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Continuous EEG Findings in Autoimmune Encephalitis

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Abstract

Purpose: Autoimmune encephalitis (AE) is a cause of new-onset seizures, including new-onset refractory status epilepticus, yet there have been few studies assessing the EEG signature of AE.

Methods: Multicenter retrospective review of patients diagnosed with AE who underwent continuous EEG monitoring.

Results: We identified 64 patients (male, 39%; white, 49%; median age, 44 years); of whom, 43 (67%) were antibody-proven AE patients. Of the patients with confirmed antibody AE, the following were identified: N-methyl-D-aspartate receptor (n = 17, 27%), voltage-gated potassium channel (n = 16, 25%), glutamic acid decarboxylase (n = 6, 9%), and other (n = 4, 6%). The remaining patients were classified as probable antibody-negative AE (n = 11, 17%), definite limbic encephalitis (antibody-negative) (n = 2, 3%), and Hashimoto encephalopathy (n = 8, 13%). Fifty-three percent exhibited electrographic seizures. New-onset refractory status epilepticus was identified in 19% of patients. Sixty-three percent had periodic or rhythmic patterns; of which, 38% had plus modifiers. Generalized rhythmic delta activity was identified in 33% of patients. Generalized rhythmic delta activity and generalized rhythmic delta activity plus fast activity were more common in anti-N-methyl-D-aspartate AE (P = 0.0001 and 0.0003, respectively). No other periodic or rhythmic patterns exhibited AE subtype association. Forty-two percent had good outcome on discharge. Periodic or rhythmic patterns, seizures, and new-onset refractory status

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epilepticus conferred an increased risk of poor outcome (OR, 6.4; $P = 0.0012$; OR, 3; $P = 0.0372$; OR, 12.3; $P = 0.02$, respectively).

Conclusion: Our study confirms a signature EEG pattern in anti-N-methyl-D-aspartate AE, termed extreme delta brush, identified as generalized rhythmic delta activity plus fast activity in our study. We found no other pattern association with other AE subtypes. We also found a high incidence of seizures among patients with AE. Finally, periodic or rhythmic patterns, seizures, and new-onset refractory status epilepticus conferred an increased risk of poor outcome regardless of AE subtype.

Keywords

Continuous EEG; Autoimmune encephalitis; Electrographic findings in autoimmune encephalitis; Encephalitis; Anti-NMDA-receptor encephalitis; Limbic encephalitis; Hashimoto encephalopathy; NORSE

Autoimmune encephalitis (AE) is characterized by rapidly progressive encephalopathy with subacute memory impairment, confusion, and often seizures caused by inflammation of the central nervous system.[1–3] The pathophysiology involves autoimmune attack against specific neuronal molecular structures through various immune-mediated mechanisms. The major mechanisms are related to antibodies directed against extracellular and intracellular neuronal targets.[3,4] The reported incidence of AE is estimated to be 5 to 10 per 100,000 in high-income countries.[1]

Autoimmune encephalitis is often associated with seizures and is increasingly recognized as a common cause of new-onset refractory status epilepticus (NORSE). In a retrospective review of 130 patients with NORSE performed by Gaspard et al.,[5] in 2015, the most common identifiable cause was autoimmune (37%), 18% of whom were paraneoplastic. Of note, 52% of all 130 cases remained cryptogenic after extensive evaluations. Antibodies against the following cell surface targets have been associated with seizures: N-methyl-D-aspartate (NMDA), leucine-rich glioma inactivated 1 (LGI1), glutamic acid decarboxylase (GAD)65, gamma-aminobutyric acid (GABA)-A, GABA-B, glycine.

Continuous EEG (cEEG) is essential for detecting and managing seizures and status epilepticus in patients with AE. However, few studies have evaluated specific EEG findings in the various types of AE. Several retrospective studies have found an association between anti-NMDA AE and a newly defined pattern of rhythmic delta with superimposed beta termed “extreme delta brush” (EDB) on EEG.[6–8,17] Little is known about the EEG findings in other AE subtypes. A small retrospective study published in 2016 found no electrographic differences on routine EEGs between patients with antibody-proven epilepsy or encephalopathy and those with seronegative encephalopathy.[1] Another retrospective study found that a poorly sustained posterior dominant rhythm on routine EEGs was significantly associated with AE.[8] No systematic studies have been performed that characterize the cEEG findings in AE patients. Our study aimed to identify EEG features of various subtypes of AE in patients undergoing cEEG monitoring and association with outcome.

METHODS

We conducted a retrospective review of 400 patients who were identified through a CPT (Current Procedural Terminology) code search of the diagnosis “encephalitis.” We included patients who were 16 years or older (all hospitals in the study were adult hospitals, and therefore this age is the most common cutoff for admission to adult hospitals) who presented with symptoms consistent with AE and underwent at least 6 hours of cEEG monitoring. A diagnosis of “antibody-positive definite AE” was made if the patient exhibited positive antibody tests in cerebrospinal fluid (CSF) and/or serum consistent with AE. The diagnosis of antibody-negative AE was made based on the criteria used in the article by Graus et al. (2016) (Supplemental Digital Content 1 [see Table 1, http://links.lww.com/JCNP/A67] describes the diagnostic criteria for AE, reproduced from Graus et al. (2016).[13] Because patients with AE rarely present with a well-defined syndrome, further investigation for AE should always be made if a patient fulfills the criteria for “possible AE.” If after thorough investigation for AE, the patient does not fulfill criteria for a specific AE syndrome [including that of “probable AE”], the likelihood of AE decreases and the diagnosis should be reconsidered. This includes but is not limited to CNS infection, septic encephalopathy, drug toxicity, posterior reversible encephalopathy, cerebrovascular disease, neoplastic disorders, Creutzfedlt–Jakob disease, genetic/mitochondrial disorders, CNS vasculitis. MRI features suggestive of AE includes hyperintense T2/fluid-attenuated inversion recovery sequences signal highly restricted to one or both medial temporal lobes [limbic encephalitis] or in multifocal areas involving grey matter, white matter, or both, compatible with inflammation or demyelination.[13] Supplemental Digital Content 1 [see Tables 2 and 3, http://links.lww.com/JCNP/A67] describe demographic, clinical, and EEG findings of patients divided into autoimmune versus paraneoplastic etiology [see Table 2, Supplemental Digital Content 1, http://links.lww.com/JCNP/A67] and extracellular versus intracellular antibody groupings [see Table 3, Supplemental Digital Content 1, http://links.lww.com/JCNP/A67]. There were no statistically significant differences between the groups and demographic, clinical, and EEG features).[13] We identified 69 with suspected AE between January 1, 2012, and December 31, 2016, at the Emory University (n = 40), Grady Memorial Hospital (n = 5), Massachusetts General Hospital (n = 13), and Yale New Haven Hospital (n = 11). Five patients with “possible AE” on initial presentation did not ultimately fulfill diagnostic criteria for “definite AE” or “probable AE” and so were excluded from the final study.

Patients with known central nervous system (CNS) infections, CNS malignancy, traumatic brain injury, or known history of seizure disorder were excluded. Continuous EEG monitoring was performed at the discretion of the treating team. EEG was acquired using 21 electrode contacts, the 10–20 international system of electrode placement, and one of several standard clinical digital video EEG systems. EEG reports were retrospectively reviewed, and the following variables were noted: presence of periodic or rhythmic patterns (PRP), presence of seizures, location of seizure onset (focal or generalized), seizure type (clinical or subclinical), and presence of NORSE. New-onset refractory status epilepticus was defined as the occurrence of a prolonged period of seizures refractory to first- and second-line agents with no readily identifiable cause in a healthy individual.[9] We coded EEG patterns and

seizures according to the American Clinical Neurophysiology Society critical care EEG Nomenclature.[10]

Demographic data, as well as clinical features and laboratory investigations, were collected via retrospective chart review. Outcomes at discharge were measured using the Glasgow outcome scale.[11] Patients with Glasgow outcome scale scores of 4 and 5 were considered as a favorable outcome, whereas those with scores between 1 and 3 were classified as poor outcomes.

The primary purpose of the study was to describe the cEEG findings of AE patients and to identify potential EEG patterns unique to AE subtype. We also aimed to identify EEG features and AE subtype association with outcome.

Associations between age and antibody type were assessed using a one-way analysis of variance. Associations between age, etiology, and antibody type were tested using two-sample *t*-test. Associations between antibody (AB) type, etiology, antibody location, and other factors (EEG, MRI findings, CSF findings, outcome) were performed with χ^2 or Fisher exact test. Odds ratio and 95% confidence intervals (CIs) were used to assess risk between EEG patterns and outcome. For statistical significance, a certainty level of $\alpha = 0.05$ was used. Data were analyzed using SAS.[12]

RESULTS

We identified 64 patients (male, 39%; white, 50%; median age, 44 years) with definite or probable AE. Forty-three of the patients (67%) had confirmed antibody-proven AE. Eleven patients (17%) had probable antibody-negative AE (five of these patients exhibited anticalcium antibodies, one exhibited anti-Sjogren's-syndrome-related antigen A (SSA) antibodies, and one exhibited antiphospholipid antibodies, acetylcholine receptor antibodies, anti-beta-2-glycoprotein antibodies, and lupus anticoagulant antibodies). Two (3%) had definite limbic encephalitis (antibody negative). Eight (13%) had Hashimoto encephalopathy (Table 1).

Of the 43 patients with confirmed antibody AE, 17 (27%) had NMDA receptor, 16 (25%) had voltage-gated potassium channel, 6 (9%) had GAD, and 4 had other antibody-positive confirmed AE (anti-Hu [$n = 1$, 1.4%], collapsin response–mediator protein 5 [$n = 1$, 1.4%], anti-Ma [$n = 1$, 1.4%], mixed antibody type [$n = 1$, 1.4%]).

There were no statistically significant differences between AE groupings and demographics, clinical features, radiographic findings, CSF findings, NORSE rates, or outcomes at discharge (Table 1 and 2). There were no other statistically significant differences between autoimmune and paraneoplastic or between extracellular versus intracellular, respectively, when tested for the characteristics listed above (Supplemental Digital Content 1 [see Tables 2 and 3, http://links.lww.com/JCNP/A67] describes the diagnostic criteria for AE, reproduced from Graus et al. (2016).[13] Because patients with AE rarely present with a well-defined syndrome, further investigation for AE should always be made if a patient fulfills the criteria for "possible AE. " If after thorough investigation for AE, the patient does not fulfill criteria for a specific AE syndrome [including that of "probable AE"], the likelihood of AE

decreases and the diagnosis should be reconsidered. This includes but is not limited to CNS infection, septic encephalopathy, drug toxicity, posterior reversible encephalopathy, cerebrovascular disease, neoplastic disorders, Creutzfedlt–Jakob disease, genetic/mitochondrial disorders, and CNS vasculitis. MRI features suggestive of AE includes hyperintense T2/fluid-attenuated inversion recovery sequences signal highly restricted to one or both medial temporal lobes [limbic encephalitis] or in multifocal areas involving grey matter, white matter, or both, compatible with inflammation or demyelination.[13] Supplemental Digital Content 1 [see Tables 2 and 3, http://links.lww.com/JCNP/A67] describe demographic, clinical, and EEG findings of patients divided into autoimmune versus paraneoplastic etiology [see Table 2, Supplemental Digital Content 1, http://links.lww.com/JCNP/A67] and extracellular versus intracellular antibody groupings [see Table 3, Supplemental Digital Content 1, http://links.lww.com/JCNP/A67]. There were no statistically significant differences between groups and demographic, clinical, and EEG features).

cEEG Findings

Table 2 describes the cEEG findings of the patients. Sixty-three percent had PRP on cEEG. Thirty-eight percent of those with periodic or rhythmic patterns had plus modifiers. Electrographic seizures were seen in approximately half of the patients (53%). New-onset refractory status epilepticus was seen in 19% of all patients.

Generalized rhythmic delta activity (GRDA) was identified in 33% of patients and was seen significantly more often in anti-NMDA receptor AE ($P = 0.0001$). Moreover, anti-NMDA receptor AE exhibited plus modifiers more often than other groups ($P = 0.0037$). Anti-NMDA was the only AE subtype that exhibited GRDA plus fast activity (+F) ($P = 0.0001$).

Lateralized rhythmic delta activity, lateralized periodic discharges, generalized periodic discharges, and bilateral independent periodic discharges were seen in 16%, 22%, 16%, and 3% of patients, respectively (without specific antibody association).

When patients were divided into extracellular versus intracellular antibody groups and autoimmune versus paraneoplastic etiology, there were no statistical differences between groups and EEG features (Supplemental Digital Content 1 [see Table 1, http://links.lww.com/JCNP/A67] describes the diagnostic criteria for AE, reproduced from Graus et al. (2016).[13] Because patients with AE rarely present with a well-defined syndrome, further investigation for AE should always be made if a patient fulfills the criteria for “possible AE.” If after thorough investigation for AE, the patient does not fulfill criteria for a specific AE syndrome [including that of “probable AE”], the likelihood of AE decreases and the diagnosis should be reconsidered. This includes but is not limited to CNS infection, septic encephalopathy, drug toxicity, posterior reversible encephalopathy, cerebrovascular disease, neoplastic disorders, Creutzfedlt–Jakob disease, genetic/mitochondrial disorders, and CNS vasculitis. MRI features suggestive of AE includes hyperintense T2/fluid-attenuated inversion recovery sequences signal highly restricted to one or both medial temporal lobes [limbic encephalitis] or in multifocal areas involving grey matter, white matter, or both, compatible with inflammation or demyelination.[13] Supplemental Digital Content 1 [see Tables 2 and 3, http://links.lww.com/JCNP/A67] describe demographic,

clinical, and EEG findings of patients divided into autoimmune versus paraneoplastic etiology [see Table 2, Supplemental Digital Content 1, http://links.lww.com/JCNP/A67] and extracellular versus intracellular antibody groupings [see Table 3, Supplemental Digital Content 1, http://links.lww.com/JCNP/A67]. There were no statistically significant differences between groups and demographic, clinical, and EEG features).

Clinical Outcomes

Forty-two percent of patients had good outcome on discharge. There were no statistically significant differences in outcome among AE subtypes. PRP, seizures, and NORSE conferred an increased risk of poor outcome (OR, 6.4; 95% CI, 2.1–19.6; $P = 0.0012$; OR, 3; 95% CI, 1.1–8.4; $P = 0.0372$; OR, 12.3; 95% CI, 1.5–103; $P = 0.02$, respectively) (Table 3). Lateralized rhythmic delta activity, generalized periodic discharge, and GRDA and plus modifiers were associated with an increased risk of poor outcome (OR, 9; 95% CI, 1.1–76; $P = 0.04$; OR, 9; 95% CI, 1.1–76; $P = 0.04$; OR, 5.4; 95% CI, 1.5–18.6; $P = 0.008$; OR, 10.7; 95% CI, 1.2–95; $P = 0.03$, respectively). Interestingly, GRDA + F did not result in increased risk of poor outcome.

DISCUSSION

Our study systematically describes the cEEG findings of various types of AE based on the updated proposed AE criteria defined by Graus et al.[13] in 2016. Our most relevant findings are as follows: (1) The lack of characteristic signature of any antibodies with specific EEG findings aside from anti-NMDA receptor AE and GRDA and GRDA + F (EDB pattern). (2) The high incidence of electrographic seizures in all AE encephalitis cases. (3) An increased risk of poor outcome with PRP, seizures, and NORSE, regardless of AE subtype.

In this study, GRDA was more commonly seen in anti-NMDA receptor AE. Furthermore, GRDA + F was associated with anti-NMDA receptor AE and likely is synonymous with the previously described EDB pattern.[6] One potential reason why “GRDA + F” is described in our study rather than “EDB” is because of the nature of the American Clinical Neurophysiology Society critical care EEG nomenclature. Although some of the reports reviewed in our study reported a connection between the GRDA + F pattern and EDB in the clinical correlation section, not all reports made this connection. Our findings are in line with previous studies that identify EDB as highly specific for anti-NMDA AE.[6,7,14,15] Thus, the EDB/GRDA + F pattern likely serves as a useful biomarker for anti-NMDA AE. In our study, the presence of GRDA + F did not result in increased odds of poor outcome in our study. The correlation of EDB and outcome is controversial because some studies report an association between EDB and poor outcome,[17,21,22] whereas others report no association between EDB and clinical outcome.[16,23,24]

No additional characteristic signatures were found with other AE subtypes. Fifty-three percent of AE patients had seizures on cEEG. To the best of our knowledge, only two other studies have been published describing EEG findings of patients with AE, with the incidence of electrographic seizures listed as 5% ($n = 20$) and 43% ($n = 7$), respectively.[1,8] These studies involved the use of routine EEG studies rather than cEEG, and thus may not accurately reflect electrographic seizure incidence. Our study is the first to identify seizure

incidence of a relatively large cohort of AE patients (n = 64) undergoing cEEG. The higher incidence of seizures in our study compared with other studies may be related to the larger cohort. The greater seizure incidence also could be related to the longer duration of EEG recording in our study. Given that cEEG holds greater utility in detecting subclinical seizures compared with routine EEG,[18] our study suggests that there may be a high incidence of seizures in patients with AE. Thus, cEEG may be more helpful than routine EEG in monitoring and detecting seizures in this group, especially if there is concern for seizures. However, the study excluded AE patients who did not undergo cEEG, which may have led to selection bias.

The presence of a PRP, seizures, and NORSE conferred an increased risk of poor outcome (Table 3). More specifically, the presence of lateralized rhythmic delta activity, generalized periodic discharge, GRDA, and plus modifiers resulted in an increased risk of poor outcome. Although the association between lateralized rhythmic delta activity, generalized periodic discharge, plus modifiers, and subsequent seizure risk may explain the relation to poor outcome,[20] one would also expect lateralized periodic discharge to confer an increased risk of poor outcome. However, in our study, lateralized periodic discharge did not result in an increased risk of poor outcome. Because faster PRP frequencies have been shown to result in higher seizure risk,[20] the same may apply to outcome. Therefore, future studies of this subject may consider measuring frequency of PRP. The presence of GRDA might confer increased risk of poor outcome because it reflects more severe global cerebral dysfunction.

The presence of NORSE conferred the highest risk of poor outcome (OR, 12.4; 95% CI, 1.5–103; P = 0.0372). This is supported by other studies that identify poor outcomes in patients with NORSE, regardless of underlying etiology.[5,19] The risk of poor outcome in those with NORSE regardless of AE subtype suggests that outcome may not be associated with AE subtype, but rather the presence of NORSE itself. Similar findings were confirmed by Iizuka et al.[19] in 2017 who discovered that patients with cryptogenic NORSE exhibited worse outcomes than those with antibody-confirmed anti-NMDA AE (who did not necessarily exhibit NORSE).

A major limitation to this study is that it used retrospective review of EEG reports; the authors did not review raw EEG data. Therefore, all data on EEG are based on the impression of different EEG readers, and interrater reliability was not assessed. Also, the EEG findings that were recorded were not quantified. Moreover, the collection of a narrow set of EEG findings (PRP, seizures, and NORSE) may have missed more subtle EEG differences between AE subtypes (i.e., presence or absence of a posterior dominant rhythm, continuity, etc). Another limitation is that outcomes were only recorded at discharge, and long-term outcome data were not recorded. Gaspard et al.[5] 2016 found that although those with NORSE have poor outcomes at discharge, outcome improves during follow-up. The same may possibly apply to AE. However, this was not addressed in this study. The majority of our study's patients with poor outcomes on discharge exhibited a Glasgow outcome scale of 3 (placed in the "poor outcome" group) (Table 4). This may have improved during later follow-up to a Glasgow outcome scale of 4 or 5 (grouped as "good outcome"). Due to the well-known connection between AE and NORSE, future studies on AE should be sure to include follow-up outcome data. Finally, anesthesia use and other comorbidities were not

recorded for patients in our study. Thus, higher risk of poor outcome in those with PRP, seizures, and NORSE may have been confounded by other factors.

In summary, our findings support that GRDA + F pattern is likely synonymous to the EDB pattern identified in anti-NMDA AE. Our findings also confirm the close association between GRDA and GRDA + F/EDB and anti-NMDA AE. Interestingly, although GRDA was associated with increased risk for poor outcome, GRDA + F did not confer a higher risk of poor outcome in our study. Our study also suggests that seizures are common in encephalopathic patients with AE, and thus cEEG may be helpful to identify subclinical seizures, especially if PRP are identified on EEG due to the well-known association between most PRP and seizure risk noted in other studies.[20] Finally, the presence of PRP, seizures, and NORSE was associated with poor outcome. The poor prognosis associated with NORSE secondary to AE in our study and cryptogenic NORSE in other studies[5,19] suggests that identifying the pathophysiology of NORSE and more effective therapies for NORSE (regardless of etiology) should be pursued in larger prospective studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE 1.

Demographics of Patients With AE

	All Cases (*n* = 64) (%)	NMDA (*n* = 17) (%)	VGKC (*n* = 16) (%)	GAD (*n* = 6) (%)	Probable AE (*n* = 13) (%)	Hashimoto (*n* = 8) (%)	Other* (*n* = 4) (%)	*P*
White	32 (50)	4 (23)	10 (63)	2 (33)	7 (54)	6 (75)	3 (75)	0.0867
Male	25 (39)	4 (23)	10 (63)	3 (50)	3 (23)	4 (50)	1 (25)	0.1617
Median age (years)	44 (16–86)	29 (16–67)	63 (18–86)	33 (23–47)	46 (21–73)	68 (32–77)	50 (39–62)	

*Groups with low “n” were grouped together into the “other” category for statistical analysis. This group included anti-Hu (*n* = 1), anti-Ma (*n* = 1), anti–collapsin response–mediator protein (*n* = 1), and mixed AB (*n* = 1). Definite limbic encephalitis with negative antibodies (*n* = 2) was grouped together with probable AE (without antibodies) (*n* = 11), for a total of *n* = 13.

AE, autoimmune encephalitis; GAD, glutamic acid decarboxylase; NMDA, N-methyl-D-aspartate; VGKC, voltage-gated potassium channel.

TABLE 2.

Imaging, CSF, Outcomes, and EEG Findings in Patients With AE

	All Cases (*n* = 64) (%)	NMDA (*n* = 17) (%)	VGKC (*n* = 16) (%)	GAD (*n* = 6) (%)	Probable AE (*n* = 13) (%)	Hashimoto (*n* = 8) (%)	Other* (*n* = 4) (%)	*P*
MRI abnormal	44 (69)	9 (53)	11 (69)	6 (100)	10 (77)	6 (75)	2 (50)	0.3205
CSF abnormal	44 (69)	14 (82)	10 (63)	4 (67)	8 (62)	6 (75)	2 (50)	0.0902
Poor outcome	36 (56)	14 (82)	6 (38)	2 (33)	7 (54)	4 (50)	3 (75)	0.0957
Seizures	34 (53)	10 (59)	10 (63)	5 (83)	6 (46)	2 (25)	1 (25)	0.2273
NORSE	12 (19)	4 (24)	1 (6)	3 (50)	4 (31)	0	0	0.0913
Focal seizures	19 (30)	3 (18)	9 (56)	2 (33)	2 (15)	2 (25)	1 (25)	0.1625
Generalized seizures	4 (6)	2 (12)	0	1 (17)	1 (8)	0	0	0.5820
Multifocal seizures	5 (8)	1 (6)	0	2 (33)	2 (15)	0	0	0.1180
Unknown seizure location	4 (6)	3 (18)	0	0	1 (8)	0	0	0.4394
No seizures	27 (42)	5 (29)	7 (44)	1 (17)	7 (54)	6 (75)	1 (25)	0.2086
PRP	40 (63)	15 (88)	6 (38)	4 (67)	7 (54)	4 (50)	4 (100)	0.0219†
GRDA	21 (33)	12 (71)	0	3 (50)	2 (15)	2 (25)	2 (50)	0.0001‡
LRDA	10 (16)	6 (35)	3 (19)	0	1 (8)	0	0	0.1957
LPD	14 (22)	3 (18)	5 (31)	2 (33)	2 (15)	2 (25)	0	0.7762
GPD	10 (16)	2 (12)	1 (6)	1 (17)	4 (31)	1 (13)	1 (25)	0.5013
BIPD	2 (3)	1 (6)	0	0	1 (8)	0	0	0.8651
Plus modifier§	15 (23)	9 (53)	1 (6)	3 (50)	2 (15)	0	0	0.0037‡
GRDA + F	8 (13)	8 (47)	0	0	0	0	0	0.0003‡

*Groups with low "*n*" were grouped together into the "other" category for statistical analysis. This group included Anti-Hu (*n* = 1), anti-Ma (*n* = 1), anti-collapsin response-mediator protein (*n* = 1), and mixed AB (*n* = 1). Definite limbic encephalitis with negative antibodies (*n* = 2) was grouped together with probable AE (without antibodies) (*n* = 11), for a total of *n* = 13.

†$P < 0.05$.

‡$P < 0.01$.

§Plus modifier is defined as an additional feature "which renders the pattern more ictal-appearing than the usual term without the plus."[17]

AE, autoimmune encephalitis; BIPD, bilateral independent periodic discharge; GAD, glutamic acid decarboxylase; GPD, generalized periodic discharge; GRDA, generalized rhythmic delta activity; LPD, lateralized periodic discharge; LRDA, lateralized rhythmic delta activity; NMDA, N-methyl-D-aspartate; NORSE, new-onset refractory status epilepticus; VGKC, voltage-gated potassium channel.

TABLE 3.

EEG Patterns and Outcome

	Poor Outcome* (*n* = 36)	Good Outcome (*n* = 27)	Odds Ratio (95% CI)	*P*
Periodic or rhythmic patterns (*n* = 40)	29	11	6.4 (2.1–19.6)	0.0012†
Seizures (*n* = 33)*	23	10	3.0 (1.1–8.5)	0.0372†
NORSE (*n* = 12)	11	1	12.4 (1.5–103.1)	0.0200†
LRDA (*n* = 10)	9	1	9.0 (1.1–76.0)	0.0436†
LPD (*n* = 16)	8	8	0.7 (0.2–2.2)	0.5614
BIPD (*n* = 3)	3	0	6.0 (0.3–120.2)	0.2445
GPD (*n* = 10)	9	1	9.0 (1.1–76.0)	0.0436†
GRDA (*n* = 21)	17	4	5.4 (1.5–18.6)	0.0081‡
GRDA + F (*n* = 8)	8	0	9.2 (0.4–210.3)	0.1662
Modifier (*n* = 16)	15	1	10.7 (1.2–94.9)	0.0331†

Good outcome is identified as a Glasgow outcome scale of 4 or 5. Poor outcome is identified as a Glasgow outcome scale of 1, 2, or 3.

*One patient's outcome upon discharge was unknown.

†P ≤ 0.05.

‡P ≤ 0.01.

BIPD, bilateral independent periodic discharge; GPD, generalized periodic discharge; GRDA, generalized rhythmic delta activity; LPD, lateralized periodic discharge; LRDA, lateralized rhythmic delta activity; NORSE, new-onset refractory status epilepticus.

TABLE 4.

EEG Patterns and GOS *

	GOS 1 (*n* = 3)	GOS 2 (*n* = 1)	GOS 3 (*n* = 32)	GOS 4 (*n* = 24)	GOS 5 (*n* = 3)	*P*
PRP (*n* = 40)	3	1	25	11	0	0.0033†
Seizures‡	3	1	19	8	2	0.0571
NORSE	2	1	8	1	0	0.0103§

Total number of known outcomes *n* = 63.

*Glasgow Outcome Scale.

†$P < 0.01$.

‡One patient's outcome upon discharge was unknown.

§$P < 0.05$.

GOS, Glasgow outcome scale; NORSE, new-onset refractory status epilepticus.

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