




Electroconvulsive Therapy for Patients with Catatonia: Current Perspectives

This article was published in the following Dove Press journal:
Neuropsychiatric Disease and Treatment

Jenifer R Lloyd ¹
Eric R Silverman ¹
Joseph L Kugler²
Joseph J Cooper ¹

¹Department of Psychiatry, University of Illinois at Chicago, Chicago, IL, USA;

²Department of Psychiatry, University of Texas-Dell Medical School, Austin, TX, USA

Abstract: Catatonia is a serious, common syndrome of motoric and behavioral dysfunction, which carries high morbidity and mortality. Electroconvulsive therapy (ECT) is the definitive treatment for catatonia, but access to ECT for the treatment of catatonia remains inappropriately limited. Catatonia is observable, detectable, and relevant to various medical specialties, but underdiagnosis impedes the delivery of appropriate treatment and heightens risk of serious complications including iatrogenesis. Current understanding of catatonia's pathophysiology links it to the current understanding of ECT's mechanism of action. Definitive catatonia care requires recognition of the syndrome, workup to identify and treat the underlying cause, and effective management including appropriate referral for ECT. Even when all of these conditions are met, and despite well-established data on the safety and efficacy of ECT, stigma surrounding ECT and legal restrictions for its use in catatonia are additional critical barriers. Addressing the underdiagnosis of catatonia and barriers to its treatment with ECT is vital to improving outcomes for patients. While no standardized protocols for treatment of catatonia with ECT exist, a large body of research guides evidence-based care and reveals where additional research is warranted. The authors conducted a review of the literature on ECT as a treatment for catatonia. Based on the review, the authors offer strategies and future directions for improving access to ECT for patients with catatonia, and propose an algorithm for the treatment of catatonia with ECT.

Keywords: catatonia, electroconvulsive therapy, underdiagnosis, algorithm

Introduction

A man in his late 70s sat inanimate, his eyes staring unfocused at a great distance, and arms stiffly suspended in mid-air. Upon removal of his pillow, his head remained elevated off the mattress. He had become severely constipated and retained his urine. Half an hour after receiving treatment, the return of fluid movement and spontaneous joking bears witness to his apparent revival from this strange, frozen state. The medical students – one of the authors (JJC) included – were astonished. Yet the nurses, anesthesia team, and psychiatry attending were not surprised, having regularly witnessed his recoveries. The catatonic syndrome separating this man from his world and its exquisite responsiveness to electroconvulsive therapy (ECT) had inspired countless cohorts of medical students, and was eventually reported.¹

Catatonia and ECT share an interwoven past over the last century. Catatonia is a neuropsychiatric syndrome characterized by behavioral and motor disturbances. Accurately described by Karl Kahlbaum as a distinct clinical phenotype in the late 19th century, catatonia was subsequently subsumed by Emil Kraepelin as a type of

Correspondence: Jenifer R Lloyd
Department of Psychiatry, University of Illinois at Chicago, 912 S Wood St (MC 913), Chicago, IL 60612, USA
Tel +1 312-996-0906
Fax +1 312-996-9517
Email jllloyd5@uic.edu

dementia praecox, later schizophrenia, where it remained in psychiatric nosology until the 2013 publication of the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5). The phenomenological and epidemiological errors in this categorization of catatonia have been well documented,^{2,3} and likely contribute to significant misconceptions and underdiagnosis of this psychomotor syndrome.

ECT is a treatment which relies upon the therapeutic benefits of inducing a seizure in the brain, is exquisitely effective for catatonia, and can be lifesaving in severe catatonic states. Even before larger observational studies describing the effectiveness of ECT in treating catatonia, inducing seizures to provide rapid recovery was reported as far back as the late 1930s.⁴ Moreover, these findings have been further strengthened by studies with increasingly rigorous study designs, and have revealed previously unrecognized causes of catatonia, while delineating catatonia's varied phenotypes.

In spite of being among the safest and most effective of known neuropsychiatric treatments, ECT remains underutilized. A multitude of factors likely influence underutilization. Principal among them are suboptimal recognition of catatonia by psychiatric and non-psychiatric physicians, mismanagement of catatonia when recognized, ongoing stigmatization of ECT, lack of patient access to ECT, and remaining neuroscience gaps in our understanding of the pathophysiology of catatonia and corresponding mechanisms of therapeutic action of ECT. This confluence of potentially contributing reasons predicts that many patients suffering from catatonia will not be presented with ECT as a treatment option.

Here, we review the evidence to date correlated with our current neuroscience-informed understanding of catatonia and ECT, how we assess and treat catatonia, the tolerance and safety of ECT, and disparities in access to ECT as a treatment. Finally, we offer practical strategies for improving recognition of catatonia, considering ECT early in its treatment course, and present an algorithmic approach to treatment.

Catatonia: The Syndrome Features

Catatonia is known to occur in the setting of a variety of psychiatric, neurologic, and general medical conditions. The DSM-5 defines catatonia as the presence of three or more of the following 12 psychomotor features: stupor,

cataplexy, waxy flexibility, mutism, negativism, posturing, mannerism, stereotypy, agitation, grimacing, echolalia, and echopraxia.⁵ Of the several rating scales for catatonia, many have been previously reviewed^{6,7} and are summarized in Table 1.⁸⁻¹⁴

Of these, the Bush–Francis catatonia rating scale (BFCRS) is widely used in both research and clinical settings, was published with standardized exam instructions making it relatively straightforward to teach to trainees, and is the scale used in the authors' practices. The BFCRS incorporates 23 clinical features to assess symptom severity and measure response to treatment.⁹ The two clinical states of catatonia most described and represented in this scale are the stuporous state and the excited state. Stuporous catatonia manifests as a paucity of movement with symptoms including immobility, unresponsiveness, mutism, rigidity, staring, and refusal of oral intake. Excited catatonia is characterized by excessive motor activity, combativeness, echophenomena, impulsivity, and repetitive speech and behavior. Alternation between these seemingly opposite catatonic states is not uncommon, and the rapid alternation itself was historically recognized as a catatonic symptom, despite not being recognized in most modern scales.¹⁵ With the most notable exception being the Northoff Catatonia Scale, most scales also leave out affective features, such as emotional lability, anxiety, flat affect, and ambivalence, despite Kahlbaum's original characterization of catatonia as having an affective domain.¹²

Mechanisms

While the pathophysiology of catatonia remains unclear, symptomatology and response to treatment have provided the beginning for exploration of the underlying pathophysiology. Pharmacological interventions used to manage catatonia involve targeting γ -aminobutyric acid (GABA)-A, glutamate, and dopamine, suggesting dysfunction in these neurotransmitter systems may play a role in catatonia.^{16,17} Some evidence supports the idea that potency of dopamine D2 receptor blockade is directly related to the risk of exacerbating catatonia or provoking malignant features.¹⁸ In comparing catatonic subjects to non-catatonic subjects, decreased GABA-A receptor density in the left sensorimotor cortex was visualized in catatonic subjects on functional imaging.¹⁹ In addition, a deficiency of cortical GABA has been observed in catatonia and is hypothesized to alter basal ganglia modulation and lead to motor symptomatology.²⁰ This disturbance has been shown to be corrected with the administration of

Table I Features of Rating Scales for Catatonia^{8–14}

Catatonia Rating Scale	Description	Items	Screening Instrument	Inter-Rater Reliability	Validity Testing
Modified Rogers Scale, Catatonia Subscale or MRS-C (1991)	A broad psychomotor scale used to rate extrapyramidal, catatonic, and other motor abnormalities in severe psychiatric illnesses. Only after completion of the MRS can the catatonia subscale be calculated.	18	No	–	–
Bush-Francis Catatonia Rating Scale (1996)	First standardized and quantifiable scale for the assessment of catatonia. Scale is supplemented by a nine-step examination procedure to identify specific symptoms.	23	If ≥ 2 two signs present in first 14 items	Screening= 0.95 Rating scale= 0.93	Sens. 100% Spec. 75–100%
Rogers Catatonia Scale (1996)	Revision of MRS-C to exclude diagnostic criteria not present in DSM-IV and further separate parkinsonian symptoms from catatonic symptoms.	22	No	0.81	Sens. and spec. 100% in DSM-IV depressive subgroup
Northoff Catatonia Rating Scale (1999)	Focuses on theory that affective, hypokinetic and hyperkinetic symptoms are equally essential components of catatonia. Scale also added time criterion for stupor and akinesia.	40	No	0.8–0.96	Sens. and spec. 100%
Braunig Catatonia Rating Scale (2000)	Excludes overlapping motor symptoms seen in parkinsonism and other motor disorders to achieve a higher specificity for catatonia.	21	No	>0.83	–
Kanner Scale (2008)	Developed to improve identification of catatonia in autism and other pervasive developmental disorders. Unlike other scales, it specifies the distinction between stupor and immobility.	18	If ≥ 2 two signs present in first 11 items	–	–

Abbreviations: Sens, sensitivity; Spec, specificity.

lorazepam, providing the theory that the quick reversal of catatonic symptoms with lorazepam may be related to the normalization of regulatory circuits.^{19,21} Dopamine hypoactivity and glutamate hyperactivity have also been postulated to have a role in catatonia as dopamine antagonists can induce a catatonic state and N-methyl-D-aspartate (NMDA) antagonists have been shown to treat catatonia. Vagal theories of catatonia, which help explain the autonomic instability, have also been elaborated.^{22,23}

Genetics may also play a role in the pathogenesis of catatonia as a study of multiplex families reported significant heritability estimates for catatonia symptoms, frequency, and severity.²⁴ In addition, studies have identified a locus of interest on chromosome 15q15 in families with inherited vulnerability to periodic catatonia, a psychomotor disturbance during acute psychosis.²⁵ The Prader Willi Syndrome, a genetic syndrome whose behavioral phenotype includes catatonia, compulsive

behaviors, stereotypies, psychosis, and excessive somnolence, is also related to an abnormality on chromosome 15, interestingly in a region containing several GABA-A receptor subunit genes.¹⁶ The Klein–Levin syndrome of episodic hypersomnolence has been proposed as a model for how diencephalic dysfunction can contribute to the catatonic phenotype.¹⁶ Additionally, theories have suggested an intense evolutionary-based fear response can induce catatonia.²⁶ Functional imaging of catatonic subjects during negative emotional states has shown alterations in activation of the orbitofrontal cortex and in the functional connectivity to the premotor cortex,²⁷ which provides a potential link from emotional/limbic signals to motor control circuits. Dysfunction in the posterior parietal cortex has been postulated to contribute to the termination of movements, resulting in motor posturing, while medial prefrontal and anterior cingulate dysfunction, regions typically involved in the initiation of activity, has been hypothesized to contribute to mutism and stupor.²⁰

Much is now known about the effects of ECT at neurochemical, neuroendocrine, synaptic, and cellular levels.²⁸ Recent data have demonstrated regional increases in brain volume post-ECT, which are likely related to neurogenic and synaptogenic effects.²⁹ While a full mechanistic understanding of the relative contributions of each of these components to the therapeutic effects of ECT for catatonia (and other states) remains incomplete, the same is true for many other treatments for neuropsychiatric disease. The current understanding of ECT's mechanism compares favorably to many psychotropic medications, anticonvulsant medications, and vagus nerve stimulation, none of which suffer the same level of stigmatization.⁶

Morbidity and Mortality

Though research has estimated the prevalence of catatonia to be 5–18% on inpatient psychiatric units, the syndrome remains under-recognized.^{30–32} Not identifying catatonia as the appropriate diagnosis and the resulting lack of treatment can lead to dangerous medical complications including pressure ulcers, nutritional deficiencies, electrolyte disturbances, venous thrombosis, pulmonary embolism, urinary tract infections, muscle contractures, and aspiration pneumonia. Without timely treatment, a patient may develop autonomic instability with hyperthermia, intense excitement, rigidity, and delirium. These symptoms indicate a life-threatening state called malignant catatonia, with a mortality rate as high as 20% if untreated.³⁰ The symptoms can be indistinguishable from neuroleptic malignant syndrome (NMS), a condition associated with exposure to dopamine antagonists such as antipsychotic drugs. As there are no identifying clinical or laboratory markers that distinguish the two, and no differential response to treatment, NMS is best considered to be a drug-induced cause of malignant catatonia.¹⁸

Differential Diagnosis

The differential diagnosis of catatonia must include numerous conditions which can present similarly or comorbidly.^{17,33,34} Here we provide several examples of how to consider catatonia and its differential diagnosis. However, this is by no means intended as a comprehensive list of all of the differential considerations, which must be tailored to the history and exam findings of each individual case. Catatonia can worsen with the addition of dopamine antagonists; however, patients can also experience drug-induced parkinsonism with overlapping symptoms of

immobility, staring, and rigidity. Akathisia, literally the inability to remain seated, is an internally excited motoric state, commonly mistaken for anxiety. Active catatonic motor features such as maintaining postures anti-gravity, repetitive movements or speech, or echophenomena would not be expected in drug-induced parkinsonism or akathisia alone. Nonconvulsive status epilepticus can lead to odd behavioral automatisms which might look like stereotypies or mannerisms, and indeed epilepsy is a relatively common cause of catatonia, but some features, such as the prolonged holding of induced postures (catalepsy) or echophenomena, would be less commonly expected in epilepsy. Akinetic mutism can lead to a mute and immobile state with a refusal to eat, but should not have active motor features, and is typically associated with a structural brain lesion. Symptoms of stuporous catatonia and hypoactive delirium can overlap, as can excited catatonia and hyperactive delirium. Despite controversy in the DSM-5 criteria, it is clear that delirium and catatonia frequently co-occur, leading to difficulty in diagnosis and appropriate treatment as benzodiazepines can improve catatonia but exacerbate delirium.^{35,36} Delirium alone should not display active catatonic motor features. The serotonin syndrome is an example of a cause of a hyperkinetic state, where the clinical features will commonly include those of both excited catatonia and hyperactive delirium. A physical motor exam encompassing assessment for catatonia-specific motor findings (eg, the BFCRS) and additional motor components of a traditional neurology exam (eg, tremor, tone, strength, coordination) is needed to rule catatonia in or out.

Prevalence and Etiology

Catatonia's prevalence varies widely in different neuropsychiatric states. Its prevalence in different psychiatric conditions is summarized in [Figure 1](#).^{14,31,37–54}

Listed at the bottom of the figure are conditions widely recognized as presenting comorbidly with catatonia (and/or for which catatonia is on the differential diagnosis), yet no systematic data regarding the prevalence of catatonia in these conditions were found. Studies have estimated that catatonia has a medical or neurological etiology in 21–46% of cases,³³ though precise and specific prevalence numbers are not available, and in some acute medical and surgical settings the rate may be even higher.⁵⁵ Potential causes are varied and numerous, and include metabolic derangements (eg, electrolyte disturbances, cardiac, renal, liver dysfunction, and vitamin deficiency), inflammatory

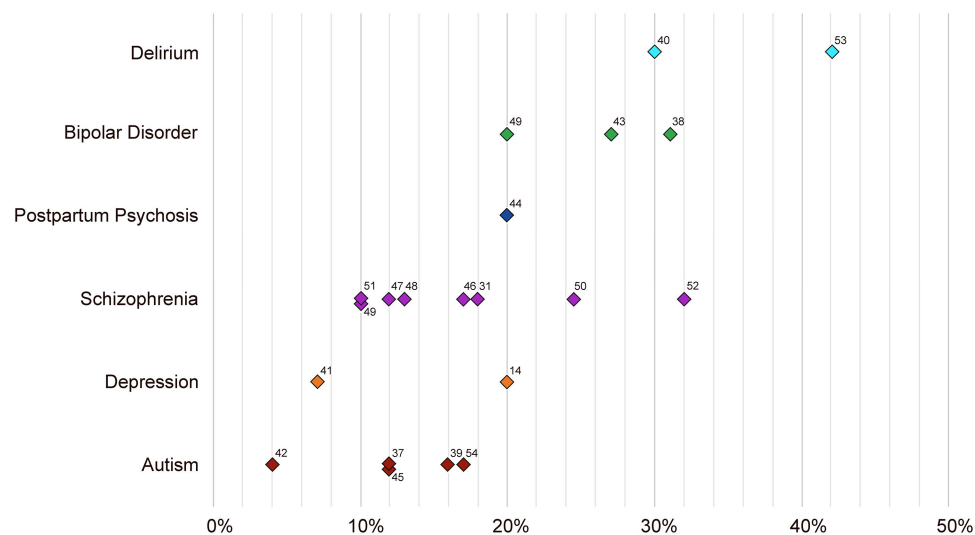


Figure 1 Prevalence of catatonia. Insufficient prevalence data for other conditions frequently cooccurring with catatonia include: obsessive-compulsive disorder, Tourette's syndrome, alcohol/sedative withdrawal, and selective mutism.

states (infectious, autoimmune, or paraneoplastic), neurologic conditions (eg, vascular, structural, seizure, degenerative, and genetic/developmental disorders), toxidromes (eg, use of recreational substances, certain medications), and withdrawal phenomena.

Evaluation and Management

Workup and Supportive Care

Regardless of etiology, catatonia is best treated by addressing both the syndrome itself and the underlying cause.^{30,56} Once the syndrome is recognized on exam, a thorough workup is warranted.^{17,36} Depending on the history, presence of comorbid symptoms, and physical exam findings, corresponding serum, urine, and cerebrospinal fluid studies, electroencephalogram, and magnetic resonance imaging of the brain should be considered.

In particular, medication regimens and recent medication changes should be evaluated, specifically the presence of dopamine antagonists, or the recent discontinuation of GABA-ergic or dopaminergic drugs. The risk of worsening catatonia or provoking malignant features is high with dopamine antagonist medications, which should be held when catatonia is recognized.¹⁸ Monitoring signs for the development of malignant catatonia such as hyperautonomia and fever is essential, with other less specific markers including elevated creatine phosphokinase, decreased serum iron, and leukocytosis.^{17,57}

Additionally, supportive care to manage medical complications of catatonia is vital. Frequent repositioning in the setting of prolonged immobility can prevent muscle

contractures and pressure ulcers.⁵⁸ Other measures include controlling pyrexia and hyperautonomia, ensuring adequate oxygenation, electrolyte repletion, appropriately hydrating to prevent acute kidney injury and rhabdomyolysis, maintaining adequate nutrition, venous thromboembolism prophylaxis, catheter use in the setting of urinary retention, bowel regimens for constipation, and implementing protocols to reduce aspiration risk.⁵⁸ Finally, throughout care, a catatonia rating scale score should be tracked regularly to monitor the severity of symptoms and response to treatment.

Treatment

Catatonia responds well to treatment. An established feature of catatonia is its robust response to benzodiazepines. Benzodiazepines have become the mainstay of first-line treatment with remission rates as high as 70–80%.^{55,59} The administration of 1–2 mg of lorazepam can function as both a treatment and diagnostic tool, known as the lorazepam challenge, with a reduction in catatonic symptoms confirming the diagnosis.⁵⁷ If the initial dose is ineffective, it can be repeated every 30–60 minutes with serial symptom assessments. Intravenous administration is preferred to ensure adherence and rapid absorption. When catatonia responds partially to lower doses, patients may require rapid titration to doses of 20–30 mg/day of lorazepam to achieve full symptom resolution.⁶⁰ Monitoring for sedation and respiratory depression is essential when escalating the dose of benzodiazepine; however, sedation typically precedes respiratory depression and thus serves as a signal

to slow or halt titration,⁶¹ which can often be done on a general medical or psychiatric unit of a general hospital by including “hold for sedation” in the medication order. Furthermore, catatonia is a state where these high doses are typically tolerated without inducing over-sedation.³⁰ However, additional precautions may be needed in situations where medical backup is less robust and in patients with a higher risk of respiratory depression, such as those with known pulmonary disease. Though lorazepam is the most common benzodiazepine used in catatonia, successful use of diazepam, oxazepam, and clonazepam has also been reported.¹⁷ Zolpidem, a positive allosteric modulator of GABA-A receptors, has also been shown to be a safe and effective alternative treatment to catatonia. Similar to the lorazepam challenge, a zolpidem challenge has been proposed, using doses from 7.5 mg to 40 mg daily.^{55,62} After, or in concert with, GABA-ergic medications, ECT is the definitive treatment for catatonia, as will be discussed below. NMDA antagonists, amantadine and memantine, have some evidence to support their use as second or third line agents.⁶³ It is unclear if these agents work through direct glutamate antagonism or indirect effects on GABA and dopamine.^{64,65} Case reports have also published support for the use of mood stabilizers in the treatment of catatonia, including valproate, topiramate, and carbamazepine, with their effects possibly mediated through GABA-ergic actions.^{55,66-68} Several case reports describe the effective treatment of catatonia with repetitive transcranial magnetic stimulation⁶⁹ or second-generation antipsychotic medications,⁵⁶ but if the latter are given, each dose should be given in combination with a benzodiazepine.⁶³ Algorithmic approaches to these treatments have been published.^{63,64}

ECT

Indication

There is wide consensus that in cases refractory to benzodiazepine treatment or in life-threatening conditions that require rapid resolution, such as malignant catatonia, ECT should be initiated.^{30,70} Other considerations which may drive ECT’s use earlier in the course of catatonia include situations that may have relative contraindications to benzodiazepine use. These could include catatonia in pregnancy or the peripartum period, comorbid substance use disorders, and psychosocial circumstances which present a concern for safely prescribing high doses of controlled substances, among others. Some have suggested that ECT

should be elevated to first-line status for the treatment of catatonia due to the safety profile and rapidity of response.⁷¹

Efficacy

Response rates of catatonia to ECT are excellent, with most modern studies reporting response in 80–100% of cases, including in the setting of non-response to benzodiazepine.^{44,59,70-73} Response rates approached 80% in a literature review of catatonia in children and adolescents with diverse underlying etiologies.⁷⁴ Lower response rates (59% and 71%) described in two retrospective studies^{75,76} may be attributable to study populations with higher rates of underlying psychotic disorder, delay in appropriate treatment, and/or recent use of dopamine antagonists.⁵⁵ There is little standardization regarding what constitutes benzodiazepine non-response. As noted above, high doses of benzodiazepines are often needed, but are often not trialed adequately in routine clinical care. Zisselman and Jaffe recommend preparing for ECT early: immediately upon non-response to initial lorazepam challenge, even while lorazepam doses are being uptitrated.⁵⁶ Hatta et al suggest ECT should be the treatment of choice for catatonia.⁷¹ Their randomized controlled trial (RCT) of catatonic patients (n=50) had several successive arms pitting ECT against various pharmacotherapies: first lorazepam, then intravenous haloperidol or oral risperidone, followed by chlorpromazine, with ECT offered to patients who failed pharmacotherapy at each step. All patients who received ECT at any step achieved remission (100% response rate). Response rates for all other treatments were considerably less impressive, including just 2% for lorazepam (though the maximum daily dose was limited to just 3 mg per day). On a larger scale, the 2016 updated Canadian Network for Mood and Anxiety Treatments guidelines for the treatment of major depressive disorder recommend ECT as a first-line treatment when catatonic features are present,⁷⁷ with level 3 evidence.

Of note, this body of evidence includes very few RCTs, and those that do exist are limited in rigor. A 2018 systematic review of 28 studies – the majority observational and including 3 RCTs – on the treatment of 564 catatonic patients with ECT concluded that none of the studies adequately demonstrated efficacy (ECT superior to placebo) or effectiveness (ECT superior to comparable treatment), despite robustly showing that catatonic symptoms improve significantly following ECT.⁷⁸ However, a sham-controlled trial of ECT for catatonia would be ethically

impermissible due to lack of equipoise based on the available evidence, combined with the grave risks of withholding or delaying treatment for catatonia, and thus may be considered similar to the lack of RCT evidence supporting the use of a parachute to prevent death when falling from an airplane.⁷⁹

There are case reports of ECT effectively treating catatonia caused by myocardial infarction,⁵⁵ lupus,⁸⁰ encephalomyelitis,⁸¹ multiple sclerosis,⁸² and other complex medical conditions.⁸³ Safe and effective use of ECT to treat delirium⁸⁴ suggests likely benefit when co-occurring with catatonia. Additionally, there are case reports of dramatic improvement in symptoms of chronic catatonia once the syndrome was recognized and ECT administered, regardless of etiology;⁵⁵ in parallel, a 1999 RCT demonstrated that lorazepam failed to treat chronic catatonia in eighteen patients (though all patients had chronic schizophrenia and the total daily dose of lorazepam was limited to 6 mg/day).⁸⁵ Limited but compelling evidence also supports the use of ECT for catatonia associated with autism,^{86–89} anti-NMDA receptor encephalitis,^{90,91} toxic psychosis,⁹² obsessive compulsive disorder,^{93–95} and repetitive self-injury and tics.⁸

Predictors of Response

Attempts to elucidate predictors of response to ECT trace back to observations made by Laszlo Meduna in 1934, where longer duration of illness predicted poorer response in the first nine catatonic patients to be treated with (chemically induced) convulsive therapy.^{4,55} Small studies since then support this duration of illness finding, but have otherwise offered few consistent findings of additional predictors of response. A small retrospective study of 27 patients found improvement to be significantly associated with younger age and autonomic dysregulation, especially elevated temperature.⁷⁵ An observational study of 63 patients with catatonic schizophrenia demonstrated that faster response was associated with a shorter duration of illness, higher initial BFCRS score, and higher rates of waxy flexibility and gegenhalten (a term used to describe a form of hypertonia involving motoric resistance to passive movements); echophenomena predicted slower response.⁷⁰

Evidence supporting the high response rate of catatonia to ECT is such that, if a suboptimal response is seen, a more extensive workup for an underlying neurologic condition should be considered.⁹⁶ Swartz et al described four patients with chronic neurologic pathology

(Alzheimer disease; cerebellar atrophy with complex partial seizures; spinal cord injury; post-encephalitis cognitive deficits) whose catatonia responded poorly to ECT.⁹⁷ A study of ECT in 26 patients with catatonia and bipolar disorder demonstrated that patients prescribed anticholinergics or dopamine agonists (suggestive of possible underlying neurologic pathology) were more frequently nonresponders.⁹⁸ The authors hypothesized that this might represent a “structural” variant of catatonia that is less responsive to ECT. Further evidence supporting this idea is a series showing that catatonia as a sequela of hypoxic brain injury was unresponsive to ECT.⁹⁹

It is well established that catatonia due to underlying mood disorders has a better response to treatment, including ECT, compared to catatonia due to underlying psychotic disorders,⁵⁵ leading some to postulate that catatonia in schizophrenia is an altogether different syndrome. Response to ECT in co-occurring catatonia and schizophrenia is likely augmented when combined with clozapine,⁵⁵ though a 2005 Cochrane Review concluded that ECT for chronic catatonia in schizophrenia is not significantly beneficial,¹⁰⁰ the updated Review from 2019 offered no new insight.¹⁰¹

Administration

Lack of rigorous comparison studies has hindered the development of a standardized treatment protocol for catatonia with ECT. Most evidence supports a “robust” approach: bitemporal ECT, standard pulse width (brief pulse), with a substantially suprathreshold stimulus,⁵⁵ with some arguing that stuporous catatonia in particular should be conceptualized as always potentially life-threatening, and that potential for cognitive side effects should be a distant secondary consideration.^{102,103} Numerous case reports describe successful treatment of catatonia with alternative electrode placements, including right unilateral (RUL),^{104–110} left anterior right temporal,¹¹¹ and biparietotemporal,¹¹² and/or ultrabrief pulse (UB) stimuli,^{81,106,107,109,110} but it is unclear whether or not there is benefit to choosing them over the traditional “robust” approach to treating catatonia. Reasons for alternate placement/stimulus varied and included lack of consent for bitemporal placement and hopes of inducing fewer cognitive side effects based on extrapolating data from studies on UB-RUL ECT in depression.¹¹³ Many of these studies commented on the preservation of patients’ pre-morbid cognitive function or the lack of ECT-induced cognitive impairments, but most did not systematically

evaluate cognition. One used brief bedside cognitive testing (of attention, concentration, short-term recall, and biographical recall), in a single case, and only post-ECT.¹⁰⁶ A second compared Mini-Mental State Examination scores in a case, pre (26/30) and post-ECT (28/30).¹¹⁰ A third described a single case in which extensive formal cognitive batteries were completed post-ECT; they showed some deficits but were suspected to be premorbid.¹⁰⁹

There is some agreement that if the ECT-induced convulsive response lasts less than 25 seconds, the stimulus dose should be increased.⁹⁶ Minimal data exist regarding the frequency of treatments for catatonia; the most common protocol is thrice weekly, except in cases of malignant catatonia where daily treatment may be considered until symptoms improve.⁵⁵ The total number of treatments typically ranges between 12 and 20 in order to achieve meaningful improvement or remission, although rapid response can also be seen.⁵⁵ The number of treatments should be titrated to clinical response and cannot be accurately predicted ahead of time.¹⁰² Recurrence of catatonia is common upon ECT cessation, and maintenance ECT (mECT) has been described as helping to prevent relapse,^{55,82,88,114–116} with some suggesting this approach may be preferred over polypharmacy.⁹⁶ While it is well established that mECT is beneficial in both mood disorders and schizophrenia for preventing relapse following successful treatment with acute ECT,^{117–119} evidence supporting the same for catatonia is based mostly on case reports. In one retrospective study of 42 older patients with a serious mental illness (approximately 25% with catatonia), mECT was highly effective in preventing hospital readmission and reducing readmission length of stay.¹²⁰ Based on these data and on direct experience, we propose the treatment algorithm in [Figure 2](#).

Electrographic markers of seizure quality have been primarily evaluated in patients with depression, not catatonia.¹²¹ If there is a concern for inadequate seizure, in addition to increasing stimulus dose, optimizations include ensuring pre-stimulus hyperventilation, changing anesthetic to an agent with less anticonvulsant properties (etomidate or ketamine), adjusting psychotropics (removing anticonvulsants and/or adding medications that lower seizure threshold, such as flumazenil,¹²² or less commonly, caffeine¹²³). In cases of prolonged immobility, the use of succinylcholine increases the risk of hyperkalemia, and non-depolarizing neuromuscular blockade (now safely reversible with sugammadex¹²⁴) should be considered.⁵⁶ Historically, all psychotropics were discontinued prior to

starting ECT; however, updated evidence and clinical practice argue against this. Current guidelines recommend carefully considering each patient's medications and adjusting only if necessary.^{125,126}

In Combination with Benzodiazepine

In practice, ECT is often administered in the setting of ongoing benzodiazepine administration. Previously, recommendations against the practice were common, citing possibly reduced benefit.^{127,128} A later case series of catatonic patients receiving bitemporal, brief-pulse ECT suggested that combined therapy was superior to monotherapy.¹²⁹ The authors observed that symptoms improved more dramatically and rapidly once one of the treatments was added to the other, regardless of which was initiated first; they thus alluded to a possible “synergistic” effect between benzodiazepines and ECT.¹²⁹ An additional case report described a patient with catatonia and OCD whose symptoms resolved only after coadministration of lorazepam and ECT.⁹³ While the literature remains small, the combination is often feasible, though may require benzodiazepine reversal with flumazenil to achieve therapeutic seizures.

Safety and Tolerability

ECT is generally safe. In 2018, the FDA reclassified ECT devices from high risk (class III) to moderate risk (class II) when used for catatonia that is treatment-resistant or requiring a rapid response in patients 13 years old and above.¹³⁰ A 2009 review determined ECT to be low risk when using American College of Cardiology/American Heart Association guidelines for non-cardiac surgery,¹³¹ and a meta-analysis published in 2017 showed a mortality rate of 2.1 per 100,000 treatments, no higher than rates of general anesthesia alone, with only one ECT-related death in 414,747 included treatments published since 2001.¹³²

Due to the immediately life-threatening nature of some ECT-responsive states (eg, malignant catatonia), there are no absolute contraindications to ECT. Any relative contraindications must be weighed against the risks of leaving a likely ECT-responsive catatonic state untreated. ECT can be performed safely in the setting of most neurological¹³³ and cardiovascular¹³¹ comorbidities. Some conditions present particularly heightened risk (eg, space-occupying brain lesion causing increased intracranial pressure; pheochromocytoma; recent myocardial infarction; cerebrovascular hemorrhage; severe pulmonary disease,^{131,134} and

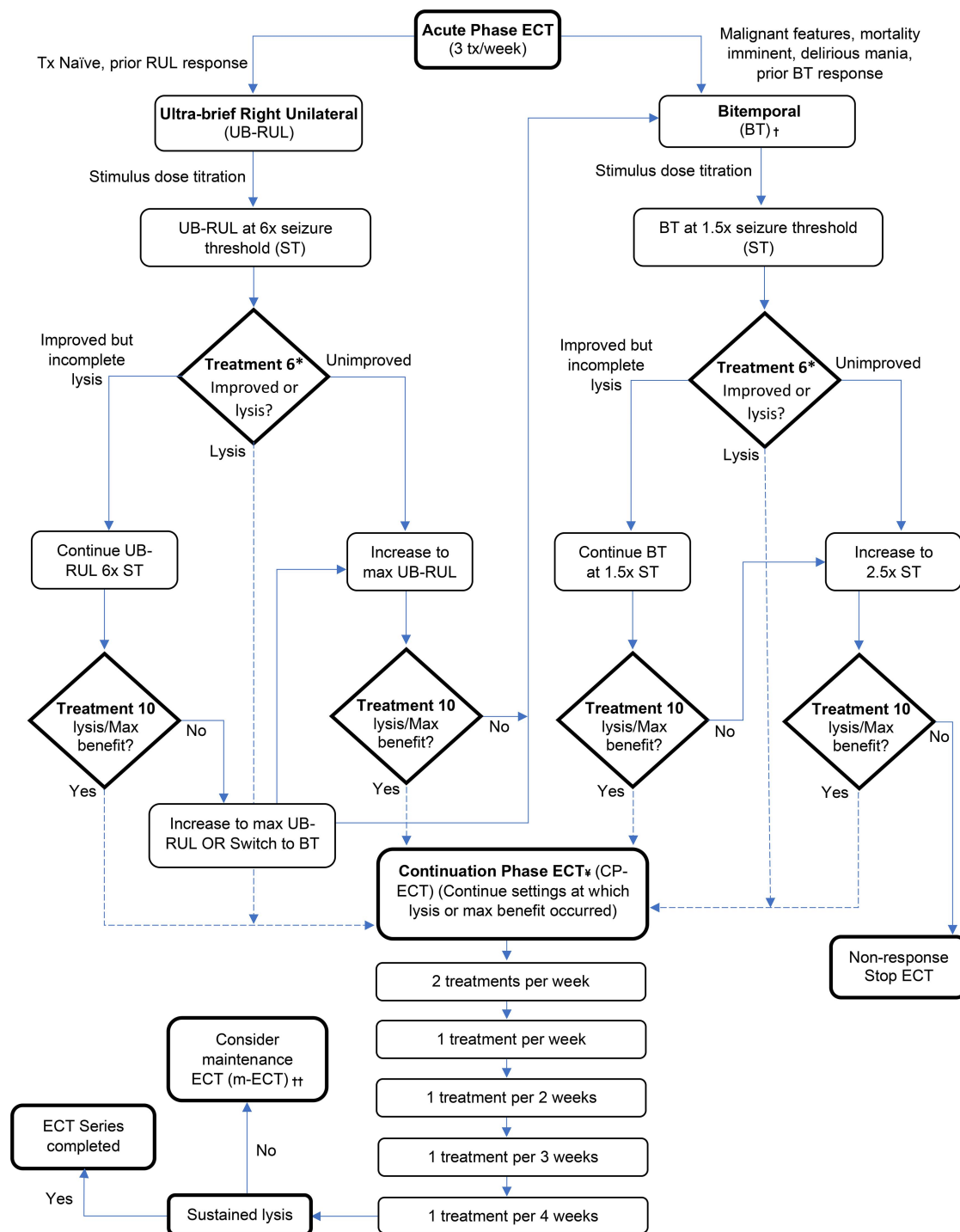


Figure 2 Proposed algorithm for ECT treatment of catatonia.^{81,102-110}

Notes: †If malignant features, consider daily BT treatment. ††Consider maintenance ECT for cases of catatonia of unclear etiology, recurrence of catatonic features in setting of continuation-phase ECT, or history of recurrent catatonia with pharmacologic treatment-resistance. *Monitor treatment response and consider seizure optimization throughout. If seizure quality is in question between treatment 1–5, first consider increasing to max UB-RUL, switching to BT, or increasing BT to 2.5× ST prior to treatment #6. Also consider optimizing via hyperventilation, switch to etomidate or ketamine, tapering or d/c anticonvulsants, or adding flumazenil or caffeine. ‡- If lysis or max benefit is lost during CP-ECT, consider further optimization of seizure parameters, increase in stimulus dosing, and return to the previous treatment level where lysis or max benefit is achieved, and proceed according to algorithm.

Abbreviations: UB-RUL, ultra-brief pulse width, right unilateral placement; BT, brief pulse width, bitemporal placement; ST, seizure threshold; CP-ECT, continuation-phase ECT; m-ECT, maintenance ECT.

hypoxic brain injury⁹⁹). Prior to ECT, patients should undergo a thorough medical evaluation, and specialty consultation should be obtained, when indicated, to assist with risk stratification and optimization of comorbidities. Guidelines around this have been published.^{131,134}

ECT has been shown to be relatively safe in pregnancy,^{135–137} in the elderly,¹³⁸ and in children and adolescents,^{92,139} though some have challenged that safety data on ECT in children with autism were not systematically collected.¹¹⁶ It has been demonstrated definitively that ECT does not cause structural brain damage,¹⁴⁰ even in patients who have received hundreds of lifetime treatments.¹ Additionally, cognitive side effects from acute ECT do not worsen with mECT.¹¹⁹ Reports suggest ECT has no long-term impact on cognition,¹⁴¹ even in patients receiving upward of 100 lifetime treatments,¹⁴² in patients with preexisting dementia,^{143,144} or in the still-developing brain.¹⁴⁵ While few systematic studies of long-term cognitive outcomes have been reported, two large cohort studies found ECT was not associated with incident dementia in those who received ECT.^{146,147}

Common side effects are headache, myalgias, and memory deficits. Memory impairments, when present, typically return to normal within weeks after an ECT course, and objectively resolve by six months post-treatment.¹³¹ Memory effects were improved markedly with the move from sine to square wave ECT,¹⁴⁸ and can be reduced further with other techniques including electrode placement and pulse width modifications.^{113,148} The majority of studies actually show improvement in subjective memory with ECT,¹⁴⁹ likely related to symptom improvements, though in some cases, subjective memory impairment may last beyond six months.¹³¹ To the authors' knowledge, there are no studies specifically looking at cognitive side effects in catatonic patients, though it is worth noting that catatonia itself significantly impairs cognition,^{27,150} and improvement on a brief cognitive measure, such as a clock drawing test, has been reported in catatonia responsive to ECT.^{80,150,151} Studies looking at depression and other conditions have shown overall improvement of cognition with ECT,^{152,153} suggesting that benefits of treatment outweigh the impact of side effects; this is likely true for catatonia as well. Risk for post-ECT delirium may be elevated in patients with catatonia compared to other indications for ECT; a study looking at associated factors found that presence of catatonia, longer seizure duration, high stimulus intensity, and bitemporal electrode placement increased risk, but that

dexmedetomidine was preventive.¹⁵⁴ There is a single report of four cases of catatonia emerging during ECT thought to be attributable to the rapid discontinuation of benzodiazepine pre-procedure.¹⁵⁵

Informed Consent

Evaluation for treatment with ECT should be done by clinicians with experience administering ECT, and, specific to catatonia, with experience in assessing catatonic signs. The informed consent process is conceptually no different for ECT than that for any other medical intervention.¹⁵⁶ Patients with catatonia are often unable to provide consent, though capacity is dynamic and should be reassessed at appropriate intervals, especially as treatment improves symptoms.¹⁵⁷ A 2018 case series reported that in 3 cases of catatonia for which ECT was initially administered involuntarily, each patient regained capacity and consented to additional ECT treatment.¹⁵⁸

Access

Legal

Laws regarding ECT vary widely across the United States¹⁵⁹ and can be quite restrictive, often making it extremely challenging to provide appropriate and timely treatment. This is especially true when decisional capacity is limited, as is often the case in catatonia. In the most restrictive states, court order, guardianship, or advance directive is required when a patient lacks decisional capacity (ie, surrogate decision-makers who would otherwise be legally permitted to consent to other medical interventions are prohibited from consenting to ECT), and/or ECT is entirely prohibited for certain age groups.^{56,159} Many have argued that these restrictions are arbitrary¹⁶⁰ and violate the ethical principle of justice in health care.¹⁶¹ Others have described cases where restrictive consent processes delayed care and thusly contributed to extreme morbidity and increased risk of mortality.^{56,58,87,162} In one case, it took 19 days to obtain a court order.⁵⁶ The question has been raised as to whether catatonia, particularly when caused by underlying medical or neurologic disease, should be subject to mental health-specific ECT laws.^{160,163}

Stigma and Myth

Even when treatment is not legally or decisionally limited, the pursuit of ECT is often hindered by stigma and fear. Misinformation in the media, film, on the internet, and spread by anti-ECT groups has perpetuated myths

regarding outdated methods and extreme side effects. Health-care providers can additionally be a source of misinformation. Several studies demonstrated that the extent of ECT knowledge positively correlated with a positive view of ECT in both providers and patients.¹⁵⁶ Furthermore, two studies of patients who underwent ECT demonstrated that the majority felt ECT was beneficial (79% and 83%) and would undergo ECT again (81% and 98%),¹⁵⁶ while in a third study, 80% of patients reported overall satisfaction with ECT, regardless of whether their treatment was voluntary or involuntary.¹⁶⁴

Provider Experience

Appropriate recommendation of ECT for catatonia remains limited worldwide by provider comfort with ECT. A few studies show that limited experience with ECT prevents providers from appropriately recommending it.^{165–167} Use in Germany is relatively low, despite the fact that psychiatrists there generally had positive views of ECT and felt it was underused.¹⁶⁸ Even in Norway, where ECT is widely available and viewed very positively, psychiatrists expressed concern about its underuse.¹⁶⁹

Under-Recognition of Catatonia

Under-recognition of catatonia is significant, and it follows then that this limits access to appropriate treatment with ECT. In 2005, van der Heijden et al demonstrated significant underdiagnosis of catatonia; clinicians diagnosed catatonia in only 2% of 139 patients, whereas a research team identified it in 18%.³¹ In one retrospective review, neurology residents failed to identify catatonia on emergency room consultation in all of the 12 patients who eventually received a catatonia diagnosis.¹⁷⁰ A three-year retrospective chart review determined that 59% of patients meeting three or more of the DSM-5 criteria for catatonia in a general medical hospital were not diagnosed with catatonia, even in the third of those cases for which psychiatric consult was obtained.³² The precise reasons for this under-recognition are not known, but may include the historic errors in nosology,¹⁶ low catatonia knowledge,^{31,171,172} lack of physical examinations done by psychiatrists,^{173,174} or confusion regarding the opposing clinical features and variable presentations of catatonia. Unfamiliarity with catatonia has been evidenced in a study showing markedly lower catatonia knowledge in internal medicine residents compared to psychiatry residents.¹⁷¹ At the same time, low catatonia knowledge has also been demonstrated among psychiatrists.^{31,171,172}

Additional Barriers

Additional barriers in the US include required post-procedure transportation with escort,¹⁷⁵ a decrease in the number of hospitals providing ECT,¹⁷⁶ geographic limitations, and disparities in insurance coverage.¹⁷⁷ Disproportionately low ECT use in people of color points to sociodemographic barriers as well.^{178–180} Globally, use of ECT is heterogeneous,^{181–187} and geographic limitations, lack of training, lack of anesthesiologists, cost, stigma, health-care inequity, and national laws have been described as obstacles to access.^{183,188–192} Outdated treatment protocols and heavy use for conditions less responsive to ECT (ie, schizophrenia) are common across Asia, based on a study of 334 institutions in 29 Asian countries.¹⁹³ In Scandinavia, ECT is widely available and tends to follow updated treatment guidelines, but unequal geographic distribution can limit access.^{169,194,195}

Discussion

Despite catatonia officially being moved out from under the umbrella of schizophrenia with the publication of DSM-5 in 2013, it continues to be misunderstood and artificially siloed, within the already artificially siloed specialty of psychiatry. Fink et al argued for the recognition of catatonia as a systemic medical syndrome.¹⁹⁶ Others have argued for catatonia to be viewed as a type of altered mental status, akin to and co-occurring with delirium,³⁶ a syndrome with which general medical practitioners have much greater familiarity. Under-recognition of catatonia among psychiatric and non-psychiatric physicians, along with cumbersome legal restrictions placed on ECT, to which very few other medical interventions are subject (rivaled only by pregnancy termination), leaves catatonia oddly disenfranchised, at significant detriment to patients.

Psychiatry as a clinical neuroscience specialty must be better integrated with the rest of medicine,^{197,198} and catatonia is a chief case-study in the argument. It is imperative that clinicians across many disciplines improve recognition and diagnosis of catatonia. There is reason to be hopeful, as two small studies demonstrated that catatonia-specific education is correlated with improved knowledge of the syndrome and increased comfort managing catatonia in practice.^{171,172} Other resources for learning catatonia are available including the Catatonia Information Center¹⁹⁹ <catatonia.org> run by Dr Andrew Francis, and the National Neuroscience Curriculum Initiative, an open-access educational collaborative which

has a module on the use of ECT for catatonia in autism,²⁰⁰ and which hosted a live case conference on catatonia as part of their Quarantine Curriculum's Mind-Body Day.²⁰¹

Widespread legal restrictions on ECT that place legal systems in between a doctor and patient in the therapeutic relationship, or disallow surrogate decision-makers, impede potentially life-saving or morbidity-reducing treatment in catatonia, and are inappropriate, inequitable, and harmful. Advocacy for changes to these laws will help our patients with catatonia suffer less discrimination in their access to care. In the meantime, psychiatric advance directives should be encouraged whenever possible. A patient with a history of ECT-responsive catatonia, who faces significant difficulty with the prospect of surrogate consent (eg, due to psychosocial or local jurisdiction factors), would be an excellent candidate for long-term planning with psychiatric advance directives providing consent to ECT in future catatonic states.

Access to appropriate diagnosis and care for ECT is a problem worldwide. Possible solutions include training more ECT providers, developing standardized methods for performing catatonia exams via telemedicine, and advocating for hospital inclusion of dedicated space for ECT. Misinformation is also widespread. Correcting this begins with standardized, adequate education of providers, and is then followed by education of our colleagues, patients, and the broader public. An example of how to perform psychoeducation about ECT using modern neuroscience-informed language has been published.²⁰²

There is currently no standardized, evidence-based approach to the ECT treatment of patients with catatonia. Based on direct experience with treating catatonia in two separate academic medical centers and this review of the literature, we suggest a practical, flexible ECT algorithm for the treatment of catatonia [Figure 2]. Influenced by the best available published evidence, our proposed algorithm also leverages over a decade of direct experience with its implementation for treating catatonia at the University of Texas at Austin.²⁰³ While not specifically in use at the University of Illinois at Chicago, the algorithm is overall consistent with ECT practice there as well. The suggested algorithm provides a general decision-making framework for ECT practitioners treating patients with catatonic syndromes across a spectrum of phenotypes and severity. Our algorithm prioritizes a balance of safety, tolerability, and relative effectiveness. Others have recently proposed pharmacologic algorithms for the treatment of catatonia utilizing similar approaches.^{63,64} The proposed algorithm may also be considered as a rational tool with the potential to inform RCTs

and high-powered studies that compare various ECT practices in the treatment of catatonia. Finally, a standardized approach to ECT treatment of catatonia could improve communication and coordination of clinical care for patients receiving treatments across several different medical centers. Our suggested algorithm is not a substitute for the application of clinical expertise, nor does it subvert individualized decision-making. All ECT treatment decisions should weigh the possible consequences of under-treating a catatonic syndrome in any given clinical context.

The limitations of our review center on the lack of high-quality evidence for ECT in catatonia. While this is partially mitigated by the high quantity of such evidence, we must recognize the need to improve our evidence base for treating catatonia with ECT. Designing ethically permissible controlled studies of ECT for catatonia is challenging but not impossible. As described, case reports and one of the authors' practices (JLK) suggest that nontraditional (ie, other than

Table 2 Catatonia Clinical Points

Catatonia Clinical Points
Awareness of the catatonic syndrome, and its prevalence across diverse medical settings is the essential first step in the care of patients with catatonia.
A psychomotor exam, such as that published with the Bush–Francis catatonia rating scale (BFCRS), should be employed broadly to screen for catatonia.
Measuring catatonia with a standardized instrument, such as the BFCRS, can aid in monitoring severity and treatment responsiveness.
Workup to determine the underlying etiology, particularly in first-lifetime episodes, should consider the broad list of neurologic, psychiatric, and general medical causes.
A review of current medications should be undertaken with particular concern for use of dopamine antagonists and/or cessation GABA-ergic or dopaminergic drugs.
Supportive care measures with adequate hydration and nutrition, appropriate mobilization and repositioning, and protocols for bowel regimens and anticoagulation are essential to prevent further complications.
A lorazepam challenge test should typically be undertaken, as both a treatment and diagnostic tool.
ECT should be used in cases refractory to benzodiazepines or in patients requiring urgent resolution.
Treatment of the underlying etiology should occur concurrently.
Maintenance treatment with benzodiazepines and/or ECT is often necessary.

bitemporal) electrode placements are effective to some degree for catatonia. Bitemporal placement could be compared to other techniques (such as UB-RUL ECT), to examine efficacy and tolerability, with strict clinical parameters for abandoning the less-efficacious treatment. These, or other, techniques would have to be chosen because of a theoretical advantage, such as improved cognitive outcomes, and if one arm shows less efficacy, the study can be interpreted as having been an unintentional partial “sham” (as the clinical interaction, anesthesia, and stimulus-induced seizure would all be similar). These data would further solidify the evidence base for the superior treatment arm. An intentional “sham” ECT study in catatonia is not ethically permissible due to the risks of undertreatment or delayed treatment of catatonia. Our proposed algorithm provides multiple possible decision-points which could be compared in future clinical trials.

In summary, there are several crucial elements to the effective treatment of catatonia, which are highlighted in Table 2. Through catatonia education, measurement-based care (BFCRS), access to medical workups from psychiatric settings, and social and legal advocacy for ECT, we can address these barriers, and improve outcomes in catatonia.

Disclosure

The authors report no conflicts of interest in this work.

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