Electroconvulsive Therapy in Multiple Sclerosis:
A Review of Current Evidence

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ABSTRACT

Objective: To review the published literature over the last 5 years on the use of electroconvulsive therapy (ECT) in multiple sclerosis (MS), focusing on the efficacy, safety, and tolerability. MS commonly has neuropsychiatric comorbidity. ECT is used in MS for severe and life-threatening forms of mental illness when other treatment options have failed or when a rapid response is required.

Data Sources: English-language literature published in the last 5 years (January 2015–June 2, 2020) was searched using the terms: *ECT*, *electroconvulsive therapy*, *shock therapy*, *electroshock therapy*, *electroconvulsive therapies*, *multiple sclerosis*, *chronic progressive multiple sclerosis*, *acute relapsing multiple sclerosis*, and *multiple sclerosis, relapsing and remitting*. KnowledgeShare, a National Health Service library application providing updates on evidence-based practice, was used along with EMBASE, PsycInfo, MEDLINE, PubMed, the TRIP database (which offers a complete and updated list of evidence-based online resources), HDAS (Healthcare Databases Advanced Search), CRDWeb (Centre for Reviews and Dissemination), and the Cochrane Library. Reference lists of articles identified in the search were also reviewed.

Study Selection: Our initial search revealed 30 articles of potential relevance. However, after individually evaluating these articles, only 6 case studies and 1 review article detailing the use of ECT in MS were included.

Data Extraction: The studies were analyzed by both authors to obtain clinical information relevant to meeting the objectives of the review.

Data Synthesis: The efficacy and safety in using ECT for MS is derived only from case series and case reports. There were no controlled trials or systematic reviews, and the evidence collated was of low quality.

Conclusions: The consensus is that ECT is an effective treatment for specific mental disorders in MS including catatonia. We have used ECT successfully in our clinic for patients with MS. However, there are concerns about the potential effects of ECT on neurologic and cognitive function. There are also possible risks with using anesthetic agents and particularly neuromuscular blockers.

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Multiple sclerosis (MS) is estimated to affect 2.5 million people worldwide.[1] MS is an autoimmune demyelinating disease that follows a chronic course. The mean age at onset is 30 years of age, and the female to male ratio is 3:1.[1] In most cases (85%–90%), the disease initially presents with episodic neurologic symptoms, which are described as a clinically isolated syndrome.[1] Symptoms may include optic neuritis, myelitis, or brain stem involvement. Symptoms commonly peak within 4 weeks, and there is partial or complete remission.[1]

The disease can take on a varied trajectory, with most patients following a relapsing-remitting (RRMS) course within 5 years of the clinically isolated syndrome.[1] In other cases, the disease takes a progressive course, usually 15–20 years after disease onset, and this is conceptualized as secondary progressive MS.[1] In a smaller cohort of patients (about 15% with mean onset at 40 years of age), the disease follows a progressive course from the beginning and is described as primary progressive MS.[1] These 2 classifications of progressive MS constitute more than 50% of people with MS globally.[2]

Acute relapses of MS manifest with focal demyelinating lesions in the white and gray matter of the brain and spinal cord.[1] Magnetic resonance imaging (MRI) can visualize these macroscopic lesions, with T2 hyperintensities representing edema and inflammation, demyelination, remyelination, gliosis, and axonal loss.[1] Neurodegenerative changes occur in parallel and become more prominent after the disease enters a progressive course.[2]

Neuropsychiatric comorbidity is common in MS and can include refractory affective disorders, catatonia, and psychotic illness.[1,3–5] The rate of suicide is increased in patients with MS compared to that of the general population.[3,6,7] One study[6] reported suicidal ideation in nearly 33% of community-dwelling patients, and just over 20% of these individuals had attempted suicide. Depression was cited as a risk factor by the authors.[6] In another study,[7] suicide was the leading cause of death in up to 15% of MS clinic outpatients.[3] In patients with an MS diagnosis, depression has a point prevalence of 14%–31% and a lifetime prevalence of up to 50%.[8] Electroconvulsive therapy (ECT) may be clinically indicated for the aforementioned psychiatric conditions and particularly for those who are at higher risk and present with active suicidality or severe depression.

In this review, we analyze the most recent evidence for the efficacy of ECT in MS and potential complications in neurologic and cognitive functioning. Our aim is to inform colleagues from psychiatry, neurology, and neuropsychiatry

Clinical Points

- Neuropsychiatric comorbidity is common in multiple sclerosis (MS).
- Electroconvulsive therapy (ECT) may be used for MS patients with severe refractory depression that has not responded to pharmacology and psychotherapy or for those with catatonic or psychotic symptoms or at high risk of suicide.
- Patients with active magnetic resonance imaging (MRI) lesions may be at greater risk of neurologic deterioration, and MRI imaging should be considered for all MS patients before ECT.
- Before ECT, there should be a discussion with the anesthetist regarding the agent used for muscle relaxation.

on the latest developments with regard to use of ECT in this patient population.

METHODS

We conducted a comprehensive evidence search of the published literature in the last 5 years (January 2015–June 2, 2020) using the search terms: *ECT*, *electroconvulsive therapy*, *shock therapy*, *electroshock therapy*, *electroconvulsive therapies*, *multiple sclerosis*, *chronic progressive multiple sclerosis*, *acute relapsing multiple sclerosis*, and *multiple sclerosis, relapsing and remitting*. The review was limited to articles written in the English language.

Our team used KnowledgeShare, which is a National Health Service library application providing updates on evidence-based practice. We searched a number of databases including EMBASE, PsycINFO, MEDLINE, PubMed, the Trip database (which offers a complete and updated list of evidence-based practice online resources), HDAS (Healthcare Databases Advanced Search), CRDWeb (Centre for Reviews and Dissemination), and the Cochrane Library. We finished with a supplementary citation search by looking through the reference lists of our sources.

Our initial search revealed 30 articles of potential relevance. However, after individually evaluating these articles, we found only 6 case studies and 1 review article detailing the use of ECT in MS. There were no controlled trials or systematic reviews, and the evidence collated was of low quality. We summarize our findings here.

RESULTS

Review by Steen et al (2015)

Steen et al[9,10] published a review article in 2015. The authors identified a 2007 review by Rasmussen and Keegan[11] of 17 case reports published since 1951. Three cases were discussed in detail and the other 14 were summarized.[11] Steen et al[9] also reviewed those 3 case reports as well as others, including 2 cases of patients with MS and comorbid psychiatric illness who received ECT.

The authors[9] initially refer to a case report by Mattingly et al[12] who found the correlation between existing baseline MRI gadolinium-enhancing lesions and new neurologic dysfunction following ECT. Mattingly et al[12] hypothesized that these active lesions, which increase the permeability of the blood-brain barrier, may prove to be a contraindication for ECT. They recommended baseline MRI imaging before commencing ECT.[12]

The 3 patients described by Rasmussen and Keegan[11] experienced no neurologic decline with ECT. The subjects were women, and their ages ranged from 23 to 61 years. The patients had individual differences in the course and severity of their MS disease. They also varied in their pretreatment neurologic functioning. All 3 patients reported significant improvement in mood following treatment. There was no longer-term follow-up, so it was not possible to ascertain the neurologic and psychiatric sequelae of ECT. In the other 14 cases, a "handful" reported neurologic deterioration. Very few of these patients had pre or post ECT MRI scans to identify new or worsening lesions.[9,11] Steen et al[9] maintain that no firm conclusions could be drawn regarding the safety and efficacy of ECT from these studies.

The 2 case reports of MS patients with comorbid psychiatric illness provided inconsistent findings.[9] One case[13] involved a 28-year-old man who was treated for recurrent catatonia. He responded well to treatment and developed no neurologic complications. The other patient was a man with psychotic depression who had a grand mal seizure following his 14th ECT treatment.[14] ECT was discontinued after this event. There is no detail about the doses used or the laterality of electrode placement.

Case Report by Oligmueller et al (2019)

Oligmueller et al[15] report the case of a 42-year-old woman with a 14-year history of RRMS and recurrent depressive disorder. She had episodic depression of a moderate to severe degree. She was married with 2 children and retired from work after developing MS. There was no history of suicidality, self-injurious behavior, or psychiatric inpatient admissions. She occasionally used alcohol, and there was no history of substance misuse.

ECT was offered because of the severity and treatment-resistant nature of her depression. Various psychotropic medications were trialed with little benefit, including antidepressant, antipsychotic, anticonvulsant, benzodiazepine, and stimulant medications. Some of these agents were used as monotherapy, and some were combined or used for augmentation effects. Her current medications included venlafaxine XR 150 mg once daily, modafinil 300 mg daily in divided doses, methylphenidate 2.5 mg daily, fingolimod 0.5 mg orally 3 times per week, omeprazole 20 mg daily, trospium XR 60 mg daily, naproxen 500 mg twice daily as needed, and alprazolam 1.5 mg twice daily as needed for anxiety.[15]

The patient had ECT without muscle relaxation because of concerns regarding succinylcholine-induced hyperkalemia and hyperthermia in MS patients. There is

the possibility of unexpectedly prolonged paralysis with nondepolarizing muscle relaxants. She had right unilateral ECT to minimize cognitive adverse effects and a total of 11 treatments. Her mood improved significantly, and there were no complications or exacerbation of neurologic symptoms.[15] There is no mention about her cognition pre or post ECT.

Case Report by Clayton et al (2018)

Clayton et al[16] discuss the case of a 54-year-old woman with a 20-year history of secondary progressive MS and moderate neurologic disability. She had comorbid bipolar disorder presenting with severe recurrent depressive episodes. There was cognitive deterioration marked by memory loss after bilateral ECT. She had previous courses of unilateral ECT. The authors[16] refer to the possible cognitive-enhancing effects of transcranial direct current stimulation (tDCS). The patient was trialed with a course of tDCS and demonstrated considerable improvement in her mood. This was monitored by standardized rating scales including the Hamilton Depression Rating Scale.[17] She had cognitive testing at baseline and after completion of tDCS to assess information processing and verbal memory. There was consistent and significant improvement in cognitive function across various domains. The authors[16] conclude that tDCS may be a useful therapy to continue the mood benefits from ECT while minimizing cognitive adverse effects.

Case Report by Harley et al (2019)

Harley et al[18] report use of ECT to treat a 41-year-old female MS patient with catatonia secondary to neuroleptic malignant syndrome. She had experienced RRMS from the age of 16 years. She presented to the hospital with symptoms of a potentially drug-induced affective psychosis, which included a 3-day history of insomnia, agitation, pressured speech, and hallucinations. The symptoms coincided with her obtaining cannabis from a new supplier. She received rapid tranquilization with parenteral antipsychotics including olanzapine and haloperidol. She developed neuroleptic malignant syndrome and catatonia secondary to this treatment. MRI with contrast, electroencephalography (EEG), and cerebrospinal fluid results were unremarkable.

Bitemporal ECT was commenced following an unsuccessful trial of high-dose lorazepam up to 16 mg daily. Rocuronium, which is a neuromuscular blocker,[19] was used as the muscle relaxant. She received 12 treatments over 6 weeks with full remission of her catatonic symptoms. Over the next 12 months, she remained symptom free. There was no deterioration of MS symptoms during treatment nor was there a relapse over the next year. However, her husband reported that she had new difficulties with forming memories. Her baseline cognition was not assessed before ECT given the nature of her initial presentation.[18]

Case Report by Narita et al (2018)

Narita et al[20] report the case of a 42-year-old Japanese woman with primary progressive MS who developed both neurologic and psychiatric symptoms concurrently at the time of onset. There was no recent history of substance misuse. She experienced auditory hallucinations, anxiety, depersonalization, and suicidal ideation. There were no cognitive symptoms.

Pharmacologic treatment included methotrexate (4 mg daily), azathioprine (75 mg daily), prednisolone (5 mg daily), and steroid pulse therapy. There was no resolution of her neurologic or psychiatric symptoms. She was also treated with various antipsychotics including risperidone (up to 4 mg daily), quetiapine (up to 400 mg daily), olanzapine (up to 20 mg daily), and asenapine (10 mg daily).

Twelve sessions of bilateral ECT improved the patient's auditory hallucinations. Validated standardized rating scales were not used to measure outcome. The patient subjectively rated the auditory hallucinations and feeling of security on a scale of 0–100. After ECT, the score for the auditory hallucinations decreased from 100 to 70 and the scores for feelings of security increased from 0 to 30. There was no change in her anxiety, suicidal ideation, or neurologic symptoms, which included an unsteady gait and involuntary movements of her upper limbs. The authors[20] conclude that there is a possible benefit of using ECT for treatment-resistant psychosis in primary progressive MS.

Case Report by Drane et al (2017)

Drane et al[21] present the case of a 49-year-old woman with rapid-cycling bipolar affective disorder, 2 × meningioma, and RRMS who developed a seizure following ECT. Her MS was treated with dimethyl fumarate. There was no history of seizures, and she had previously responded to ECT. The patient was initially admitted to the hospital with depression, and her antidepressants (nortriptyline and escitalopram) were stopped to reduce the rapid cycling. There was an emergence of an affective switch complicated by a transient delirium. She was discharged with olanzapine and lithium but was readmitted with depressed mood within a week. The authors[21] state that there are only 2 previous case reports of seizures post ECT in patients with MS or space-occupying lesions.[14]

The patient was treated with right unilateral ultrabrief ECT. Her seizure threshold was found at 19mC. She did not receive a suprathreshold dose, and there was no clear seizure endpoint on the EEG. She developed a spontaneous generalized tonic-clonic seizure 20 minutes after the ECT stimulus, which was stopped with pharmacologic treatment. Prior to treatment, there was no radiographic evidence of active demyelination or mass effect. ECT was discontinued, and she was later discharged on a combination of lithium and lamotrigine.

The authors[21] refer to previous literature[14] and suggest that the seizure was a complication of the MS, as ECT theoretically increases the seizure threshold. They also hypothesize that the patient may have had continued epileptiform activity following the treatment that resulted in a generalized seizure. Other potential causal factors may have been the meningioma, history of delirium, and olanzapine, which can reduce the seizure threshold. They[21] conclude

that the current literature indicates that ECT can be safely used in MS,[22] although there needs to be more awareness and understanding about the relationship between ECT, MS, and space-occupying lesions.

Case Report by Tran et al (2015)

Tran et al[23] report successful use of ECT in the treatment of a 61-year-old woman with bipolar depression and a 26-year history of secondary progressive MS. The patient's MS was managed with glatiramer and baclofen. After an acute flare-up of MS, she had a depressive relapse that was resistant to various psychotropic medications including paroxetine, agomelatine, lithium, and olanzapine. The doses are not provided nor is there any mention if combination therapy was used. The authors[23] comment on polypharmacy, given that the patient experienced adverse effects from the psychotropic agents. She had 10 bifrontal ECT treatments with good clinical response. There was no neurologic or cognitive complication post treatment.

The patient initially had hyperkalemia and was administered rocuronium with sugammadex reversal for muscle relaxation to avoid suxamethonium-induced hyperkalemia. Rocuronium was preferred for its faster onset of action with specific and predictable reversal by sugammadex. Sugammadex is a unique neuromuscular reversal drug.[24] The authors[23] note that this complication is more marked in MS, and a nondepolarizing muscle relaxant is preferred.

Tran and colleagues[23] conclude that ECT is a safe and effective treatment in MS and refer to 21 previous published case studies, whereby 80% experienced no neurologic deterioration. They add that suxamethonium may not be appropriate in these patients because of the hyperkalemia risk.

CONCLUSIONS

There are no large controlled studies on the psychiatric and neurologic effects of using ECT in MS. There is a paucity of literature reporting on outcome and the short- and longer-term sequelae. *The ECT Handbook*[5] concludes that the role of ECT in MS has been focused on treating the most severe neuropsychiatric cases. According to the handbook,[5] there is some evidence to indicate that patients with active white matter lesions would be at greater risk of neurologic deterioration. There are concerns about the anesthetic risks and particularly using neuromuscular-blocking agents in MS. However, the most recent case studies[15,18,20,23] generally report that patients have experienced benefit from ECT in treating comorbid severe psychiatric disorder.

Longstanding concerns about cognitive adverse effects with ECT limit the wider use of this effective treatment. In our clinical experience, the cognitive effects tend to be mostly transient, and patients recover quickly to their baseline function. This observation has been supported by the latest research. A meta-analysis conducted by Semkovska and McLoughlin[25] showed that the decline in cognition was only evident during the first 3 days following a treatment session. The open, uncontrolled study by Kirov et al[26] added further reassurance, demonstrating that there is a lack of cumulative cognitive deterioration following an increasing number of ECT treatments. However, the study design for this trial[26] may raise doubts about data validity.

Theoretically, patients with MS would be at greater risk of poorer cognitive outcomes. Cognitive impairment already contributes to poor quality of life in MS. In cross-sectional studies, cognitive impairment is prevalent in up to 40%–70% of cases.[1] Individuals may have preexisting cognitive deficits including impaired learning, decreased IQ, and problems with executive function, information processing, and working memory.[1]

The decision to use ECT in MS must be on an individualized basis and involves a comprehensive assessment of risk versus benefit. There should be detailed discussion with patients and relatives. The treatment team may consider organizing MRI imaging before treatment to look for signs of active lesions. Further research is needed into the use of ECT in MS for conclusive evidence on its safety and efficacy.

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REFERENCES

1. Ron MA. The neuropsychiatry of multiple sclerosis. *BJPsych Advances*. 2018;24(3):178–187.
2. Thompson AJ. A much-needed focus on progression in multiple sclerosis. *Lancet Neurol*. 2015;14(2):133–135.
3. Moghadasi AN, Pourmand S, Sharifian M, et al. Behavioral neurology of multiple sclerosis and autoimmune encephalopathies. *Neurol Clin*. 2016;34(1):17–31.
4. Pérez LP, González RS, Lázaro EB. Treatment of mood disorders in multiple sclerosis. *Curr Treat Options Neurol*. 2015;17(1):323.
5. Ferrier NI, Waite J. ECT in Neuropsychiatric Disorders. In: Waite J, ed. *The ECT Handbook*. 4th ed. Ferrier, IN: Cambridge University Press; 2020:96–108.
6. Feinstein A. An examination of suicidal intent in patients with multiple sclerosis. *Neurology*. 2002;59(5):674–678.
7. Chwastiak LA, Ehde DM. Psychiatric issues in multiple sclerosis. *Psychiatr Clin North Am*. 2007;30(4):803–817.
8. Taylor D, Barnes TRE, Young AH. Drug treatment of psychiatric symptoms occurring in the context of other disorders. In: *Maudsley Prescribing Guidelines*. 13th ed. Hoboken, NJ: Wiley Blackwell; 2018:679–728.
9. Steen K, Narang P, Lippmann S. Electroconvulsive therapy in multiple sclerosis. *Innov Clin Neurosci*. 2015;12(7-8):28–30.
10. Kalali A. Editor's message: issue highlights, July–August 2015. *Innov Clin Neurosci*. 2015;12(7–8):3.
11. Rasmussen KG, Keegan BM. Electroconvulsive therapy in patients with multiple sclerosis. *J ECT*. 2007;23(3):179–180.
12. Mattingly G, Baker K, Zorumski CF, et al. Multiple sclerosis and ECT: possible value of gadolinium-enhanced magnetic resonance scans for identifying high-risk patients. *J Neuropsychiatry Clin Neurosci*. 1992;4(2):145–151.
13. Pontikes TK, Dinwiddie SH. Electroconvulsive therapy in a patient with multiple sclerosis and recurrent catatonia. *J ECT*. 2010;26(4):270–271.
14. Urban-Kowalczyk M, Rudecki T, Wróblewski D, et al. Electroconvulsive therapy in patient with psychotic depression and multiple sclerosis. *Neurocase*. 2014;20(4):452–455.
15. Oligmueller J, Sharma A, Egbert M, et al. Safety

of electroconvulsive therapy in treatment-refractory depression in the setting of multiple sclerosis. *J ECT*. 2019;35(3):e36–e37.
16. Clayton AM, Howard J, Dobbs B, et al. Remotely supervised transcranial direct current stimulation after ECT improves mood and cognition in a patient with multiple sclerosis: a case study. *J ECT*. 2018;34(1):e15.
17. Hamilton M. Development of a rating scale for primary depressive illness. *Br J Soc Clin Psychol*. 1967;6(4):278–296.
18. Harley JA, Peebles C, Porter RJ. Electroconvulsive therapy for catatonia secondary to neuroleptic malignant syndrome in a patient with multiple sclerosis. *Aust N Z J Psychiatry*. 2019;53(7):703–704.
19. Rocuronium 10 mg/ml solution for injection/infusion. emc website. https://www.medicines.org.uk/emc/product/553/smpc.
20. Narita Z, Satake N, Sato W, et al. Possible effects of electroconvulsive therapy on refractory psychosis in primary progressive multiple sclerosis:a case report. *Neuropsychopharmacol Rep*. 2018;38(2):92–94.
21. Drane A, Agalawatta N, Lyndon W, et al. Seizure, sclerosis or space-occupying lesions? *Aust N Z J Psychiatry*. 2017;51(1):101.
22. Palm U, Ayache SS, Padberg F, et al. Non-invasive brain stimulation therapy in multiple sclerosis: a review of tDCS, rTMS and ECT results. *Brain Stimul*. 2014;7(6):849–854.
23. Tran T, Tibrewal P, Dhillon R, et al. Is electroconvulsive therapy safe in multiple sclerosis? *Aust N Z J Psychiatry*. 2015;49(10):942–942.
24. Nag K, Singh DR, Shetti AN, et al. Sugammadex: a revolutionary drug in neuromuscular pharmacology. *Anesth Essays Res*. 2013;7(3):302–306.
25. Semkovska M, McLoughlin DM. Objective cognitive performance associated with electroconvulsive therapy for depression: a systematic review and meta-analysis. *Biol Psychiatry*. 2010;68(6):568–577.
26. Kirov GG, Owen L, Ballard H, et al. Evaluation of cumulative cognitive deficits from electroconvulsive therapy. *Br J Psychiatry*. 2016;208(3):266–270.