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Analysis of electroencephalogram characteristics of anti-NMDA receptor encephalitis patients in China

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HIGHLIGHTS

- The majority of anti-NMDAR encephalitis patients (98.4%) had abnormal EEG.
- Diffuse slowing was the most common EEG pattern in patients with anti-NMDAR encephalitis.
- Extreme delta brush (EDB) mainly occurred in patients at the peak stage.

ABSTRACT

Objective: To explore the characteristics of electroencephalogram (EEG) in patients with anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis.
Methods: Anti-NMDAR encephalitis patients admitted to the Department of Neurology between January 2012 and June 2016 were enrolled. All patients underwent electroencephalogram (EEG) at least once in the disease peak stage, and received tumor screening, symptomatic therapy, and immunotherapy. Patients received outcome evaluation every 6 months after the immunotherapy, and modified Rankin scale (mRS) 0–2 was defined as favorable outcome.
Results: This study enrolled 62 cases of anti-NMDAR encephalitis patients, including 29 males (46.8%) and 33 females (53.2%). The patient ages were between 10 and 59 (mean 26.3 ± 11.3) years. A total of 93 instances of EEG monitoring were performed on 62 patients. At the peak stage, EEG presentations showed 61 cases (98.4%) were abnormal, cranial MRI showed 29 cases (46.8%) were abnormal among all 62 patients. The main presentations of abnormal EEG were diffuse slowing (25 cases, 40.3%), epileptiform discharges (11 cases, 17.7%), extreme delta brush (EDB) (10 cases, 16.1%), polymorphic delta rhythm (6 cases, 9.7%), focal slowing (5 cases, 8.1%), and diffuse beta activities (4 cases, 6.5%). Patients with normal background, epileptiform discharges, polymorphic delta rhythm, and diffuse beta activity in EEG all had favorable long-term outcome.
Conclusions: The majority of anti-NMDAR encephalitis patients had abnormal EEG. EEG could sensitively reflect the abnormal brain functions of patients and could assist with early clinical diagnosis and prognosis prediction.
Significance: Diffuse slowing was the most common presentation on the EEG in patients with anti-NMDAR encephalitis. The EEG pattern of normal background, epileptiform discharges, polymorphic delta rhythm, and diffuse beta activities at the peak stage might suggest favorable long-term prognosis.

1. Introduction

Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis was first reported by Dalmau et al. (2007). This autoimmune encephalitis is serious and can be fatal; however, the disease condition can be significantly improved or even cured after early diagnosis and active treatment. Due to the limitations of detection techniques, the identification of anti-NMDAR encephalitis or the rapid obtainment of detection of anti-NMDAR encephalitis-specific antibodies cannot be achieved in many regions. Therefore, it is very important to further understand the clinical and auxiliary examination characteristics of anti-NMDAR encephalitis and to perform accurate diagnosis as early as possible. Previous studies have shown that electroencephalogram (EEG) of anti-NMDAR encephalitis patients usually has abnormalities; a non-specific

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diffuse slowing is the common EEG presentation in anti-NMDAR encephalitis (Dalmau et al., 2011). In addition, EEGs are helpful for clinical differentiation between non-convulsive status epilepticus (NCSE) occurring in anti-NMDAR encephalitis patients and frequent involuntary movements; therefore, EEGs can be used as a powerful tool for disease diagnosis, clinical symptom identification, and anti-epilepsy treatment guidance (Chanson et al., 2016; Dalmau et al., 2011; Dericioglu et al., 2013). In 2012, Schmitt et al. (2012) first reported that 30.4% (7/23 cases) of adult anti-NMDAR encephalitis patients had extreme delta brush (EDB) on EEG. The presentation of this EDB was a wave peak of 1–3 Hz delta waves superimposed with a large amount of 20–30 Hz beta waves and was considered to be the possible characteristic EEG change for anti-NMDAR encephalitis. However, the association between the outcome and EEG presentation at the peak stage in anti-NMDAR encephalitis patients and the occurrence rate of EDB in Chinese patients are still not clear. Therefore, this study was performed to analyze the EEG characteristics of Chinese anti-NMDAR encephalitis patients.

2. Subjects and methods

2.1. Patients

Anti-NMDAR encephalitis patients admitted to the Department of Neurology in Xuanwu Hospital of Capital Medical University between January 1st, 2012 and June 30th, 2016 were enrolled. The inclusion criteria are as follows: (1) Patients who met the anti-NMDAR encephalitis diagnostic criteria (Graus et al., 2016) and had rapid development (disease course < 3 months) of one or more of the following symptoms: Mental behavior disorder, cognitive impairment, language impairment, disturbance of consciousness, epilepsy, involuntary movement, autonomic nervous system dysfunction, or central hypoventilation; patients who had positive anti-NMDAR antibody IgG in their cerebrospinal fluid (CSF) with or without combined positive anti-NMDAR antibody IgG in their serum; and exclusion of the diagnosis of other diseases, such as viral encephalitis, brain tumor, metabolic diseases, and drug poisoning; (2) Patients within 60 d of disease onset; and (3) Obtainment of informed consent of patients or family members.

Clinical information of patients, such as basic conditions, past history, clinical presentations, and treatment, was recorded in detail and included gender, age, time of disease onset, time between disease onset and hospital admission, clinical manifestations, whether combined with teratoma or other tumors, modified Rankin Scale (mRS) scores before treatment (Titulaer et al., 2013), immunotherapy, and whether the patient had been admitted into neuro-intensive care unit (NCU). According to the staging methods in the studies of Gitiaux et al. (2013) and Nosadini et al. (2015), the following clinical stages were used: The initial stage was within 14 d of symptom onset, the peak stage was 14–60 d after the presence of symptoms, the improvement stage was 3–6 months after disease onset, and the recovery stage was 6 months after disease onset. All patients underwent at least one EEG, lumbar puncture, and cranial magnetic resonance imaging (MRI) at the peak stage.

2.2. EEG examination and analytic indicators

EEG monitoring was performed using the 32-channel video-EEG monitoring system (DAVINCI-SAM; Micromed, Mogliano Veneto, Italy). Recording electrodes were placed according to the international 10–20 system. EEG was assessed offline by at least two certified neurophysiologists. EEG analytic patterns included epileptiform discharges, diffuse slowing, focal slowing, polymorphic delta rhythm, diffuse beta activities, and EDB (Schmitt et al., 2012). The definition of the EEG patterns was as follows: The epileptiform discharges pattern was defined when there were epileptiform discharges, the EDB pattern was defined when there was EDB in EEG activities, and the other patterns were defined according to the main form of EEG activities. The use of anti-epileptic drugs and sedative drugs was recorded simultaneously.

2.3. Lumbar puncture examination

The lumbar puncture pressure and white blood cell count, glucose, protein, chlorides, and oligoclonal bands in CSF were recorded. In addition, the NMDAR antibody titers in CSF and serum were detected (according to the antibody titer levels, samples were classified into strong positive (titer of 1:100 and above), positive (1:32), weak positive (1:10), and negative.

2.4. Treatment

All patients received tumor screening, symptomatic supportive treatment, and immunotherapy. All cancer patients received tumor resection. The immunotherapy included intravenous glucocorticoid therapy (1000 mg or 500 mg methylprednisolone for 3 or 5 d), intravenous gamma immunoglobulin (IVIG) (0.4 g/kg/d for each course for 5 d), plasma exchange (3–5 times in each course), or immunosuppressants (rituximab, cyclophosphamide, mycophenolate mofetil, or thiopurine).

2.5. Outcome evaluation

Patients received outcome evaluation every 6 months after the immunotherapy. The mRS (Titulaer et al., 2013) was used for outcome evaluation. After discharge, outcome evaluation was performed during the clinical visit to the neurologist or via telephone follow-up. The evaluation standards were as follows: mRS score of 0–2 points was a favorable outcome, and 3–6 points was an unfavorable outcome.

2.6. Statistical analysis

Data input and statistical analyses were performed using Statistical Package for Social Sciences (SPSS) 22.0 (IBM Corporation, Armonk, NY, USA). All measurement data were subject to the normality test. Data with a normal distribution were expressed as means ± standard deviations, while data with a non-normal distribution were expressed as medians (interquartile ranges). Count data were described as the number of cases (%). The significance levels of differences in gender, clinical presentations, and patient outcome between the two groups of patients with or without EDB on the EEG were analyzed using Fisher's exact test or the chi-square test. $P < 0.05$ indicated statistical significance.

3. Results

In total, this study enrolled 62 cases of anti-NMDAR encephalitis patients, including 29 males (46.8%) and 33 females (53.2%). The patient ages were between 10 and 59 (mean 26.3 ± 11.3) years; 58 cases were first disease onset, and 4 cases were first recurrence. A total of 5 (5/33, 8.1%) female patients had combined ovarian teratoma, and they all received teratoma resection within one month of admission; no other patients were found any tumors.

A total of 31 (50%) patients had precursory symptoms such as fever, headache, and dizziness before disease onset. Mental behavior disorder (27 cases, 43.5%) and epileptic seizure (19 cases, 30.6%) were the more common initial symptoms. The more common clin-

Table 1
The first onset symptoms and clinical features of patients with anti-NMDAR encephalitis.

	First onset symptoms		Clinical features	
	Number	Percentage	Number	Percentage
Mental behavior disorder	27	43.5	48	77.4
Epileptic seizure	19	30.6	46	74.2
Cognitive impairment	5	8.1	37	59.7
Limb weakness	5	8.1	5	8.1
Involuntary movement	4	6.5	29	46.8
Disturbance of consciousness	2	3.2	33	53.2
Language impairment	0	0	25	40.3
Autonomic nervous dysfunction	0	0	14	22.6
Central hypoventilation	0	0	13	21.0

Table 2
The EEG presentations in different clinical stages of anti-NMDAR encephalitis patients.

EEG	Clinical stage							
	Initial stage		Peak stage		Improvement stage		Recovery stage	
	$n = 10$	Percentage	$n = 62$	Percentage	$n = 13$	Percentage	$n = 4$	Percentage
Normal	2	20.0	1	1.6	1	7.7	2	50.0
Epileptiform discharges	2	20.0	11	17.7	3	23.1	0	0
Diffuse slowing	4	40.0	25	40.3	7	53.8	0	0
Focal slowing	1	10.0	5	8.1	0	0	1	25.0
Polymorphic delta rhythm	0	0	6	9.7	0	0	0	0
Diffuse beta activities	0	0	4	6.5	0	0	1	25.0
EDB	1	10.0	10	16.1	2	15.4	0	0

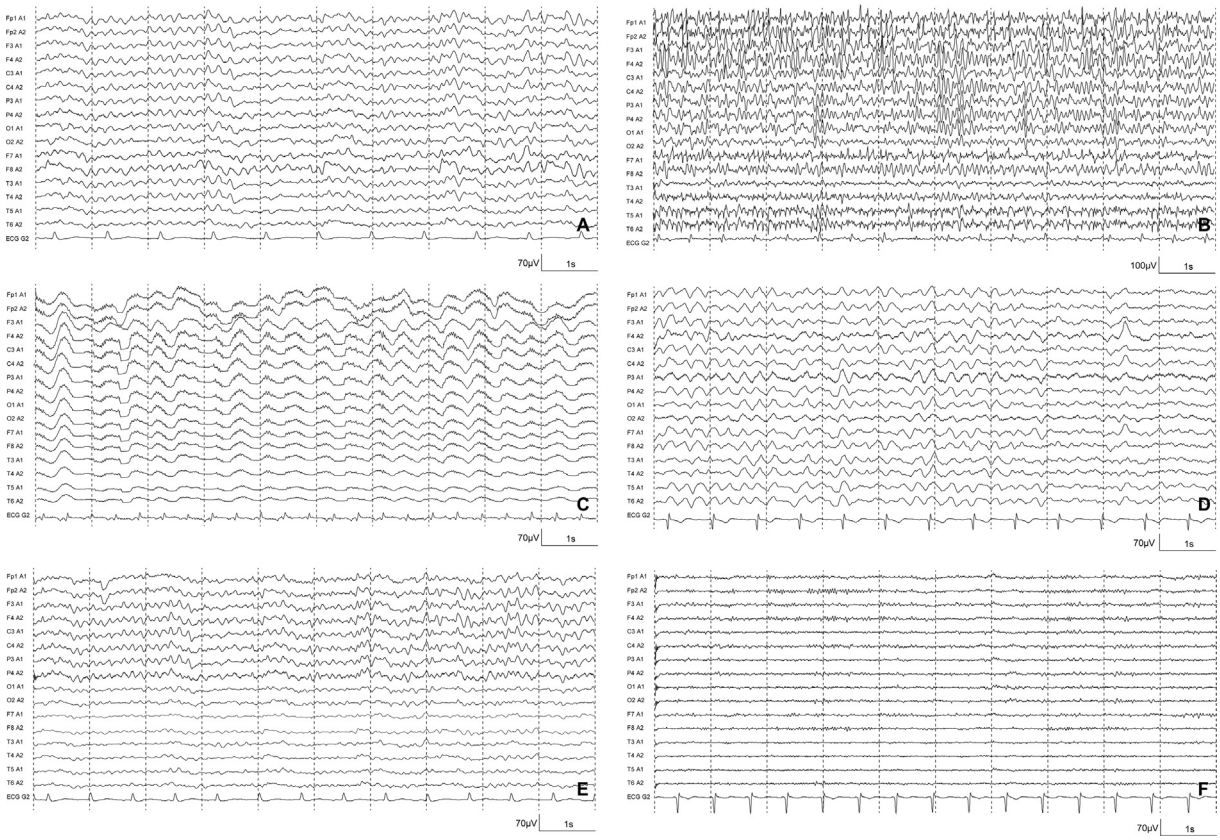

Fig. 1. Examples of abnormal EEG patterns: (A) diffuse slowing; (B) epileptiform discharges; (C) EDB; (D) polymorphic delta rhythm; (E) focal slowing; (F) beta activities.

ical presentations included 48 cases of mental behavior disorder (77.4%), 46 cases of epileptic seizure (74.2%) with 2 cases (3.2%) of status epilepticus, 37 cases (59.7%) of cognitive impairment, 33 cases (53.2%) of disturbance of consciousness, of which 6 cases were sedative drug-related, and 13 cases (21%) with Glasgow coma scale (GCS) scores < 8 points (Table 1). A total of 24 cases (38.7%) were admitted into the NCU for treatment. Before treatment, mRS scores were 1–5 (mean 3.7 ± 1.3).

Table 3
The EEG presentations in peak stage and NMDAR antibody titers in CSF and serum of anti-NMDAR encephalitis patients.

NMDAR antibody titers	Normal (%)	Epileptiform discharges (%)	Diffuse slowing (%)	Focal slowing (%)	Polymorphic delta rhythm (%)	Diffuse beta activities (%)	EDB (%)
CSF							
1:10	0(0)	0(0)	2(3.2)	0(0)	1(1.6)	0(0)	0(0)
1:32	1(1.6)	9(14.5)	14(22.6)	4(6.5)	3(4.8)	1(1.6)	6(9.7)
≥1:100	0(0)	2(3.2)	9(14.5)	1(1.6)	2(3.2)	3(4.8)	4(6.5)
Serum							
(−)	1(1.6)	7(11.3)	16(25.8)	2(3.2)	1(1.6)	0(0)	6(9.7)
1:10	0(0)	2(3.2)	3(4.8)	1(1.6)	3(4.8)	0(0)	1(1.6)
1:32	0(0)	2(3.2)	6(9.7)	2(3.2)	2(3.2)	3(4.8)	3(4.8)
≥1:100	0(0)	0(0)	0(0)	0(0)	0(0)	1(1.6)	0(0)
Total	1(1.6)	11(17.7)	25(40.3)	5(8.1)	6(9.7)	4(6.5)	10 (16.1)

Table 4
The clinical manifestations and outcomes of anti-NMDAR encephalitis patients had EDB on EEG.

Items		*n*	EDB		P value
			No *n* (%)	Yes *n* (%)	
Total		62	52(83.9)	10(16.1)	–
Gender	Male	29	24(82.8)	5(17.2)	1.000
	Female	33	28(84.8)	5(15.2)	
Mental behavior disorder	No	14	11(78.6)	3(21.4)	0.681
	Yes	48	41(85.4)	7 (14.5)	
Epileptic seizure	No	16	13(81.2)	3(18.8)	0. 709
	Yes	46	39(84.8)	7(15.2)	
Cognitive impairment	No	25	23(92.0)	2(8.0)	0.182
	Yes	37	29(78.4)	8(21.6)	
Disturbance of consciousness	No	29	23(79.3)	6(20.7)	0.493
	Yes	33	29(87.9)	4(12.1)	
Involuntary movement	No	33	29(87.9)	4(12.1)	0.493
	Yes	29	23(79.3)	6(20.7)	
Language impairment	No	37	33 (89.2)	4 (10.8)	0.291
	Yes	25	19 (76.0)	6 (24.0)	
Autonomic nervous dysfunction	No	48	39(81.2)	9(18.8)	0.431
	Yes	14	13(92.9)	1(7.1)	
Mechanical ventilation	No	49	41(83.7)	8(16.3)	1.000
	Yes	13	11(84.6)	2(15.4)	
Teratoma	No	57	48(84.2)	9(15.8)	1.000
	Yes	5	4(80.0)	1(20.0)	
Stay in neuro-intensive care unit	No	38	32(84.2)	6(15.8)	1.000
	Yes	24	20(83.3)	4(16.7)	
Sedation	No	33	28(84.8)	5(15.2)	1.000
	Yes	29	24(82.8)	5(17.2)	
Modified Rankin Scale before immunotherapy	1	4	3(75.0)	1(25.0)	–
	2	10	9(90.0)	1(10.0)	
	3	17	14(82.4)	3(17.6)	
	4	3	3(100)	0(0)	
	5	28	23(82.1)	5(17.9)	
The NMDAR antibody titers strong positive in CSF	No	41	35(85.4)	6(14.6)	0.722
	Yes	21	17(81.0)	4(19.0)	
Cranial MRI	Normal	32	26(81.2)	6(18.8)	0.733
	Abnormal	30	26(86.7)	4(13.3)	
Outcome after 6 months	Favorable	54	46(85.2)	8(14.8)	0.604
	Unfavorable	8	6(75.0)	2(25.0)	
Outcome after 6–54 months	Favorable	48	43(89.6)	5(10.4)	0.214
	Unfavorable	7	5(71.4)	2(28.6)	

EEG results: A total of 93 instances of EEG monitoring were performed on 62 patients; 40 patients received EEG monitoring once, 15 cases received monitoring twice, 5 cases received monitoring three times, and 2 cases received monitoring 4 times. The patients underwent a median of 4 (range 2–144) hours of continuous EEG monitoring. The conditions of EEG monitoring at different clinical stages were as follows. At the initial stage, 10 cases underwent EEG monitoring. At the peak stage, all 62 patients received EEG monitoring at least once, and 4 out of the 62 patients received EEG monitoring twice; moreover, because 3 of these 4 patients had consistent results between the two EEGs, only one result was selected for statistical analysis. For the patient whose first EEG showed EDB but whose second EEG after 1 month showed diffuse slowing, only the first EEG result was selected for statistical analysis. At the improvement stage, 13 cases received EEG monitoring. At the recovery stage, 4 cases received EEG monitoring (Table 2).

EEG presentations at the peak stage: Among the EEG results of the 62 patients, 1 case (1.6%) was normal, and 61 cases (98.4%) were abnormal. The main presentations of abnormal EEG were diffuse slowing (25 cases, 40.3%), epileptiform discharges (11 cases, 17.7%), EDB (10 cases, 16.1%), polymorphic delta rhythm (6 cases, 9.7%), focal slowing (5 cases, 8.1%), and diffuse beta activities (4 cases, 6.5%) (Fig. 1). All non-EDB beta activities were due to admin-

istration of sedatives. There was no association between the EEG presentations in peak stage and NMDAR antibody titers in CSF and serum (Table 3). The presence of EDB could exclude the influences of benzodiazepines or sedative drugs. The clinical presentations, cranial MRI presentations, and outcome between the two groups of patients with or without EDB were not significantly different (Table 4). EEG presentations at the peak stage and outcomes (Fig. 2): Patients with normal background, epileptiform discharges, polymorphic delta rhythm, and diffuse beta activity in their EEG findings all had favorable long-term outcome.

Lumbar puncture examination results: The lumbar puncture pressure ranged from 80 to 330 (mean 188 ± 56) mmH_2O, and 20 cases (32.3%) had increased pressure. The white blood cell count in the CSF ranged from 0 to 764×10^6/L, with a median of 10×10^6/L (interquartile range: 3×10^6/L–25×10^6/L); 29 cases (46.8%) had increased white blood cell count, with dominant monocytes. The glucose and chloride levels in the CSF were all normal. The CSF protein level ranged from 6 to 153 (mean 28 ± 22) mg/dl. Oligoclonal bands in CSF were positive in 27 cases (43.5%). Detection of NMDAR antibodies in CSF was positive in all 62 cases, of which 21 cases (33.9%) were strongly positive, 38 cases (61.3%) were positive, and 3 cases (4.8%) were weakly positive.

Serum NMDAR antibody detection results: One case (1.6%) were strongly positive, 18 cases (29.0%) were positive, 10 cases (16.1%) were weakly positive, and 33 cases (53.2%) were negative.

Cranial MRI: Among these 62 patients, 33 cases (53.2%) were normal, and 29 cases (46.8%) were abnormal. Five patients had lesions extensively involving the cerebral cortex. Other lesions visible in cranial MRIs showed that 8 cases had frontal lobe involvement, 7 cases had temporal lobe involvement, 6 cases had hippocampal involvement, 6 cases had cerebral white matter involvement, 4 cases had parietal lobe involvement, 4 cases had insular involvement, 3 cases had cingulate gyrus involvement, and 1 case had occipital lobe involvement.

Treatment and outcome: All patients received immunotherapy; 56 cases (90.3%) received glucocorticoid therapy, 41 cases (66.1%) received IVIG therapy, 12 cases (19.4%) received plasma exchange therapy, and 10 cases (16.1%) received immunosuppressant therapy. After 6 months of immunotherapy, mRS scores ranged from 0 to 6 (mean 1.1 ± 1.3), 54 of the 62 patients (87.1%) had favorable outcomes, and 8 cases (12.9%) had unfavorable outcome; one patient died because of renal failure. Subsequently, 61 survivors were followed up once every 6 months, of which 7 patients were lost to follow-up; the longest follow-up time was 54 months after the immunotherapy. The long-term follow-up results of 54 cases showed that the mRS scores ranged from 0 to 6 (mean 1.0 ± 1.3), 48 cases (88.9%) had favorable outcomes, 6 cases (11.1%) had unfavorable outcomes (Fig. 3). The remaining symptoms included cognitive impairment in 13 cases, personality change in 3 cases, language impairment in 2 cases, epileptic seizure in 2 cases, slow action in 1 case, and involuntary movement in 1 case.

4. Discussion

EEG is a tool commonly used in the diagnosis of nervous system diseases. Its diagnostic value in anti-NMDAR encephalitis has received increasing attention (Schmitt et al., 2012). This study confirmed that EEG had important significance in the early diagnosis of anti-NMDAR encephalitis and the differentiation between epilepsy and involuntary movement. Our data showed that at the disease peak stage, the majority of patients (98.4%) had an abnormal EEG and that the abnormal cranial MRI rate was 46.8%; thus, the EEG was more sensitive than cranial MRI and had important significance in the diagnosis of patients who only exhibited psychiatric symptoms at the early stage of disease onset (Mangalwedhe et al., 2015). For example, 43.5% patients in this study had disease onset with abnormal mental behaviors. EEG could help to discover abnormalities as early as possible to avoid delayed treatment of patients due to long-term treatment in the psychiatry department.

Consistent with previous study (Da et al., 2014), results in this study also showed that diffuse slowing was the most common type of EEG presentation in anti-NMDAR encephalitis. NMDAR is an ionotropic glutamate receptor; it has many regulatory sites with different structures and ligand-gated channels with high calcium permeability and is distributed in all brain tissues. Following the interaction between NMDAR and NMDAR antibodies, cell depolarization is shortened, causing slow waves in the EEG (Carvajal et al., 2016). In addition, encephalitis itself will cause damage in certain locations, such as the cerebral cortex, cerebral white matter, basal ganglia, and midbrain. Cortical damage or disorders of the ascending reticular activating system will both induce the presence of slow waves. According to different locations of damage, focal slowing or diffuse slowing might occur (Sutter et al., 2015).

Acute symptomatic seizure is a common symptom in anti-NMDAR encephalitis. Some researchers have shown that autoimmune encephalitis was the most common reason for new-onset refractory status epilepticus (Gaspard et al., 2015). EEG has an important role in the diagnosis and treatment efficacy evaluation of epilepsy and status epilepticus. The EEG results at the peak stage in this study revealed 11 cases (17.7%) of epileptic wave, and epilepsy seizure was the clinical presentation in 46 cases (74.2%); of these cases, 2 had status epilepticus. Similarly, previous study showed that the majority (near 80%) of patients had limb twitching, but only a very low percentage of patients had epileptiform discharges in the EEG (Schmitt et al., 2012). There are a couple of possible reasons for this presentation. (1) Many patients had epileptic seizures or even status epilepticus at the early stage of disease onset; however, epileptic seizures in some patients were easy to control, and epileptiform discharges could not be recorded during EEG detection. (2) Epilepsy and involuntary movement were present at the same time, or the epilepsy-like attack observed in clinical practices was actually involuntary movement; therefore, the detection rate of epileptiform discharges on the EEG was low. It is sometimes difficult to distinguish between epilepsy and involuntary movement in patients with anti-NMDAR encephalitis only by clinical presentations, especially in patients with disturbance of consciousness; therefore, EEG monitoring is very important. Anti-NMDAR encephalitis patients usually have extensive delta rhythms on the EEG (Da et al., 2014); some results have suggested that the delta rhythm reflects NCSE (Kirkpatrick et al., 2011). However, some studies also showed that this type of delta rhythm was not associated with epilepsy; even after several months of disease onset, patients with improved clinical presentations still had this type of delta rhythm (Da et al., 2014). In our study, 9.7% (6/62 cases) of patients exhibited polymorphic delta rhythm without concurrent beta waves on the EEG at the peak stage; additionally, the presentation was not associated with epilepsy.

EDB has received clinical attention since Schmitt et al. (2012) showed that it might be a characteristic EEG change in anti-NMDAR encephalitis. This study showed that EDB emerged in patients at the initial stage, mainly occurred at the peak stage, and gradually disappeared at the recovery stage. This study also confirmed that EDB was neither an artifact resulting from non-involuntary movement nor a drug-related fast wave caused by anti-epileptic drugs or sedative drugs and was not associated with sleep-wake cycles (Schmitt et al., 2012). The EDB could help in the diagnosis of anti-NMDAR encephalitis; in particular, it could be used as the basis of early diagnosis of atypical cases. If the EDB is discovered in the clinical workup, the possibility of anti-NMDAR encephalitis should be highly suspected. In contrast to previous reports showing that patients with EDB had more serious diseases

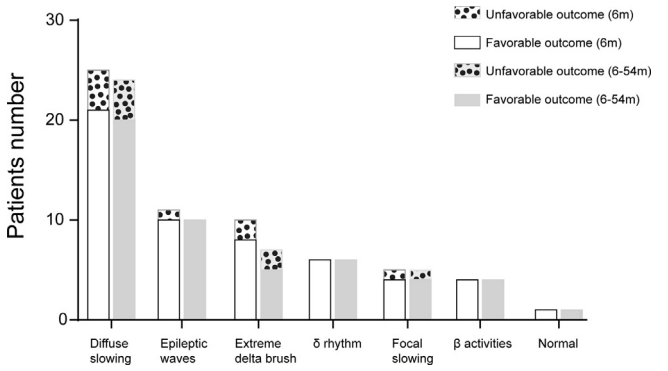

Fig. 2. EEG presentations on the disease peak stage and outcomes.

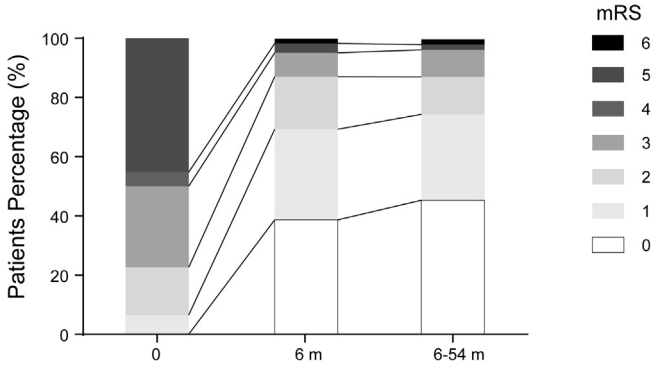

Fig. 3. The outcome after 6 months and outcome of long-term follow-up (6–54 months) of patients with anti-NMDAR encephalitis.

(Da et al., 2014; Schmitt et al., 2012; VanHaerents et al., 2014), the present study showed that the conditions of disturbance of consciousness, requirement of mechanic ventilation, and admission into the NCU, which reflected the disease severity between the two groups with or without EDB, were not significantly different. In addition, the 16.1% (10/62 cases) EDB occurrence rate in this study was lower than the 30.5% rate reported by Schmitt et al. (2012). There are a couple of possible reasons for this difference. (1) It might be associated with the lower percentage of severe patients enrolled in this study. In the study of Schmitt et al. (2012), 61% (14/23 cases) of patients were severe patients with GCS < 8 points; in this study, only 21% (13/62) of patients had GCS < 8 points. (2) It might be associated with the shorter duration of EEG monitoring in this study. The patients underwent a median of 7 (range 1–123) days of continuous EEG monitoring in Schmitt et al. (2012) study. However, the duration of EEG monitoring was a median of 4 (range 2–144) hours in our study. (3) It is possible that the EDB occurrence rate among Chinese patients is not very high. The results of two studies focusing on EEG from children with anti-NMDAR encephalitis in China showed that approximately 7% (7/105 cases and 2/28 cases) of patients had EDB (Gao et al., 2016; Li et al., 2016); the percentages were both significantly lower than the 1/3 occurrence rate.

Currently, the prognosis of patients with the presence of EDB is still controversial. Previous studies have shown that patients with EDB had worse outcome (Da et al., 2014; Schmitt et al., 2012; VanHaerents et al., 2014). However, a different study also suggested that patients with EDB had a median mRS score of 0 (0–3) at the recovery stage and had favorable outcomes (Li et al., 2016). One study showed that patients with the presence of beta waves imposed in between wave peaks of delta waves, rather than on the wave peaks, had better outcome than patients with EDB (Wang et al., 2015). The outcomes after 6 months and after longer periods of follow-up in this study were not significantly different between the two groups with or without EDB, suggesting that EDB did not have specificity in prediction of unfavorable prognosis. Since the patients with EEG pattern of normal background, epileptiform discharges, polymorphic delta rhythm, and diffuse beta activities at the peak stage all had favorable outcome after 6–54 months, these 4 EEG patterns might indicate favorable long-term prognosis for patients.

In summary, the majority of anti-NMDAR encephalitis patients had abnormal EEG. The diffuse slowing was the most common presentation on the EEG. EDB mainly occurred in patients at the peak stage. EEG could sensitively reflect the abnormal brain functions of patients and could assist with early clinical diagnosis and prognosis prediction.

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Conflict of interest: None of the authors have potential conflicts of interest to be disclosed.

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