Electroconvulsive Therapy in Anti-N-Methyl-D-Aspartate Receptor Encephalitis

A Case Report and Review of the Literature

M. Justin Coffey, MD and Joseph J. Cooper, MD

Objectives: There is a growing scientific literature describing the neuropsychiatric symptoms of anti-N-methyl-D-aspartate (NMDA) receptor encephalitis, including the use of electroconvulsive therapy (ECT) to treat those symptoms. We sought to consolidate this literature into a review that highlights its relevance to ECT practitioners.

Methods: We performed a PubMed search using the terms *electroconvulsive therapy* and *encephalitis*, *autoimmune encephalitis*, or *anti-NMDA receptor encephalitis*. We reviewed all relevant studies in detail, cross-referenced all bibliographies, and collected key clinical information related to the practice of ECT.

Results: We identified 6 studies offering patient-level descriptions of the use of ECT in patients with anti-NMDA receptor encephalitis. In all cases ECT was used to target symptoms of catatonia. Electroconvulsive therapy was delivered safely and effectively irrespective of the timing of diagnosis, tumor removal, or immunotherapy.

Conclusions: There are no controlled data on the use of ECT in anti-NMDA receptor encephalitis. Further investigation is needed to determine whether ECT has a disease-modifying effect on this form of autoimmune encephalitis.

Key Words: ECT, catatonia, anti-NMDA receptor encephalitis, autoimmune encephalitis

(*J ECT* 2016;32: 225–229)

Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis is a recently described and increasingly understood autoimmune disorder with a prominent neuropsychiatric presentation.[1,2] The clinical syndrome is characterized typically by a nonspecific, flu-like prodrome followed by acute development of severe neuropsychiatric symptoms over 1 to 3 weeks.[3] Predominant symptoms are movement disorders, such as catatonia and dyskinesias, cognitive impairments in memory and executive function, and behavioral symptoms, such as impulsivity, disinhibition, or aggression.[4] The vast majority of patients are seen first by a psychiatrist, rather than a neurologist.[3] Roughly two thirds of patients then progress to a neuroautonomic phase characterized by seizures, hypoventilation, coma, and even death.

The precise incidence of anti-NMDA receptor encephalitis is not established, although epidemiologic data suggest it is the second most common form of autoimmune encephalitis and is even more common than viral encephalitis in young people.[4] The antibody implicated in the disorder was first described in the year 2007.[2] Since then, then number reported cases rapidly expanded as the antibody test became more widely available, with the largest reported series including 577 individuals.[4] The pathophysiology involves antibody-mediated crosslinking and internalization of the GluN1 subunit of the NMDA receptor, which results in receptor hypofunction and altered synaptic plasticity. In roughly 50% of patients, a tumor is identified as the source of antibody production.[4] The typical finding is a mature ovarian teratoma in a woman older than 18 years, although the condition has been reported in men with testicular teratoma as well as in men and women without tumor.[3] The diagnosis is suspected based on clinical presentation and confirmed by the presence of IgG anti-GlunN1 antibodies in the cerebrospinal fluid.

Treatment centers on surgical removal of a tumor (if identified) and immunotherapies such as intravenous immunoglobulin (IVIG), plasma exchange, corticosteroids, and chemotherapies. The prognosis is generally favorable, with 75% of patients achieving full or nearly full recovery.[5]

The management of the neuropsychiatric symptoms is challenging. The condition is easily misdiagnosed,[6] and there is often a delay of days to weeks between symptom onset and laboratory confirmation of the diagnosis,[7] leaving clinicians to deliver symptomatic treatments off-label before establishing a diagnosis. The use of antipsychotics in these patients may worsen symptoms or cause neuroleptic malignant syndrome (NMS).[8] Benzodiazepines may improve catatonia, but sedating medications carry increased risk in these patients who are already vulnerable to hypoventilation and decreased arousal.[8]

Electroconvulsive therapy is a safe and effective treatment for catatonia, including when it is associated with neurologic or general medical disorders.[9] Electroconvulsive therapy has been used safely in cases of infectious encephalitis[10,11] and encephalitis lethargica[12,13] where the target symptoms have been catatonia, seizures, or both. In such cases, ECT is delivered before, after, or along with treatment for the underlying etiology of the encephalitis (eg, antiviral therapy for herpes encephalitis). The optimal ECT technique in such cases is not established.

Similarly, in cases of anti-NMDA receptor encephalitis, the timing of ECT may vary. Although definitive treatment is tumor removal and immunotherapy, the symptoms of anti-NMDA receptor encephalitis are severe enough to warrant intervention prior to receiving laboratory confirmation of the diagnosis. During such times, patients may be on psychiatry wards or neurology wards, in neurological intensive care units, or even in emergency departments.[14] They may be receiving concomitant medications, such as anticonvulsants for seizure activity, lorazepam for catatonia, and antipsychotics for psychosis. They may be undergoing major surgery (eg, laparotomy), systemic immunotherapy (eg, steroids, cyclophosphamide, rituximab, IVIG), or plasma exchange. Although certain patients may be communicative and cognitively intact, others may be mute, cognitively impaired, or even comatose. Each of these factors may be relevant to delivering safe and optimally effective ECT.

To call ECT practitioners' attention to anti-NMDA receptor encephalitis and the important role ECT may play in treating it, we reviewed the existing scientific literature on this topic.

METHODS

We performed a search of the PubMed database using the terms *electroconvulsive therapy* and *encephalitis*, *autoimmune*

From the Menninger Clinic, Houston, TX.
Received for publication March 5, 2016; accepted April 13, 2016.
Reprints: M. Justin Coffey MD, The Menninger Clinic, 12301 Main St, Houston, TX 77035 (e-mail: jcoffey@menninger.edu).
M.J.C. receives author royalties from UpToDate and MedLink Neurology. J.J.C. has no conflicts of interest to disclose.

DOI: 10.1097/YCT.0000000000000334

encephalitis, or *anti-NMDA receptor encephalitis*. Results were limited to studies with human subjects written in the English language. One of us (M.J.C.) reviewed all abstracts for relevance, and then both authors reviewed all relevant studies in full, including their bibliographies. We excluded studies of viral encephalitis or encephalitis lethargica. We excluded studies of paraneoplastic or autoimmune encephalitis other than anti-NMDA receptor encephalitis, even if the clinical syndrome described was sufficient to have a high suspicion of anti-NMDA receptor encephalitis. We also excluded conference abstracts unless published. From each of the remaining studies, we collected clinical information pertinent to the practice of ECT.

RESULTS

We identified a total of eight studies describing the use of ECT in patients with anti-NMDAR encephalitis.[3,8,15–20] Two studies including patients with anti-NMDAR encephalitis who received ECT were excluded as they contained no individual level data.[3,20] Of the 6 remaining studies, all were case reports (Table 1). Four of six case reports described a patient 18 years or younger. The case reports describe clinical features inconsistently and ECT parameters incompletely, such that descriptive statistics of the sample are not meaningful. Therefore, we summarize these reports below in the order of their publication.

Case 1

Braakman and colleagues[15] describe a 47-year-old man with no apparent neuropsychiatric history who developed an upper respiratory infection followed three weeks later by derealization, anxiety, musical hallucinations, insomnia, disorientation, memory impairments, bradyphrenia, restlessness, excessive sweating, and suicidal thoughts. The report mentions a psychiatric diagnosis of "psychosis with hallucinations of unknown origin" but does not mention if antipsychotic medication was started. A few days later, the patient developed paroxysmal upward eye deviations, extreme agitation, dystonic posturing, rigidity, dyskinesias, dyspnea, laryngospasms with oxygen desaturation, pathologic affect, and mutism. Brain magnetic resonance imaging (MRI) was unremarkable, electroencephalogram (EEG) showed diffuse slow wave activity over bilateral frontal areas predominantly, and cerebrospinal fluid (CSF) analysis revealed lymphocytic pleocytosis. The patient received acyclovir for presumed herpes encephalitis until microbiology studies identified no viral agents, at which point acyclovir was withdrawn and the diagnosis was changed to encephalitis lethargica. Intravenous lorazepam up to 10 mg daily and methylprednisolone 1.00 mg daily were administered for three days with no improvement, after which ECT was recommended.

The patient received seven bilateral ECT treatments with technical parameters, treatment schedule, anesthesia regimen, concomitant medications, and seizure quality not specified. The patient's "agitation, laryngospasm, mutism, hallucinations, catatonia, oculogyric crises, and extrapyramidal symptoms had disappeared," and he "regained a normal level of consciousness." The course of ECT concluded, and the patient had lingering attention and memory impairments for 1 year and was able to resume work as a teacher after 2 years. The diagnosis of anti-NMDAR encephalitis was made retrospectively by identifying the presence of NMDAR antibodies were identified in an archived sample of CSF.

Case 2

Mann and colleagues[8] describe a 14-year-old African America girl with no apparent neuropsychiatric history who developed a blistering, erythematous facial rash and headache that resolved

TABLE 1. Case Reports of ECT in Anti-NMDA Receptor Encephalitis

Bibliographic Information	Patient Demographics	Immunotherapy	Timing of ECT	ECT Technique	Outcome
Braakman HMH, et al. *Neurology*, 2010	47-year-old man	Methylprednisolone	Initiated before diagnosis of encephalitis	7 bilateral ECT treatments with concomitant lorazepam	Improved behavior, cognition, and motor abnormalities
Mann A, et al. *J Neuropsychiatry Clin Neurosci*, 2012	14-year-old African American girl	Prednisolone, IVIG, rituximab, plasma exchange, cyclophosphamide	Initiated after diagnosis of encephalitis	7 ECT treatments on alternating days with concomitant lorazepam	Improved hemodynamics, behavior, cognition, and motor abnormalities; persistent impulsivity
Matsumoto T, et al. *Psychiatry and Clinical Neurosci*, 2012	18-year-old Japanese man	None	Initiated before diagnosis of encephalitis	13 ECT treatments with concomitant antipsychotics	Improved hemodynamics, behavior, cognition, psychosis, and motor abnormalities
Wilson JE, et al. *Psychosomatics*, 2013	14-year-old African American girl	High-dose steroids, IVIG, tumor removal, rituximab	Initiated before diagnosis of encephalitis	14 total ECT treatments: 5 daily with concomitant lorazepam, then 9 treatments following tumor removal	Improved hemodynamics, behavior, cognition, and motor abnormalities
Jones KC, et al. *Psychiatric Practice*, 2015	17-year-old boy	IVIG	Initiated prior to diagnosis of encephalitis	2 bitemporal ECT treatments with concomitant lorazepam anticonvulsants, and antipsychotics	Improved hemodynamics, behavior, cognition, and motor abnormalities
Sunwoo JS, et al. *J ECT* (2016)	27-year-old woman	IVIG, tumor removal, rituximab	Initiated after diagnosis of encephalitis	13 bitemporal ECT treatments, twice weekly schedule, with concomitant cisatracurium	Improved hemodynamics, behavior, cognition, and motor abnormalities

spontaneously followed by "acute-onset auditory hallucinations and paranoia" and then "hyperactivity, irritability, increased speech, and insomnia." CSF analysis revealed lymphocytic pleocytosis, EEG showed frontal slowing, and brain MRI showed minimal nonspecific periventricular white matter changes. She received vancomycin, ceftriaxone, and acyclovir for presumed viral encephalitis, but went on to develop generalized tonic-clonic seizures, incontinence, mutism, and the inability to feed herself, followed by "periods of dystonia, dyskinesia, spastic rigidity, cogwheel rigidity, bilateral upper extremity hyperreflexia," and "unintelligible verbal communication." Six weeks after symptom onset, anti-NMDAR antibodies were detected in her CSF, and she was given IVIG with no improvement. Over the next 2 weeks, she received trials of risperidone, diphenhydramine, and carbidopa-levodopa, as well as intravenous lorazepam 2 mg every 6 hours when she developed "symptoms consistent with worsening catatonia: waxy flexibility, echololalia, muscle rigidity, negativism, stereotypy (lip and tongue biting; fidgeting with clothes), blank staring, and a grasp reflex." The lorazepam was associated with "temporary but dramatic improvement." A course of rituximab was terminated early due to "autonomic instability and worsening catatonia within 24 hours," at which point ECT was recommended.

The patient received 7 ECT treatments on alternating days with electrode location, technical parameters, anesthesia regimen, concomitant medications, and seizure quality not specified. ECT normalized the patient's blood pressure, pulse and temperature, and "she became more aware of her surroundings, could name her location, play a simple card game, eat and toilet with assistance, and ambulate independently," although "she remained impulsive and aggressive" with "sleep-cycle inversion." The course of ECT was concluded, and valproic acid, trazodone, and plasma exchange were administered, followed one month later by the addition of rituximab, cyclophosphamide, risperidone, and lorazepam. No tumor was identified, and the patient was discharged to an inpatient rehabilitation program, where over the course of 8 months her neuropsychiatric symptoms and functional status gradually improved.

Case 3

Matsumoto and colleagues[16] describe an 18-year-old Japanese man who, 5 days after recovering from influenza, developed "acute-onset behavioral abnormalities and personality change," followed by delusions, violence, confusion, "catalepsy, stereotypy, convulsions, and involuntary movements of the tongue." Brain MRI was normal, as was EEG. He was treated for "catatonic schizophrenia with antipsychotics, lorazepam, and sodium valproate," which "only reduced his confusional state," at which point ECT was recommended.

The patient received 13 ECT treatments with electrode location, technical parameters, treatment schedule, anesthesia regimen, and seizure quality not specified. He continued to receive antipsychotic medication during ECT, after which he "made a full recovery." After the patient's discharge, the CSF study results indicated the presence of anti-NMDAR antibodies, and the diagnosis of anti-NMDAR encephalitis was made. No tumor was identified, and no immunotherapy was ever administered.

Case 4

Wilson and colleagues[17] describe a 14-year-old African American girl who, 3 months after being diagnosed with mononucleosis, developed "progressive weight loss, fatigue, weakness, and headache, followed by the onset of insomnia, agitation, echolalia, and bizarre posturing of her upper extremities," as well as "a prolonged period of somnolence and unresponsiveness" after receiving an injection of haloperidol in a local emergency department. Brain MRI and EEG were normal, and CSF analysis showed pleocytosis. She received acyclovir for a presumed diagnosis of herpes encephalitis, in addition to valproic acid and levetiracetam for "spells characterized by flexion of her arms and legs with eyes deviating to the right." Roughly 2 weeks later, she developed "unstable blood pressure, tachycardia, decreased respiratory drive, and an elevated core body temperature," and aspiration pneumonia was diagnosed. A positive lorazepam challenge was consistent with a diagnosis of catatonia, and she then received empirical immunotherapy with high-dose steroids and intravenous immunoglobulin. Despite these measures, her condition worsened, she underwent tracheostomy and gastrostomy tube placement, and "transfer to hospice was discussed with the family." Roughly 1 week later, during a psychiatry consultation for possible NMS, the patient's Bush Francis Catatonia Rating Scale score was 21, and she received a trial intravenous lorazepam at escalating doses for a presumed diagnosis of malignant catatonia. Her autonomic instability improved, but improvement in her motor abnormalities was transient, at which point ECT was recommended.

While receiving 36 mg of lorazepam per day, the patient received 5 daily ECT treatments with electrode location, technical parameters, anesthesia regimen, and seizure quality not specified. "Subtle improvements in her mental status and catatonic symptoms" allowed the lorazepam dose to be decreased to 12 mg per day and a CT of the chest, abdomen, and pelvis to be obtained. The CT revealed an ovarian mass diagnosed on pathology as a mature teratoma, and the patient immediately underwent left salpingo-oopherectomy and received a course of high-dose steroids while lorazepam was continued. Autonomic instability recurred, so the course of ECT was resumed, while she also received intravenous immunoglobulin and rituximab. She displayed gradual improvement and "more purposeful and goal-directed movements," and after her fourteenth ECT treatment, "her catatonia was almost completely resolved," the tracheostomy was removed, and she began speaking in whispers. She was discharged to an inpatient rehabilitation facility and after one year "had returned to her cognitive and physical baseline."

Case 5

Jones and colleagues[18] describe a 17-year-old boy with a history of genital herpes and no neuropsychiatric history who presented to a local emergency department with "new-onset confusion, seizures, and symptoms of catatonia." Diagnostic work-up, including normal EEG and head CT, was unrevealing, and he received acyclovir, lorazepam, and antipsychotic medications for presumed viral encephalitis. When his symptoms did not improve, he was transferred to a tertiary care academic medical center, where he received a regimen of anti-viral, antipsychotic, and anticonvulsant medications. Brain MRI and microbiology studies were normal, whereas long-term video-EEG revealed frontally dominant delta wave activity. A psychiatry consultant identified "signs of catatonia," including "labile mood with uncontrollable crying, repetition of phrases, posturing, purposeless motor movements, negativism, cataplexy, stereotyping, waxy flexibility, hyperverbal speech with loose associations, echolalia, and disorientation." No improvement was seen after 2 mg lorazepam challenges. The patient received no benefit from additional trials of antipsychotic medications as well as memantine, at which point ECT was recommended to treat malignant catatonia.

The patient received 2 bitemporal ECT treatments with initial settings of pulse width of 1 ms, 40 Hz frequency, 0.8 mA current, and 2 second stimulus duration, and ultimate settings of pulse width of 1 ms, 60 Hz frequency, 0.8 mA current, and 3 second

stimulus duration. The treatment schedule, concomitant medications, and anesthesia regimen were not specified. The initial treatment elicited a seizure of 91 seconds, with no report of seizure quality for the second treatment. Electroconvulsive therapy resulted in "notable improvement in his catatonic symptoms, including autonomic instability, stereotyped behaviors, and agitation." The course of ECT was concluded as CSF analysis results returned and demonstrated the presence of anti-NMDAR antibodies, at which point immunotherapy with intravenous immunoglobulin was pursued in lieu of ECT, although lorazepam was continued as needed. Tumor surveillance yielded no findings. Over an unspecified time course, the patient showed "gradual improvement in cognition and physical functioning, with resolution of seizure activity, dysautonomia, and agitation." He was eventually discharged to an inpatient rehabilitation facility, and no long-term follow-up data were reported.

Case 6

Chu and colleagues[19] describe a 27-year-old woman with no neuropsychiatric history developed headache and insomnia, followed a few days later by "confusion, visual and auditory hallucinations, and disorganized speech," as well as reduced levels of arousal. Infectious work-up was unrevealing, brain MRI was normal, but CT of abdomen and pelvis identified a 2-cm lesion suggestive of an ovarian teratoma. She received intravenous immunoglobulin daily for five days due to a "high suspicion of anti-NMDA receptor encephalitis," but her condition progressively worsened. Despite tumor removal and a trial of rituximab, she developed seizures and "hyperkinetic repetitive movements predominantly affecting perioral areas, hands, and feet." Long-term video-EEG showed generalized slowing with delta brush patterns and no epileptiform activity. Her symptoms did not improve on anticonvulsant medication, and the administration of olanzapine was associated with rhabdomyolysis, rigidity, and autonomic instability requiring intubation. "Over several months," she received intravenous cisatracurium to prevent self-injury. When there was no improvement in her symptoms despite eight additional doses of rituximab, ECT was recommended to treat "ongoing dyskinesia and catatonia."

The patient received 13 bitemporal ECT treatments on a twice weekly schedule with settings of pulse width of 1 ms, 0.8 mA current, and a stimulus dose ranging from 192 to 432 millicoulombs. During the first 12 treatments, anesthesia was achieved with fentanyl. During the final treatment, anesthesia was changed to propofol, and muscle relaxation was achieved with succinylcholine rather than cisatracurium. Seizure duration ranged from 33 to 63 seconds. Electroconvulsive therapy progressively improved the patient's motor abnormalities as measured by "sequential reduction of cisatracurium infusion rate." In addition, the patient's alertness improved, although other cognitive disabilities persisted. Anti-NMDA receptor antibodies remained present in the CSF, and no additional tumor was identified.

DISCUSSION

Anti-NMDA receptor encephalitis is a systemic autoimmune disorder with severe neurotoxic effects. Patients are hemodynamically unstable, unable to communicate or maintain alertness, may have an unidentified tumor, may be receiving immunotherapy or chemotherapy, and may be suffering seizures, all factors that may increase the risks associated with ECT. Nevertheless, in all 6 cases described above, ECT was administered safely in a person who was gravely ill. Moreover, some patients may have rigidity, immobility, or muscle atrophy, all risk factors for transient hyperkalemia, which may make a non-depolarizing muscle relaxant a safer alternative to succinylcholine. Only 1 case report in this series included a description of anesthesia and muscle relaxation, and only 1 case report included a detailed description of ECT technique. Still, there were no reports of adverse effects associated with ECT, as have been reported when ECT is used to treat NMS.[21] Overall, these outcomes suggest that ECT is safe and has an important role to play in the management of anti-NMDA receptor encephalitis.

In all 6 cases ECT was used to treat signs and symptoms of catatonia, and it was effective at doing so. Whereas in some cases, the catatonia was malignant and possibly attributable to the use of dopamine-blocking medications, in other cases the catatonia presumably stemmed from the encephalitis itself. It does not appear that quantifiable outcome measures, such as the Bush Francis Catatonia Rating Scale, were used to evaluate the effectiveness of ECT. Rather, global clinical impressions are what most authors reported. Notwithstanding the desire for more methodical outcome measurement, ECT was an effective therapy even after numerous other therapies had been unsuccessful. This effectiveness is particularly important given the fact that there is often a significant delay from symptom onset to diagnosis, during which time empiric therapy must be attempted to alleviate suffering and prevent harm. Indeed, in the majority of case reports, ECT was initiated before the diagnosis of anti-NMDA receptor encephalitis being made, suggesting that ECT can safely be considered early in the course of patients suspected to have autoimmune encephalitis, particularly if patients exhibit signs of catatonia. In such cases, the early administration of ECT may help patients avoid adverse reactions to dopamine-blocking medications (eg, NMS), as occurred in the majority of the cases included in our sample.

The timing of ECT administration may have special importance for additional reasons. Some patients had improvement after ECT but before immunotherapy; some patients had improvement after ECT after not improving with immunotherapy; and 1 patient had improvement with ECT and did not require immunotherapy. Two additional case reports describing the use of ECT in limbic encephalitis may also be relevant. First, Lee and colleagues[22] describe an 11-year-old African American girl with "paraneoplastic limbic encephalitis" that is remarkably consistent with anti-NMDA receptor encephalitis, but was reported in 2006 before the NMDA receptor antibody test was available. Symptoms of malignant catatonia "responded rapidly" to 8 bilateral ECT treatments over 2 weeks, at which point was put on hold, and ultrasound and abdominal computed tomography revealed an ovarian mass that was then surgically removed and found to be a "nonimmature cystic teratoma." By the fourth postoperative day, her neuropsychiatric exam had returned to normal, aside from mild-to-moderate short-term memory impairments that persisted for 2 years after hospital discharge. In a similar report, Slooter and colleagues describe a 13-year-old girl with malignant catatonia attributed to "encephalitis of unknown origin" that is also highly suggestive of anti-NMDA receptor encephalitis.[23] Her condition responded after four bilateral ECT treatments and continued to improve with nine additional treatments. No tumor was identified, and no form of immunotherapy was administered.

These observations raise the question of whether ECT has a disease-modifying effect on anti-NMDA receptor encephalitis. If so, what might be the mechanism of such an effect? The pathophysiology of anti-NMDA receptor encephalitis appears to be mediated by antibodies to the NR1 (glycine-binding) subunit of the NMDA receptor.[3] These antibodies bind to the NR1 subunit and crosslink surface NMDA receptors, causing internalization and receptor hypofunction. Dalmau et al[5] propose that this decrease in NMDA receptor function results in downstream effects on dopaminergic, noradrenergic, and cholinergic systems

(producing autonomic instability); GABAergic neurons (producing a frontostriatal syndrome); and medullopontine circuits (producing hypoventilation and coma). These effects are reversible and dependent on titer levels of antibody, perhaps explaining why surgically removing an antibody-producing tumor early in the course of the illness is so important. Electroconvulsive therapy, on the other hand, may exert its beneficial effects by acting directly on the NMDA receptor system. Although human data are lacking, animal data indicate that electroconvulsive shock upregulates NMDA receptors, an effect possibly mediated by the rapid increase in tissue plasminogen activator that follows an electrically induced seizure.[24] This theory of action remains speculative and overly simplistic, but it calls attention to the need to investigate more formally the important role that ECT might play in treating this severe and potentially devastating neuropsychiatric illness.

The main limitation of this review is the incomplete reporting of the technical parameters of the ECT delivered to each patient. Although the total number of ECT treatments was reported (range, 2–14), the electrode location, treatment schedule, stimulus waveform and intensity, and ECT device were often not included. Furthermore, the anesthesia regimen and concomitant medication regimen were also difficult to discern, even though these factors influence ECT technique. Also, perhaps most importantly, none of the case reports contains quantitative measures of outcomes, including side effects. So as to enable the generation of valid hypotheses related to ECT, future publications should follow established recommendations for including these important technical details.[25]

When prescribed to patients suffering from anti-NMDA receptor encephalitis, ECT can be reasonably expected to treat symptoms of catatonia, malignant catatonia, and NMS. The safety profile cannot be well assessed by case reports, but a favorable risk-to-benefit ratio is indicated by the severity of the clinical states described. Clinicians should consider ECT early in the course of a neuropsychiatric illness consistent with anti-NMDA receptor encephalitis. In the authors' experience with these challenging cases, the urgent need for a rapid, definitive treatment response is an indication for prescribing a course of brief pulse ECT using bitemporal electrode placement and a stimulus dose at least 1.5 times above seizure threshold. Further research is needed to investigate whether ECT has a disease modifying effect exclusive of its beneficial effects on symptoms of catatonia.

REFERENCES

1. Vitaliani R, Mason W, Ances B, et al. Paraneoplastic encephalitis, psychiatric symptoms, and hypoventilation in ovarian teratoma. *Ann Neurol*. 2005;58:594–604.
2. Dalmau J, Tuzun E, Wu HY, et al. Paraneoplastic anti-NMDA receptor encephalitis associated with ovarian teratoma. *Ann Neurol*. 2007;61:25–36.
3. Dalmau J, Gleichman AJ, Hughes EG, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol*. 2008;7:1091–1098.
4. Titulaer MJ, McCracken L, Gabilondo I, et al. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis. *Lancet Neurol*. 2013;12:157–165.
5. Dalmau J, Lancaster E, Martinez-Hernandez E, et al. Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. *Lancet Neurol*. 2011;10:63–74.
6. Maneta E, Garcia G. Psychiatric manifestations of anti-NMDA receptor encephalitis: neurobiological underpinnings and differential diagnostic implications. *Psychosomatics*. 2014;55:37–44.
7. Wandinger KP, Saschenbrecker S, Stoecker W, et al. Anti-NMDA receptor encephalitis: a severe, multistage, treatable disorder presenting with psychosis. *J Neuroimmunol*. 2011;231:86–91.
8. Mann A, Machado NM, Liu N, et al. A multidisciplinary approach to the treatment of anti-NMDA receptor antibody encephalitis: a case and review of the literature. *J Neuropsychiatry Clin Neurosci*. 2012;24: 247–254.
9. Luchini F, Medda P, Mariani M, et al. Electroconvulsive therapy in catatonic patients: efficicacy and predictors of response. *World J Psychiatr*. 2015;5:182–192.
10. Shukla L, Narayanaswamy J, Gopinath S, et al. Electroconvulsive therapy for the treatment of organic catatonia due to viral encephalitis. *J ECT*. 2012;28:e27–e28.
11. Hart D, Lineberry T, Philbrick K, et al. Highlight the use of electroconvulsive therapy in a case of post-infectious encephalitis. *J ECT*. 2005;21:57–58.
12. Dekleva KB, Husain MM. Sporadic encephalitis lethargica: a case treated successfully with ECT. *J Neuropsychiatr Clin Neurosci*. 1995;7:237–239.
13. Ali S, Welch CA, Park LT, et al. Encephalitis and catatonia treated with ECT. *Cogn Behav Neurol*. 2008;21:46–51.
14. Chapman MR, Vause HE. Anti-NMDA receptor encephalitis: diagnosis, psychiatric presentation, and treatment. *Am J Psychiatry*. 2011;168: 245–251.
15. Braakman HMH, Moers-Hornicks VMP, Arts BMG, et al. Pearls and oysters: electroconvulsive therapy in anti-NMDA receptor encephalitis. *Neurology*. 2010;75:e44–e46.
16. Matsumoto T, Matsumoto K, Kobayashi T, et al. Electroconvulsive therapy can improve psychotic symptoms in anti-NMDA receptor encephalitis. *Psychiatr and Clin Neurosci*. 2012;66:242–243.
17. Wilson JE, Shuster J, Fuchs C. Anti-NMDA receptor encephalitis in a 14-year-old female presenting as malignant catatonia: medical and psychiatric approach to treatment. *Psychosomatics*. 2013;54:585–589.
18. Jones KC, Schwartz AC, Hermida AP. A case of anti-NMDA receptor encephalitis treated with ECT. *J Psychiatr Pract*. 21:374–380.
19. Sunwoo J-S, Jung DC, Choi JY, et al. Successful treatment of refractory dyskinesia secondary to anti-N-methyl-D-aspartate receptor encephalitis with electroconvulsive therapy. *J ECT*. 2016;32:e13–e14.
20. Florance NR, Davis RL, Lam C, et al. Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis in children and adolescents. *Ann Neurol*. 2009;66:11–18.
21. Mann SC, Caroff SN, Bleier HR, et al. Electroconvulsive therapy of the lethal catatonia syndrome. *Convuls Ther*. 1990;6:239–247.
22. Lee A, Glick DB, Dinwiddie SH. Electroconvulsive therapy in a pediatric patient with malignant catatonia and paraneoplastic limbic encephalitis. *J ECT*. 2006;22:267–270.
23. Slooter AJ, Braun KPJ, Balk FJE, et al. Electroconvulsive therapy for malignant catatonia in childhood. *Peidatr Neurol*. 2005;32:190–192.
24. Hoirisch-Clapauch S, Mezzasalma MAU, Nardi AE. Pivotal role of tissue plasminogen activator in the mechanism of action of electroconvulsive therapy. *J Psychopharm*. 2014;28:99–105.
25. Weiner RD, Weaver LA Jr, Sackeim HA. Reporting of technical parameters in ECT publications: recommendations for authors. *Convulsive Ther*. 1988;4:88–91.