Suicidality is a common and serious feature of anti-N-methyl-D-aspartate receptor encephalitis

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Abstract

Purpose: We aimed to assess suicidality risk amongst people who had had anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis.

Method: All people with a definitive diagnosis of anti-NMDAR encephalitis in West China Hospital between June 2012 and February 2017 were identified and their notes were retrospectively reviewed. Demographic and clinical characteristics and risk predictors for suicidality were summarized; those with suicidality were compared to those without.

Result: Seventeen of 133 people (13%) presented suicidality symptoms: 7 (5%) with suicidal ideation; 8 (6%) who attempted suicide; and 2 (1.5%) who completed suicide. Median age was 27 (16-78) years, most were female (13 [76%]). Compared with those with no suicidality, psychiatric symptoms as the initial symptoms were higher in those who reported suicidality ($p=0.039$); insomnia, aggression, mania, depression and delusion were also more common ($P<0.05$), but multivariate analysis did not identify any independent predictor. Recurrence of encephalitis was higher in people with suicidality than in those without ($p=0.020$). Other characteristics were not significantly different in those who had suicidality and those who did not.

Conclusion: Suicidality is a common and potentially lethal risk for people with anti-NMDAR encephalitis. Those presenting with psychiatric symptoms as the initial symptom and with insomnia, aggression, mania, depression and delusion should be carefully screen for suicidality.

Keywords: Anti-NMDAR encephalitis, suicidal rate, psychiatric symptom, predictors.

Introduction

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an autoimmune disease caused by autoantibodies against the NR1 subunit of the NMDA receptor (1, 2). More than 1,000 cases have been reported since the original diagnosis in 2007 (2,3). Typical features include psychiatric symptoms, seizures, cognitive impairment, speech impairment, movement disorders, autonomic instability, central hypoventilation, and decreased consciousness (3-6). Psychiatric symptoms are the most important and commonest symptom (3-6). Disorganization, delusions, hallucinations, agitation, aggression and insomnia are common psychiatric symptoms reported amongst those presenting with the condition (3, 4, 7). The symptoms are often similar to those of schizophrenia and this may result in misdiagnosis. Suicidality may be a complication of schizophrenia; in some series up to 40% of people with schizophrenia attempted suicide (8-10).No studies, however, apart from some case series, appear to focus on suicidality amongst survivors of anti-NMDAR encephalitis (11-17). In view of the similarity in presentation, we attempted to characterize suicidality in people who had had anti-NMDAR encephalitis, and summarize their clinical characteristics, risk factors and potential predictors.

Materials and methods

Patients

People who were admitted to the wards of West China Hospital between June 2012 and February 2017 with a definitive diagnosis of anti-NMDAR encephalitis were enrolled into this retrospective study based on an existing registry. Diagnosis was based on clinical characteristics and confirmed by anti-NMDAR IgG antibody screening in serum and cerebrospinal fluid (CSF). Serum and CSF samples of suspected cases were simultaneously obtained and sent to Peking Union Medical College Hospital, China, or Oumeng Biotechnology Corporation, Beijing, China, for testing. Samples were assessed by indirect immunofluorescence using EU 90 cells; the method was previously reported in detail (6,18). After diagnostic confirmation, immunotherapy was started. Subjects were also enrolled into an anti-NMDAR encephalitis registry after written informed consent was obtained from either the patient or their families or representatives.

The registry and this study were approved by the Ethical Committee of West China Hospital, Sichuan University (No.20110818).

Data extraction and management

People who developed suicidality were identified mainly through reviewing the registry and evaluating inpatient and follow-up records. Demographics, clinical manifestations, results of auxiliary examination, treatment strategies and treatment outcomes were extracted. Clinical manifestations were divided into: psychiatric symptoms; seizures; cognitive impairment; dyskinesias and movement disorders; speech dysfunction; autonomic instability; central hypoventilation; and decreased consciousness. Psychiatric symptoms included mainly disorganization, insomnia, agitation, mania, aggression, hallucinations, depression, anxiety, delusions and

psychomotor inhibition. Mood was assessed by the Zung Depression Scale (ZDS) (19) and anxiety by the Zung Anxiety Scale (ZAS) (20). Participants were considered to be depressed if their ZDS score was ≥ 50, and anxious if their ZAS score was ≥ 45. EEG results were considered abnormal if clear-cut epileptiform discharges or abnormal slow waves were recorded. For this study, only encephalitis-induced abnormalities were considered abnormal findings on MRI; other abnormalities were not recorded as abnormal. CSF results were considered abnormal if the white blood cell (>5/mm^3) or/and protein (>0.45g/L) were elevated. A titer of anti-NMDAR antibody in CSF ≥ 1:100 was defined as strongly positive. All individuals were also screened for an underlying tumor by MRI, ultrasound examination, contrast-enhanced computed tomography, and tumor markers. All were followed-up through telephone contact or outpatient clinic visits after the first month and every 3 months after the initiation of immunotherapy. Outcomes of treatment were evaluated at the final follow up using the modified Rankin Scale (mRS). Good outcome was defined as mRS score 0-2 and poor outcome as mRS score 3-6. Relapse of encephalitis was defined as new onset or worsening of symptoms occurring after an initial improvement or stabilization of at least 2 months (5).

Definition of suicidality

Suicidality was classified according to the degree of severity: “suicidal ideation,” “attempted suicide,” and “completed suicide”. “Suicidal ideation” referred to expression of the thought of killing oneself without any practical attempt. “Attempted suicide” and “completed suicide” were regarded as suicidal behavior where life-threatening behavior occurred with the intention of jeopardizing life. Self-injurious behavior with unknown intent was not included in suicidal behavior (21).

Statistical analysis

Statistical analyses were performed using SPSS version 21.0. Univariate analyses were performed to compare gender, age, initial symptoms, psychiatric symptoms, other symptomatic presentations, tumor findings, abnormal EEG results, abnormal MRI results, abnormal CSF results, strongly positive NMDAR-Ab in the CSF, positive NMDAR-Ab in the serum, treatment, duration of follow-up, treatment outcomes, and rate of relapse between individuals with and without suicidality and between those with suicidal ideation and with suicidal behavior. Age and duration of follow-up were analyzed as continuous variables, while the remaining variables were analyzed as categorical variables. Wilcoxon test was used for continuous variables. Fisher’s exact test or the chi-squared test were used for other categorical variables. All predictive factors identified by univariate analyses were included into a further multivariable logistic regression model. A two-sided p-value of 0.05 or less was considered to be statistically significant.

Results

General clinical characteristics of individuals who presented with suicidality

A total of 133 people were diagnosed with anti-NMDAR encephalitis during the period of interest. Seventeen (13%) presented suicidality after the onset of

encephalitis; 7 (5%) had suicidal ideation, 8 (6%) attempted suicide and 2 (1.5%) who completed suicide. A further five people with self-injurious behavior were not included as the intention was not known; one of them later died due to multiple organ dysfunction. The median time interval between the initial symptoms of anti-NMDAR encephalitis and suicidality was 1 month (range, 2 days-24 months); 10 of 17 had suicidality prior to admission, 3 during hospitalization, 2 after discharge, and 2 during relapse. The demographic and clinical characteristics of those with suicidality are presented in table 1. Median age was 27 years (range, 16-78 years), and 13 (76%) were female. Educational level among them included one with only primary school education, 5 with middle school education, 3 with high school education, and 8 with higher education.

Fourteen individuals (82%) presented with psychiatric symptoms as the initial symptoms, while 2 presented with a seizure and one with speech dysfunction. Detailed information regarding psychiatric symptoms experienced by each individual is listed in Table 2. Two (12%) were found to have neoplasia (one ovarian teratoma and one adrenal adenoma).

All 17 individuals with suicidality had positive NMDAR-Ab in the CSF, with 6/17 being strongly positive; only 8/17 had positive serum antibodies. Brain MRI was abnormal in 3 individuals, including one who had a lesion near the left anterior horn of the lateral ventricle. The other two individuals with abnormal MRIs had multifocal lesions; one had involvement of the left pons, cerebral peduncle, thalamus, callosum, frontal lobe, periventricular area, and bilateral internal capsules, while the other had involvement of the bilateral frontal and parietal lobes, periventricular triangle, and left anterior horn of the lateral ventricle. Abnormal EEG results were present in 13 of 16 patients (81%) who had results available. Eight had abnormal CSF results. The median follow-up duration was 13.5 months (range, 1-48 months). Treatment outcomes of those with suicidality at the end of follow-up were assessed; 12 (71%) had a good outcome (mRS 0-2). Of those with good outcome, 6 (50%) made a full recovery (mRS 0). Five (29%) had a poor outcome (mRS 3-6) and of those, 3 died. Of the 16 individuals with follow-up of 2 months or more, 5 (31%) had a recurrence.

Comparisons between those with and without suicidality

We compared the 17 individuals who had suicidality with the 116 without suicidality (table 3). Sixty-five (56%) without suicidality had psychiatric symptoms as their initial symptoms; and this was significantly lower than those with suicidality (56% vs. 82%, p=0.039). Psychiatric symptoms in those with suicidality were also different from those without. Univariable analysis showed that the proportion with delusion, mania, insomnia, aggression, and depression were higher in those with suicidality than those without suicidality (table 3). Multivariable logistic regression analysis, however, did not identify independent predictors of suicidality (table 4). There were no significant differences among other psychiatric symptoms (including disorganization, anxiety, agitation, hallucination and psychomotor inhibition). There were no significant differences between the two groups with regards to gender, age, educational background, duration of follow-up, other clinical symptoms and auxiliary examination results (table 3). There were no significant differences in treatment

outcomes at final follow-up between the two groups, but those with suicidality had a higher rate of recurrence than those without suicidality (31% vs. 8%, p=0.020).

Comparisons between those with suicidal ideation and those with suicidal behavior

Detailed information comparing results for those with suicidal ideation only and those with attempted suicide or who completed suicide is presented in Figure 1. The proportion of people with abnormal CSF results was higher in those with suicidal behavior than in those with suicidal ideation (70% vs. 14%, p=0.050). Gender, clinical manifestations, psychiatric symptoms, tumor findings, auxiliary examination results, treatment outcomes, and recurrence rates were not significantly different between these two groups.

Discussion

This study focusing on suicidality in people with anti-NMDAR encephalitis found that suicidality is not rare and was seen in over 10% of individuals, with 1.5% eventually committing suicide. This is a higher suicide rate than suggested by the Chinese national disease surveillance system which provided annual figures between 7.72/100,000 and 7.69/100,000 for completed suicide rate in the general population around the time of the study (21). This increase had already been reported in a small case series in which 3 of 12 people with anti-NMDAR encephalitis had suicidality (one with suicidal ideation and two with suicide attempts) (23). Another study of the NMDAR, NMDAR sub-unit mRNAs, and post-synaptic density protein 95 (PSD 95) in postmortem brain tissue demonstrated that NMDAR sub-unit mRNAs levels and PSD 95 levels in people with suicidality were different from the control group (24). Another study suggested that the levels of NMDAR antagonists and agonists were also related to suicidality (21). Suicidality should, therefore, be seen not as rare, but as a common and potentially serious manifestation of anti-NMDAR encephalitis. The specific mechanism, however, warrants further study.

The demographic characteristics of those with suicidality suggested that it can affect individuals of different ages, and educational backgrounds. It can also present in different stages of encephalitis, from prior to admission, to after discharge and also during recurrence. One of the affected committed suicide eight months post discharge after suffering from suspected depression for about one month. In this particular individual, follow up prior to the onset of depression had noted full clinical recovery. It is possible that, as there was full recovery of consciousness, speech function, cognitive abilities, and other psychiatric symptoms, mood was overlooked and an evaluation of suicidality risk was not performed. Two further individuals had suicidal ideation or attempted suicide post discharge. Assessing the risk of suicidality is essential during telephone and outpatient clinic visits, even in those who appear to have had a good recovery.

We also analyzed clinical manifestations. Our cases presented with a variety of clinical symptoms (Table 1). Of interest is that those whose initial presentation included florid psychiatric symptoms were more likely to have suicidality than those who didn’t present with psychiatric symptoms. Psychiatric symptoms were also different between the two groups on univariable analysis throughout the course of

the disease. Insomnia, aggression, mania, depression, and delusions were more common in those with suicidality ($p<0.05$). These findings are also consistent with previous studies of risk factors for suicidal behavior in other mental disorders (25-29).More attention should be paid to people with anti-NMDAR encephalitis with florid psychiatric symptoms, and assessment of the risk of suicidal behavior should be made. Multivariate analysis, however, did not identify independent predictors of suicidality in this study. This could be due to the small sample size and further studies with larger samples are needed to identify the predictors of suicidality of people with anti-NMDAR encephalitis.

Previous studies have shown that higher antibody titers were related to poorer outcomes (30, 31). In this study, the preliminary analysis of those with strongly positive antibodies in the CSF showed no significant difference between those with and without suicidality ($p=0.257$) nor between those with suicidal ideation and those with suicidal behavior ($p=0.644$). The MRI results of individuals with suicidality may be normal, but may also show focal or multifocal lesions affecting limbic system, frontal and parietal lobes, periventricular areas, internal capsule, callosum, pons, cerebral peduncles, and thalamus. A previous study showed that some lesions, such as smaller right parahippocampal cortex volume and superior temporal gyrus volume could be related to suicidality (31). Due to small numbers and a relatively low rate of abnormal MRI in anti-NMDAR encephalitis, we could not ascertain relationships between suicidality and lesion location. Compared to individuals without suicidality, no significant differences were found among MRI, EEG, and CSF results. Abnormal CSF results were more common in those with suicidal behavior than in those with only suicidal ideation (70% vs. 14%, $p=0.05$). Abnormal CSF results have also been shown to be predictive of poor outcomes (3, 6). Other studies have also shown that elevated levels of inflammatory factors in the CSF, such as interleukin-6, were related to suicide attempts (33), and the abnormal CSF results were likely related to inflammatory activation. People with abnormal CSF results warrant screening for suicidality. Further studies are needed to identify potential biomarkers for suicidality in people with anti-NMDAR encephalitis.

Treatment outcomes at last follow up were not significantly different between those with and without suicidality. Interestingly, two individuals had suicidality during a relapse but not during the first episode. Individuals with suicidality also had a higher rate of recurrence of encephalitis (31% vs. 8%, $p=0.020$).We speculate, therefore, that there may be a relationship between relapse and suicidality. Previous reports suggest that symptomatology during relapse may be less severe than the first episode (5).In those with recurrence, therefore, more attention should be paid to the increased risk of suicidality, rather than to the less severe symptoms. Studies with larger samples are needed to confirm these suggestions.

Our study has several limitations. Firstly, mainly due to study design bias and the limitations inherent in uncontrolled retrospective research, we have not assessed suicidality consistently throughout the study period, particularly in the earlier stages. We have also not used a scale to estimate the severity of suicidality and this could have led to inevitable recall bias although this may lead an underestimation of the

suicidality. Secondly, due to the small sample of people with suicidality comparative results might be compromised. Lastly, the initial symptom was defined according to the clinician's expertise and the families' descriptions, which might cause interpretative bias, especially, when the initial symptom were not characteristic.

Conclusion

Our findings suggest that suicidality is a common, potentially lethal risk in people with anti-NMDAR encephalitis which should not be ignored by clinicians. People presenting with psychiatric symptoms such as insomnia, aggression, mania, depression, or delusions at the initial and subsequent presentation may be at particular risk. Our study, however has several limitations so our findings should be interpreted with caution. Further prospective studies with larger sample sizes and more precise classification of suicidality are urgently needed.

Disclosure of conflict of interest

No author has any conflict of interest in respect to this work. LH, LZ, XYJ, KS, ATA, DZ and JML have no disclosures to make. JWS has received research grants and honoraria from UCB, Eisai, and Janssen.

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Table 1. The demographic characteristics and clinical information of patients with suicidality

No./suicidal classification	Sex/age (year)	Educational background	Initial symptom	IT from onset to suicidality	Tumor	Brain MRI	EEG	CSF	NMDAR-Ab	mRS
1[a]/SI	F/25	Middle school	Disorganization	14m (during relapse)	No	Normal	Abnormal	WBC <5/mm^3 Pro <0.45g/L	CSF + Serum +	6
2/SI	F/38	Middle school	Insomnia, depression	1m (prior to admission)	No	Normal	Normal	WBC <5/mm^3 Pro <0.45g/L	CSF + Serum +	1[e]
3[a]/SI	F/29	College	Agitation, insomnia, depression	1m (prior to admission)	No	Abnormal[b]	Normal	WBC <5/mm^3 Pro <0.45g/L	CSF + Serum -	2[f]
4/SI	F/52	Middle school	Depression, anxiety	1m (prior to admission)	No	Normal	Normal	WBC <5/mm^3 Pro <0.45g/L	CSF + Serum -	0
5/SI	F/19	Middle school	Seizure	3m (during hospitalization)	No	Normal	Abnormal	WBC <5/mm^3 Pro <0.45g/L	CSF + Serum -	0
6/SI	M/27	High school	Disorganization	20d (prior to admission)	No	Normal	Abnormal	WBC 12/mm^3 Pro <0.45g/L	CSF + Serum +	0
7/SI	M/35	College	Anxiety, delusion	14d (during hospitalization)	No	Abnormal[c]	Abnormal	WBC <5/mm^3 Pro <0.45g/L	CSF + Serum -	0
8/AS	F/24	College	Speech dysfunction	2m (prior to admission)	No	Normal	Abnormal	WBC 20/mm^3 Pro <0.45g/L	CSF + Serum +	1[g]
9[a]/AS	F/25	High school	Delusion, hallucination	24m (prior to admission)	No	Normal	Abnormal	WBC 10/mm^3 Pro <0.45g/L	CSF + Serum -	1[h]
10/AS	F/27	College	Insomnia, depression	5m (prior to admission)	No	Normal	Normal	WBC <5/mm^3 Pro <0.45g/L	CSF + Serum -	0
11/AS	M/78	College	Agitation,	2m (during	Left	Normal	Abnormal	WBC <5/mm^3	CSF +	4[i]

			disorganization	hospitalization)	adrenal adenoma			Pro 0.48g/L	Serum -	
12/As	F/28	College	Delusion, hallucination	2d (prior to admission)	Right ovarian teratoma	Normal	NA	WBC 54/mm^3 Pro <0.45g/L	CSF + Serum +	1[j]
13/AS	M/33	College	Insomnia, depression	7d (prior to admission)	No	Normal	Abnormal	WBC 50/mm^3 Pro <0.45g/L	CSF + Serum +	1[k]
14[a]/AS	F/46	College	Insomnia, delusion	10d (prior to admission)	No	Normal	Normal	WBC 10/mm^3 Pro <0.45g/L	CSF + Serum -	4[l]
15/AS	F/16	Middle school	Seizure	1m (post discharge)	No	Normal	Abnormal	WBC <5/mm^3 Pro <0.45g/L	CSF + Serum -	0
16/CS	F/27	High school	Disorganization, hallucination	9m (post discharge)	No	Abnormal[d]	Abnormal	WBC 20/mm^3 Pro 0.79g/L	CSF + Serum +	6
17[a]/CS	F/24	Primary school	Insomnia, anxiety	17m (during relapse)	No	Normal	Abnormal	WBC <5/mm^3 Pro <0.45g/L	CSF + Serum +	6

Abbreviations: AS = attempted suicide; CS = completed suicide; CSF = cerebrospinal fluid; EEG = electroencephalogram; F=female; FLAIR = fluid attenuated inversion recovery sequence; IT=interval time M=male; MRI = magnetic resonance imaging; mRS = modified Rankin Scale; NA = data not available; NMDAR-Ab = N-methyl-D-aspartate receptor antibody; Pro = protein; SI = suicidal ideation; T2WI = T2-weighted Imaging; WBC = white blood cell.

a. Patients relapsed;

b. Lesions involving left pons, cerebral peduncle, thalamus, callosum, frontal, periventricular, and bilateral internal capsule with high signal on T2WI and FLAIR;

c. Lesion nearby left anterior horn of lateral ventricle with high signal on T2WI and FLAIR;

d. Lesions involving bilateral frontal, parietal, periventricular triangle, and nearby left anterior horn of lateral ventricle with high signal on T2WI and FLAIR;

Residual deficits are: e. Agitation, anterograde amnesia; f. Weakness and occasionally movement disorder of right limb; g. Agitation; h. Memory deterioration; i. Cognitive impairment, weakness of limb, lack of self-care ability; j. Agitation; k. Anterograde amnesia; l. Insomnia, disorganization, agitation, aggression, mania, anxiety, delusion, suicidal ideation.

Table 2. Psychiatric symptoms of patients with suicidality

No.	Disorganization (88%)	Agitation (88%)	Insomnia (82%)	Mania (82%)	Depression (65%)	Aggression (59%)	Hallucination (59%)	Anxiety (53%)	Delusion (53%)	Psychomotor inhibition (6%)
1	+	+	+	+	+	-	-	+	+	-
2	+	+	+	+	+	+	-	+	-	-
3	-	+	+	+	+	+	-	-	-	-
4	+	+	+	+	+	+	+	+	+	-
5	+	+	+	+	-	+	+	-	-	-
6	+	+	-	+	-	+	-	-	-	-
7	+	+	+	+	-	+	-	+	+	-
8	+	+	+	+	-	+	+	-	+	-
9	+	+	+	+	+	+	+	+	+	-
10	+	+	+	+	+	-	+	+	-	-
11	+	-	-	-	+	-	+	-	-	-
12	-	+	-	+	-	-	+	-	+	-
13	-	-	+	-	+	-	+	-	-	-
14	+	+	+	+	+	+	+	+	+	-
15	+	+	+	+	-	-	-	-	-	-
16	+	+	+	-	+	-	-	+	+	+
17	+	+	+	+	+	+	+	+	+	-

Table 3. Comparisons between patients with and without suicidality

	All n (%)	Suicidality n (%)	No suicidality n (%)	P values
Total	133	17	116	
Sex (female)	79 (59)	13 (76)	66 (57)	0.125[a]
Age, year, median (range)	25 (9-78)	27 (16-78)	24 (9-71)	0.071[b]
Education background (college or above)	45 (34)	8 (47)	37 (32)	0.217[a]
Psychiatric symptoms as initial symptom	79 (59)	14 (82)	65 (56)	0.039[a]
Psychiatric symptoms				
Disorganization	113 (85)	15 (88)	98 (85)	1.000[c]
Agitation	109 (82)	15 (88)	94 (81)	0.737[c]
Insomnia	69 (52)	14 (82)	55 (47)	0.007[a]
Mania	68 (51)	14 (82)	54 (47)	0.006[a]
Depression	55 (41)	11 (65)	44 (38)	0.036[a]
Aggression	42 (32)	10 (59)	32 (28)	0.010[a]
Hallucination	54 (41)	10 (59)	44 (38)	0.101[a]
Anxiety	53 (40)	9 (53)	44 (38)	0.238[a]
Delusion	30 (23)	9 (53)	21 (18)	0.003[c]
Psychomotor inhibition	22 (17)	1 (6)	21 (18)	0.304[c]
Seizure	111 (84)	12 (71)	99 (85)	0.159[c]
Cognitive impairment	83 of 97 (86)	11 of 14 (79)	72 of 83 (87)	0.420[c]
Dyskinesias and movement disorders	57 (43)	8 (47)	49 (42)	0.708[a]
Speech dysfunction	43 (32)	6 (35)	37 (32)	0.780[a]
Autonomic instability	39 (29)	5 (29)	34 (29)	1.000[c]
Decreased consciousness	81 (61)	7 (41)	74 (64)	0.074[a]
Central hypoventilation	29 (22)	3 (18)	26 (22)	1.000[c]
Tumor	23 (17)	2 (12)	21 (18)	0.736[c]
Abnormal EEG	97 of 116 (84)	13 of 16 (81)	84 of 100 (84)	0.725[c]
Abnormal MRI	49 of 127 (39)	3 of 17 (18)	46 of 110 (42)	0.057[a]
Abnormal CSF	86 (65)	8 (47)	78 (67)	0.104[a]
Strongly positive Ab in CSF	64 (48)	6 (35)	58 (50)	0.257[a]
Positive Ab in serum	79 (59)	8 (47)	71 (61)	0.267[a]
Treatment				
IVIG	123 (92)	17 (100)	106 (91)	0.360[c]
MTP	69 (52)	8 (47)	61 (53)	0.670[a]
Duration of follow-up, month, median (range)	15.0 (1-48)	13.5 (1-48)	15.0 (2-46)	0.512[a]
Good outcome	104 of 123 (85)	12 of 17 (71)	92 of 106 (87)	0.139[c]
Relapse	14 of 122 (11)	5 of 16 (31)	9 of 106 (8)	0.020[c]

Abbreviations: Ab = N-methyl-D-aspartate receptor antibody; CSF = cerebrospinal fluid; EEG = electroencephalogram; IVIG = intravenous immunoglobulin; MTP = methylprednisolone; MRI =

magnetic resonance imaging.

a. Chi-squared test;

b. Wilcoxon test;

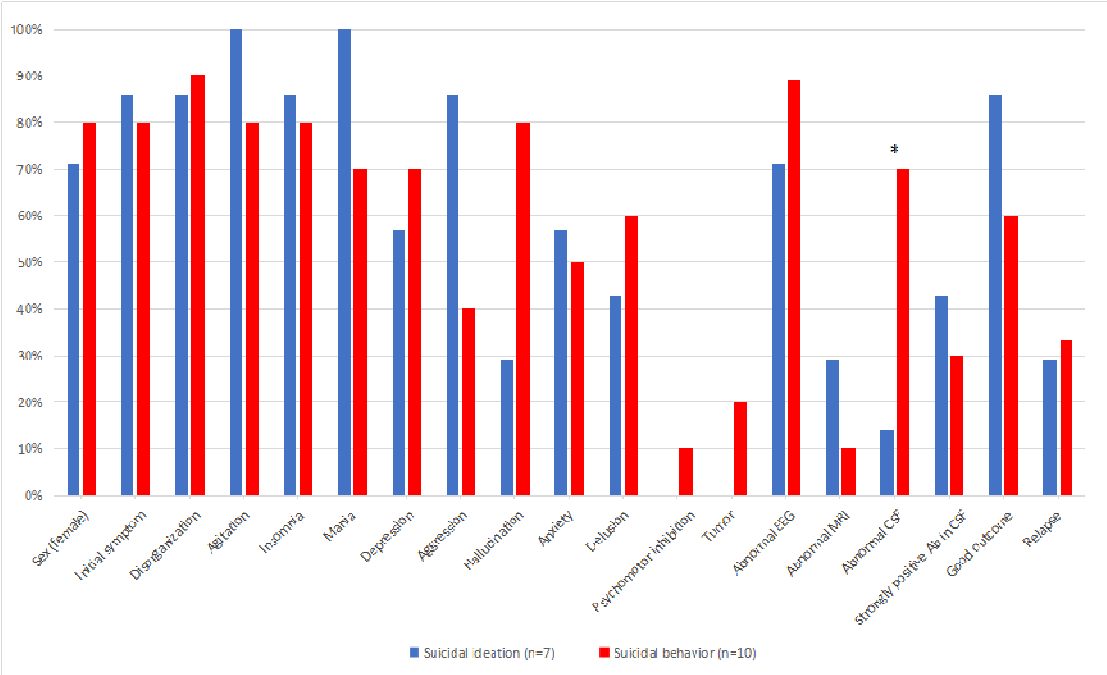
c. Fisher's exact test.

Table 4. Multivariate analysis of factors associated with suicidality in people with anti-NMDAR encephalitis.

Variables	Adjusted odds ratio	95% CI	P value
Psychiatric symptoms as initial symptom	2.973	0.730-12.114	0.128
Aggression	1.409	0.356-5.576	0.625
Depression	1.137	0.310-4.176	0.847
Mania	3.273	0.626-17.119	0.160
Insomnia	2.841	0.663-12.164	0.159
Delusion	2.681	0.761-9.443	0.125

Abbreviations: CI = confidence interval.

Figure 1. Comparisons between people with suicidal ideation and those with suicidal behavior



The blue bar represents people with suicidal ideation, the red bar represents people with suicidal behavior. *P value of 0.05 or less, Fisher's exact test.

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