Brazilian consensus recommendations on the diagnosis and treatment of autoimmune encephalitis in the adult and pediatric populations

Consenso brasileiro sobre o diagnóstico e o tratamento de encefalites autoimunes nas populações adulta e pediátrica

Lívia Almeida Dutra[1]   Pedro Victor de Castro Silva[1]   João Henrique Fregadolli Ferreira[1]
Alexandre Coelho Marques[1]   Fabio Fieni Toso[1]   Claudia Cristina Ferreira Vasconcelos[2]
Doralina Guimarães Brum[3]   Samira Luisa dos Apóstolos Pereira[4]   Tarso Adoni[4]
Leticia Januzi de Almeida Rocha[5]   Leticia Pereira de Brito Sampaio[6]
Nise Alessandra de Carvalho Sousa[7]   Renata Barbosa Paolilo[6]   Angélica Dal Pizzol[8]
Bruna Klein da Costa[9,10]   Caio César Diniz Disserol[11,12]   Camila Pupe[13]
Daniel Almeida do Valle[14]   Denise Sisterolli Diniz[15]   Fabiano Ferreira de Abrantes[16]
Felipe da Rocha Schmidt[17]   Fernando Cendes[18]   Francisco Tomaz Meneses de Oliveira[19]
Gabriela Joca Martins[20]   Guilherme Diogo Silva[4]   Katia Lin[21]   Lécio Figueira Pinto[4]
Mara Lúcia Schimtz Ferreira Santos[14]   Marcus Vinícius Magno Gonçalves[22]
Mariana Braatz Krueger[23]   Michel Elyas Jung Haziot[19]   Orlando Graziani Povoas Barsottini[16]
Osvaldo José Moreira do Nascimento[13,24]   Paulo Ribeiro Nóbrega[25]   Priscilla Mara Proveti[26]
Raphael Machado do Castilhos[27]   Vanessa Daccach[28]   Felipe von Glehn[25]

[1] Hospital Israelita Albert Einstein, Instituto do Cérebro, São Paulo, São Paulo SP, Brazil.
[2] Universidade Federal do Estado do Rio de Janeiro, Rio de Janeiro, Rio de Janeiro RJ, Brazil.
[3] Universidade Estadual Paulista, Faculdade de Medicina de Botucatu, Departamento de Neurologia, Psicologia e Psiquiatria, Botucatu SP, Brazil.
[4] Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Departamento de Neurologia e Neurocirurgia, São Paulo SP, Brazil.
[5] Universidade Federal de Alagoas, Hospital Universitário, Maceió AL, Brazil.
[6] Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Instituto da Criança, São Paulo SP, Brazil.
[7] Universidade Federal do Amazonas, Manaus AM, Brazil.
[8] Hospital Moinhos de Vento, Departamento de Neurologia, Porto Alegre RS, Brazil.
[9] Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre RS, Brazil.
[10] Santa Casa de Misericórdia de Porto Alegre, Porto Alegre RS, Brazil.
[11] Universidade Federal do Paraná, Hospital das Clínicas, Curitiba PR, Brazil.

Address for correspondence Livia Almeida Dutra,
(email: livia.dutra@einstein.br).

[12] Instituto de Neurologia de Curitiba, Curitiba PR, Brazil.
[13] Universidade Federal Fluminense, Niterói RJ, Brazil.
[14] Hospital Pequeno Príncipe, Curitiba PR, Brazil.
[15] Universidade Federal de Goiás, Goiânia GO, Brazil.
[16] Universidade Federal de São Paulo, São Paulo SP, Brazil.
[17] Universidade do Estado do Rio de Janeiro, Rio de Janeiro RJ, Brazil.
[18] Universidade Estadual de Campinas, Campinas SP, Brazil.
[19] Santa Casa de Misericórdia de São Paulo, São Paulo SP, Brazil.
[20] Hospital Geral de Fortaleza, Fortaleza CE, Brazil.
[21] Universidade Federal de Santa Catarina, Florianópolis SC, Brazil.
[22] Universidade da Região de Joinville, Joinville SC, Brazil.
[23] Hospital Infantil Albert Sabin, Fortaleza CE, Brazil.
[24] Academia Nacional de Medicina, Rio de Janeiro RJ, Brazil.
[25] Universidade Federal do Ceará, Fortaleza CE, Brazil.
[26] Universidade de Brasília, Faculdade de Medicina, Brasília DF, Brazil.
[27] Hospital de Clínicas de Porto Alegre, Porto Alegre RS, Brazil.
[28] Universidade de São Paulo, Faculdade de Medicina de Ribeirão Preto, Ribeirão Preto SP, Brazil.

Abstract

Background   Autoimmune encephalitis (AIE) is a group of inflammatory diseases characterized by the presence of antibodies against neuronal and glial antigens, leading to subacute psychiatric symptoms, memory complaints, and movement disorders. The patients are predominantly young, and delays in treatment are associated with worse prognosis.

Objective   With the support of the Brazilian Academy of Neurology (Academia Brasileira de Neurologia, ABN) and the Brazilian Society of Child Neurology (Sociedade Brasileira de Neurologia Infantil, SBNI), a consensus on the diagnosis and treatment of AIE in Brazil was developed using the Delphi method.

Methods   A total of 25 panelists, including adult and child neurologists, participated in the study.

Results   The panelists agreed that patients fulfilling criteria for possible AIE should be screened for antineuronal antibodies in the serum and cerebrospinal fluid (CSF) using the tissue-based assay (TBA) and cell-based assay (CBA) techniques. Children should also be screened for anti-myelin oligodendrocyte glucoprotein antibodies (anti-MOG). Treatment should be started within the first 4 weeks of symptoms. The first-line option is methylprednisolone plus intravenous immunoglobulin (IVIG) or plasmapheresis, the second-line includes rituximab and/or cyclophosphamide, while third-line treatment options are bortezomib and tocilizumab. Most seizures in AIE are symptomatic, and antiseizure medications may be weaned after the acute stage. In anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis, the panelists have agreed that oral immunosuppressant agents should not be used. Patients should be evaluated at the acute and postacute stages using functional and cognitive scales, such as the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), the Modified Rankin Scale (mRS), and the Clinical Assessment Scale in Autoimmune Encephalitis (CASE).

Conclusion   The present study provides tangible evidence for the effective management of AIE patients within the Brazilian healthcare system.

Keywords
► Autoimmune Encephalitis
► Anti-N-Methyl-D-Aspartate Receptor Encephalitis
► Delphi Technique
► Rituximab
► Tocilizumab

Resumo

Antecedentes   Encefalites autoimunes (EAIs) são um grupo de doenças inflamatórias caracterizadas pela presença de anticorpos contra antígenos neuronais e gliais, que ocasionam sintomas psiquiátricos subagudos, queixas de memória e distúrbios anormais do movimento. A maioria dos pacientes é jovem, e o atraso no tratamento está associado a pior prognóstico.

Objetivo   Com o apoio da Academia Brasileira de Neurologia (ABN) e da Sociedade Brasileira de Neurologia Infantil (SBNI), desenvolvemos um consenso sobre o diagnóstico e o tratamento da EAIs no Brasil utilizando a metodologia Delphi.

Métodos   Um total de 25 especialistas, incluindo neurologistas e neurologistas infantis, foram convidados a participar.

Resultados   Os especialistas concordaram que os pacientes com critérios de possíveis EAIs devem ser submetidos ao rastreio de anticorpos antineuronais no soro e no líquido cefalorraquidiano (LCR) por meio das técnicas de ensaio baseado em tecidos (*tissue-based assay*, TBA, em inglês) e ensaio baseado em células (*cell-based assay*, CBA, em inglês). As crianças também devem ser submetidas ao rastreio de de anticorpo contra a glicoproteína da mielina de oligodendrócitos (*anti-myelin oligodendrocyte glycoprotein*, anti-MOG, em inglês). O tratamento deve ser iniciado dentro das primeiras 4 semanas dos sintomas, sendo as opções de primeira linha metilprednisolona combinada com imunoglobulina intravenosa (IGIV) ou plasmaférese. O tratamento de segunda linha

Palavras-chave
► Doenças Autoimunes do Sistema Nervoso
► Encefalite Antirreceptor de N-Metil-D-Aspartato
► Técnica Delphi
► Rituximab
► Tocilizumab

inclui rituximabe e ciclofosfamida. Bortezomib e tocilizumab são opções de tratamento de terceira linha. A maioria das crises epilépticas nas EAIs são sintomáticas, e os fármacos anticrise podem ser desmamadas após a fase aguda. Em relação à encefalite antirreceptor de N-metil-D-aspartato (*anti-N-methyl-D-aspartate receptor*, anti-NMDAR, em inglês), os especialistas concordaram que agentes imunossupressores orais não devem ser usados. Os pacientes devem ser avaliados na fase aguda e pós-aguda mediante escalas funcionais e cognitivas, como Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Modified Rankin Scale (mRS), e Clinical Assessment Scale in Autoimmune Encephalitis (CASE).

Conclusão   Esta pesquisa oferece evidências tangíveis do manejo efetivo de pacientes com EAIs no sistema de saúde Brasileiro.

INTRODUCTION

Autoimmune encephalitis (AIE) comprises a group of inflammatory diseases characterized by the presence of antibodies (abs) against neuronal and glial antigens. The disease was first described in 2005,[1] but the first case series was published by Dalmau et al.[2] in 2008, who reported a group of female patients with a severe form of encephalitis associated with orofacial dyskinesia, psychosis, memory impairment, ovarian teratoma, and abs against the anti-N-methyl-D-aspartate receptor (anti-NMDAR). In the past 15 years, more than 12 other abs directed against cell-surface antigens have also been associated with AIE, most of them directed against neurotransmitter receptors, or proteins of the neuronal surface and glial antigens.[3] Additionally, epidemiological studies[4] conducted in developed countries have indicated that AIE predominantly affects children and young adults, with a prevalence rate of 7–13.5 cases per 100 thousand individuals. This rate is comparable to the estimated prevalence of neuromyelitis optica spectrum disorder in people of African descendant, of $\sim$ 10 cases per 100 thousand individuals,[5] suggesting that the prevalence rate of AIE might be similar to, or even higher than, that of other neuroimmunological diseases.

The most common clinical symptoms in this novel group of diseases are psychiatric and cognitive impairment, seizures, abnormal movements, and autonomic symptoms.[3] Further clinical characterization shows that specific symptoms are associated with AIE subtypes, producing a phenotype-antibody correlation, as described in previous reports.[3,6] Anti-NMDAR encephalitis is the most common AIE subtype, primarily affecting children and young women.[7] Anti-leucine-rich glioma-inactivated 1 (anti-LGI1) antibody-associated encephalitis is the second most common type, mostly affecting older male patients and characterized by memory and behavioral changes, hyponatremia, and seizures, especially faciobrachial dystonic seizures.[6,8,9] Other abs associated with AIE include anti-contactin-associated protein-like 2 (anti-CASPR2), anti-alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (anti-AMPAR,) anti-gamma-aminobutyric acid type-A receptor (anti-GABA$_A$R), anti-gamma-aminobutyric acid type-B receptor (anti-GABA$_B$R), anti-immunoglobulin-like cell-adhesion molecule 5 (anti-IgLON5), and anti-glutamic acid decarboxylase (anti-GAD).[3]

Adult patients with AIE are diagnosed using the clinical criteria described by Graus et al.[10] in 2016 (►**Table 1**). In view of the specificities of the developing brain and the variability of symptoms among children, the criteria were modified in 2020 for the pediatric population.[11] The detection of anti-neuronal abs against cell-surface antigens is performed using two complementary laboratory techniques, tissue-based assay (TBA) and cell-based assay (CBA) in paired samples of the cerebrospinal fluid (CSF) and serum.[6,12–17] Currently, most available commercial diagnostic kits use the CBA technique. However, data have shown that the use of CBAs alone may yield rates of 4 to 14% of false negative results, especially in the detection of anti-LGI1, anti-GABA$_B$R and anti-AMPAR abs.[13] A growing body of literature[18–21] indicates that misdiagnosis in AIE occurs, often because the disease is not readily recognized by specialists or due to misinterpretation of results.

Autoimmune encephalitis represents a high economic burden for the health care system, as patients often need intensive care units (ICU) beds, advanced complementary investigation, specific testing, and treatment with intravenous immunoglobulin (IVIG), plasmapheresis (PLX) and rituximab (RTX).[22] At present, treatment recommendations are based on expert opinions and retrospective series, since few randomized clinical trials involving AIE patients have been conducted.[3,6–8,11,23–29]

The Delphi method is a validated technique for scientific discussions among a panel of experts, intending to generate knowledge on topics with limited scientific information, such as AIE.[30] This method has four key characteristics: anonymity, iteration, controlled feedback, and statistical response from the group, to promote an equitable forum for discussion and the exchange of opinions.[31] Thus, a selected group of experts contribute to the creation of a scientifically-recognized consensus on the proposed topic. The method has been previously used in the international consensus for pediatric AIE.[27]

Table 1 Diagnostic criteria for autoimmune encephalitis (AIE)

Diagnostic criteria for possible autoimmune encephalitis in adults (all three of following criteria met):
1. Subacute onset (rapid progression in fewer than than three months) of working memory deficits (short-term memory loss), altered mental status (decreased level of consciousness, lethargy or personality changes), or psychiatric symptoms 2. At least one of the following: 　New focal CNS findings 　Seizures not explained by a previously-known seizure disorder 　CSF pleocytosis 　MRI suggestive of encephalitis 3. Reasonable exclusion of alternative causes.
Diagnostic criteria for possible autoimmune encephalitis in the pediatric population (all three of following criteria met):
1. Onset of neurologic and/or psychiatric symptoms over ≤ 3 months in a previously-healthy child. 2. Two of the following: 　Altered mental status/level of consciousness, or EEG with slowing or epileptiform activity (focal or generalized) 　Focal neurologic deficits 　Cognitive difficulties 　Acute developmental regression 　Movement disorder (except tics) 　Psychiatric symptoms 　Seizures not explained by a previously-known seizure disorder or other condition 3. Reasonable exclusion of alternative causes, including other causes of CNS inflammation.

Abbreviations: CNS, central nervous system; CSF, cerebrospinal fluid; EEG, electroencephalogram; MRI, magnetic resonance imaging.
Note: Adapted from Graus et al.[10] (2016) and Cellucci et al.[11] (2020).

Two recent papers[32,33] have highlighted several barriers to the treatment and diagnosis of AIE in Brazil. The challenges faced by patients and the healthcare system encompass limited test availability, restricted access to treatment, and insufficient staff knowledge about the disease. A median delay of 6 months for AIE diagnosis has been reported in a Brazilian series.[33] In collaboration with the Brazilian Academy of Neurology (Academia Brasileira de Neurologia, ABN) and the Brazilian Society of Child Neurology (Sociedade Brasileira de Neurologia Infantil, SBNI), the objective of the present study was to formulate evidence-based guidelines for the diagnosis and treatment of AIE in Brazil, employing the Delphi method. Given the distinct pathophysiology of neurological immune-mediated diseases, the present study specifically focuses on seropositive AIE associated with cell-surface abs. It is important to note that the current study does not encompass immune-mediated conditions linked to high-risk abs that target intracellular antigens (such as anti-Hu, anti-Yo, and anti-Ma2) or synaptic antigens (such as anti-GAD and anti-amphiphysin). Consequently, the recommendations herein presented are not applicable to high-risk syndromes or other forms of immune-mediated encephalitis.

METHODS

Study design
A cross-sectional study was conducted in which invited experts participated in the development of a consensus on the diagnosis and treatment of AIE using the Delphi method.

A steering committee (ST) was established comprising 4 principal investigators, 7 members of the neuroimmunology scientific section of the ABN, and 1 member of the SBNI. The ST played a key role in overseeing the planning and implementation of the study but was not involved in the voting process.

The present study was overseen by an external consultant with expertise in the Delphi method, who ensured its methodological rigor. The process included meticulous participant selection, an exhaustive literature review, and implementation of two Delphi rounds, complemented by a pivotal online meeting (►**Figure 1**).

Participant selection
All members of the ABN and SBNI were invited to participate through the respective societies via the local mailing systems. Additional information was collected from the 87 individuals who expressed an interest in taking part, including details on:

- specialty and subspecialty;
- Brazilian region of medical residency;
- number of years dedicated to the specialty after residency; and
- number of seropositive patients treated in the last 2 years.

After receiving the initial data, the ST selected participants to provide representation for all Brazilian regions, using the following criteria:

- three or more years in the specialty after residency;
- experience in treating at least 5 patients with confirmed seropositive autoimmune encephalitis in the past 2 years; and
- availability to participate in the project.

Participants undergoing training (residency or fellowship) and those employed by the pharmaceutical industry or a diagnostics laboratory were excluded. Each institution included one expert for every five confirmed cases. In cases in which an institution had more than one expert, senior level professionals were selected.
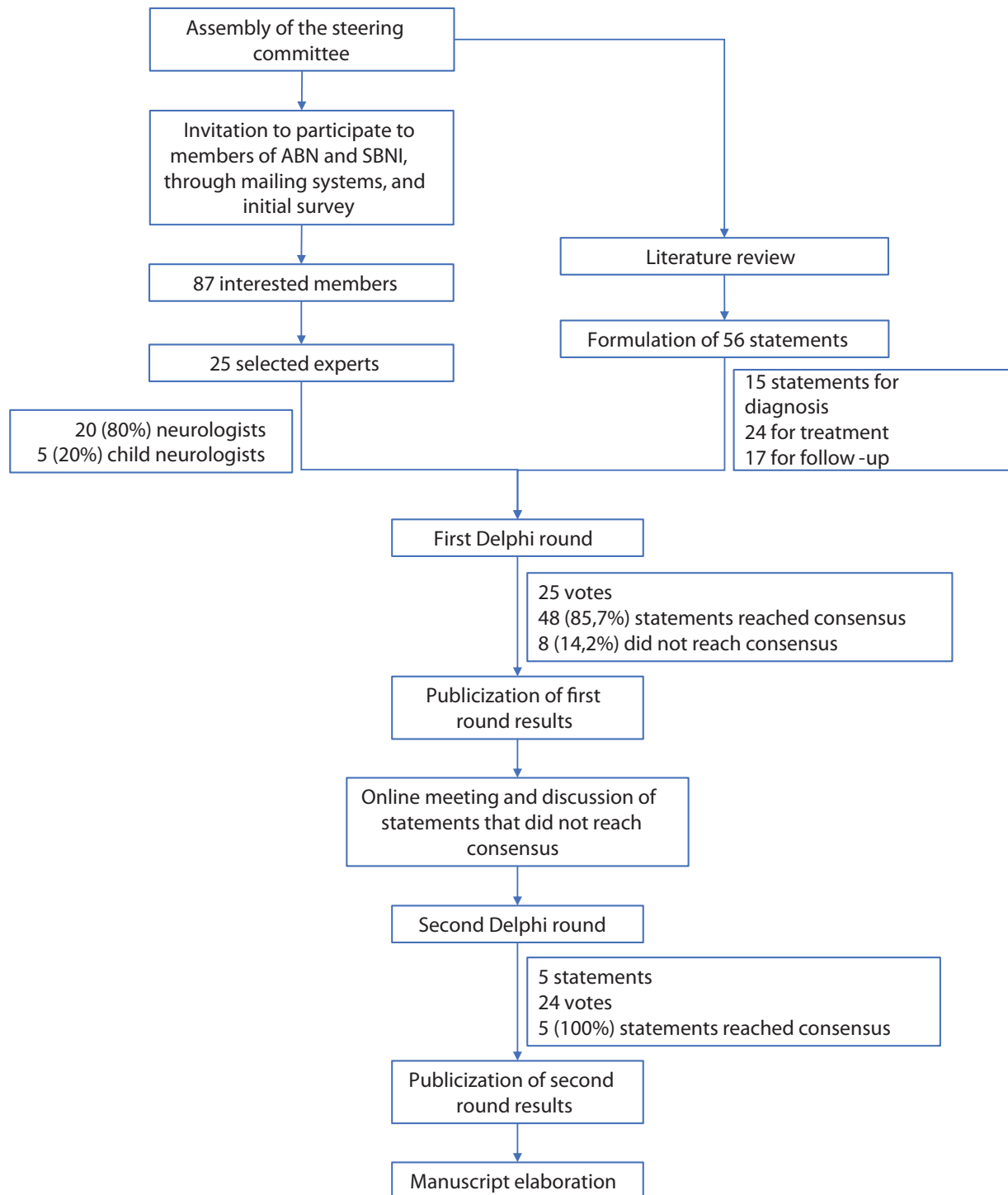
Figure 1 Brazilian consensus on AIE, study design.

A convenience sample of 25 experts comprised the expert panel, and they were invited to participate by email in the ensuing Delphi rounds. In total, 20 (80%) panelists were adult neurologists, and 5 (20%) were pediatric neurologists. All participants had experience working in both the public and private health systems. Regarding region, 12 participants (48%) were from Brazil's Southeastern region, 3 (12%), from the Northeastern region, 2 (8%), from the Midwestern region (8%), and 8 (32%), from the Southern region. All panelists

provided informed consent, and the study was approved by the local Ethics Committee, under permit registration no. 63315922.1.0000.0071.

Literature review and Delphi rounds
The ST conducted a comprehensive systematic review focusing on the diagnosis and treatment of AIE. The team elected key themes derived from the literature for discussion during the Delphi rounds. The literature search was based on main

topics of the Medical Subject Headings (MeSH) controlled vocabulary thesaurus, including *autoimmune diseases* and *autoimmune diseases of the nervous system*. The inclusion criteria covered all available studies published in English or Portuguese between 2007 and 2023, excluding case reports. A total of 278 articles were initially identified on the PubMed/MEDLINE and EMBASE databases, 188 of which underwent a thorough review.

The first Delphi round consisted of an online questionnaire (see ►**Supplementary Materials**; https://www.arquivosde-neuropsiquiatria.org/wp-content/uploads/2024/05/ANP-2023.0302-Supplementary-Material-1-to-4.zip) containing 56 statements on the diagnosis, treatment, and follow-up of AIE patients. The questionnaire was delivered using the Survey-Monkey app (SurveyMonkey Inc., San Mateo, CA, United States). All statements had a 5-point Likert scale voting option, ranging from "strongly disagree" to "strongly agree."

In the initial Delphi survey, all 25 participants received the questions and provided their responses after an introductory kickstart meeting designed to explain the study methodology and objectives. The statements presented encompassed evidence-based recommendations and drew on the personal clinical experiences of the ST members. Consensus was defined when 75% or more of the votes fell within the Likert scale range of 4 or 5. The Answers were collected anonymously within a 14-day period and shared exclusively with the third-party consultant, ensuring the ST remained blinded to individual responses. The results of this survey were then summarized and distributed to all participants.

Twenty days after the online voting, the expert panel took part in an online meeting, at which the ST presented the results for each statement. Statements for which no consensus was reached were discussed by the panel. All participants had an equal opportunity to express their opinions, and the suggestions made by the panel were compiled. This online meeting lasted 2 hours and had a rate of 96% of attendance (24/25 experts), with 1 participant excluded from subsequent rounds for failing to participate in this meeting. Following additional refinements in wording, statements that initially failed to achieve consensus underwent a subsequent round of voting. The voting outcomes were then summarized and expressed as numbers and percentages.

RESULTS

The percentage agreement on statements related to the diagnosis of AIE are presented in ►**Table 2**. A summary of the percentage agreement for treatment is provided in ►**Table 3**, while details regarding the consensus on statements about the follow-up of AIE patients are shown in ►**Table 5**. Delphi voting results are available in the ►**Supplementary Material S1** to **S4** (online only; https://www.arquivosdeneuropsiquiatria.org/wp-content/uploads/2024/05/ANP-2023.0302-Supplementary-Material-1-to-4.zip). No consensus was reached for statements 14, 32, 50, and 52 during the first round of voting. These statements were adjusted after the online meeting, and consensus was reached on them after a second round of voting.

Diagnosis of AIE patients

Autoimmune encephalitis should be suspected in patients presenting with acute or subacute ($<$ 3 months) psychiatric symptoms, memory complaints, seizures and/or movement disorders. Adult patients fulfilling the Graus criteria for possible AIE,[10] or the pediatric Cellucci criteria,[11] should be tested for antineuronal abs (►**Table 1**). All patients should be investigated using brain MRI, EEG, and CSF analysis, including the immunoglobulin G (IgG) index and oligoclonal bands (OCBs).

Antineuronal abs should be investigated in paired serum and CSF samples using TBAs and CBAs.[3,6,10,34] The panelists recommended adding anti-MOG testing for all pediatric patients with possible AIE, regardless of the MRI findings.[11] Moreover, the panelists recommended against testing for anti-voltage-gated potassium channel (anti-VGKC) abs.

Treatment of AIE patients

All patients fulfilling the criteria for possible or definite AIE should receive treatment within 4 weeks of symptom onset. Sample collection (of the CSF and serum) for abs testing should preferably be performed before immunotherapy, but its initiation should not be delayed while waiting for the results.

The first-line treatment should be methylprednisolone (MP) plus IVIG, or MP plus PLX. The choice of regimen should be based on local availability and the expertise of the attending physician. No consensus was reached on the clinical features indicating first-line treatment with MP plus PLX.

The experts agreed that satisfactory clinical response is defined as clinical and/or functional improvement within 10 to 14 days after starting the treatment. Treatment response should be monitored using clinical parameters such as reduced seizure frequency, partial improvement in cognitive and psychiatric symptoms, restored level of consciousness, or improvements in abnormal movements, ataxia, and in signs of brainstem dysfunction.[35] Patients failing to partially improve within 14 days should receive the second-line treatment, which includes RTX or/and cyclophosphamide ($0.75 \, mg/m^2$). The use of RTX (1,000 mg and repeat after 14 days) has been associated with better prognosis and lower relapse rate, and RTX can be prescribed alone or in association with cyclophosphamide in patients aged $>$ 16 years.[36]

The panelists agreed that the third-line treatment options include tocilizumab and bortezomib. Other treatment options should be discussed with an AIE expert team. Oral immunosuppression with azathioprine or mycophenolate should not be routinely prescribed, especially for patients with anti-NMDAR encephalitis, according to data from a meta-analysis.[29] The panelists strongly agreed (92%) that, if required, RTX should be the choice for maintenance immunosuppression.

Antiseizure medications (ASMs) should be prescribed only if the patient presents with seizures. Neurologists should consider weaning of ASMs in the months after the acute stage of the disease if the patient is stable. Further treatment recommendations are presented in ►**Table 3** and ►**Figure 2**. Proposed doses and regimens are summarized in ►**Table 4**.

Table 2 Brazilian consensus on AIE – diagnosis statements

Statement		% Agree (n)
1. AIE should be suspected in patients with acute or subacute (< 3 months) onset of focal or diffuse neurological symptoms, psychiatric symptoms, epileptic seizures, movement disorders, or dysautonomia.		100% (25)
2. In adults, the definition of possible AIE follows the criteria proposed by Graus et al., 2016.[10]		100% (25)
3. In adults, the definition of probable seronegative AIE follows the criteria proposed by Graus et al.[10].		96% (25)
4. In children, the definition of possible AIE follows the criteria review proposed by Cellucci et al., 2020.[11]		100% (25)
5. The definition of definite AIE follows the criteria proposed by Graus et al.[10]		100% (25)
6. The definition of autoimmune limbic encephalitis follows the criteria proposed by Graus et al.[10]		96% (25)
7. All patients meeting the criteria for possible AIE should be tested for autoantibodies in paired serum and CSF samples.		84% (25)
8. In cases of suspected AIE, patients should be investigated with:	Brain MRI	100% (25)
	EEG	96% (25)
	OCBs (in the CSF)	88% (25)
	IgG Index (in the CSF)	84% (25)
	PCR for herpesvirus (in the CSF)	92% (25)
9. The following findings on brain MRI are suggestive of AIE: hyperintensities on T2 and FLAIR sequences restricted to the medial temporal lobe, either unilateral or bilateral; multifocal involvement of white and/or gray matter that is suggestive of demyelination or inflammation.		92% (25)
10. The search for antineuronal antibodies should be performed using the TBA and CBA methodologies.		96% (25)
11. For the detection of anti-MOG and anti-glycine antibodies, the CBA technique should be used.		96% (25)
12. Laboratory findings that should be interpreted with caution	Low titers of anti-GAD anti-GAD antibodies in the serum.	100% (24)
	Anti-TPO antibodies at any titer.	96% (25)
	Low titers of antibodies detected by other methodologies (such as radioimmunoassay).	96% (25)
	Exclusive presence of anti-NMDAR antibodies in the serum.	100% (25)
	Low titers of anti-CASPR-2 antibodies.	87% (23)
13. The detection of antibodies solely in the serum should be interpreted with caution. The determination of pathogenicity should consider the specific antibody detected, the clinical presentation, and discussion with experts in AIE.		100% (25)
14. Antibodies against the VGKC complex should not be requested.		65% (23)
14a. Antibodies against the VGKC complex should not be requested in the investigation of AIE		92% (24)
15. Anti-MOG testing should be requested in children with suspected autoimmune encephalitis, regardless of the findings on brain MRI.		84% (25)

Abbreviations: AIE, autoimmune encephalitis; anti-CASPR-2, contactin-associated protein-like 2; CBA, cell-based assay; CSF, cerebrospinal fluid; EEG, electroencephalogram; FLAIR, fluid-attenuated inversion recovery; GAD65, glutamic acid decarboxylase 65-kilodalton isoform; IgG, immunoglobulin G; MOG, myelin oligodendrocyte glycoprotein; MRI, magnetic resonance imaging; NMDAR, N-methyl-D-aspartate receptor; OCBs, oligoclonal bands; PCR, polymerase chain reaction; TBA, tissue-based assay; TPO, thyroid peroxidase; VGKC, voltage-gated potassium channel.

Follow-up of AIE patients

The experts agreed that patients should be screened for neoplasia at the time of clinical presentation. Screening options should be individualized according to the specific ab identified and its association with neoplasms. Screening in patients that exhibit abs commonly associated with neoplasm should be performed annually for 4 years. The initial screening should be performed though chest, abdominal and pelvic computed tomography (CT) scans with whole-body fluorodeoxyglucose-positron emission tomography (FDG-PET) ordered if initial CT scans prove inconclusive or negative. In addition, women should also be investigated using transvaginal ultrasonography and mammography to exclude ovarian and breast cancers respectively, while men should undergo scrotal ultrasonography to exclude testicular cancer.[6]

Table 3 Brazilian consensus on AIE – treatment statements

Statement	% agree (n)
1. Treatment should be initiated for patients with criteria for possible or definite AIE.	96% (25)
2. The collection of paired serum and CSF samples for diagnosis should be performed before initiating treatment.	96% (25)
3. Treatment should be considered for patients who meet the criteria for possible AIE following HSV (types 1 and 2) encephalitis.	92% (24)
4. The first-line treatment should preferably be the combination of MP and IVIG or MP and PLX.	100% (25)
5. MP can be administered concomitantly with PLX.	100% (25)
6. IVIG can be prescribed concomitantly with MP.	100% (25)
7. The choice between the combination of MP and PLX or IGIV should be made based on the availability and experience of the attending medical team.	96% (25)
8. In my practice, PLX would be considered the first therapeutic option in the following clinical manifestations: need for ICU admission; autonomic dysfunction; status epilepticus; and rapid progression to severe disease nadir.	52% (25) 52% (25) 68% (25) 72% (25)
9. The second-line treatment should be initiated after 10 to 14 days of the start of the initial treatment if there is no satisfactory clinical response.	88% (25)
10. Satisfactory clinical response is defined as clinical and/or functional improvement within a period of 10 to 14 days after initiating treatment.	96% (25)
11. Treatment response should be monitored using parameters such as seizure control, cognitive symptoms, psychiatric symptoms, level of consciousness, movement disorders, gait and coordination, signs of brainstem dysfunction, and muscle weakness. Currently, there is no structured tool to quantify treatment response.	100% (25)
12. In my clinical practice, if maintenance treatment with immunosuppressive drugs is prescribed, it can be performed with: monthly IVIG infusions; oral corticosteroids; azathioprine; mycophenolate mofetil; and rituximab.	72% (25) 60% (25) 68% (25) 63% (24) 92% (24)
13. The options for second-line treatment are rituximab alone or in combination with cyclophosphamide.	80% (25)
14. The use of rituximab in AIE is associated with improved functional outcomes and lower recurrence rates.	92% (25)
15. The use of cyclophosphamide is indicated for patients older than 16 years of age in cases of refractory AIE, contraindication to or unavailability of rituximab.	96% (25)
16. The options for third-line treatment include tocilizumab and bortezomib.	88% (24)
17. Patients with AIE should not receive long-term immunosuppression (> 6 months) with azathioprine, corticosteroids, methotrexate, or mycophenolate.	36% (25)
32a. As a routine practice, patients with AIE should not receive immunosuppression with azathioprine or mycophenolate, especially in cases of anti-NMDAR encephalitis.	100% (24)
18. AEDs should only be prescribed if the patient presents with epileptic seizures.	92% (25)
19. AEDs should be withdrawn after the treatment of the acute stage, considering the low risk of developing autoimmune epilepsy.	52% (25)
34a. In general, patients with AIE may present with symptomatic epileptic seizures, but most of them do not develop epilepsy in the long term.	100% (23)
20. The drugs of choice for hyperkinetic movements are: benzodiazepines; anticholinergics; valproate; and neuroleptics.	92% (25) 32% (25) 68% (25) 56% (25)

Table 3 (*Continued*)

Statement	% agree (n)
21. The use of neuroleptics should be rationalized due to the potential risk of developing neuroleptic malignant syndrome.	100% (25)
22. Refractory cases of movement disorders that pose a risk to patient care can be managed with propofol, midazolam, or tetrabenazine. After the acute stage, medications should be tapered and discontinued.	88% (25)
23. For symptomatic treatment of Morvan syndrome (peripheral hyperexcitability) the following drugs can be used: carbamazepine; and phenytoin.	96% (23) 75% (24)
24. The principles of the treatment for relapses should be similar to those used for the initial manifestation of AIE.	92% (25)

Abbreviations: AEDs, antiepileptic drugs; AIE, autoimmune encephalitis; CSF, cerebrospinal fluid; HSV, herpes simplex virus; ICU, Intensive Care Unit; IVIG, intravenous immunoglobulin; MP, methylprednisolone; NMDAR, N-methyl-D-aspartate receptor; PLX, plasmapheresis.

Table 4 Proposed treatment regiments for AIE

First-line options	Dose/mode of administration
IVIG	2 g/kg for 2–5 days.
IV methylprednisolone	Children: 20–30 mg/kg/day (maximum: 1 g/day) for 3–5 days. Adults: 1,000 mg for 3–5 days.
Plasmapheresis	5–7 sessions over 7–14 days.
Second-line options	**Dose/mode of administration**
IV rituximab	The following doses are acceptable: 500–1,000 mg (500 mg for < 40 kg, 1,000 mg for > 40 kg) given twice and separated by 2 weeks, or 750 mg/m^2 (maximum: 1 g), given twice and separated by 2 weeks, or 375 mg/m^2 (maximum: 1 g) weekly for 4 weeks.
IV cyclophosphamide	500–1,000 mg/m^2 (maximum: 1,500 mg) monthly pulses.
Third-line options	**Dose/mode of administration**
IV tocilizumab	Children: 12 mg/kg/dose for < 30 kg, 8 mg/kg/dose for > 30 kg (maximum: 800 mg). Adults: 8 mg/kg/dose (maximum: 800 mg), given monthly.
SC bortezomib	Three cycles of 21 days, each one composed of 1.3 mg/m^2 on days 1, 4, 8 and 11.

Abbreviations: AIE, autoimmune encephalitis; IV, intravenous; IVIG, intravenous immunoglobulin; SC, subcutaneous.

Regular assessment of cognitive outcomes is recommended, utilizing the Modified Rankin Scale (mRS), the Montreal Cognitive Assessment (MoCA), and the Mini-Mental State Examination (MMSE) tools, despite their inherent limitations. The Clinical Assessment Scale in Autoimmune Encephalitis (CASE) constitutes a robust tool to predict outcomes during the acute stage of the disease in both the adult and pediatric populations.[35] While not formally validated for use in the Brazilian population, the panelists suggest drawing on its items to monitor symptom improvement.

The experts do not recommend follow-up of ab titers as a routine practice, except in cases of anti-MOG encephalitis, in which monitoring can be useful, although there is no clearly-defined clinical relevance.[37] Other follow-up recommendations are presented in ►**Table 5**.

DISCUSSION

In the present study, using the Delphi method, detailed information on the diagnosis, treatment, and follow-up of AIE patients is reported, to establish a framework for the clinical management of these patients. The study findings are in line with those of previously reported results, showing that neurologists should use the clinical criteria available to select patients for antineuronal abs detection, and that the clinical picture is of vital importance when AIE is suspected.[38–40]

The panelists agreed that a preliminary investigation using brain MRI, electroencephalography (EEG) and CSF analysis with OCBs is important to exclude alternative diagnoses, which include Creutzfeldt-Jakob disease, systemic lupus erythematosus, Alzheimer disease, and other degenerative conditions.[10,21,33] Herpesvirus encephalitis should be ruled out with CSF polymerase chain reactions (PCRs). The use of the clinical criteria helps prevent misdiagnosis, as previously described,[18–21] while data show that the laboratory yield in patients not fulfilling clinical criteria is low.[18,33] Morever, AIE can be triggered by herpes viral infections,[6] such as herpesvirus 1, varicella-zoster, and Epstein-Barr, and patients with herpetic encephalitis that present with relapse should be screened for AIE.[41–43]

Although a few reported cases[39,40] indicate that some AIE types (anti-LGI1, anti-IgLON5, anti-dipeptidyl-peptidase-
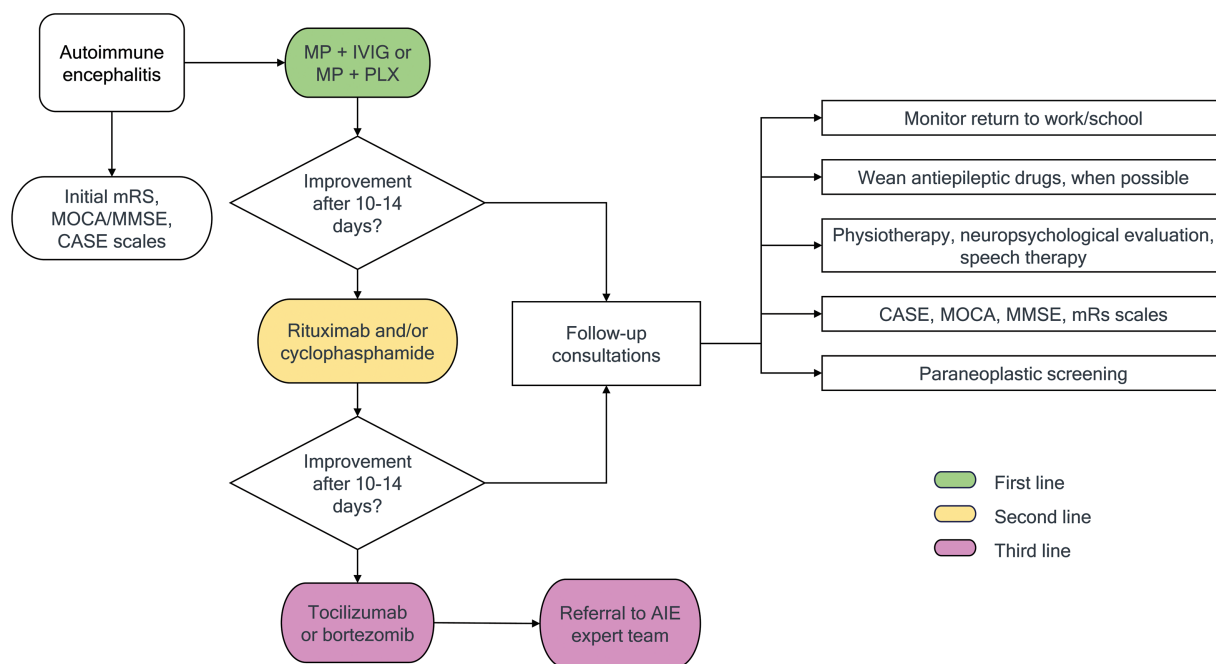
Abbreviations: mRs, modified Rankin scale; MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; CASE, Clinical Assessment in Autoimmune Encephalitis; MP, methylprednisolone; IVIG, intravenous immunoglobulin; PLX, phasmapheresis.
Figure 2 Proposed algorithm for AIE management.

Table 5 Brazilian consensus on AIE – follow-up statements

Statement	% agree (N)
1. Screening for neoplasia should be performed in all patients with AIE at the time of clinical presentation.	100% (25)
2. Paraneoplastic screening should be individualized according to the specific antibody identified and its association with neoplasms.	80% (25)
3. In cases of AIE with antibodies frequently associated with neoplasms, screening should be performed every 12 months for 4 years.	76% (25)
4. The initial screening for neoplasms should include contrast-enhanced CT scans of the chest, abdomen, and pelvis. If CT is contraindicated, consider using MRI as an alternative.	92% (25)
5. Children and adults with a typical clinical syndrome of anti-NMDAR antibody encephalitis should be specifically investigated for teratoma using ovarian/testicular ultrasound or abdominal and pelvic MRI.	100% (25)
6. Whole-body FDG-PET can be requested when the initial CT scan is negative or inconclusive.	84% (25)
7. The prognosis is associated with treatment within the first 4 weeks of symptom onset.	92% (25)
8. During follow-up consultations for patients with AIE, it is important to evaluate cognition, psychiatric/behavioral symptoms, frequency of epileptic seizures, presence of abnormal movements, gait and coordination abnormalities, muscle weakness, presence of dysautonomia, and symptoms suggestive of brainstem dysfunction (such as ophthalmoparesis and dysphagia).	100% (25)
9. The performance cognitive screening tests at least semi-annually for ongoing monitoring and assessment of cognitive function is recommended.	92% (25)
10. Cognitive monitoring can be performed using the MoCA scale in adults.	78% (23)
11. Cognitive monitoring can be performed using the MMSE scale in adults.	61% (23)
50a. Cognitive monitoring can be performed using the MMSE scale in adults, considering the limitations of this assessment in cognitive domains such as memory and executive function.	79% (23)
12. Serial measurement of antibody titers is not indicated as a prognostic factor or as an indicator for second-line treatment or maintenance therapy.	92% (25)
13. In cases of anti-MOG-associated encephalitis, antibody titers should be monitored.	52% (25)
52a. In cases of encephalitis associated with anti-MOG antibodies, monitoring of anti-MOG titers can be useful, although there is no clearly-defined clinical relevance.	95.8% (24)

Abbreviations: AIE, autoimmune encephalitis; CT, computed tomography; FDG-PET, fluorodeoxyglucose-positron emission tomography; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; MOG, myelin oligodendrocyte clycoprotein; MRI, magnetic resonance imaging; NMDAR, N-methyl-D-aspartate receptor.

like protein 6 [anti-DPPX], and anti-NMDAR) may sometimes have a progressive initial presentation and might not fulfill the criteria for AIE, the data available remain scarce, and the present consensus recommends discussing these specific cases with the AIE expert team.

In the present study, the experts recommended testing for antineuronal abs using the TBA and CBA techniques in the serum and CSF. This is paramount, and clinicians should be aware of the different techniques available when ordering laboratory tests.[13] The optimal balance between sensitivity and specificity can be achieved with cross-validation of the combined methods in the serum and CSF samples.[12,15,16,44,45] The TBA is an immunohistochemistry assay conducted in the rat brain, providing supplementary information on novel or noncommercially-tested abs. This includes abs not routinely assessed by commercial CBAs, such as anti-metabotropic glutamate receptor (anti-mGluR) 1 and 5, and anti-GABA-$_A$R. It is important to test both the serum and CSF, as the sensitivity of commercial kits may differ for these two sample types.[12,46]

The panelists emphasized that anti-VGKC abs should not be ordered.[38,47,48] While preliminary reports[49,50] have linked AIE to these abs, subsequent studies[51,52] have clarified that LGI1 and CASPR-2 are the specific epitopes associated with AIE, rather than the VGKC complex. Moreover, a study[53] evaluating 1,455 patients showed that anti-VGKC positivity in the absence of abs to LGI1 and CASPR-2 is not a clear marker for autoimmune inflammation and does not appear to contribute to the clinical practice.

An interesting outcome of the present study was the recommendation of anti-MOG testing for children with AIE, based on results from Brazilian, Spanish,[54] Danish, and Chinese[56] pediatric cohorts, which identified anti-MOG as the second most common ab associated with AIE among children.[11,54-57] Although the literature[37,58-60] shows that anti-MOG titers may predict recurrent myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), its clinical significance in MOGAD encephalitis is not fully understood.

In Brazil, the panelists suggested that the first-line treatment should be the combination MP plus IVIG or MP plus PLX. Given that the most common AIE subtype is anti-NMDAR, and that a meta-analysis[29] has shown better functional outcomes in patients initially treated with IVIG plus MP, with borderline results for IVIG plus PLX, combined with the fact that treatment within 4 weeks of the initial presentation is associated with better prognosis,[24,29,61,62] the panel agreed that combined initial therapy should be offered to all patients. This treatment regimen has been ratified by a recent Canadian consensus on AIE.[63] Debate remains over whether other AIE subtypes, especially anti-LGI1, respond to treatment with steroids alone. Nevertheless, in most anti-LGI1 reports,[8,64-66] more than 50% of the patients received additional immunotherapy (mostly IVIG) besides corticosteroids, while other studies suggest IVIG may also be beneficial for this AIE subtype.

The preferred option as the second-line treatment, RTX should be started early in the course of the disease. This approach is in line with growing evidence supporting RTX use in AIE. The GENERATE group[36] enrolled 358 patients with anti-NMDAR, anti-GAD65, anti-LGI1, and anti-CASPR2 for a mean follow-up of 41 months, and they showed that patients treated with RTX presented better clinical outcomes and lower relapse rates, especially in cases of anti-NMDAR. Other reports also support the use of RTX in adults and children.[6,7,24,27-29,62,63,67-81] The third-line options are bortezomib and tocilizumab, and they should be offered to refractory patients.[67,72,73,78-80,82-90]

Regarding maintenance therapy, the consensus among the panelists was that the existing evidence does not support the use of oral immunosuppressants, such as azathioprine (AZA) or mycophenolate mofetil (MMF), in the treatment of AIE. The total contingent of patients treated with oral immunosuppressants represents less than 10% of the reported cases, and the benefits remain unclear.[2,7,29,68,71,82,91,92] Furthermore, the available evidence supports the use of RTX, tocilizumab and bortezomib to treat refractory AIE (including real-world data and an ongoing randomized clinical trial),[36,85,86] particularly in cases of anti-NMDAR encephalitis.

Seizures are considered acute symptomatic events in AIE, resulting from cortical injury or dysfunction caused by the autoimmune process.[93-95] Therefore, the occurrence of seizures in AIE does not meet the diagnostic criteria for epilepsy, which specify a sustained predisposition to recurrent seizures.[96] Sodium channel blockers (phenytoin, carbamazepine, oxcarbazepine, lamotrigine, and lacosamide) are the first-line ASMs. However, caution is advised regarding the potential adverse effects of ASMs, which may resemble encephalitis symptoms, such as cognitive impairment (topiramate, phenobarbital, benzodiazepines), behavioral changes (levetiracetam, perampanel), and hyponatremia (carbamazepine, oxcarbazepine).[97]

When used for seizure management, ASMs should be continued for a defined period and then reassessed for further need. There is no routine recommendation for chronic use, even in cases evolving with residual brain lesions. Numerous studies have shown that most patients with AIE are seizure-free after one year.[65,93,98-104] Treatment following acute symptomatic seizures is typically recommended for 12 weeks, although the autoimmune process associated with encephalitis may remain active for an extended period.[105]

During follow-up, AIE patients should be evaluated though cognitive and functional assessments. Actively investigating symptoms such as fatigue, psychiatric and behavioral alterations, and assessing milestones such as returning to work or school and neurodevelopmental progress, is important.[106-108] Cognitive dysfunction is common after AIE, in which severity can range from mild and selective impairment to more generalized involvement of cognitive domains.[109] Episodic memory deficits are the most frequently reported, which is consistent with the limbic involvement in many AIE types.[107,110-112] Cognitive deficits may persist for several years and are a major cause of functional decline and difficulty in resuming previous activities.[107,113] Notably, disease severity and delayed immunotherapy have been reported as predictors of long-term cognitive outcomes, highlighting the importance of early diagnosis and adequate

treatment.[8,61,113] A cognitive-psychiatric syndrome that resembles schizophrenia spectrum disorders has been described in the postacute stage of anti-NMDAR,[108] and both sleep disorders and mood symptoms have been frequently reported.[111]

Patients should be screened using the MoCA, MMSE and mRS upon diagnosis and again at subsequent follow-up consultations. Nonetheless, clinicians must consider the inherent limitations of the aforementioned scores. The MMSE, for instance, provides limited information on memory and executive function, whereas the mRS can underestimate cognitive and functional outcomes.[114–117] The CASE scores demonstrate consistency in measuring the main AIE dysfunctions, serving as a useful instrument for the clinical practice, even for pediatric patients.[35,110,118–120]

The present study has certain limitations. The treatment of patients with probable seronegative AIE was not evaluated by the panelists. This was mainly due to the fact that the data available was controversial, as many studies have not classified patients according to the Graus criteria for probable seronegative AIE and did not perform the appropriate diagnostic workup with the TBA and CBA techniques.[21,38] At the moment, if a patient fulfills the criteria for probable seronegative AIE, treatment should follow the recommendations for AIE seropositive cases.[10]

In conclusion, the present study reports the results of the Delphi consensus on the diagnosis and management of AIE in Brazil, with the support of the ABN SBNI, as a guide for the general neurologist. Given the continental dimensions of Brazil and the shortage of trained specialists, further discussions on optimal strategies to deliver care to AIE patients within the Brazilian healthcare system should be explored. Considering that AIE is an acute condition with a chronic course, predominantly affecting young patients with viable treatment options, systematizing patient care through evidence-based practices is imperative.

Authors' Contributions
LAD, PVCS: conceptualization, data curation, formal analysis, investigation, methodology, project administration, supervision, validation, writing of the original draft, and writing – review and editing. JHFF, ACM, FFT, CCFV, DGB, SLAP, TA, LJAR, LPBS, NACS, FVG: conceptualization, methodology, supervision, and writing – review and editing. ADP, BKDC, CCDD, CP, DADV, DSD, FFA, FRS, FTM, GJM, GDS, KL, LFP, MLSFS, MVMG, MBK, MEJH, OGPD, OJMN, PRN, PMP, RMPC, VD: writing – review and editing. All authors approved the final version of the manuscript and agree to be responsible for all aspects of the work.

Conflict of Interest
LAD reports that she has received a grant for the Brazilian Autoimmune Encephalitis Network (Rede Brasileira de Encefalites Autoimunes), from Laboratório Fleury.

Acknowledgments
The authors would like to express their sincere gratitude to Dr. Rieder, for the invaluable support provided by

References

1   Vitaliani R, Mason W, Ances B, Zwerdling T, Jiang Z, Dalmau J. Paraneoplastic encephalitis, psychiatric symptoms, and hypoventilation in ovarian teratoma. Ann Neurol 2005;58(04): 594–604. Doi: 10.1002/ana.20614

2   Dalmau J, Gleichman AJ, Hughes EG, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. Lancet Neurol 2008;7(12):1091–1098. Doi: 10.1016/S1474-4422(08)70224-2

3   Dalmau J, Graus F. Antibody-Mediated Encephalitis. N Engl J Med 2018;378(09):840–851. Doi: 10.1056/NEJMra1708712

4   Dubey D, Pittock SJ, Kelly CR, et al. Autoimmune encephalitis epidemiology and a comparison to infectious encephalitis. Ann Neurol 2018;83(01):166–177. Doi: 10.1002/ana.25131

5   Hor JY, Asgari N, Nakashima I, et al. Epidemiology of Neuromyelitis Optica Spectrum Disorder and Its Prevalence and Incidence Worldwide. Front Neurol 2020;11:501. Doi: 10.3389/fneur.2020.00501

6   Dutra LA, Abrantes F, Toso FF, Pedroso JL, Barsottini OGP, Hoftberger R. Autoimmune encephalitis: a review of diagnosis and treatment. Arq Neuropsiquiatr 2018;76(01):41–49. Doi: 10.1590/0004-282X20170176

7   Titulaer MJ, McCracken L, Gabilondo I, et al. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. Lancet Neurol 2013;12(02):157–165. Doi: 10.1016/S1474-4422(12)70310-1

8   van Sonderen A, Thijs RD, Coenders EC, et al. Anti-LGI1 encephalitis: Clinical syndrome and long-term follow-up. Neurology 2016; 87(14):1449–1456. Doi: 10.1212/WNL.0000000000003173

9   Gadoth A, Nisnboym M, Alcalay Y, Weinstein T. LGI1 encephalitis associated hyponatremia, is it all in the brain? (2256). Neurology 2021;96(15, Supplement)2256

10   Graus F, Titulaer MJ, Balu R, et al. A clinical approach to diagnosis of autoimmune encephalitis. Lancet Neurol 2016;15(04): 391–404. Doi: 10.1016/s1474-4422(15)00401-9

11   Cellucci T, Van Mater H, Graus F, et al. Clinical approach to the diagnosis of autoimmune encephalitis in the pediatric patient. Neurol Neuroimmunol Neuroinflamm 2020;7(02):e663. Doi: 10.1212/nxi.0000000000000663

12   Ricken G, Schwaiger C, De Simoni D, et al. Detection Methods for Autoantibodies in Suspected Autoimmune Encephalitis. Front Neurol 2018;9:841. Doi: 10.3389/fneur.2018.00841

13   Ruiz-García R, Muñoz-Sánchez G, Naranjo L, et al. Limitations of a Commercial Assay as Diagnostic Test of Autoimmune Encephalitis. Front Immunol 2021;12:691536. Doi: 10.3389/fimmu.2021.691536

14   Fredrich SE, Vernino S, Blackburn KM. Antibody Testing for Neurological Autoimmune Disorders: Evaluation of Best Practices at a Tertiary Referral Center. Front Neurol 2021;12:690415. Doi: 10.3389/fneur.2021.690415

15   Bien CG, Bien CI, Dogan Onugoren M, et al. Routine diagnostics for neural antibodies, clinical correlates, treatment and functional outcome. J Neurol 2020;267(07):2101–2114. Doi: 10.1007/s00415-020-09814-3

16 McCracken L, Zhang J, Greene M, et al. Improving the antibody-based evaluation of autoimmune encephalitis. Neurol Neuroimmunol Neuroinflamm 2017;4(06):e404. Doi: 10.1212/NXI.0000000000000404

17 Dalmau J, Geis C, Graus F. Autoantibodies to Synaptic Receptors and Neuronal Cell Surface Proteins in Autoimmune Diseases of the Central Nervous System. Physiol Rev 2017;97(02):839–887. Doi: 10.1152/physrev.00010.2016

18 Flanagan EP, Geschwind MD, Lopez-Chiriboga AS, et al. Autoimmune Encephalitis Misdiagnosis in Adults. JAMA Neurol 2023;80(01):30–39. Doi: 10.1001/jamaneurol.2022.4251

19 Dinoto A, Zara P, Mariotto S, et al. Autoimmune encephalitis misdiagnosis and mimics. J Neuroimmunol 2023;378:578071. Doi: 10.1016/j.jneuroim.2023.578071

20 Van Steenhoven RW, de Vries JM, Bruijstens AL, et al. Mimics of Autoimmune Encephalitis: Validation of the 2016 Clinical Autoimmune Encephalitis Criteria. Neurol Neuroimmunol Neuroinflamm 2023;10(06):e200148. Doi: 10.1212/NXI.0000000000200148

21 Dalmau J, Graus F. Autoimmune Encephalitis-Misdiagnosis, Misconceptions, and How to Avoid Them. JAMA Neurol 2023;80(01):12–14. Doi: 10.1001/jamaneurol.2022.4154

22 Cohen J, Sotoca J, Gandhi S, et al. Autoimmune encephalitis: A costly condition. Neurology 2019;92(09):e964–e972. Doi: 10.1212/WNL.0000000000006990

23 Uy CE, Binks S, Irani SR. Autoimmune encephalitis: clinical spectrum and management. Pract Neurol 2021;21(05):412–423. Doi: 10.1136/practneurol-2020-002567

24 Abboud H, Probasco JC, Irani S, et al; Autoimmune Encephalitis Alliance Clinicians Network. Autoimmune encephalitis: proposed best practice recommendations for diagnosis and acute management. J Neurol Neurosurg Psychiatry 2021;92(07):757–768. Doi: 10.1136/jnnp-2020-325300

25 Ganesh A, Wesley SF. Practice Current: When do you suspect autoimmune encephalitis and what is the role of antibody testing? Neurol Clin Pract 2018;8(01):67–73. Doi: 10.1212/CPJ.0000000000000423

26 Nissen MS, Ryding M, Meyer M, Blaabjerg M. Autoimmune Encephalitis: Current Knowledge on Subtypes, Disease Mechanisms and Treatment. CNS Neurol Disord Drug Targets 2020;19(08):584–598. Doi: 10.2174/1871527319666200708133103

27 Nosadini M, Thomas T, Eyre M, et al. International Consensus Recommendations for the Treatment of Pediatric NMDAR Antibody Encephalitis. Neurol Neuroimmunol Neuroinflamm 2021;8(05):e1052. Doi: 10.1212/NXI.0000000000001052

28 Ellul M, Solomon T. Acute encephalitis - diagnosis and management. Clin Med (Lond) 2018;18(02):155–159. Doi: 10.7861/clinmedicine.18-2-155

29 Nosadini M, Eyre M, Molteni E, et al; International NMDAR Antibody Encephalitis Consensus Group. Use and Safety of Immunotherapeutic Management of N-Methyl-d-Aspartate Receptor Antibody Encephalitis: A Meta-analysis. JAMA Neurol 2021;78(11):1333–1344. Doi: 10.1001/jamaneurol.2021.3188

30 Beiderbeck D, Frevel N, von der Gracht HA, Schmidt SL, Schweitzer VM. Preparing, conducting, and analyzing Delphi surveys: Cross-disciplinary practices, new directions, and advancements. MethodsX 2021;8:101401. Doi: 10.1016/j.mex.2021.101401

31 Schmalz U, Spinler S, Ringbeck J. Lessons Learned from a Two-Round Delphi-based Scenario Study. MethodsX 2020;8:101179. Doi: 10.1016/j.mex.2020.101179

32 Vasconcelos GA, Barreira RM, Antoniollo KENT, et al. Autoimmune Encephalitis in Latin America: A Critical Review. Front Neurol 2021;11:606350. Doi: 10.3389/fneur.2020.606350

33 de Freitas Dias B, Fieni Toso F, Slhessarenko Fraife Barreto ME, et al. Brazilian autoimmune encephalitis network (BrAIN): antibody profile and clinical characteristics from a multicenter study. Front Immunol 2023;14:1256480. Doi: 10.3389/fimmu.2023.1256480

34 Dalmau J, Graus F. Antibody-mediated neuropsychiatric disorders. J Allergy Clin Immunol 2022;149(01):37–40. Doi: 10.1016/j.jaci.2021.11.008

35 Lim J-A, Lee S-T, Moon J, et al. Development of the clinical assessment scale in autoimmune encephalitis. Ann Neurol 2019;85(03):352–358. Doi: 10.1002/ana.25421

36 Thaler FS, Zimmermann L, Kammermeier S, et al; German Network for Research on Autoimmune Encephalitis (GENERATE) Rituximab Treatment and Long-term Outcome of Patients With Autoimmune Encephalitis: Real-world Evidence From the GENERATE Registry. Neurol Neuroimmunol Neuroinflamm 2021;8(06):e1088. Doi: 10.1212/NXI.0000000000001088

37 Wendel EM, Thonke HS, Bertolini A, et al; BIOMARKER Study Group. Temporal Dynamics of MOG Antibodies in Children With Acquired Demyelinating Syndrome. Neurol Neuroimmunol Neuroinflamm 2022;9(06):e200035. Doi: 10.1212/NXI.0000000000200035

38 Dalmau J, Graus F. Diagnostic criteria for autoimmune encephalitis: utility and pitfalls for antibody-negative disease. Lancet Neurol 2023;22(06):529–540. Doi: 10.1016/S1474-4422(23)00083-2

39 Bastiaansen AEM, van Steenhoven RW, Te Vaarwerk ES, et al. Antibodies Associated With Autoimmune Encephalitis in Patients With Presumed Neurodegenerative Dementia. Neurol Neuroimmunol Neuroinflamm 2023;10(05):e200137. Doi: 10.1212/NXI.0000000000200137

40 Venkatesan A, Probasco JC. Autoimmune encephalitis: chasing a moving target. Lancet Neurol 2023;22(06):460–462. Doi: 10.1016/S1474-4422(23)00165-5

41 Armangué T, Olivé-Cirera G, Martínez-Hernandez E, et al. Neurologic complications in herpes simplex encephalitis: clinical, immunological and genetic studies. Brain 2023;146(10):4306–4319. Doi: 10.1093/brain/awad238

42 Danieli D, Moraes ACM, Alves MP, et al. Anti-N-methyl-D-aspartate receptor encephalitis and Epstein-Barr virus: another tale on autoimmunity? Eur J Neurol 2017;24(08):e46–e47. Doi: 10.1111/ene.13332

43 Armangue T, Spatola M, Vlagea A, et al; Spanish Herpes Simplex Encephalitis Study Group. Frequency, symptoms, risk factors, and outcomes of autoimmune encephalitis after herpes simplex encephalitis: a prospective observational study and retrospective analysis. Lancet Neurol 2018;17(09):760–772. Doi: 10.1016/S1474-4422(18)30244-8

44 Budhram A, Dubey D, Sechi E, et al. Neural Antibody Testing in Patients with Suspected Autoimmune Encephalitis. Clin Chem 2020;66(12):1496–1509. Doi: 10.1093/clinchem/hvaa254

45 Budhram A, Mirian A, McFadden S, Edmond P, Bhayana V, Yang L. Neural Antibody Testing for Autoimmune Encephalitis: A Canadian Single-Centre Experience. Can J Neurol Sci 2021;48(06):859–863. Doi: 10.1017/cjn.2021.23

46 Budhram A, Yang L, Bhayana V, Mills JR, Dubey D. Clinical Sensitivity, Specificity, and Predictive Value of Neural Antibody Testing for Autoimmune Encephalitis. J Appl Lab Med 2022;7(01):350–356. Doi: 10.1093/jalm/jfab127

47 Bastiaansen AEM, van Sonderen A, Titulaer MJ. Autoimmune encephalitis with anti-leucine-rich glioma-inactivated 1 or anti-contactin-associated protein-like 2 antibodies (formerly called voltage-gated potassium channel-complex antibodies). Curr Opin Neurol 2017;30(03):302–309. Doi: 10.1097/WCO.0000000000000444

48 Michael S, Waters P, Irani SR. Stop testing for autoantibodies to the VGKC-complex: only request LGI1 and CASPR2. Pract Neurol 2020;20(05):377–384. Doi: 10.1136/practneurol-2019-002494

49 Buckley C, Oger J, Clover L, et al. Potassium channel antibodies in two patients with reversible limbic encephalitis. Ann Neurol 2001;50(01):73–78. Doi: 10.1002/ana.1097

50 Shillito P, Molenaar PC, Vincent A, et al. Acquired neuromyotonia: evidence for autoantibodies directed against K+ channels of

peripheral nerves. Ann Neurol 1995;38(05):714–722. Doi: 10.1002/ana.410380505

51 Lai M, Huijbers MG, Lancaster E, et al. Investigation of LGI1 as the antigen in limbic encephalitis previously attributed to potassium channels: a case series. Lancet Neurol 2010;9(08):776–785. Doi: 10.1016/S1474-4422(10)70137-X

52 Irani SR, Alexander S, Waters P, et al. Antibodies to Kv1 potassium channel-complex proteins leucine-rich, glioma inactivated 1 protein and contactin-associated protein-2 in limbic encephalitis, Morvan's syndrome and acquired neuromyotonia. Brain 2010;133(09):2734–2748. Doi: 10.1093/brain/awq213

53 van Sonderen A, Schreurs MW, de Bruijn MA, et al. The relevance of VGKC positivity in the absence of LGI1 and Caspr2 antibodies. Neurology 2016;86(18):1692–1699. Doi: 10.1212/WNL.0000000000002637

54 Armangue T, Olivé-Cirera G, Martínez-Hernandez E, et al; Spanish Pediatric anti-MOG Study Group. Associations of paediatric demyelinating and encephalitic syndromes with myelin oligodendrocyte glycoprotein antibodies: a multicentre observational study. Lancet Neurol 2020;19(03):234–246. Doi: 10.1016/S1474-4422(19)30488-0

55 Han JY, Kim SY, Kim H, et al. Clinico-radiological characteristics of anti-myelin oligodendrocyte glycoprotein antibody-associated autoimmune encephalitis in children. Dev Med Child Neurol 2022;64(08):998–1007. Doi: 10.1111/dmcn.15174

56 Kang Q, Liao H, Yang L, Fang H, Hu W, Wu L. Clinical Characteristics and Short-Term Prognosis of Children With Antibody-Mediated Autoimmune Encephalitis: A Single-Center Cohort Study. Front Pediatr 2022;10:880693. Doi: 10.3389/fped.2022.880693

57 de Bruijn MAAM, Bruijstens AL, Bastiaansen AEM, et al; CHANCE Study Group. Pediatric autoimmune encephalitis: Recognition and diagnosis. Neurol Neuroimmunol Neuroinflamm 2020;7 (03):e682. Doi: 10.1212/NXI.0000000000000682

58 Hennes EM, Baumann M, Schanda K, et al; BIOMARKER Study Group. Prognostic relevance of MOG antibodies in children with an acquired demyelinating syndrome. Neurology 2017;89(09): 900–908. Doi: 10.1212/WNL.0000000000004312

59 Huda S, Whittam D, Jackson R, et al. Predictors of relapse in MOG antibody associated disease: a cohort study. BMJ Open 2021;11 (11):e055392. Doi: 10.1136/bmjopen-2021-055392

60 Di Pauli F, Mader S, Rostasy K, et al. Temporal dynamics of anti-MOG antibodies in CNS demyelinating diseases. Clin Immunol 2011;138(03):247–254. Doi: 10.1016/j.clim.2010.11.013

61 Balu R, McCracken L, Lancaster E, Graus F, Dalmau J, Titulaer MJ. A score that predicts 1-year functional status in patients with anti-NMDA receptor encephalitis. Neurology 2019;92(03):e244–e252. Doi: 10.1212/WNL.0000000000006783

62 Zuliani L, Nosadini M, Gastaldi M, et al. Management of antibody-mediated autoimmune encephalitis in adults and children: literature review and consensus-based practical recommendations. Neurol Sci 2019;40(10):2017–2030. Doi: 10.1007/s10072-019-03930-3

63 Hahn C, Budhram A, Alikhani K, et al. Canadian Consensus Guidelines for the Diagnosis and Treatment of Autoimmune Encephalitis in Adults. Can J Neurol Sci 2024;•••:1–21. Doi: 10.1017/cjn.2024.16

64 Dubey D, Britton J, McKeon A, et al. Randomized Placebo-Controlled Trial of Intravenous Immunoglobulin in Autoimmune LGI1/CASPR2 Epilepsy. Ann Neurol 2020;87(02):313–323. Doi: 10.1002/ana.25655

65 Alkabie S, Budhram A. Prolonged Corticosteroids Without Maintenance Immunotherapy for Treatment of Anti-LGI1 Encephalitis: Analysis of Outcomes and Relapse Rate. Neurol Neuroimmunol Neuroinflamm 2023;10(03):e200115. Doi: 10.1212/NXI.0000000000200115

66 Rodriguez A, Klein CJ, Sechi E, et al. LGI1 antibody encephalitis: acute treatment comparisons and outcome. J Neurol Neurosurg Psychiatry 2022;93(03):309–315. Doi: 10.1136/jnnp-2021-327302

67 Stingl C, Cardinale K, Van Mater H. An Update on the Treatment of Pediatric Autoimmune Encephalitis. Curr Treatm Opt Rheumatol 2018;4(01):14–28. Doi: 10.1007/s40674-018-0089-z

68 Dale RC, Brilot F, Duffy LV, et al. Utility and safety of rituximab in pediatric autoimmune and inflammatory CNS disease. Neurology 2014;83(02):142–150. Doi: 10.1212/WNL.0000000000000570

69 Dou X, Li D, Wu Y, et al. Efficacy and Safety of Rituximab in Chinese Children With Refractory Anti-NMDAR Encephalitis. Front Neurol 2020;11:606923. Doi: 10.3389/fneur.2020.606923

70 Ellul MA, Wood G, Tooren HVD, Easton A, Babu A, Michael BD. Update on the diagnosis and management of autoimmune encephalitis. Clin Med (Lond) 2020;20(04):389–392. Doi: 10.7861/CLINMED.2020-0241

71 Nosadini M, Mohammad SS, Ramanathan S, Brilot F, Dale RC. Immune therapy in autoimmune encephalitis: a systematic review. Expert Rev Neurother 2015;15(12):1391–1419. Doi: 10.1586/14737175.2015.1115720

72 Ciano-Petersen NL, Muñiz-Castrillo S, Vogrig A, Joubert B, Honnorat J. Immunomodulation in the acute phase of autoimmune encephalitis. Rev Neurol (Paris) 2022;178(1-2):34–47. Doi: 10.1016/j.neurol.2021.12.001

73 Dinoto A, Ferrari S, Mariotto S. Treatment Options in Refractory Autoimmune Encephalitis. CNS Drugs 2022;36(09):919–931. Doi: 10.1007/s40263-022-00943-z

74 Bien CG. Management of autoimmune encephalitis. Curr Opin Neurol 2021;34(02):166–171. Doi: 10.1097/WCO.0000000000000909

75 Lee WJ, Lee ST, Byun JI, et al. Rituximab treatment for autoimmune limbic encephalitis in an institutional cohort. Neurology 2016;86 (18):1683–1691. Doi: 10.1212/WNL.0000000000002635

76 Nepal G, Shing YK, Yadav JK, et al. Efficacy and safety of rituximab in autoimmune encephalitis: A meta-analysis. Acta Neurol Scand 2020;142(05):449–459. Doi: 10.1111/ane.13291

77 Du Y, Zhao C, Liu J, et al. Simplified regimen of combined low-dose rituximab for autoimmune encephalitis with neuronal surface antibodies. J Neuroinflammation 2022;19(01):259. Doi: 10.1186/s12974-022-02622-8

78 Lee WJ, Lee ST, Shin YW, et al. Teratoma Removal, Steroid, IVIG, Rituximab and Tocilizumab (T-SIRT) in Anti-NMDAR Encephalitis. Neurotherapeutics 2021;18(01):474–487. Doi: 10.1007/s13311-020-00921-7

79 Nguyen L, Wang C. Anti-NMDA Receptor Autoimmune Encephalitis: Diagnosis and Management Strategies. Int J Gen Med 2023; 16:7–21. Doi: 10.2147/IJGM.S397429

80 Smets I, Titulaer MJ. Antibody Therapies in Autoimmune Encephalitis. Neurotherapeutics 2022;19(03):823–831. Doi: 10.1007/s13311-021-01178-4

81 Wang B, Wang C, Feng J, Hao M, Guo S. Clinical Features, Treatment, and Prognostic Factors in Neuronal Surface Antibody-Mediated Severe Autoimmune Encephalitis. Front Immunol 2022;13:890656. Doi: 10.3389/fimmu.2022.890656

82 Behrendt V, Krogias C, Reinacher-Schick A, Gold R, Kleiter I. Bortezomib Treatment for Patients With Anti-N-Methyl-d-Aspartate Receptor Encephalitis. JAMA Neurol 2016;73(10): 1251–1253. Doi: 10.1001/jamaneurol.2016.2588

83 Dinoto A, Cheli M, Bratina A, Sartori A, Manganotti P. Bortezomib in anti-N-Methyl-d-Aspartate-Receptor (NMDA-R) encephalitis: A systematic review. J Neuroimmunol 2021;356:577586. Doi: 10.1016/j.jneuroim.2021.577586

84 Li YH, Jiang L. Recent research on immunotherapy for anti-N-methyl-D-aspartate receptor encephalitis. Zhongguo Dang Dai Er Ke Za Zhi 2022;24(08):948–953. Doi: 10.7499/j.issn.1008-8830.2204021

85 Scheibe F, Prüss H, Mengel AM, et al. Bortezomib for treatment of therapy-refractory anti-NMDA receptor encephalitis. Neurology 2017;88(04):366–370. Doi: 10.1212/WNL.0000000000003536

86 Schwarz L, Akbari N, Prüss H, Meisel A, Scheibe F. Clinical characteristics, treatments, outcome, and prognostic factors of severe autoimmune encephalitis in the intensive care unit:

Standard treatment and the value of additional plasma cell-depleting escalation therapies for treatment-refractory patients. Eur J Neurol 2023;30(02):474–489. Doi: 10.1111/ene.15585

87 Benucci M, Tramacere L, Infantino M, et al. Efficacy of Tocilizumab in Limbic Encephalitis with Anti-CASPR2 Antibodies. Case Rep Neurol Med 2020;2020:5697670. Doi: 10.1155/2020/5697670

88 Dale RC. Interleukin-6 Blockade as Rescue Therapy in Autoimmune Encephalitis. Neurotherapeutics 2016;13(04):821–823. Doi: 10.1007/s13311-016-0471-1

89 Lee W-J, Lee S-T, Moon J, et al. Tocilizumab in Autoimmune Encephalitis Refractory to Rituximab: An Institutional Cohort Study. Neurotherapeutics 2016;13(04):824–832. Doi: 10.1007/s13311-016-0442-6

90 Randell RL, Adams AV, Van Mater H. Tocilizumab in Refractory Autoimmune Encephalitis: A Series of Pediatric Cases. Pediatr Neurol 2018;86:66–68. Doi: 10.1016/j.pediatrneurol.2018.07.016

91 Irani SR, Bera K, Waters P, et al. N-methyl-D-aspartate antibody encephalitis: temporal progression of clinical and paraclinical observations in a predominantly non-paraneoplastic disorder of both sexes. Brain 2010;133(Pt 6):1655–1667. Doi: 10.1093/brain/awq113

92 Hacohen Y, Absoud M, Hemingway C, et al. NMDA receptor antibodies associated with distinct white matter syndromes. Neurol Neuroimmunol Neuroinflamm 2014;1(01):e2. Doi: 10.1212/NXI.0000000000000002

93 Rada A, Birnbacher R, Gobbi C, et al. Seizures associated with antibodies against cell surface antigens are acute symptomatic and not indicative of epilepsy: insights from long-term data. J Neurol 2021;268(03):1059–1069. Doi: 10.1007/s00415-020-10250-6

94 Vogrig A, Joubert B, André-Obadia N, Gigli GL, Rheims S, Honnorat J. Seizure specificities in patients with antibody-mediated autoimmune encephalitis. Epilepsia 2019;60(08):1508–1525. Doi: 10.1111/epi.16282

95 Vogrig A, Gigli GL, Nilo A, Pauletto G, Valente M. Seizures, Epilepsy, and NORSE Secondary to Autoimmune Encephalitis: A Practical Guide for Clinicians. Biomedicines 2022;11(01):44. Doi: 10.3390/biomedicines11010044

96 Fisher RS, Acevedo C, Arzimanoglou A, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia 2014;55(04):475–482. Doi: 10.1111/epi.12550

97 Cabezudo-García P, Mena-Vázquez N, Villagrán-García M, Serrano-Castro PJ. Efficacy of antiepileptic drugs in autoimmune epilepsy: A systematic review. Seizure 2018;59:72–76. Doi: 10.1016/j.seizure.2018.05.004

98 de Bruijn MAAM, van Sonderen A, van Coevorden-Hameete MH, et al. Evaluation of seizure treatment in anti-LGI1, anti-NMDAR, and anti-GABA$_B$R encephalitis. Neurology 2019;92(19):e2185–e2196. Doi: 10.1212/WNL.0000000000007475

99 Ilyas-Feldmann M, Prüß H, Holtkamp M. Long-term seizure outcome and antiseizure medication use in autoimmune encephalitis. Seizure 2021;86(86):138–143. Doi: 10.1016/j.seizure.2021.02.010

100 Liu X, Guo K, Lin J, et al. Long-term seizure outcomes in patients with autoimmune encephalitis: A prospective observational registry study update. Epilepsia 2022;63(07):1812–1821. Doi: 10.1111/epi.17245

101 Britton JW, Dalmau J. Recognizing autoimmune encephalitis as a cause of seizures: Treating cause and not effect. Neurology 2019;92(19):877–878. Doi: 10.1212/WNL.0000000000007444

102 Elkhider H, Sharma R, Kapoor N, Vattoth S, Shihabuddin B. Autoimmune encephalitis and seizures, cerebrospinal fluid, imaging, and EEG findings: a case series. Neurol Sci 2022;43(04):2669–2680. Doi: 10.1007/s10072-021-05617-0

103 Shen CH, Fang GL, Yang F, et al. Seizures and risk of epilepsy in anti-NMDAR, anti-LGI1, and anti-GABA$_B$ R encephalitis. Ann

Clin Transl Neurol 2020;7(08):1392–1399. Doi: 10.1002/acn3.51137

104 Wesselingh R, Butzkueven H, Buzzard K, Tarlinton D, O'Brien TJ, Monif M. Seizures in autoimmune encephalitis: Kindling the fire. Epilepsia 2020;61(06):1033–1044. Doi: 10.1111/epi.16515

105 Flammer J, Neziraj T, Rüegg S, Pröbstel AK. Immune Mechanisms in Epileptogenesis: Update on Diagnosis and Treatment of Autoimmune Epilepsy Syndromes. Drugs 2023;83(02):135–158. Doi: 10.1007/s40265-022-01826-9

106 Blum RA, Tomlinson AR, Jetté N, Kwon CS, Easton A, Yeshokumar AK. Assessment of long-term psychosocial outcomes in anti-NMDA receptor encephalitis. Epilepsy Behav 2020;108:107088. Doi: 10.1016/j.yebeh.2020.107088

107 de Bruijn MAAM, Aarsen FK, van Oosterhout MP, et al; CHANCE Study Group. Long-term neuropsychological outcome following pediatric anti-NMDAR encephalitis. Neurology 2018;90(22):e1997–e2005. Doi: 10.1212/WNL.0000000000005605

108 Guasp M, Rosa-Justicia M, Muñoz-Lopetegi A, et al; Spanish anti-NMDAR Encephalitis Study Group. Clinical characterisation of patients in the post-acute stage of anti-NMDA receptor encephalitis: a prospective cohort study and comparison with patients with schizophrenia spectrum disorders. Lancet Neurol 2022;21(10):899–910. Doi: 10.1016/S1474-4422(22)00299-X

109 Nicolle DCM, Moses JL. A Systematic Review of the Neuropsychological Sequelae of People Diagnosed with Anti N-Methyl-D-Aspartate Receptor Encephalitis in the Acute and Chronic Phases. Arch Clin Neuropsychol 2018;33(08):964–983. Doi: 10.1093/arclin/acy005

110 Abboud H, Briggs F, Buerki R, et al. Residual symptoms and long-term outcomes after all-cause autoimmune encephalitis in adults. J Neurol Sci 2022;434:120124. Doi: 10.1016/j.jns.2021.120124

111 Ariño H, Armangué T, Petit-Pedrol M, et al. Anti-LGI1-associated cognitive impairment: Presentation and long-term outcome. Neurology 2016;87(08):759–765. Doi: 10.1212/WNL.0000000000003009

112 Finke C, Kopp UA, Prüss H, Dalmau J, Wandinger K-P, Ploner CJ. Cognitive deficits following anti-NMDA receptor encephalitis. J Neurol Neurosurg Psychiatry 2012;83(02):195–198. Doi: 10.1136/jnnp-2011-300411

113 Heine J, Kopp UA, Klag J, Ploner CJ, Prüss H, Finke C. Long-Term Cognitive Outcome in Anti-N-Methyl-D-Aspartate Receptor Encephalitis. Ann Neurol 2021;90(06):949–961. Doi: 10.1002/ana.26241

114 Devenney E, Hodges JR. The Mini-Mental State Examination: pitfalls and limitations. Pract Neurol 2017;17(01):79–80. Doi: 10.1136/practneurol-2016-001520

115 Naugle RI, Kawczak K. Limitations of the Mini-Mental State Examination. Cleve Clin J Med 1989;56(03):277–281. Doi: 10.3949/ccjm.56.3.277

116 New PW, Buchbinder R. Critical appraisal and review of the Rankin scale and its derivatives. Neuroepidemiology 2006;26(01):4–15. Doi: 10.1159/000089536

117 Kapoor A, Lanctôt KL, Bayley M, et al. "Good Outcome" Isn't Good Enough: Cognitive Impairment, Depressive Symptoms, and Social Restrictions in Physically Recovered Stroke Patients. Stroke 2017;48(06):1688–1690. Doi: 10.1161/STROKEAHA.117.016728

118 Zhou H, Deng Q, Yang Z, et al. Performance of the clinical assessment scale for autoimmune encephalitis in a pediatric autoimmune encephalitis cohort. Front Immunol 2022;13:915352. Doi: 10.3389/fimmu.2022.915352

119 Cai MT, Lai QL, Zheng Y, et al. Validation of the Clinical Assessment Scale for Autoimmune Encephalitis: A Multicenter Study. Neurol Ther 2021;10(02):985–1000. Doi: 10.1007/s40120-021-00278-9

120 Zhang Y, Tu E, Yao C, Liu J, Lei Q, Lu W. Validation of the Clinical Assessment Scale in Autoimmune Encephalitis in Chinese Patients. Front Immunol 2021;12:796965. Doi: 10.3389/fimmu.2021.796965