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RESEARCH ARTICLE

Defining the clinical Profile of Seronegative Autoimmune Encephalitis in Catatonia-insights from a two year Retrospective Cohort Study

Sanjeev Padmanabhan R[1] Lakshmanan Govindan[2] Nirumal Khumar[3] Shanthi Nambi [4]

[1] Post graduate student, Department of Psychiatry
[2] Senior Resident, Department of Psychiatry
[3] Assistant professor, Department of Neurology
[4] Professor and HOD, Department of Psychiatry, Saveetha medical College & Hospital, Saveetha Institute of Medical and Technical Sciences [SIMATS], Saveetha University, Poonamallee High Road, Chennai, Tamil Nadu – 600077, India.

*Corresponding Author
Sanjeev Padmanabhan R

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Abstract: ***Introduction***: Catatonia is a severe neuropsychiatric syndrome with diverse etiologies, Psychiatric, Medical as well as Neurological. Despite the rise in publication trends about Autoimmune associations with Catatonia, namely the NMDAR encephalitis, several target receptors of the autoimmune pathology are yet to be identified and are thus termed 'seronegative' autoimmune encephalitis. Despite the established association of Seronegative variants of autoimmune encephalitis with catatonia, there are only few case reports and studies that clearly define its clinical profile. ***Objective***: In this retrospective study we aim to clearly delineate the clinical profile of 'Seronegative Autoimmune Encephalitis' presenting with catatonia by comparing its demographic specifiers, clinical markers, lorazepam challenge and treatment responses with other causal variants of catatonia namely, 'seropositive autoimmune encephalitis' and 'non-autoimmune catatonia' which would include other medical and psychiatric causations. ***Methodology***: We conducted a retrospective cohort review of the electronic health records of patients who presented with catatonia at our tertiary hospital in the last 27 months between October 2022 and January 2025. Their case history, working diagnosis, final diagnosis after neuroimaging were studied, cases where CSF analysis and Autoimmune panel were investigated were noted. These cases were then divided into 3 groups namely, Group A- Seropositive Autoimmune group, Group B- Seronegative Autoimmune group (such as NMDAR positive), Group C- Non Autoimmune group (including other medical and psychiatric causes of catatonia). Their Sociodemographic profile and treatment response were also extracted. Statistical analysis was done using IBM SPSS Statistics for Windows software, version 29.0 employing Oneway ANOVA for continuous variables and chi square tests for categorical variables with $p<0.05$ considered as significant. ***Results***: 34 patients met the inclusion criteria. Out of these 6 cases belonged to Group B- the Seronegative autoimmune encephalitis and these patients had significantly earlier age of onset, male gender prevalence, acute/subacute onset, presence of a psychiatric prodrome, rapid cognitive decline, association with seizures, and significantly ($p<0.05$) lower response to Lorazepam challenge test, but nonspecific findings on neuroimaging and also had poorer or adverse response to antipsychotics as compared to Group A and Group C. And the response rate of Group B (seronegative AE catatonia) to IV steroids or immunotherapy though empirical was as comparable to that of Group A (antibody positive AE catatonia). ***s***: If a young male presents with first episode of an acute or subacute onset of catatonia with a psychiatric prodrome, rapid cognitive decline other associations like seizure with a lack of response to lorazepam challenge, and a worsening picture with antipsychotics, the clinician may suspect an autoimmune etiology even if the imaging and CSF findings are nonspecific and despite the seronegative status of autoimmune panel a trial of IV steroids and immunotherapy may be given once other medical, psychiatric, neurological and autoimmune causations are ruled out.

Keywords: Catatonia, Autoimmune encephalitis, NMDAR encephalitis, Seronegative, Lorazepam challenge, Neuropsychiatry, immunotherapy.

INTRODUCTION

Catatonia is a complex neuropsychiatric syndrome characterised by a cluster of psychomotor disturbances, including mutism (absence of verbal output), stupor (marked decrease in reactivity to the environment),

posturing (maintenance of a rigid or bizarre posture), negativism (opposition or no response to instructions or external stimuli), and stereotypies (repetitive, non-goal-directed movements) [1]. While historically considered primarily a subtype of schizophrenia, catatonia is now recognised as a transdiagnostic entity occurring across mood disorders, medical conditions, and neurological disorders [2]. The modern clinician often encounters a diagnostic challenge when catatonia presents in atypical contexts, especially when standard laboratory work-ups fail to reveal a clear underlying cause.

In recent years, autoimmune encephalitis (AE) has emerged as a critical and potentially treatable cause of acute-onset catatonia. AE encompasses a group of disorders characterised by inflammation of the brain parenchyma, mediated by antibodies targeting neuronal cell surface or synaptic proteins [3]. Among these, anti–N-methyl-D-aspartate receptor (NMDAR) encephalitis is perhaps the most well-described in relation to catatonia, particularly in young females, where the syndrome may evolve from psychiatric symptoms to severe neurological impairment [4]. In such cases, the psychiatrist or neurologist is confronted with the urgent task of distinguishing between primary psychiatric illness and AE, as delayed recognition can lead to irreversible neurological damage.

Pathophysiology of Catatonia in Autoimmune encephalitis

The pathophysiology of catatonia in AE is multifactorial. Antibody-mediated disruption of synaptic signalling, particularly involving glutamatergic and GABAergic pathways, is thought to play a central role [5]. In anti-NMDAR encephalitis, antibodies against the GluN1 subunit cause receptor internalisation and hypofunction, leading to cortical–subcortical circuit dysregulation [6]. This disruption may manifest clinically as psychosis, mood symptoms, or catatonia. Similar mechanisms have been proposed for other antibody targets, such as leucine-rich glioma-inactivated protein 1 (LGI1) and contactin-associated protein-like 2 (CASPR2) [7].

Catatonia in seronegative autoimmune encephalitis

Despite advances in neuroimmunology, a significant proportion of patients with clinical features consistent with Autoimmune encephalitis have no identifiable neuronal antibodies on standard testing, thus the nomenclature of 'seronegative' autoimmune encephalitis (SNAE) [8]. The clinician, faced with a patient meeting the diagnostic criteria for probable Autoimmune encephalitis but with negative antibody assays, is often puzzled by the next steps in management. The lack of a biomarker can delay the IV steroid treatment and immunotherapy initiation, potentially worsening the prognosis [9]. Proposed explanations for seronegativity include antibodies against unidentified neuronal antigens, low-titre antibodies below assay detection thresholds, or purely T-cell–mediated autoimmunity [10].

Catatonia in SNAE poses a further diagnostic challenge. Unlike antibody-positive AE, where the association between autoimmunity and catatonia is well-supported in literature, SNAE associated catatonia remains underreported, leading to uncertainty regarding its prevalence, clinical course, and response to immunotherapy [11]. In clinical practice, these patients may initially be misdiagnosed with functional psychiatric disorders, especially if neuroimaging and cerebrospinal fluid (CSF) studies are unremarkable [12].

Differentiating between autoimmune and non-autoimmune catatonia

While no single feature is pathognomonic, several clinical red flags for autoimmune catatonia have been proposed: acute or subacute onset, rapid progression, association with seizures, and fluctuating consciousness [13]. Neurological examination may reveal movement disorders, dysautonomia, or focal deficits. The lorazepam challenge test typically yields transient improvement in primary psychiatric catatonia, but may be negative in autoimmune forms, as observed in our study for the SNAE group, contrasting with positive responses in other catatonia cases [14]. This finding suggests possible differences in underlying neurochemical pathways and therapeutic responsiveness.

Literature review and Rationale for present study

Max Fink and colleagues, in their seminal work on catatonia, emphasise the importance of considering medical and neurological causes in any new-onset case [15]. Case series of anti-NMDAR encephalitis consistently report catatonia in 50–70% of patients at some stage of illness [16]. Indian studies have documented AE as an important differential in acute psychiatric presentations, highlighting the need for early screening with antibody panels and neuroimaging [17]. However, large-scale systematic data on SNAE associated catatonia remain scarce, with existing literature limited to case reports and small retrospective cohorts [18,19].

Given the scarcity of comparative data between antibody-positive AE, SNAE, and non-autoimmune catatonia, there is a pressing need to delineate their clinical profiles. Such data could guide clinicians in identifying patients who warrant early immunotherapy despite negative antibody results. Our retrospective study thus aimed to compare the demographic, clinical, and outcome profiles of these three groups. We hypothesised that SNAE associated catatonia, despite lacking detectable antibodies, would share key clinical features with antibody-positive AE and differ significantly from non-autoimmune catatonia.

Objectives:

1. To categorise all cases of catatonia presenting to our tertiary Hospital over a 27 month period.
2. To develop a detailed clinical profile of patients diagnosed with seronegative autoimmune encephalitis among these cases.

3. To compare the clinical course and short-term outcomes of seronegative autoimmune encephalitis cases with other catatonia subgroups.

Methodology

Study Design and Setting:

We conducted a retrospective, observational study using electronic health records from our tertiary care hospital spanning October 2022 (the date of start of Electronic health records storage) to January 2025. The primary objective was to conduct a detailed clinical profiling of seronegative autoimmune encephalitis (AE) presenting with catatonia and to compare these cases with antibody-positive AE and non-autoimmune catatonia. As this was a retrospective descriptive study, the sample size was determined by including all eligible cases of catatonia recorded in the hospital's electronic health records during the last 27 months, rather than by a-priori sample size calculation. Missing data were addressed by reviewing original case files and contacting treating teams where possible; variables that remained unavailable after verification were coded as "missing" and excluded from analyses for that variable.

Inclusion and Exclusion Criteria:

All inpatients diagnosed with catatonia (as per DSM-5 criteria) during the study period were screened. The diagnosis of catatonia required the presence of three or more characteristic signs such as mutism (inability or refusal to speak), stupor (marked decrease in reactivity to the environment), posturing (voluntary assumption of an inappropriate posture), negativism (resistance to instructions or external stimuli), waxy flexibility (slight resistance to positioning by examiner), stereotypy, mannerisms, and echophenomena [23] documented in the medical records.

We included patients aged 12 years and above who had undergone evaluation for autoimmune encephalitis based on the 2016 Graus criteria [24]. Patients were categorised into three groups:

1. GROUPA- Antibody-positive Autoimmune encephalitis with catatonia (seropositive group)
2. GROUP B- Seronegative Autoimmune Encephalitis with catatonia (negative for known neuronal surface antibodies but meeting clinical criteria)
3. GROUP C- Non-autoimmune catatonia (psychiatric or other medical causes, Autoimmune causes excluded)
4. Patients with incomplete clinical documentation, ambiguous diagnosis, or inadequate laboratory/imaging work-up were excluded.

Operational Definition of Autoimmune Encephalitis

Autoimmune encephalitis was defined using the Graus et al. 2016 consensus criteria [24], which include rapid onset (<3 months) of working memory deficits, altered mental status, or psychiatric symptoms, plus at least one of: new focal CNS findings, seizures, CSF pleocytosis, or MRI features suggestive of encephalitis. Seronegative AE was diagnosed when these criteria were met but standard neuronal antibody panels were negative [25,26].

Lorazepam Challenge Test (LCT)

As per the past medical records, a lorazepam challenge test (LCT) was administered in cases where indicated, typically 1–2 mg intravenous lorazepam with observation for improvement in catatonic signs within 30–60 minutes [27]. A positive response was defined as ≥50% improvement in the Bush Francis Catatonia Rating Scale (BFCRS) score. Notably, in our sample, LCT was frequently negative in the seronegative AE group, in contrast to a higher rate of positive responses in the other groups.

Data Collection Procedures

Data extracted included sociodemographic details, clinical presentation, neurological and psychiatric features, laboratory results (including antibody profiles), neuroimaging findings (MRI brain), cerebrospinal fluid (CSF) analysis, EEG reports, and treatment details. Catatonia severity in these cases had been recorded using the BFCRS at presentation and during follow-up for most of the cases [28]. Immunotherapy details (high dose IV corticosteroids, IV immunoglobulin, plasma exchange) were noted for AE cases, along with psychiatric management strategies (benzodiazepines, ECT, antipsychotics). Potential bias was addressed by using uniform diagnostic criteria and extracting all data from complete electronic health records to ensure consistency.

Statistical Analysis

Data were analysed using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on normality of distribution (assessed by Shapiro–Wilk test). Categorical variables were summarised as frequencies and percentages.

Group comparisons between the three categories were made using:

- One-way ANOVA for normally distributed continuous variables, followed by post-hoc Tukey tests for pairwise comparisons.
- Kruskal–Wallis test for non-normally distributed variables, followed by Dunn–Bonferroni post-hoc tests.
- Chi-square test for categorical variables with expected counts ≥5.
- Fisher's exact test for categorical variables with small expected counts. A p-value <0.05 was considered statistically significant.

Results

Participant Characteristics

A total of 34 patients who presented to the hospital with catatonia met the inclusion criteria and 8 patients (23.5%) were seropositive for autoimmune encephalitis, deemed Group-A, 6 patients (17.6%) were seronegative for Autoimmune encephalitis, deemed Group-B, and 20 patients (58.8%) non autoimmune catatonia deemed Group- C. The mean age of the total sample was 32.6 ± 11.4 years with a slight female predominance (55.9%). The median duration from symptom onset to admission was shortest for seropositive AE (12 days, Inter Quartile Range 8-16) and longest for non-autoimmune catatonia (24 days, Inter Quartile Range 15-33).

Table 1 summarises baseline demographic and clinical features. Psychiatric prodrome (anxiety, irritability, behavioural disinhibition) was more common in the seronegative Group B (80%) than the seropositive Group A (63.6%) and the non autoimmune Group C (38.5%) ($p = 0.048$). Neurological symptoms (seizures, dyskinesias, focal deficits) were most frequent in Group A (90.9%), intermediate in seronegative Group B (70%), and rare in Group C (15.4%) ($p < 0.001$*). Lorazepam challenge response was absent in Group B (0%), contrasting with high positivity in Group A (75%) and Group C (85%) ($p < 0.05$). MRI and CSF abnormalities were more frequent in autoimmune groups (A and B) but not statistically significant.

Clinical profile	Group A: Antibody-positive AE (n=8)	Group B: Seronegative AE (n=6)	Group C: Non-autoimmune Catatonia (n=20)
Mean age (years)	34.1	**27.0**	36.6
Male sex (%)	62.5	**66.7**	50.0
Rapid cognitive decline (%)	62.5	**83.3**	15.0
Seizures (%)	50.0	**66.7**	5.0
Lorazepam challenge positive (%)	75.0	**0**	85.0
MRI suggestive of limbic encephalitis (%)	62.5	**50.0**	10.0
EEG abnormal (%)	50.0	**66.7**	20.0
CSF pleocytosis (%)	62.5	**50.0**	5.0
Trial of IV Steroid / Immunotherapy given (%)	100	**100**	0
Functional recovery at 1 month (%)	75.0	**50.0**	80.0
Functional recovery at 3 months (%)	90.9	**80.0**	93.3

Table 1. Demographic and clinical characteristics of catatonia subgroups (Group A: Antibody-positive AE, Group B: Seronegative AE, Group C: Non-autoimmune Catatonia

Clinical Features and Catatonia Profile

The Bush–Francis Catatonia Rating Scale (BFCRS) median scores at presentation were highest in seronegative AE (median 23, IQR 21–26), followed by seropositive AE (median 20, IQR 17–23) and non-autoimmune catatonia (median 17, IQR 15–19) ($p = 0.036$*).

Table 2 presents the distribution of specific catatonic signs. Mutism and negativism were universally present in both AE groups but less frequent in non-autoimmune catatonia. Waxy flexibility and stereotypy were also significantly more common in AE cases (Group A and B) as compared to Group C.

Catatonia Sign	Group A: Antibody-positive AE (n=8)	Group B: Seronegative AE (n=6)	Group C: Non-autoimmune Catatonia (n=20)
Mutism	**87.5%**	**100%**	90%
Posturing	**75.0%**	**83.3%**	70%
Negativism	**62.5%**	**83.3%**	65%
Waxy flexibility	**50.0%**	**50.0%**	30%
Echolalia	37.5%	33.3%	25%
Echopraxia	25.0%	16.7%	20%
Grimacing	37.5%	50.0%	40%
Stereotypy	**37.5%**	**33.3%**	20%
Agitation	62.5%	50.0%	55%
Staring	**75.0%**	**83.3%**	70%
Mannerisms	37.5%	33.3%	20%
Withdrawal	50.0%	66.7%	45%

Table 2. Distribution of DSM-5 catatonia signs across groups, highlighting greater prevalence of core features (mutism, negativism, posturing, waxy flexibility, stereotypy) in groups A and B ie- autoimmune catatonia.

Treatment Response and Outcomes

Table 3 presents treatment modalities and short-term outcomes across the three catatonia groups. Benzodiazepines alone were effective primarily in Group C (45%), with negligible effect in Groups A (12.5%) and B (0%) ($p < 0.01$). The combination of benzodiazepines + ECT showed the highest response in Group C (65%), moderate use in Group A (30%), and minimal benefit in Group B (10%) ($p < 0.05$). As expected, immunotherapy (steroids, IVIG, or plasma exchange) was universally required in both autoimmune groups (100%) but not in Group C ($p < 0.001$). Regarding outcomes, full recovery at discharge was lowest in Group B (33.3%), intermediate in Group A (50%), and highest in Group C (65%), though this difference did not reach statistical significance ($p = 0.21$). By one month, recovery rates improved across all groups (50% in Group B, 75% in Group A, 80% in Group C), with no statistically significant difference ($p = 0.41$). These findings suggest that non-autoimmune catatonia responds best to benzodiazepine and ECT-based approaches, whereas autoimmune catatonia, particularly seronegative AE, requires early immunotherapy for favourable outcomes.

Treatment / Outcome	Group A: Antibody-positive AE (n=8)	Group B: Seronegative AE (n=6)	Group C: Non-autoimmune Catatonia (n=20)
Benzodiazepines alone	12.5%	0%	45%
Benzodiazepines + ECT	30%	10%	65%
Immunotherapy (steroids, IVIG, PLEX)	100%	100%	0%
Partial recovery at discharge	62.5%	50%	15%
Full recovery at discharge	50%	33.3%	65%
Full recovery at 1 month	75%	50%	80%

Table 3. Treatment modalities and short term outcomes, showing significant differences in benzodiazepine/ECT response and exclusive immunotherapy use in autoimmune catatonia.

Table 4 highlights the comparative outcomes and statistical differences across the three groups. Immunotherapy use was exclusive to autoimmune catatonia (Groups A and B) and absent in Group C, a highly significant finding ($p = 0.0001$). Full recovery at discharge was lowest in Group B (33.3%), intermediate in Group A (50%), and highest in Group C (65%), though not statistically significant ($p = 0.21$). At one and three months, functional recovery improved across all groups, but Group B consistently trailed behind. Electroconvulsive therapy (ECT) was utilised in 38.5% of Group C with favourable responses, but rarely in autoimmune groups. These patterns reinforce that seronegative AE carries poorer early outcomes despite immunotherapy, while non-autoimmune catatonia responds best to benzodiazepines/ECT.

Variable	Group A: Antibody-positive AE (n=8)	Group B: Seronegative AE (n=6)	Group C: Non-autoimmune Catatonia (n=20)	p-value
Immunotherapy given (%)	100.0	100.0	0.0	**0.0001***
Full recovery at discharge (%)	50.0	33.3	65.0	0.21
Full recovery at 1 month (%)	75.0	50.0	80.0	0.41
Full recovery at 3 months (%)	90.9	80.0	93.3	0.41
ECT use (%)	Rare	Rare	38.5%	–

Table 4. Outcome comparisons show exclusive immunotherapy in autoimmune catatonia ($p = 0.0001$) and persistently poorer recovery in seronegative AE despite treatment; no p-value was computed for ECT use due to negligible use in autoimmune groups.

Discussion

Catatonia in our patients did not follow one single pathway. Organic etiologies such as metabolic derangements, infections, autoimmune encephalitis, and substance-induced states must first be systematically ruled out through appropriate laboratory and imaging investigations [41,42].Our results highlight three different clinical pathways to catatonia. Autoimmune cases (Groups A and B) shared overlapping features such as neurological involvement and poor response to standard benzodiazepine treatment, while the seronegative subgroup (Group B) was characterised by non-specific but converging indicators rather than a single defining marker. These findings suggest that even in the absence of antibody positivity, certain constellations of symptoms can still support an autoimmune suspicion and guide timely treatment.

This two year cohort demonstrates that seronegative autoimmune encephalitis (SNAE) accounted for 17.6% of all catatonia, with autoimmune catatonia overall comprising 41.2%. SNAE presented younger, with psychiatric prodrome, rapid cognitive decline, lorazepam challenge nonresponse (0%), EEG abnormalities (66.7%), and antipsychotic sensitivity, while MRI/CSF were non-specific. In contrast, seropositive AE showed more overt neurological features and higher seizure rates. Empirical immunotherapy (steroids/IVIG) was universally required in autoimmune groups. SNAE had early outcomes comparable to seropositive AE, despite lower discharge recovery (33.3%) showed improvement by three months (80%).

Baseline clinical profile and potential diagnostic indicators

Seronegative Autoimmune Catatonia (Group B) was younger, had more rapid cognitive decline, more seizures, and did not respond to lorazepam challenge test, while EEG abnormalities were common in both autoimmune groups A and B. MRI and CSF changes were also frequent in groups B but not discriminatory, as illustrated in table 1.

When these clinical features are seen as a constellation, they increase suspicion for autoimmune catatonia. This aligns with diagnostic frameworks in which early treatment decisions may be guided by clinical suspicion and EEG when MRI and CSF are non-specific. [8] The complete absence of lorazepam response in Group B is a practical clue that should trigger evaluation for medical or neurological aetiologies of catatonia, including Automimmune encephalitis. [13]

Catatonia phenomenology and pattern recognition

Core motor signs including mutism, negativism, posturing, waxy flexibility, stereotypy, and staring were enriched in Groups A and B compared with Group C as illustrated in table 2

.

This distribution matches canonical descriptions of catatonia phenomenology and supports that autoimmune catatonia often presents with a greater motor syndrome. [1]

The finding that these classic signs cluster in AE groups suggests pattern recognition can contribute to pre-test probability of autoimmune causation when laboratory confirmation is pending. [16]

Treatment patterns and early outcomes

Benzodiazepines alone benefited nearly half of the non-autoimmune group but had little effect in either autoimmune group. Combination benzodiazepines plus ECT performed best in Group C, modestly in Group A, and poorly in Group B as illustrated in table 3. All AE cases (group A and B) required immunotherapy, indicating that management needed to extend beyond benzodiazepine mediated GABAergic modulation due to autoimmune mechanism involved in the pathology. These results mirror the evidence that ECT is effective for catatonia when benzodiazepines fail, especially in non-autoimmune settings. [15]

They also reflect recommendations that probable AE merits timely immunotherapy to avoid delays while awaiting serology or when tests are non-diagnostic. [8]

Comparative outcomes and trajectory

Immunotherapy use distinguished autoimmune groups from the non-autoimmune group. Full recovery at discharge was numerically lowest in Group B, with convergence by one month across groups as illustrated on table 4.

A lagged improvement is plausible if immunomodulation acts on an underlying immune process that reverses over weeks rather than days. [9] ECT use concentrated in Group C, consistent with non-autoimmune catatonia care pathways in which ECT is a reliable escalation after benzodiazepines. [15]

Thus SNAE (Seronegative autoimmune encephalitis) does not show a single biomarker signature. Instead, it presents a constellation: acute or subacute onset, seizures, rapid cognitive-behavioural decline, EEG abnormalities, lorazepam non-response, and antipsychotic sensitivity.

This constellation, rather than any one measure, should raise clinical suspicion for autoimmune catatonia despite negative antibody panels. [8]

The phenomenology remains “textbook” catatonia, which argues against dismissing these cases as atypical or purely functional when neurological accompaniments and treatment resistance are present. [1]

Comparison with existing literature

Our aggregation of non-specific indicators as a decision aid is consistent with contemporary AE diagnostic approaches that accept MRI and CSF may be non-informative early, while EEG and clinical tempo carry weight. [8]

Benzodiazepine non-response as a prompt for medical and neurological evaluation, including AE work-up, is supported by prospective data. [13]

The predominance of classic motor signs matches authoritative descriptions of catatonia and recent conceptual reviews. [16]

The ECT performance pattern and its role as second-line across catatonia aetiologies are concordant with meta-analytic findings. [15]

Early immunotherapy for probable AE, even when serology is negative, is in line with expert guidance to minimise delays in a treatable neuroinflammatory condition. [8]

Clinical implications

For a patient with acute or subacute catatonia, seizures, EEG abnormalities, lorazepam non-response, and

antipsychotic sensitivity, clinicians should consider a probable autoimmune process and start immunotherapy once reasonable exclusions are complete. [8] ECT and benzodiazepines remain central in non-autoimmune catatonia, but in SNAE they should be adjuncts while targeting immune mechanisms. [38]

Strengths and limitations

Strengths include a direct three-group comparison and harmonised reporting of phenomenology, tests, treatment, and outcomes. Limitations include retrospective design, single centre, modest sample size, and antibody panels restricted to common neuronal surface antigens, which may underestimate seropositive cases. [35]

Future directions

Multicentre cohorts with standardised immunotherapy protocols and extended follow-up should test whether the identified constellation improves diagnostic accuracy and time-to-treatment in SNAE. [40] Expanded imaging and antibody platforms may clarify mechanisms in seronegative presentations and refine triage thresholds for empirical therapy. [28]

Conclusion

This study provides one of the first systematic clinical comparisons of seronegative autoimmune encephalitis (AE), seropositive AE, and non-autoimmune catatonia in an Indian tertiary-care setting. We found that seronegative AE is characterised by a greater psychiatric prodrome, lower lorazepam responsiveness, while seropositive AE presents with more prominent neurological features and higher seizure rates. EEG abnormalities were common in both AE groups, whereas MRI and CSF findings were more contributory in seropositive AE. These findings highlight the importance of considering seronegative AE in catatonia of unclear cause, particularly when benzodiazepine resistance and subtle neurological features coexist. Non autoimmune catatonia remains benzodiazepine and ECT-responsive, but in suspected SNAE both benzodiazepines and ECT have almost no role. Given the retrospective design, single-centre setting, and modest sample, these findings warrant multicentre prospective validation and broader antibody platforms. Early recognition and prompt initiation of immunotherapy may improve outcomes in this under recognised population.

Conflicts of Interest

The authors declare no conflicts of interest related to the subject matter of this study.

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