Brief Communication

Journal of Child Neurology
2015, Vol. 30(2) 238-245

DOI: 10.1177/0883073813515947
jcn.sagepub.com
SAGE

Longitudinal Electroencephalographic (EEG) Findings in Pediatric Anti-*N*-Methyl-D-Aspartate (Anti-NMDA) Receptor Encephalitis: The Padua Experience

Margherita Nosadini, MD[1], Clementina Boniver, MD, PhD[2], Luigi Zuliani, MD[3], Luca de Palma, MD[2], Elisa Cainelli, PhD[1,2,4], Pier Antonio Battistella, MD, PhD[1], Irene Toldo, MD, PhD[1], Agnese Suppiej, MD, PhD[1], and Stefano Sartori, MD, PhD[1]

Abstract

To contribute to characterize electroencephalographic (EEG) activity in pediatric anti-*N*-methyl-D-aspartate (anti-NMDA) receptor encephalitis, we reviewed electroclinical data of 5 children with anti-NMDA receptor encephalitis diagnosed in our department. We identified 4 longitudinal electroencephalographic phases: in the early phase, background activity was normal, with intermixed non-reactive slow waves; in the florid phase, background activity deteriorated with appearance of sequences of peculiar rhythmic theta and/or delta activity unrelated to clinical changes, unresponsive to stimuli and antiepileptic medications; in the recovery phase, these sequences decreased and reactive posterior rhythm re-emerged; electroencephalogram normalized 2 to 5 months after onset. In conclusion, in the presence of evocative clinical history, recognizing a characteristic longitudinal electroencephalographic activity could provide ancillary aspects addressing the diagnosis and the overall management of children with anti-*N*-methyl-D-aspartate receptor encephalitis; in particular, knowing that peculiar and recurrent paroxysmal nonepileptic rhythmic theta-delta patterns can occur in these patients could help distinguish paroxysmal epileptic and nonepileptic electroencephalographic activity.

Keywords

anti-NMDAR encephalitis, EEG, children, seizure, rhythmic pattern

Received September 09, 2013. Received revised September 12, 2013, and October 16, 2013. Accepted for publication November 14, 2013.

Anti-*N*-methyl-D-aspartate (anti-NMDA) receptor encephalitis has been raising increasing interest in pediatric literature, and its clinical features have been progressively better defined.[1,2] A variable mixture of cognitive, motor, and psychiatric disturbances is observed in the disease and, especially in the early phases, numerous paroxysmal nonepileptic events and convulsive and nonconvulsive epileptic seizures coexist, sometimes hardly distinguishable on clinical grounds.

In contrast to its relatively well-characterized clinical phenotype, the evolution of interictal electroencephalographic (EEG) activity throughout the disease course has been little documented, especially in pediatric patients. Herein, we report and discuss the evolution of electroencephalographic activity during the course of the disease in 5 children with severe anti-*N*-methyl-D-aspartate receptor encephalitis.

Patients and Methods

Over the last 6 years, 4 children were diagnosed with anti-*N*-methyl-D-aspartate receptor encephalitis in our department (cases 1-4); an additional patient has recently been diagnosed, and is currently hospitalized (case 5). Clinical diagnosis was confirmed by the identification of anti-*N*-methyl-D-aspartate receptor antibodies in cerebrospinal fluid (case 1, retrospectively diagnosed, had a frozen serum sample tested). Video-electroencephalographic monitoring was performed in all patients using a computerized electroencephalographic system (Mizar Sirius, Galileo NT Line software, EB Neuro SpA, Florence, Italy; Nihon Kohden Italia Srl, Bergamo, Italy), and the tracings as well

[1] Pediatric Neurology Unit, Department of Pediatrics, University of Padua, Italy
[2] Pediatric Neurophysiology Unit, Department of Pediatrics, University of Padua, Italy
[3] Department of Neurology, Ca' Foncello Hospital, Treviso, Italy
[4] Lifespan Cognitive Neuroscience Laboratory, Department of General Psychology, University of Padua, Italy

Corresponding Author:
Stefano Sartori, MD, PhD, Pediatric Neurology Unit, Department of Pediatrics, University of Padua, Via Giustiniani 3, 35128 Padova, Italy.
Email: stefano.sartori@unipd.it

Table 1. Clinical Features and Electroencephalographic (EEG) Phases Throughout Disease Progression of the 5 Reported Pediatric Patients With Anti-*N*-Methyl-D-Aspartate (Anti-NMDA) Receptor Encephalitis.

	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	M	F	F	F	M
Age at onset	9 y and 1 mo	9 y 7 mo	12 y 10 mo	8 y 1 mo	6 y 7 mo
Available follow-up (mo)	72	30	18	11	2
Prodromal symptoms	No	Headache and vomit	No	No	No
Symptoms at onset	Movement disorder	Psychiatric disturbances	Psychiatric disturbances	Movement disorder	Paroxysmal spells
Seizures					
Early phase	1[a] (focal +/– SG) (not documented at EEG)	5[a] (focal +/– SG) (not documented at EEG)	2[a] (focal +/– SG) (not documented at EEG)	No	Many (focal +/– SG) (not documented at EEG)
Florid phase	No	No	No	2[a] (focal +/– SG) (not documented at EEG)	1 (focal +/– SG) (documented at EEG)
Recovery	Many (EPC[b])	No	No	No	Not available
Psychiatric symptoms	Irascibility, relational disturbances, mood instability, agitation and cry spells	Bizarre behavior, confusional state, agitation, aggressiveness, coprophagia, unintelligible speech	Irascibility, disinhibition, eruptations, psychomotor agitation	Restlessness, cry spells, visual hallucinations, unintelligible speech with catastrophic content, psychomotor agitation	Inappropriate behavior, psychomotor agitation
Movement disorders					
Orolinguofacial dyskinesias	Grimaces, involuntary lower lip movements	Grimaces, tongue protrusion	Grimaces, jaw clenching, tongue protrusion	Grimaces, tongue rolling	Grimaces, abnormal involuntary eye motricity
Limbs and pelvic movements	Choreoathetosis (right lower limb)	Choreoathetosis and dystonias (left upper limb)	Athetosis (upper limbs)	Choreoathetosis (limbs), pelvic thrusting	Hand dyskinesias (right > left)
Stereotyped movements	Yes	Yes	Yes	Yes	Yes
Posturing—freezing	Yes	Yes	Yes	Yes	No
Hypermotor spells	Yes (rare)	Yes (rare)	Yes (frequent)	Yes (frequent)	Yes (rare)
Speech	Dysarthria, mutism	Mutism	Echolalia, coprolalia, mutism	Dysarthria, mutism	Mutism
Autonomic disturbances	Hyperthermia, sleep-wake cycle dysregulation, urinary retention	Hypertension, hyperthermia, apnea, sleep-wake cycle dysregulation, urinary retention, incontinence	Bradycardic spells, hyperpnea and apnea, sleep-wake cycle dysregulation, urinary retention, hyperhidrosis	Flushing, remitting fever, sleep-wake cycle dysregulation, hyperhidrosis	Urinary retention and incontinence
Impairment of consciousness	Severe; stupor with catatonic features (bedridden)	Severe; stupor with catatonic features (bedridden)	Severe; stupor with catatonic features (bedridden)	Severe; stupor with catatonic features (bedridden)	Severe; stupor with catatonic features (bedridden)
Tumor	No	No	No	No	Not available
Etiologic treatment	Methylprednisolone, IVIg, ACTH	Methylprednisolone, IVIg, plasma exchange, cyclophosphamide	Methylprednisolone, plasma exchange, cyclophosphamide, mycophenolate	Plasma exchange, methylprednisolone, cyclophosphamide, mycophenolate	Plasma exchange, methylprednisolone
Length of hospitalization (mo)	8	6	4	3.5	Not available
PICU (length of stay)	No PICU	PICU (3 d)	No PICU	PICU (15 d)	PICU (1 d)
Outcome					
Cognitive outcome	Normal IQ at 12 mo	Normal IQ at 8 mo	Normal IQ at 5 mo	Normal IQ at 5 mo	Not available
Motor outcome	Full recovery	Full recovery	Full recovery	Full recovery	
Sequelae	Mild impairment in working memory and attentive functions	Auditory misperceptions, night awakenings for nightmares, very mild impairment in working memory	Mild learning disability, conflict/error monitoring, motor programming, impulse control	Mild mood lability, impairment in working memory, attentive functions, impulse control	Not available

(continued)

Table 1. (continued)

	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	M	F	F	F	M
Electroencephalographic phases					
Early phase (timing)	(Onset to 1st wk)	(Onset to 1st wk)	(Onset to 2nd wk)	(Onset to 4th wk)	(Onset to 1st wk)
Main clinical features:	Alpha rhythm	Alpha rhythm (left > right)	Alpha rhythm	Alpha rhythm (right > left)	Alpha rhythm (right > left)
Preserved consciousness	Nonreactive intermixed slow waves at 2-3 Hz	Nonreactive intermixed frontotemporal slow waves at 2-3 Hz	Nonreactive intermixed bilateral frontal slow waves at 1-2 Hz	Nonreactive intermixed frontotemporal slow waves at 2-3 Hz (left > right)	Nonreactive intermixed frontotemporal slow waves at 2-3 Hz (left > right)
Psychiatric disturbances (behavioral changes)					
Movement disorder (dyskinesias)					
	Later: subcontinuous and high-voltage slow waves (mainly expressed on left centroparietal regions)	Later: subcontinuous and high-voltage slow waves (right > left)	Later: subcontinuous and very-high-voltage slow waves	Later: diffuse low voltage	Later: subcontinuous and high-voltage slow waves (left > right)
	Preserved sleep stages[a]	Sleep not available[a]	Preserved sleep stages[a]	Preserved sleep stages[a]	Preserved sleep stages[a]
Florid phase (timing)	(1st wk to 3rd mo)	(1st wk to 5th wk)	(2nd wk to 2nd mo)	(4th wk to 2nd mo)	(1st wk to present)
Main clinical features:	Progressively slowed cerebral electrical activity	Globally slowed cerebral electrical activity	Globally slowed cerebral electrical activity	Globally slowed cerebral electrical activity	Globally slowed cerebral electrical activity
Impairment of consciousness					
Psychiatric symptoms (irascibility, mood instability, relational difficulties, agitation and cry spells, confusional state, unintelligible speech, hallucinations)	Intermixed slow waves at 2-3 Hz; later subcontinuous and high-voltage slow waves	Diffuse high-voltage slow waves at 1-2 Hz, with prevalence on anterior regions (right > left)	Anterior medium- to high-voltage slow waves at 1-2.5 Hz	Anterior (mainly frontal) intermixed or subcontinuous medium- to high-voltage slow waves at 1-2.5 Hz	Anterior (mainly frontal) intermixed or subcontinuous medium- to high-voltage slow waves at 1-2.5 Hz
	Disappearance of alpha rhythm (3rd wk to 4th wk)	Poor representation and subsequent disappearance of alpha rhythm (2nd wk)	Poor representation and subsequent disappearance of alpha rhythm (3rd wk)	Poor representation and subsequent disappearance of alpha rhythm (4th wk)	Poor representation and subsequent disappearance of alpha rhythm (4th wk)
Movement disorders (dyskinesias, stereotyped movements, pelvic movements, hypermotor spells, posturing, freezing, catatonia)	Intermixed discrete sequences of nonreactive rhythmic delta activity at 2-2.5 Hz and theta activity at 4-5 Hz, arising from left frontocentral regions, of medium voltage, often with sharp appearance (4th wk)	Brief sequences of nonreactive rhythmic delta activity at 1-2 Hz of medium or high voltage, with angular appearance (3rd wk)	Subcontinuous discrete sequences of nonreactive rhythmic delta activity at 2-2.5 Hz and theta activity at 4-5 Hz, arising unilaterally or simultaneously from homologous or different regions of the 2 hemispheres, or following one another on the same regions, mainly expressed on frontal regions bilaterally, of medium or high voltage, often with sharp appearance (3rd-4th wk)	Subcontinuous discrete sequences of nonreactive rhythmic delta activity at 2-2.5 Hz and theta activity at 4-5 Hz, arising unilaterally or simultaneously from homologous or different regions of the 2 hemispheres, or following one another on the same regions, mainly expressed on frontal regions bilaterally, of medium or high voltage, sometimes with sharp appearance (3rd-5th wk)	Recurrent discrete sequences of nonreactive rhythmic delta activity at 2-2.5 Hz and theta activity at 4-5 Hz, arising unilaterally or simultaneously from homologous or different regions of the 2 hemispheres, or following one another on the same regions, mainly expressed on frontal regions bilaterally, of very high voltage, often with very sharp appearance (3rd-4th wk)
Speech disturbances (dysarthria, mutism)					
Seizures (focal, SG)					
Autonomic dysregulation (hypertension, hyperthermia, apnea/hyperpnea, sleep-wake cycle dysregulation, urinary retention/incontinence, flushing, hyperhidrosis)					
	Fairly preserved sleep stages[a]	Fairly preserved sleep stages[a]	Fairly preserved sleep stages[a]	Fairly preserved sleep stages[a]	Fairly preserved sleep stages[a]
Recovery phase (timing)	(3rd mo to 10th mo)	(5th wk to 5th mo)	(2nd mo to 4th mo)	(2nd mo to 3rd mo)	Not available
Main clinical features:	EPC[b]				
Gradual and slow recovery Improvement of consciousness, speech and motor functions	Reappearance of alpha posterior rhythm (7th mo)	Reappearance of alpha posterior rhythm (7th wk)	Reappearance of alpha posterior rhythm (6th wk)	Reappearance of alpha posterior rhythm (2nd mo)	
Persistence of psychiatric symptoms (hallucinations, disinhibition)	Gradual decrease in nonreacting rhythmic delta or theta sequences	Gradual decrease in nonreacting rhythmic delta or theta sequences	Gradual decrease in nonreacting rhythmic delta or theta sequences	Gradual decrease in nonreacting rhythmic delta or theta sequences	
EEG normalization (timing)	(7th mo)	(5th mo)	(2nd mo)	(4th mo)	Not available
Main clinical features: Mild neurologic, psychiatric, emotional, neuropsychological sequelae					

Abbreviations: ACTH, adrenocorticotropic hormone; EEG, electroencephalography; EPC, epilepsia partialis continua; F, females; IQ, intelligence quotient; IVIg, intravenous immunoglobulin; M, males; NMDAR, *N*-methyl-D-aspartate receptor; PICU, pediatric intensive care unit; SG, secondary generalization; +/–, with or without.

[a]Witnessed by nonmedical personnel or medical personnel not specifically trained in neurology.

[b]Not shown.

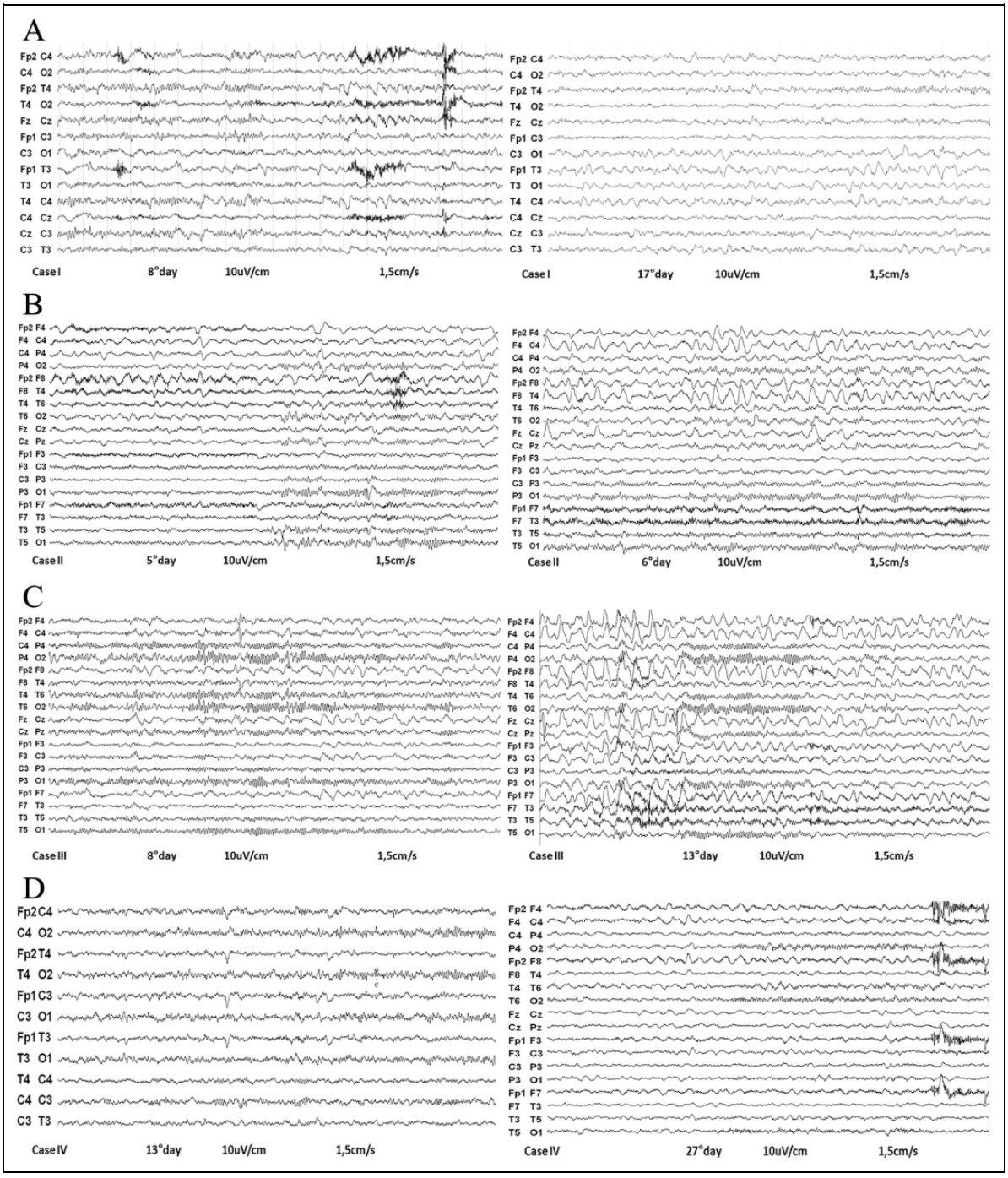

Figure 1. Electroencephalographic (EEG) tracings of patients 1 to 4 in the early electroencephalographic phase.

as a comprehensive set of clinical data were retrospectively evaluated by the principal investigators (CB, SS, MN, LDP).

Results

Clinical Data

Clinical data of the 5 pediatric patients with anti-*N*-methyl-D-aspartate receptor encephalitis diagnosed in our department between 2007 and 2013 are reported in Table 1. Data on case 5 are limited because of the short available follow-up. All patients developed a severe form of the disease and were bedridden within 3 weeks from onset. Clinical seizures were reported exclusively in the early and florid phases of disease in cases 2 to 4 (data on the recovery phase of case 5 not available yet); case 1 developed a transient picture of *epilepsia partialis continua* in the recovery phase, during her stay at another rehabilitation unit (data not available). No seizures were electrically documented during the prolonged

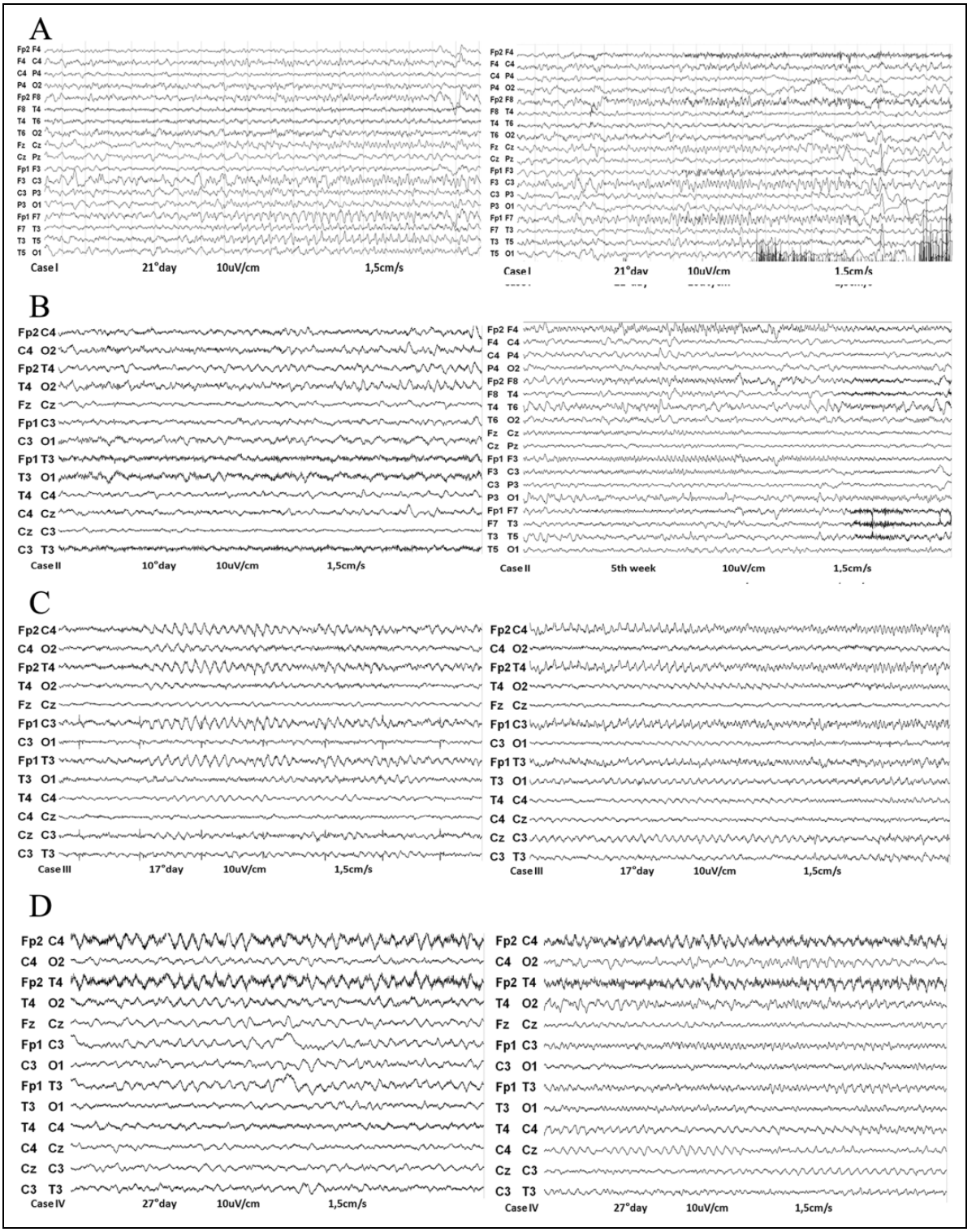

Figure 2. Electroencephalographic (EEG) tracings of patients 1 to 4 in the florid electroencephalographic phase.

electroencephalographic recordings performed at our hospital in cases 1 to 4; only in case 5, the electroencephalographic tracing performed during a paroxysmal episode disclosed an ictal pattern (Figure 4C, D).

Electroencephalographic Data

Electroencephalographic findings during the course of the disease in each of our patients are detailed in Table 1, and the corresponding iconography is reported in Figures 1 to 4. We

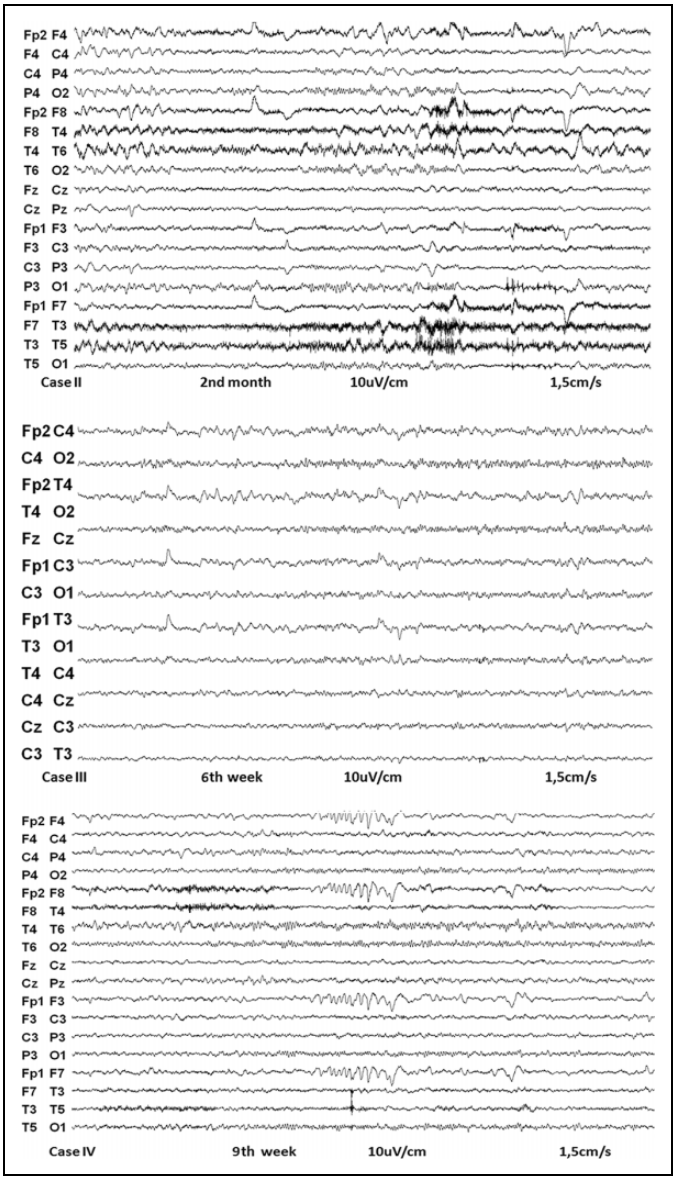

Figure 3. Electroencephalographic (EEG) tracings of patients 2 to 4 in the recovery electroencephalographic phase (iconography of case 1 not available in this phase).

identified 4 phases in electroencephalographic activity during the course of the disease in all our patients:

1. Electroencephalographic background activity in wakefulness and sleep was normal in the *early* phase (when behavioral changes and/or orofacial and limb dyskinesias were the most commonly recognized clinical features), with preserved, fairly symmetrical and reactive alpha posterior rhythm (8-12 Hz), despite the variable presence of intermittent or more subcontinuous, medium- to high-amplitude, nonreactive, sometimes monomorphic, unilateral and/or bilateral slow waves (1-3 Hz), most evident in the frontotemporal regions of the scalp (Figures 1 and 4A).
2. About 2 to 3 weeks after the onset of symptoms, in the *florid* phase of disease (when consciousness and vigilance impairment was more severe and complex stereotyped movements predominated), electroencephalographic tracings showed progressive deterioration of background activity with disappearance of reactive posterior rhythm and appearance of an unusual electrical pattern (Figures 2 and 4B). This was characterized by defined and discrete sequences of rhythmic delta and/or theta activity at 2 to 2.5 Hz and 4 to 5 Hz, respectively, of variable duration (seconds to hours), often with sharp appearance, without clinical counterpart (occurring independently from the paroxysmal intermittent movement disorders and the behavioral changes observed in these patients), not responding to stimuli, eye opening or closure, pain, antiepileptic drugs, and usually disappearing in sleep. These rhythmic sequences could arise unilaterally or simultaneously from homologous or different regions of the scalp of the 2 hemispheres, or alternate to normal electrical activity on the same region. Conversely, electrical activity in sleep was relatively well preserved.
3. Later, during the *recovery* phase, the above-mentioned rhythmic sequences gradually decreased, with reemergence of a recognizable physiological posterior rhythm and a globally well-organized background activity (Figure 3).
4. Eventually, 2 to 5 months after disease onset, an electroencephalogram showed complete *normalization* of electrical activity.

Discussion

We retrospectively identified 4 disease course–related phases in electroencephalographic activity in all our children with anti-*N*-methyl-D-aspartate receptor encephalitis. After an aspecific electroencephalographic *early* phase characterized by the presence of intermixed slow waves predominant on the anterior regions of the scalp, electric cerebral activity markedly deteriorates in the *florid* phase, giving way to a peculiar rhythmic theta-delta activity unreactive to stimuli and unrelated to clinical changes. This rhythmic activity gradually disappears in the electroencephalographic *recovery* phase along with the gradual reappearance of a physiologic posterior activity, even before a clinical turning point is obvious, and eventually *normalization* of electric cerebral activity follows.

So far, disorganization and diffuse or focal slowing of electrical cerebral activity in the delta-theta range, sometimes with rhythmical appearance, has been described in the literature,[2-5] but the evolution of electroencephalographic activity throughout the course of the disease has been little documented and characterized in children. More recently, a unique electroencephalographic pattern, resembling the delta brush pattern in premature infants has been identified in 30% of adults with anti-*N*-methyl-D-aspartate receptor encephalitis[6] and in a 14-year-old girl.[7] This "extreme delta brush" pattern, unrelated

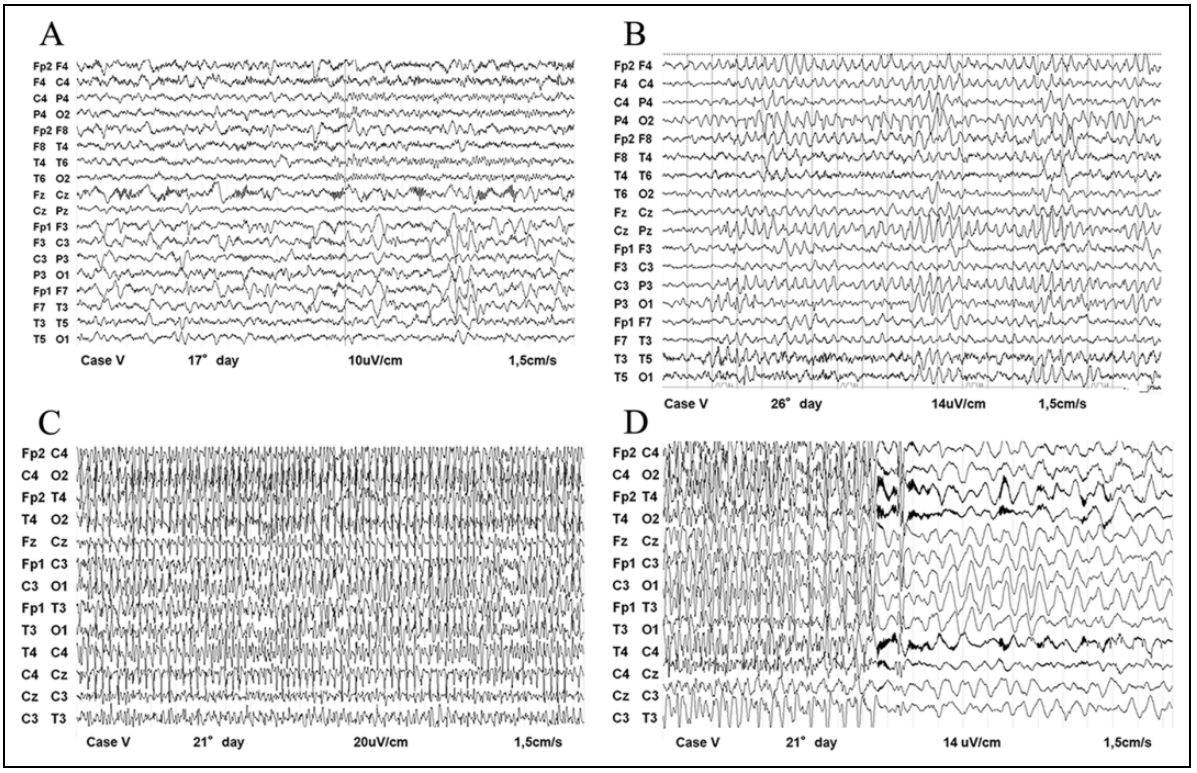

Figure 4. Electroencephalographic (EEG) tracings of case 5 in the early and florid electroencephalographic phases (A, B). Electroencephalographic recording during (C) and at the end (D) of a secondary generalized convulsive epileptic seizure, showing the abrupt cessation of an epileptic electrical pattern (D), clearly different to the rhythmic nonepileptic patterns showed above in this patient and in the other cases reported in Figure 2. Electroencephalographic recording indicates the patient has a secondarily generalized seizure characterized by upward eye deviation, chewing, clonic movements at the 4 limbs, generalized stiffness, opisthotonus, and desaturation.

to sedation and to the occurrence of dystonic spells or other paroxysmal abnormal movements, has not been reported in other children so far, and we were not able to detect it in our patients.

The nature of the peculiar delta-theta pattern observed in our patients in the florid electroencephalographic phase of disease represents an intriguing and challenging issue. Although its rhythmic appearance can seem like an epileptic phenomenon at first look, several considerations point against an epileptic nature of this electroencephalographic pattern. First, prolonged video-electroencephalograms failed to demonstrate any close and compelling correlation between the above-mentioned delta-theta sequences and the paroxysmal intermittent behavioral changes and the movement disorders observed in these patients. Second, such sequences do not display the usual electrical features of epileptic discharges for several aspects (as illustrated by the comparison between a nonepileptic rhythmic pattern and an ictal epileptic pattern in case 5, respectively, in Figure 4B and 4C, D): they are not preceded by repetitive spikes or low-amplitude fast activity, there are no frequency and amplitude changes during the sequences (the so-called recruiting/derecruiting rhythms of epileptic discharges) and no diffusion of the paroxysmal activity from one region to another (as in epileptic seizures). Finally, these sequences do not respond to nonsedative antiepileptics, and usually disappear when patients manage to fall asleep spontaneously or after benzodiazepine administration, giving way to a relatively well-organized electrical activity in sleep, and can reappear at awakening. Similarly, a pharmacologic origin of these rhythmic sequences can be reasonably ruled out, as they were observed before and/or independently from drug administration in our patients and in other reported cases.[6,8] Furthermore, this electrical activity does not evoke the activity induced by benzodiazepines or barbiturates (ie, beta activity). With the epileptic and pharmacologic nature ruled out, the origin of this rhythmic activity is still to be clarified. A direct effect of the anti-*N*-methyl-D-aspartate receptor antibodies on the cortex might be hypothesized, similar to that of ketamine, a known *N*-methyl-D-aspartate receptor antagonist that induces a dissociative anesthesia[9,10] and, at certain dosages, can produce an increase in electroencephalographic activity in the theta bands and a psychotic-like clinical picture,[11] interestingly resembling anti-*N*-methyl-D-aspartate receptor encephalitis. Alternatively, such patterns can be ascribed to the dysfunction of the subcortical (pallidostriatal) systems controlling electric cortical activity caused by antibody-mediated inactivation of inhibitory gamma-aminobutyric acid-ergic neurons.[4,5,12] Further studies are, however, warranted to evaluate these speculations and hypotheses.

Interestingly, on the same days of the completion of the present study, peculiar electroencephalographic features, partially

overlapping with our observations, were published by Gitiaux and colleagues,[13] supporting the clinical and speculative importance of electroencephalographic study in these patients.

Even if the peculiar clinical presentation of anti-*N*-methyl-D-aspartate receptor encephalitis represents the mainstay of diagnosis, recognizing characteristic longitudinal electroencephalographic patterns can provide support to an early diagnosis and a prompt and appropriate treatment.[6] Moreover, knowing that peculiar recognizable paroxysmal rhythmic nonepileptic electroencephalographic patterns can occur in pediatric anti-*N*-methyl-D-aspartate receptor encephalitis can provide a useful key element helping the interpretation of electroencephalographic tracings and the differentiation between epileptic and nonepileptic electroencephalographic activity in these patients.

Acknowledgments

This work was performed at the Pediatric Neurology and Neurophysiology Unit, Division of Pediatrics, University of Padua. We thank all the medical staff and the nurses for their precious contribution. We also thank the children and their parents for their kind collaboration.

Author Contributions

SS, CB, and MN made substantial contributions regarding conception and design, and the acquisition, analysis, and interpretation of data. SS, MN, CB, LZ, and LdP were involved in drafting the manuscript; LdP provided the iconography; EC provided the neuropsychological data. AS, IT, and PAB were involved in revising the manuscript critically for important intellectual content and have given final approval of the version to be published. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

The clinical management of the patient reported in this paper conformed to the specifications provided by our institutional review board. All investigations were performed according to the recommendations of the ethical committee of our department, and video-electroencephalographic recordings were performed after acquiring written permission from the patients' parents.

References

1. Dalmau J, Gleichman AJ, Hughes EG, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol*. 2008;7:1091-1098.
2. Irani SR, Bera K, Waters P, et al. *N*-methyl-D-aspartate antibody encephalitis: temporal progression of clinical and paraclinical observations in a predominantly non-paraneoplastic disorder of both sexes. *Brain.* 2010;133(pt 6):1655-1667.
3. Florance NR, Davis RL, Lam C, et al. Anti-*N*-methyl-D-aspartate receptor (NMDAR) encephalitis in children and adolescents. *Ann Neurol*. 2009;66:11-18.
4. Florance-Ryan N, Dalmau J. Update on anti-*N*-methyl-D-aspartate receptor encephalitis in children and adolescents. *Curr Opin Pediatr*. 2010;22:739-744.
5. Kleinig TJ, Thompson PD, Matar W, et al. The distinctive movement disorder of ovarian teratoma-associated encephalitis. *Mov Disord*. 2008;23:1256-1261.
6. Schmitt SE, Pargeon K, Frechette ES, et al. Extreme delta brush: a unique EEG pattern in adults with anti-NMDA receptor encephalitis. *Neurology*. 2012;79:1094-1100.
7. Armangue T, Titulaer MJ, Málaga I, et al. Pediatric anti-*N*-methyl-D-aspartate receptor encephalitis-clinical analysis and novel findings in a series of 20 patients. *J Pediatr*. 2013;162: 850-856.
8. Bayreuther C, Bourg V, Dellamonica J, et al. Complex partial status epilepticus revealing anti-NMDA receptor encephalitis. *Epileptic Disord*. 2009;11:261-265.
9. Corssen G, Domino EF, Bree RL. Electroencephalographic effects of ketamine anesthesia in children. *Anesth Analg*. 1969; 48:141-147.
10. Malver LP, Brokjaer A, Staahl C, et al. Electroencephalography and analgesics. *Br J Clin Pharmacol*. 2013 Apr 18. [Epub ahead of print.
11. Weiner AL, Vieira L, McKay CA, Bayer MJ. Ketamine abusers presenting to the emergency department: a case series. *J Emerg Med*. 2000;18:447-451.
12. Rigby M, Le Bourdellès B, Heavens RP, et al. The messenger RNAs for the *N*-methyl-D-aspartate receptor subunits show region-specific expression of different subunit composition in the human brain. *Neuroscience*. 1996;73:429-447.
13. Gitiaux C, Simonnet H, Eisermann M, et al. Early electro-clinical features may contribute to diagnosis of the anti-NMDA receptor encephalitis in children. *Clin Neurophysiol*. 2013 Jul 2 [Epub ahead of print].