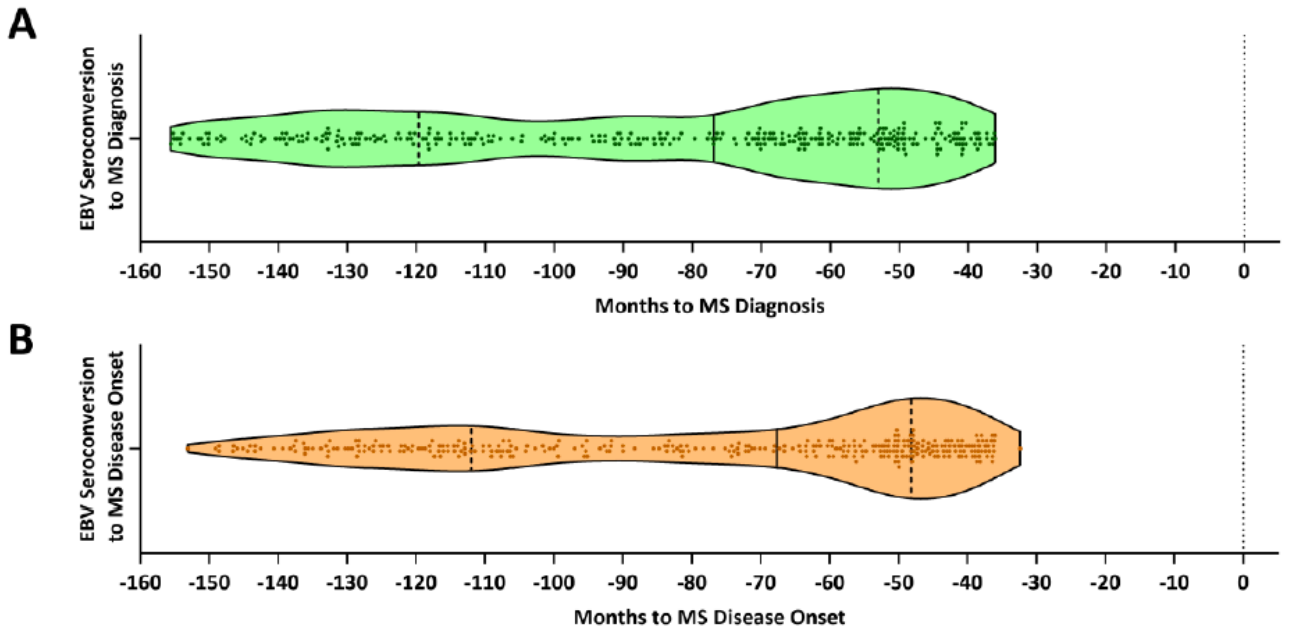


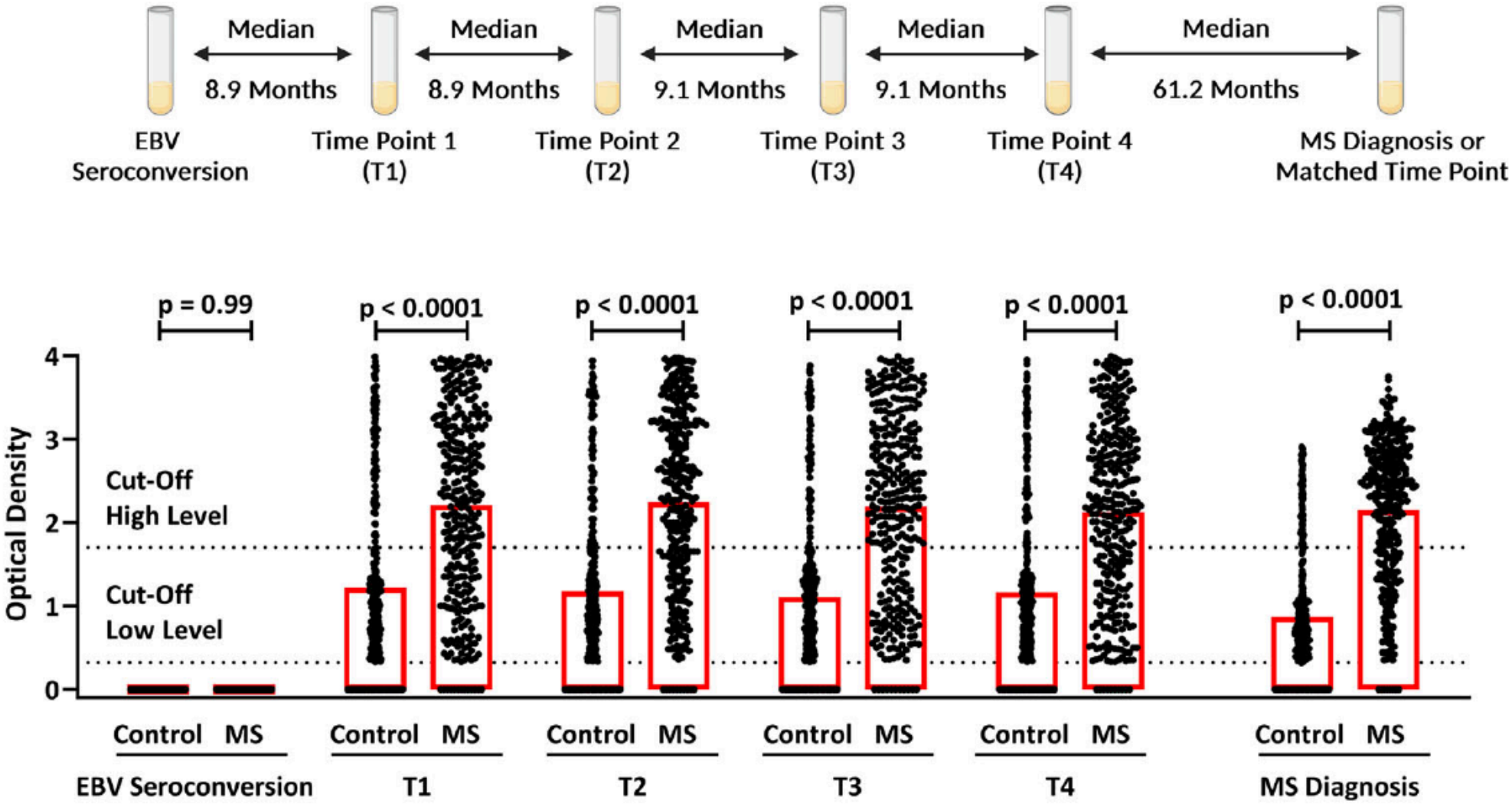


Vietzen H, Kühner LM, Berger SM, et al. Early identification of individuals at risk for multiple sclerosis by quantification of EBNA-$1_{381-452}$-specific antibody titers. *Nat Commun*. 2025;16(1):6416.

In 324 (46%) of the MS patients, the time point of EBV seroconversion could be retrospectively identified, and follow-up plasma samples were available in a 6–12 (median: 8.9) month interval from EBV seroconversion to the time point of MS diagnosis. MS was diagnosed 36–156 (median: 76.91) months after EBV seroconversion (Fig. S1A). The MS disease onset, as defined by the first occurrence of symptoms consistent with MS, occurred after 1–19 (mean: 7.92) months before the MS diagnosis.

Figure S1



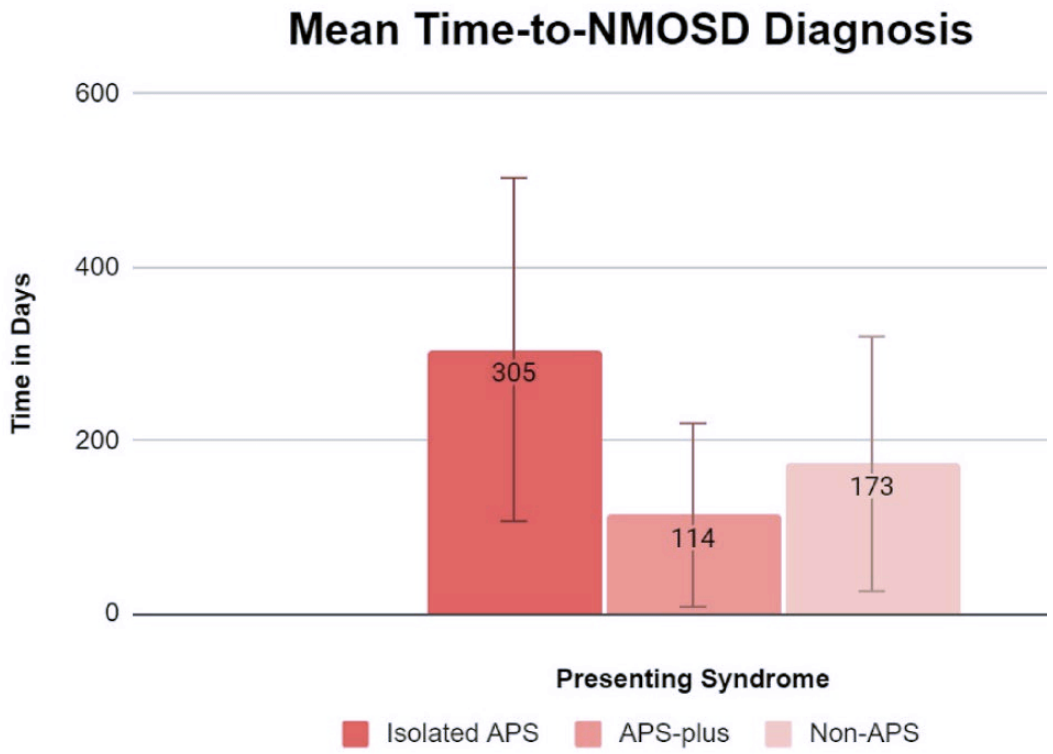


Vietzen H, Kühner LM, Berger SM, et al. Early identification of individuals at risk for multiple sclerosis by quantification of EBNA-$1_{381-452}$-specific antibody titers. *Nat Commun*. 2025;16(1):6416.

European Journal of Paediatric Neurology 56 (2025) 6–9

Delayed diagnosis in pediatric-onset aquaporin-4 positive neuromyelitis optica spectrum disorder with isolated area postrema syndrome

Quinton Mandle [a,*], Linda Nguyen [b], Paul S. Horn [c], Yolanda S. Wheeler [d], Helen Wu [e], Kelsey E. Poisson [a]



APS is characterized by intractable nausea, vomiting, anorexia, and/or hiccups. APS has characteristic and sensitive magnetic resonance imaging (MRI) findings, with most affected patients displaying T2-hyperintense lesions of the dorsal caudal medulla

Thirty-eight patients were included; 15.8 % were male and 84.2 % were female. Eighteen patients (47 %) presented with APS at first symptom onset. Ten patients (26 %) presented with isolated APS and eight patients (21 %) presented with APS-plus.

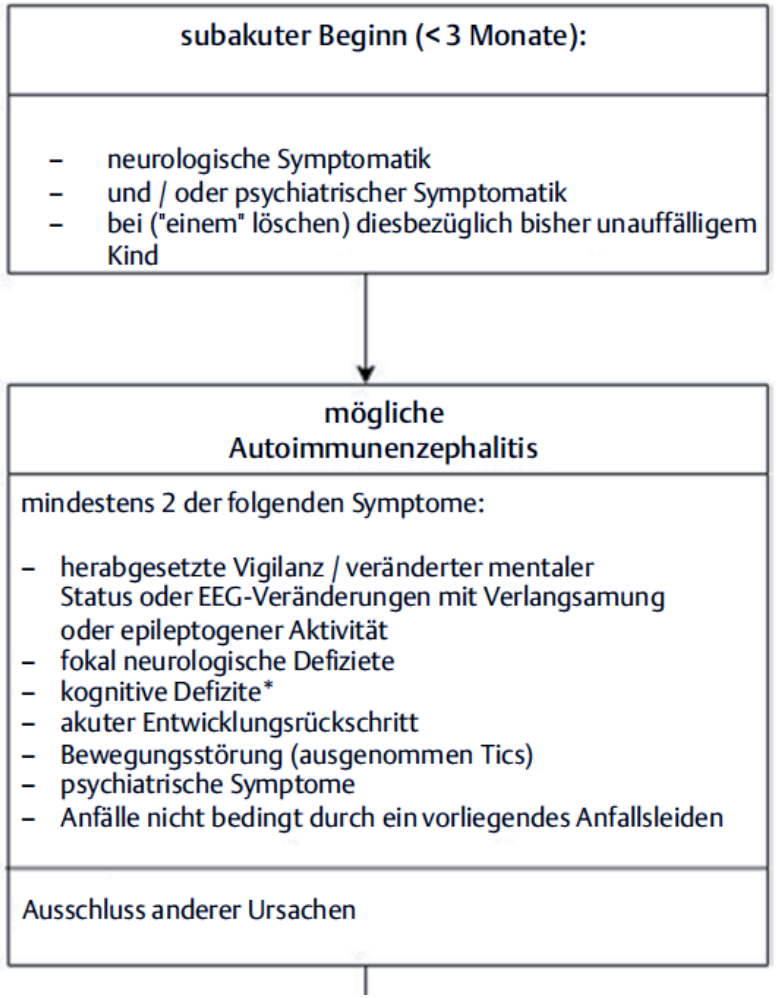
We demonstrate that isolated APS can be a manifestation in a subset of patients with AQP4+ pediatric-onset NMOSD and that these patients experience a significantly longer delay to diagnosis than patients presenting with other syndromes, with or without APS. In addition to being at risk for treatment delay and subsequent permanent disability, these patients may undergo invasive workup and experience significant frustration with misdiagnosis, as demonstrated by our illustrative case.

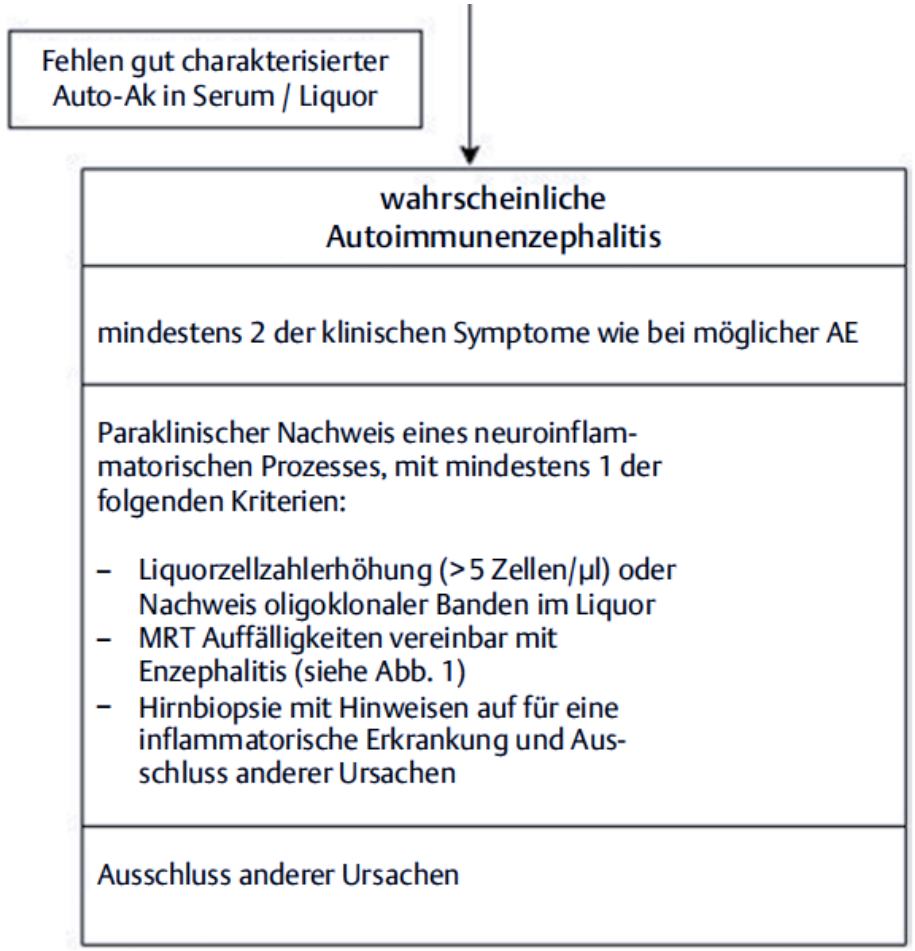
Mandle Q, Nguyen L, Horn PS, Wheeler YS, Wu H, Poisson KE. Delayed diagnosis in pediatric-onset aquaporin-4 positive neuromyelitis optica spectrum disorder with isolated area postrema syndrome. *Eur J Paediatr Neurol*. 2025;56:6-9. doi:10.1016/j.ejpn.2025.04.005

Diagnostik und Therapie bei Kindern mit antikörperbedingten ZNS-Erkrankungen

Eva-Maria Wendel, Kevin Rostasy

Klin Neurophysiol 2025; 56: 96–114





Diagnostik und Therapie bei Kindern mit antikörperbedingten ZNS-Erkrankungen

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▶ **Tab. 1** Differenzialdiagnosen einer autoimmunen Enzephalitis im Kindesalter.

Erkrankung	Differenzialdiagnosen
Primäre ZNS-Entzündung	SREAT-EnzephalitisZNS-Vaskulitisdemyelinisierende Erkrankungen: ADEM, Multiple Sklerose, Neuromyelitis-optica-SpektrumerkrankungenRasmussen-Enzephalitis
Systemische Entzündung	Autoimmunerkrankungen: Anti-Phospholipid-Syndrom, Zöliakie, Morbus Behçet, Sarkoidose, systemischer Lupus erythematodes und Sjögren-Syndromautoinflammatorische Erkrankungen: Interferonopathien und HLH
Infektionen, Post-/Parainfektiöse Enzephalopathien	B. burgdorferi, L. monocytogenes, Mycoplasma pneumoniae, M. tuberculosis, T. pallidumAdenoviren, Enteroviren, Ebstein-Barr-Virus, Influenzavirus, JC-Virus, Masern, Tollwut, Varizellen, Westnil-Fieber, StreptokokkenMalaria
Metabolische Erkrankungen	Leukodystrophie, Mitochondriopathien, Mukopolysaccharidosen, organische Azidurien, Morbus Wilson, ANE mit RNABP2-MutationHepatische Enzephalopathie
Neoplastische Erkrankungen	primäre ZNS-Tumoren (Lymphome, Gliome, Astrozytome)Metastasen (Neuroblastome, Leukämien) Ovarialteratome
Psychiatrisch	Schizophrenie, bipolare Erkrankung, psychogene Krampfanfälle, Konversionsstörung
Ernährung	Vitamin-B_{12}-Defizienz
Toxisch	DrogenIntoxikationMedikamente (z. B. Metronidazol, Ciclosporin)
Erkrankungen mit unklarem Mechanismus	FIRES, PANDAS, PANS, ANE ohne RANBP2-Mutation

Diagnostik und Therapie bei Kindern mit antikörperbedingten ZNS-Erkrankungen

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Akute Schubtherapie

- First-Line-Immuntherapie
  - Methylprednisolonpuls i. v. (20–30 mg/kg/d; maximal 1 g/d) für 3–5 Tage
  - alternativ Dexamethason p.o. (20 mg/m² KOF; maximal 12 g total) über 3 Tage
  - bei ausbleibender Besserung:
    - Immunglobuline i. v. (2 g/kgKG) verteilt auf 2–5 Tage (= 0,4 g/kgKG/d für 5 Tage)
    - Plasmapherese (wenn möglich vor Immunglobulingabe) (5–7 Zyklen)
- Second-Line-Immuntherapie
  - Rituximab (375 mg/m2; maximal 1 g) zunächst 2 Gaben im Abstand von 2 Wochen, dann nach 3–6 Monaten erneut
  - Cyclophosphamid (500–1000 mg/m2; maximal 1,5 g) monatlich für 3–6 Monate
  - Tocilizumab als Eskalationstherapie (12 mg/kgKG ED (<30 kgKG), 8 mg/kgKG ED (>30 kgKG); maximal 800 mg) monatlich über 6 Monate oder länger

Erhaltungstherapie

- Prednisolon p.o. (2 mg/kgKG/d, maximal 60 mg/d) für 1 Woche, dann ausschleichen über einige Wochen
- monatlich Immunglobuline i. v. (0,4–1,0 g/kgKG für 1 Tag), über 3–6 Monate
- Cyclophosphamid i. v. (500–1000 mg/m²; maximal 1,5 g) monatlich für bis zu 6 Monate
- Rituximab (375 mg/m2; maximal 1 g) alle 6 Monate, je nach B-Zell-Depletierung für 2 Jahre

Wendel E, Rostasy K. Diagnostik und Therapie bei Kindern mit antikörperbedingten ZNS-Erkrankungen. *Klin Neurophysiol.* 2025; 56: 96–114