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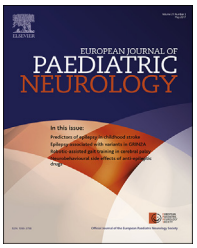

Original article

# Epileptic phenotypes, electroclinical features and clinical characteristics in 17 children with anti-NMDAR encephalitis

E. Haberlandt [a,*], M. Ensslen [b], U. Gruber-Sedlmayr [c], B. Plecko [j], M. Brunner-Krainz [c], M. Schimmel [d], S. Schubert-Bast [e], U. Neirich [f], H. Philippi [g], G. Kurleman [h], M. Tardieu [i], G. Wohlrab [j], I. Borggraefe [b], K. Rostásy [k]

[a] Clinical Department of Pediatrics I, Neuropediatrics, Medical University of Innsbruck, Innsbruck, Austria
[b] Department of Pediatric Neurology and Developmental Medicine and Social Pediatrics, Dr. von Haunersches Children's Hospital, University of Munich, Munich, Germany
[c] Department of Pediatrics, Medical University of Graz, Graz, Austria
[d] Department of Pediatrics, Klinikum Augsburg, Augsburg, Germany
[e] Department of Pediatric Neurology, University Children's Hospital Heidelberg, Heidelberg, Germany
[f] Department of Pediatrics, Neurology, Stiftungskrankenhäuser Frankfurt am Main, Clementine Kinderhospital, Frankfurt am Main, Germany
[g] Sozialpädiatrisches Zentrum Frankfurt Mitte, Frankfurt am Main, Germany
[h] Department of General Pediatrics, Neuropediatrics, University Children's Hospital Münster, Münster, Germany
[i] Assistance publique hôpitaux de Paris, Hôpitaux universitaires Paris-Sud, Université Paris-Sud, Paris, France
[j] Department of Neuropaediatrics and Neurophysiology, University Children's Hospital, Zuerich, Switzerland
[k] Department of Pediatric Neurology, Children's Hospital Datteln, University Witten/Herdecke, Witten, Germany

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ABSTRACT

*Background:* Anti-N-methyl D-aspartate receptor (NMDAR) encephalitis is a rare disorder characterized by seizures, neuropsychiatric symptoms, dyskinesia and autonomic instability.

*Objective:* Aim of the present study was to evaluate the seizure phenotypes and electroencephalogram (EEG) features in children with anti-NMDAR encephalitis.

*Methods:* Seizure types, electroclinical features and clinical characteristics of 17 children with anti-NMDAR encephalitis were analysed in a retrospective case series from nine centres in Europe.

*Results:* Nearly half (8/17) of the children presented with psychiatric symptoms, whereas in 4/17 patients seizures were the first symptom and in 5/17 both symptoms occurred at the same time. During the following course seizures were reported in 16/17 children. The first EEG detected generalized slowing in 11/17 patients, focal slowing in 3/17 and normal

*Abbreviations:* CSF, cerebrospinal fluid; EEG, electroencephalogram; EDB, extreme delta brush; NMDAR, anti N-methyl D-aspartate receptor.

* *Corresponding author*. Clinical Department of Pediatrics I, Neuropediatrics, Medical University of Innsbruck, Anichstrasse 35, A-6020 Innsbruck, Austria. Fax: +43 512 504 24904.
E-mail address: edda.haberlandt@tirol-kliniken.at (E. Haberlandt).

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Extreme
Delta brush

background activity in only 3/17 children. The extreme delta brush (EDB) pattern was detected in 9/17 (53%) patients.

*Conclusion:* In addition to psychiatric symptoms, children with anti-NMDAR encephalitis often show generalized slowing in EEG with or without seizures at initial presentation. EDB is present in half of all children and is potentially a helpful tool for early detection of this immune-mediated disease.



## 1. Introduction

Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is an immune-mediated disorder with a range of symptoms including seizures, neuropsychiatric symptoms, dyskinesia and autonomic instability.[1] Whereas it was first characterized in young women as a paraneoplastic entity with teratomas of the ovary, the number of patients diagnosed without teratoma is steadily increasing, particularly in pediatric case series. All patients have serum and/or cerebrospinal fluid antibodies against NMDAR, a ligand-gated cell surface cation channel with important functions in synaptic transmission and plasticity.[2]

Clinical symptoms usually start with psychiatric disturbances followed within weeks by encephalopathic changes, dyskinesias and autonomic instability. Seizures are present in the majority of patients. In one study of 44 patients with anti-NMDAR encephalitis including ten children, 16 had dyscognitive seizures, 12 had simple partial and 33 patients additionally had generalized seizures.[3] Epileptic phenotypes with focal motor or complex seizures developing at early stages of the disease have also been described.[4] Electroencephalographic (EEG) findings of non-specific, generalized slowing without epileptiform discharges dominate the clinical picture in adults.[4] Schmitt et al. recently described "extreme delta brush pattern" as a novel EEG finding defined as delta activity with superimposed fast activity in the beta range predominately symmetric and synchronous, typically seen across all regions.[5]

We here describe the epileptic phenotypes, electroclinical features and clinical features of 17 children with anti-NMDAR encephalitis.

## 2. Methods

### 2.1. Patients

Seventeen children with anti-NMDAR encephalitis were retrospectively enrolled between 2002 and 2012 from nine different neuropediatric centres in Europe. All patients underwent extensive diagnostic studies including magnetic resonance imaging (MRI) of the brain, EEG, serum and cerebrospinal fluid (CSF) studies. The following demographic and clinical data were obtained: age, gender, presence of tumours, NMDAR antibody status in serum and/or CSF, clinical course including symptoms (e.g. psychiatric, neurological signs), outcome, seizure semiology, treatment regimes and EEG findings. Medical information was made available by the treating physicians.

Outcome was measured with the modified Rankin Scale (mRS), ranking neurological recovery on a scale from 0 to 6. 2 mRS designates a slight disability, with the patient able to walk, being only slightly handicapped for everyday life. 3 mRS designates moderate disability with severe handicap for daily routine. Modified Rankin Scale 4–6 designates more severe motor disability.

Outcome of patients was scored as (1) full neurological recovery if they were able to return to all their daily activities without any sequelae; (2) substantial improvement if they returned to their homes with mild deficits but still improving; or (3) limited improvement if there was minimal change in the neurological status three months after initial presentation.

### 2.2. Seizures and EEG findings

Seizures were characterized as generalized (e.g. atonic seizures, generalized tonic clonic seizures) or focal (dyscognitive, focal motor seizures) with or without status epilepticus, seizure frequency <1/day (less than one seizure per day) or >1/day (more than one seizure per day) – with or without therapy resistance during the course of the disease according to the revised terminology for seizures reported by the International League against Epilepsy (ILAE) in 2010.[6]

The EEGs from initial presentation and the last available follow-up were evaluated by two pediatric neurologists as follows: presence of background activity changes (generalized slowing, focal slowing and extreme delta brushes (EDB)), presence of interictal epileptic paroxysms such as sharp waves, spike waves, polyspike waves or generalized discharges, focal interictal epileptic discharges, multifocal interictal epileptic discharges and electrographic seizures.

## 3. Results

### 3.1. Clinical characteristics and laboratory findings (Table 1)

Seventeen (5 male, 12 female) patients with a median age at disease onset of 8.7 (range: 1.8–17.3) years with antibody-confirmed anti-NMDAR encephalitis were enrolled. Median follow-up was 14 (range: 2–30) months. In 2/17 (12%) patients