International Psychogeriatrics: page 1 of 16 © International Psychogeriatric Association 2023
doi:10.1017/S104161022300039X

REVIEW

Electroconvulsive therapy in individuals with dementia/major NCD presenting with behavioral symptoms: a systematic review

Anil K. Bachu,[1,2] Vijaya Padma Kotapati,[1] Tejasvi Kainth,[3] Rikinkumar Patel,[4] Nagy A. Youssef,[5] and Rajesh R. Tampi[6,7]

[1]*Department of Psychiatry, Baptist Health - UAMS Psychiatry Residency Education Program, North Little Rock, AR, USA*
[2]*Allegheny Clinic, Psychiatry and Behavior Health Institute, Pittsburgh, PA, USA*
[3]*Department of Biomedical informatics, Stony Brook University, New York, NY, USA*
[4]*Department of Psychiatry, Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, NC, USA*
[5]*Department of Psychiatry and Behavioral Health, Ohio State University College of Medicine, Columbus, OH, USA*
[6]*Department of Psychiatry, Creighton University School of Medicine, Omaha, NE, USA*
[7]*Department of Psychiatry, Yale School of Medicine (YSM), New Haven, CT, USA*

ABSTRACT

Objective: This study aims to systematically review the literature on using electroconvulsive therapy (ECT) in patients with dementia/major NCD (Neuro cognitive disorder) presenting with behavioral symptoms.

Design: We conducted a PRISMA-guided systematic review of the literature. We searched five major databases, including PubMed, Medline, Embase, Cochrane, and registry (ClinicalTrials.gov), collaborating with "ECT" and "dementia/major NCD" as our search terms.

Measurements: Out of 445 published papers and four clinical trials, only 43 papers and three clinical trials met the criteria. There were 22 case reports, 14 case series, 4 retrospective chart reviews, 1 retrospective case–control study, 1 randomized controlled trial, and 2 ongoing trials. We evaluated existing evidence for using ECT in dementia/major NCD patients with depressive symptoms, agitation and aggression, psychotic symptoms, catatonia, Lewy body dementia/major NCD, manic symptoms, and a combination of these symptoms.

Settings: The studies were conducted in the in-patient setting.

Participants: Seven hundred and ninety total patients over the age of 60 years were added.

Results: All reviewed studies reported symptomatic benefits in treating behavioral symptoms in individuals with dementia/major NCD. While transient confusion, short-term memory loss, and cognitive impairment were common side effects, most studies found no serious side effects from ECT use.

Conclusion: Current evidence from a systematic review of 46 studies indicates that ECT benefits specific individuals with dementia/major NCD and behavioral symptoms, but sometimes adverse events may limit its use in these vulnerable individuals.

Key words: Electroconvulsive therapy, ECT, aggression, Dementia/Major NCD, agitation, bipolar disorder, depression

Introduction

Dementia/major NCD is the second leading cause of death in older individuals. In the USA, approximately 47 million people have dementia/major NCD. The Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) identifies dementia/major NCD as a condition associated with a significant decline from a previous level of performance in one or more cognitive domains, including complex attention, executive function, learning, and memory, language, perceptual-motor, or social recognition (American Psychiatric Association, 2013. Mood disturbances, psychotic features, and agitation are the distinct behavioral features evidenced in NCDs (American Psychiatric Association, 2013).

Correspondence should be addressed to: Anil K. Bachu, Department of Psychiatry, Baptist Health - UAMS Psychiatry Residency Education Program, North Little Rock, AR, USA. Tel: 9377508431. E-mail: anilbachu0181@gmail.com
Received 21 Jul 2022; revision requested 18 Apr 2023; revised version received 14 Apr 2023; accepted 18 Apr 2023.

Agitation and aggression are the most common disruptive neuropsychiatric symptoms seen in patients with dementia/major NCD (Cerejeira *et al.*, 2012). It is reported that approximately 4 5–80% of patients who have dementia/major NCD exhibit these symptoms (Testad *et al.*, 2007). These contribute to increased cost of care, hospitalization, caregiver burden, and risk of premature institutionalization (Acharya *et al.*, 2015). Agitation is characterized by disruptive motor or vocal activity. It could be moderate to severe in intensity and is most common, particularly in NCD. It often occurs in the setting of confusion and frustration and in the context of resisting the caregiver's duties, such as bathing and dressing. There are currently no treatment options approved by the US Food and Drug Administration for aggression and agitation in patients with dementia/major NCD. Implementing environmental and behavioral interventions in nursing homes is challenging because of low staff-to-resident ratios (Acharya *et al.*, 2015). Physicians utilize atypical antipsychotics to manage behavioral disturbances in patients with dementia/major NCD (Sutor and Rasmussen, 2008). There are some concerns regarding the efficacy and safety of these medications, including tardive dyskinesia, cerebrovascular adverse events, sedation, and increased risk of mortality (Sutor and Rasmussen, 2008). According to the FDA, an increased mortality risk is associated with antipsychotic use in a patient with dementia/major NCD complicated by agitation and psychosis (Lenzer 2005). Given the concern about this risk, electroconvulsive therapy (ECT) could be considered an alternative treatment with likely less risk.

ECT is effective and relatively safe in treating depression and mania in older adults, with or without dementia/major NCD (Sutor and Rasmussen, 2008). A primary concern for using ECT in such patients is its adverse effect on cognitive functioning. There are few published reports, including case studies and retrospective chart reviews, that support the utility of ECT in individuals with dementia/major NCD as a safe and beneficial intervention (Roccaforte *et al.*, 2000; Grant and Mohan, 2001a; Sutor and Rasmussen, 2008; Ujkaj *et al.*, 2012). However, little is known about the effects of these interventions on dementia/major NCD. Therefore, this study aims to review the impact of ECT on dementia/major NCD systematically.

Search strategy

This systematic review was conducted following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Figure 1) (Page *et al.*, 2021). This review aims to evaluate the data on the efficacy and tolerability of ECT in individuals with dementia/major NCD. We performed a literature search of PubMed, MEDLINE, EMBASE, Cochrane, and registry (ClinicalTrials.gov) collaboration databases through 30 March 2022, using the following keywords: ECT and dementia/major NCD. No language restrictions were imposed at the search and filtering stage. However, we only included studies published in English language journals or had official English translations in the final analysis. The search was not restricted by the age of the subjects. All studies, including clinical trials, case reports, case–control studies, case series, and retrospective chart reviews, were included if the participants were diagnosed with dementia/major NCD and were treated with ECT.

Four authors reviewed all the abstracts and full-text papers from the citations obtained via the search of the databases. The decision on which studies to be included or excluded from the final analysis was made after reviewing the full-text papers by all the authors. Disagreements between the authors were resolved by a consensus.

Results

This systematic review of the literature identified 445 published papers and 4 clinical trials using our search strategy for the evidence for using ECT among individuals with dementia/major NCD. After removing duplicates, abstracts of 242 papers and 3 clinical trials were reviewed by all the authors. Among them, 171 full-text papers were assessed for eligibility. Forty-three published papers and three clinical trials were eligible for a full-text review. We excluded 10 non-English papers without translations, letters to the editor, review papers, medical hypotheses, and 2 with pseudo-dementia/major NCD as a primary diagnosis. Of the 43 papers and 3 trials that were included in our systematic review, 22 were case reports, 14 were case series, 1 were retrospective case–control studies, 4 were retrospective chart reviews, 3 were randomized control trials (RCTs), 1 observational trial, and 1 single-group interventional trial was identified for the use of ECT among individuals with dementia/major NCD (Tables 1, 2, and 3).

Case reports

The case reports included male and female patients ranging from a 48-year-old male with frontotemporal dementia/major NCD and major depressive disorder to a 92-year-old female with dementia/

https://doi.org/10.1017/S104161022300039X Published online by Cambridge University Press

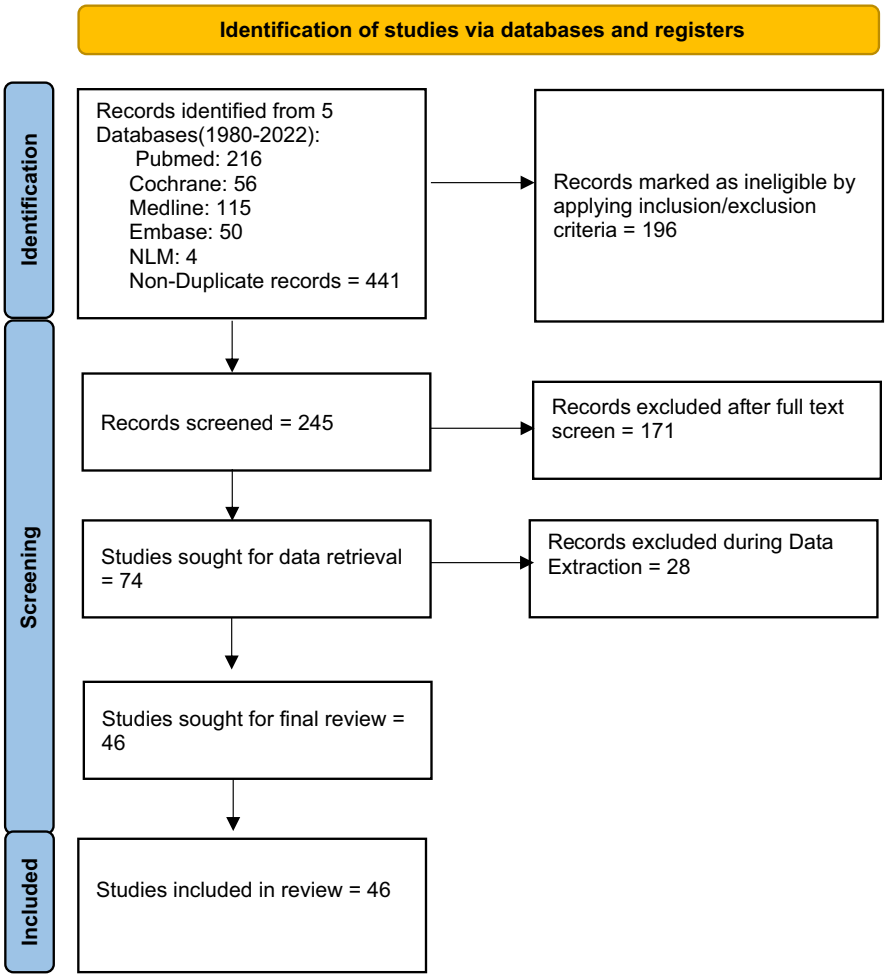

Figure 1. PRISMA 2020 flow diagram for new systematic review.

Table 1. Study type and distribution of 46 studies included in the systematic review

Type of study	Numbers
Case reports	22
Case series	14
Retrospective chart reviews	4
Retrospective case–control	1
Randomized controlled trials	3
Observational clinical trial	1
Single-group interventional trial	1

Table 2. Number of studies by isolated presenting symptoms

ECT in individuals with dementia	Number of studies
Depressive symptoms	5
Catatonic symptoms, yelling and screaming	4
Agitation and aggression	3
Psychotic depression	2
Psychosis	1
Lewy body dementia	1

major NCD and psychosis (Katagai *et al.*, 2007). Five patients received ECT for symptoms of depression (Amison and Foster, 2005; Bhat *et al.*, 2004; Arrsland and Odberg, 1996; Fàzzari *et al.*, 2009; Zink *et al.*, 2002) and showed significant improvement in scores on several rating scales, including HAM-D (Amison and Foster, 2005), Hamilton Depression Rating Scale (HDRS) (Bhat *et al.*, 2004; Zink *et al.*, 2002), Mini-Mental State Examination (MMSE) (Amison and Foster, 2005; Bhat *et al.*, 2004; Zink *et al.*, 2002), and the Cornell scale for depression in dementia/major NCD (Arrsland and Odberg, 1996) after ECT.

Roccaforte *et al.* (2000) reported the use of ECT for "screaming" in a 77-year-old female with advanced dementia/major NCD, which improved subsequently following treatment. ECT was used to treat two patients with dementia/major NCD with comorbid psychotic depression

https://doi.org/10.1017/S104161022300039X Published online by Cambridge University Press

Table 3. The type of study, age of participants, diagnosis, outcomes, and adverse events for all 46 studies

STUDY	YEAR	TYPE OF STUDY	NO. OF PARTICIPANTS	AGE OF PARTICIPANTS	DIAGNOSIS	OUTCOMES	ADVERSE EFFECTS	ADDN. COMMENTS
Fàzzari *et al.* (2009)	2009	Case report	1	69	Cotard's delusion; insomnia; depression; amnesia; cognitive deficit	6 ECT sessions; mood improved; cognitive performance increased; anxiety symptoms remitted	None noted	
Bang *et al.* (2008)	2008	Case report	2	Case 1: 88 years; case 2: 80 years	Verbal agitation with dementia	Case 1 (11 Rx) and 2 (5 Rx); no verbal agitation after ECT treatments	None noted	
Katagai *et al.* (2007)	2007	Case report	1	92 years	Dementia with psychotic features	2 ECT sessions; improved cognition after ECT	No cognitive side effects reported	
Bhat *et al.* (2004)	2004	Case report	1	76 years	AD depression on donepezil	9 ECT sessions; improvement in depression	Postictal delirium after ninth ECT	MMSE 26→23; HDRS 31→12
Rasmussen *et al.* (2003)	2003	Case report	7	60–90 years	Major depression and probable LBD	All 7 patients improved depression	1 cognitive status mild impairment	
Roccaforte *et al* (2000)	2000	Case report	1	77 years	Advanced dementia and disruptive vocalizations	6 ECT sessions; no yelling for a year after receiving ECT	None noted	
Zink *et al.* (2002)	2002	Case report	1	81 years	AD (incipient) depression on rivastigmine (ACHE-I)	Eight ECT sessions; no significant deterioration of memory and cognitive abilities after ECT treatments	Improvement in depression and ADLs	MMSE 27→24; HDRS-27→8
Grant and Mohan (2001b)	2001	Case report	4	Case 1: 56 years; case 2: 78 years; case 3: 77 years; case 4: 78 years	Agitation and aggression associated with dementia	All 4 cases reduced agitation and aggression after receiving ECT treatment	1 patient increased confusion for several hours after treatment	
Weintraub and Lippmann (2001)	2001	Case report	2	Case 1: 88 years; case 2: 84 years	Advanced dementia and affective disorder	2 patients showed improvement after treatment with ECT	None noted	
Holmberg *et al.* (1996)	1996	Case report	1	78 years	Vascular dementia with severe unremitting agitation	Decrease in agitation after receiving ECT treatment	None noted	

Table 3. Continued

STUDY	YEAR	TYPE OF STUDY	NO. OF PARTICIPANTS	AGE OF PARTICIPANTS	DIAGNOSIS	OUTCOMES	ADVERSE EFFECTS	ADDN. COMMENTS
Liang *et al.* (1988)	1988	Case report	2	Case 1: 76 years; case 2: 88 years	Case 1 Dx: AD with anxiety/agitation; case 2 Dx: AD with agitation/ depression	Case 1: anxiety improved; cognition same. Case 2: depression and agitation improved	None reported	
Perry (1983)	1983	Case report	1	50 years	Depression and catatonia associated with dementia	ECT was helpful during multiple presentations; improvement in activities of daily living	None noted.	Trials of medications before and during each admission were not effective, while ECT produced dramatic and rapid recovery. ECT is often useful in treating depression in the presence of dementia
Wu *et al.* (2010a)	2010	Case report	2	Case 1: 78 years; case 2: 71 years	Case 1: Alzheimer's type dementia; case 2: frontotemporal dementia	Case 1: received 7 ECT treatments; after fourth ECT obvious improvement in aggression; after 6th ECT decreased untoward behaviors and no behavioral problems in following 3 months while receiving maintenance ECT every 28 days. Case 2: total 6 ECTs; after 4th ECT improvement in behavior; following 6th ECT aggressive behavior resolved; maintenance ECT every 28 days.	None noted	Both cases ECT well tolerated and led to marked improvement in social comportment and quality of life.
Selvadurai *et al.* (2018)	2018	Case report	1	64 years	Dementia with acute behavioral disturbances and physical aggression	17 months of ECT with frequency of 1 ECT every 4 to 5 weeks; targeted behaviors of agitation, aggression, motor disturbances, and disinhibition significantly improved	No adverse effects	

Table 3. Continued

STUDY	YEAR	TYPE OF STUDY	NO. OF PARTICIPANTS	AGE OF PARTICIPANTS	DIAGNOSIS	OUTCOMES	ADVERSE EFFECTS	ADDN. COMMENTS
Janjua *et al.* (2019)	2019	Case report	1	67 years	Dementia with Lewy body	Eight ECT treatments; following the course of ECT, patient is less depressed and visual hallucinations disappeared.	No adverse effects	Montreal Cognitive Assessment (MOCA) improved from 19/30 to 23/30 and Quick Inventory of Depressive Symptomatology (QIDS) improved from 22 to 12.
Liang *et al.* (1988)	1988	Case series	2	Case 1: 76 years; case 2: 88 years	Case 1: primary degenerative dementia and major depressive disorder with agitation; case 2: dementia and depression with agitation	Case 1: 8 ECT treatments. Patient responded after 3rd treatment; NRS score improved from 21 to 6 posttreatment with ECT; MMSE improved from 21/30 at baseline to 19/30 2 months post-ECT. Case 2: patient responded after 2nd treatment; NRS score improved from 41 to 18 3 months posttreatment with ECT; MMSE posttreatment is 10/30.	Case 1: cognition remain unchanged; case 2: disoriented, poor short-term memory and grossly impaired abstarction and ability	
Rasmussen *et al.* (2003)	2003	Case series	7	7 patients	Lewy body dementia and depression	Significant improvement in depression associated with Lewy body dementia after treatment with ECT.	Well tolerated. No noted side effects	
Weintraub and Lippmann (2001)	2001	Case series	2	2 cases	Advanced dementia with severe affective disorder	Significant improvement in depression and mania even when complicated by moderate or severe dementia.	No adverse effects reported	

Table 3. Continued

STUDY	YEAR	TYPE OF STUDY	NO. OF PARTICIPANTS	AGE OF PARTICIPANTS	DIAGNOSIS	OUTCOMES	ADVERSE EFFECTS	ADDN. COMMENTS
Grant and Mohan (2001a)	2001	Case series	4	4 cases	Dementia with agitation and aggression	Improvement in behavioral symptoms after treatment.	No adverse effects reported	
Carlyle *et al.* (1991)	1991	Case series	3	3 cases	Case 1: major depression and cognitive impairment. Case 2: cognitive impairment only; all with verbal agitation	Bilateral ECT showed rapid resolution of their screaming behavior early in their course.	No adverse effects reported	
Sutor and Rasmussen (2008)	2008	Case series	11	59–98 years	Alzheimer disease with agitation	9/11 agitation improved; hospitalization decreased for all 11.	None noted	
Takahashi *et al.* (2009)	2009	Case series	8	> 50 years	Alzheimer disease with agitation	8 patients with therapy-resistant DLB showed improvement with ECT	No safety hazard in this study	23/167 diagnosed with DLB
Wu et al. (2010b)	2010	Case series	2	Case 1: 78 years; case 2: 71 years	Case 1: Alzheimer's dementia with behavioral dyscontrol and aggression; case 2: frontotemporal dementia with agitation and aggressive behavior	Case 1: improvement in aggression after 4th ECT session. No behavioral problems after 3-month follow-up; case 2: improvement in behavior after 4th ECT treatment. Aggressive behavior resolved after 6th session.	None noted	
Acharya *et al.* (2015)	2015	Case series	26	26 cases	Dementia with behavioral disturbance	Significant reduction in behavioral disturbances with significant decrease from baseline on Cohen Mansfield Agitation Inventory and Neuropsychiatric Inventory (CMAI).	ECT was generally well tolerated except in 2 cases where patients developed postictal delirium	

Table 3. Continued

STUDY	YEAR	TYPE OF STUDY	NO. OF PARTICIPANTS	AGE OF PARTICIPANTS	DIAGNOSIS	OUTCOMES	ADVERSE EFFECTS	ADDN. COMMENTS
Burton *et al.* (2017)	2017	Case series	6	6 cases; 79–88 years	Dementia-related agitation; three had Alzheimer dementia, 2 had vascular dementia, and 1 had unspecified dementia	Patients in the ECT and non-ECT-treated groups had comparable baseline scores. Scores on all measures of CMAI, NPI, and CGI were lower on final assessment in both groups with no statistically significant difference.	Post-ECT adverse effects occurred in 2 patients; one patient developed nausea that remitted with intravenous ondansetron, and 1 patient had postemergence agitation that resolved with intravenous valium.	
Lau *et al.* (2017)	2017	Case series	5	Above 60 years	Dementia with disruptive vocalization	After completion of a series of ECT, the mean verbal agitation score decreased from 6.8 to 2.3 with both clinical and statistical significance	No adverse effects	
Hermida *et al.* (2022)	2022	Case series	7	7 cases	Dementia with Lewy body	All 7 patients responded to ultra brief right unilateral ECT with marked improvement in their presenting symptoms of agitation and/or depression	No significant adverse effects from treatment	
Hausner *et al.* (2011)	2010	Case series	44	44 patients included	Major depressive disorder patients divided in to 3 groups [no cognitive impairment (n = 13), mild cognitive impairment (n = 19), and Alzheimer's dementia (n = 12)]	3 groups of patients received ECT; initial nonsignificant cognitive deterioration in all 3 groups; 6 weeks after termination of ECT, there was highly significant reductions on the Hamilton Depression Rating Scale (HDRS) irrespective of the patient's initial cognitive status.	No severe adverse effects reported; however it has transiter cognitive deficit	

Table 3. Continued

STUDY	YEAR	TYPE OF STUDY	NO. OF PARTICIPANTS	AGE OF PARTICIPANTS	DIAGNOSIS	OUTCOMES	ADVERSE EFFECTS	ADDN. COMMENTS
Mcdonald and Thompson (2001)	2001	Case series	3	3 patients	Dementia with manic symptoms and agitation	Acute and maintenance treatment of ECT was administered. The patients exhibited significant improvement in signs of mania, agitation, and mental status scores.	No adverse side effects reported	
Nelson and Rosenberg (1991)	1991	Retrospective chart review of 4 years	21	21 patients	Dementia with major depressive disorder	Patients had a positive response to ECT with an overall response similar to that of depressed patients without dementia.	Greater incidence of transitory increase in confusion.	
Hermida *et al.* (2020a, 2020b)	2020	Retrospective chart review	60	Mean age 77.5 ± 8.0 years	Dementia with agitation and aggression	After 3–6 ECT treatment sessions PAS* total before ECT, and it decreased significantly	No significant side effects except transient confusion	Decreased number of psychotropics prescribed along and increased GAF* score was observed after the ECT treatment course
Ujkaj *et al.* (2012)	2012	Retrospective chart review	16	16 patients with mean age 66.6 ± 8.3 years	Dementia with agitation and aggressive behavior	9 ECT treatments; patients except one patient exhibited significant reductions in their total Pittsburgh Agitation Scale scores, Clinical Global Impression (CGI) scale; however, no significant difference is observed in Global Assessment of Functioning (GAF).	Transient postictal confusion which typically resolved within 48 hours.	

Table 3. Continued

STUDY	YEAR	TYPE OF STUDY	NO. OF PARTICIPANTS	AGE OF PARTICIPANTS	DIAGNOSIS	OUTCOMES	ADVERSE EFFECTS	ADDN. COMMENTS
Isserles *et al.* (2017)	2016	Retrospective chart review	79	79 (64–88 years)	Dementia with preexisting psychiatric disorders	72% response improvement for acute treatment and 87% improvement for maintenance	Significant cognitive adverse effects	
Zhang *et al.* (2016)	2016	Retrospective case control study	23	60 years and older	Dementia	Most patients responded to ECT satisfactorily (56.5%) or partially (34.8%)	Mild-moderate transient memory impairment (30.4%)	
Forester *et al.* (2019)	2019	Single-blind	randomized trial	200	Above 65 years	Moderate to severe dementia with severe agitation	Eighteen of the 23 subjects experienced a significant reduction in agitation from baseline to discharge on the CMAI.	In a retrospective chart review study of 16 patients undergoing ECT for agitation related to AD, only two experienced more than transient confusion post-ECT that required treatment
Hermida *et al.* (2020a)	2020	Randomized control trial	200	Age more than 65 years	Dementia with agitation	ECT is safe and effective in reducing agitation in AD as measured by the Pittsburgh Agitation Scale (PAS), Global Assessment of Functioning (GAF), and number of psychotropic medications.	No significant ECT-related medical complications were observed except transient confusion	

Table 3. Continued

STUDY	YEAR	TYPE OF STUDY	NO. OF PARTICIPANTS	AGE OF PARTICIPANTS	DIAGNOSIS	OUTCOMES	ADVERSE EFFECTS	ADDN. COMMENTS
Safety and efficacy of electroconvulsive (ECT) for behavioral and psychological symptoms of dementia (BPSD) (ECTBPSD) (Clinicaltrails. Gov); NCT02969499	2021	Completed clinical trial	33	66 to 81 years	Dementia and with behavioral and psychiatric symptoms of dementia (BPSD)	Primary outcome measure: change in neuropsychiatric inventory (NPI); time frame: NPI measured 7 days pre-ECT and then 7 days after completing ECT course	All-cause mortality in 3%, 1 out of 33 2 days post-ECT due to pneumonia, unlikely due to ECT; 1 out of 33 participants had transient hypotension and bradycardia after an ECT treatment; two out of 33 participants manifested agitation/ restlessness after ECT; two out of 33 participants had ECT held temporarily due to increased confusion due to urinary tract infection; results have not been published	
ECT for agitation in Alzheimer's dementia (AD) (ECT-AD)(Clinicaltrails. Gov); NCT03926520	Estimated completion: March 2023	Ongoing clinical trial	Estimated to recruit 200 participants	55 years to 89 years	Acute management of severe agitation in Alzheimer's dementia	Primary outcome measure: The CMAI total score; time frame: The CMAI will be collected through study completion, about 13 months; not reported (ongoing clinical trial)	N/A	
ECT for treatment of Alzheimer's disease (ECTAD) (Clinicaltrials. Gov); NCT02438202	Estimated completion: January 2024	Ongoing clinical trial	Estimated to recruit 15 participants	65 years and older	Modified electroconvulsive therapy series in patients with Alzheimer's disease using Thymatron IV device (Somatics)	Primary outcome measure: change in cognition measured by individual change between initial and final Mini Mental State Examination (MMSE); time frame: 27 weeks; not reported (ongoing clinical trial)	N/A	

(Borisovskaya *et al.*, 2014) with remission of symptoms and no worsening of cognition. In a case reported by Rodríguez-Sosa *et al.* (2013), ECT was used to treat a 65-year-old female patient presenting first with refractory psychotic depression and later with catatonic symptoms who was diagnosed with frontotemporal dementia/major NCD. In this patient, the symptoms improved transiently. In a case reported by Katagai *et al.* (2007), ECT was used to treat a 92-year-old demented female with delusions, and the psychotic symptoms resolved following ECT treatment. No cardiac adverse effects or cognitive decline was reported in the case by Katagai *et al.* (2007). Authors (Aksay *et al.*, 2014; Holmberg *et al.*, 1996) described two separate case reports illustrating the use of ECT for agitation and physical aggression in patients with vascular dementia/major NCD and early-onset Alzheimer's dementia/major NCD with remission of symptoms and improved scores on the Pittsburg Agitation Scale (PAS).

Selvadurai *et al.* (2018) reported the use of ECT in a 64-year-old male diagnosed with a major neurocognitive disorder with acute behavioral disturbances and physical aggression. M-ECT was administered and was continued for 17 months at a frequency of 1 ECT every 4 to 5 weeks. The patient showed significant improvement in agitation, aggression, motor disturbances, and disinhibition with no reported adverse effects. Janjua *et al.* (2019) described another case report which elicited using ECT to treat dementia/major NCD with Lewy body (DLB) in a 67-year-old male with depression, Rapid Eye Movement (REM) sleep behavior disorder, bradykinesia, cognitive impairment, and visual hallucination. After receiving eight right unilateral ultra-brief pulse treatments of ECT over 3 weeks, the patient showed marked improvement in his MOCA and QIDS after the eighth ECT treatment. The patient did not experience any significant side effects.

ECT was generally well tolerated in all these cases except for the development of ST-segment depression in the electrocardiogram of one patient (Borisovskaya *et al.*, 2014), and high fever with liver dysfunction in another patient (Suzuki *et al.*, 2009) after the sixth ECT session, which resolved within a week and the ECT series was continued.

Case series

Out of the 14 case series, ECT was used to treat depression in six studies (Rasmussen *et al.*, 2003; Takahashi *et al.*, 2009; Weintraub and Lippmann, 2001; Hausner *et al.*, 2011; Hermida *et al.*, 2022; Liang *et al.*, 1988). Seven studies targeted agitation and yelling (Bang *et al.*, 2008; Grant and Mohan, 2001b; Acharya *et al.*, 2015; Burton *et al.*, 2017; Carlyle *et al.*, 1991; Lau *et al.*, 2017; Wu *et al.*, 2010a), and ECT was used to treat mania in one case series (Mcdonald and Thompson, 2001). The mean age group for the individuals was 50–95 years, with most patients being females. Most of the patients were diagnosed with Alzheimer's dementia/major NCD, and two case series of patients were diagnosed with Lewy body dementia/major NCD.

Rasmussen *et al.* (2003) described a case series of seven individuals with probable Lewy body dementia/major NCD, all showing improved depression following ECT treatments. Takahashi *et al.* (2009) described similar results in their case series of eight patients with dementia/major NCD with Lewy bodies and treatment-resistant depression. Pathological yelling diminished significantly in two patients with dementia/major NCD using ECT described in a case series by Bang *et al.* (2008). Similarly, three demented patients showed rapid resolution of their screaming behavior with ECT (Carlyle *et al.*, 1991). In an open-label, noncontrolled trial, Hausner *et al.* (2011) compared cognitive changes between three groups of patients with no cognitive impairment ($n = 13$), mild cognitive impairment ($n = 19$), and Alzheimer's dementia/major NCD ($n = 12$) who received ECT for depression after they had failed at least two sufficient trials with antidepressants. It was determined that 6 weeks after the termination of ECT, there were highly significant reductions on the HDRS, irrespective of the patient's initial cognitive status.

A prospective study conducted by Acharya *et al.* (2015) to investigate the safety and efficacy of ECT as a treatment for agitation and aggression in patients with dementia/major NCD included 23 patients. The results reported a significant reduction in behavioral disturbances with a substantial decrease from baseline on Cohen Mansfield Agitation Inventory and Neuropsychiatric Inventory (CMAI). ECT was generally well tolerated except in two cases where patients developed postictal delirium (Acharya *et al.*, 2015). Only one case series by Mcdonald and Thompson (2001) was done on three elderly patients with dementia/major NCD associated with agitation and mania. Patients showed significant improvement in signs of mania and agitation.

Burton *et al.* (2017) described case series of nine patients with dementia/major NCD-related agitation, out of which six received ECT, and three did not receive ECT. Patients in both groups had comparable CMAI, Neuropsychiatric inventory (NPI), and Clinical Global Impression (CGI) scores. The scores were lower on the final assessment in both groups, with no statistically significant difference.

https://doi.org/10.1017/S104161022300039X Published online by Cambridge University Press

Lau *et al.* (2017) conducted a case series of five patients with dementia/major NCD with disruptive vocalization who completed a series of ECT. The mean verbal agitation score showed statistically significant improvement. Hermida *et al.* (2022) conducted a case series on seven patients with DLB who received ultra-brief right unilateral ECT to treat agitation and depressive symptoms. All seven patients elicited marked improvement in their presenting symptoms of agitation and depression without significant adverse effects from treatment.

Retrospective chart reviews

After reviewing the literature, four retrospective chart reviews were included in this systematic review. A retrospective chart review by Nelson and Rosenberg (1991) reported treatment with ECT for 21 patients with dementia/major NCD and depression. Out of these 21 patients, 12 had refractory depression, 4 had medical contraindications to the use of antidepressants, 2 had life-threatening depression and refused to eat, and 4 had a history of good response to ECT. All patients had a positive response to ECT, with an overall response similar to depressed patients without dementia/major NCD but with a greater incidence of transitory increase in confusion.

Another retrospective chart review conducted by Ujkaj *et al.* (2012) included 16 patients diagnosed with dementia/major NCD based on DSM IV-TR who received ECT for agitation and aggressive behaviors. Patients, on average, received nine ECT treatments ranging from 2 to 15. All patients except one showed significant reductions in their total PAS scores from pre- to post-ECT measurements. The CGI scale improved after ECT treatment. The change in the Global Assessment of Functioning (GAF) was clinically and statistically insignificant. The most common side effect was transient postictal confusion which typically resolved within 48 hours.

All cognitive side effects were reversible and transient, even in dementia/major NCD subjects. Out of 11 patients with Alzheimer's dementia/major NCD treated with ECT for agitation, nine showed improved symptoms and were associated with fewer hospitalizations in the year after an ECT series (Sutor and Rasmussen, 2008).

Hermida *et al.* (2020a) conducted a retrospective chart review of 60 elderly patients with dementia/major NCD presenting with symptoms of aggression or agitation and who received ECT treatments. The baseline PAS total decreased significantly after 3–6 ECT treatments. No significant ECT-related medical complications were observed except transient confusion.

Isserles *et al.* (2017) conducted a retrospective chart review on 25 patients with dementia/major NCD and a preexisting psychiatric disorder treated with ECT. Twenty-nine acute ECT courses and 15 maintenance courses were reviewed. ECT showed clinically significant improvement in acute and maintenance treatment courses. Cognitive adverse effects affecting functioning were reported in 7% of the acute treatment courses, and two reports showed significant cognitive adverse effects in the maintenance treatment courses.

Retrospective case–control studies

After reviewing the literature, the systematic review included one retrospective case–control study by Zhang *et al.* (2016). This case–control study comprised 23 patients with dementia/major NCD treated with ECT, and 71 matched controls were treated for 8 years (2007–2014). Most patients responded to ECT satisfactorily (65%) or partially (34–8%), with only mild–moderate transient memory impairment as a side effect.

Clinical trials

This systematic review included three RCTs and two ongoing trials.

Published trials

Forester *et al.* (2019) conducted a multi-site, single-blinded, randomized trial in 200 in-patients with severe agitation and moderate-to-severe treatment-resistant dementia/major NCD. The preliminary open-label data suggested that acute ECT treatment was safe and effective in reducing agitation in this population. Hermida *et al.* (2020a) conducted a RCT on 200 randomized patients with Alzheimer's dementia/major NCD and severe agitation. The authors reported that ECT is safe and effective in reducing agitation in AD as measured by the PAS and GAF. There were no significant ECT-related medical complications observed except for transient confusion.

Completed clinical trial

The clinical trial **(Clinicaltrails. Gov, National Library of Medicine (U.S.), 2016-2020)** studied the safety and efficacy of ECT for behavioral and psychological symptoms of dementia/major NCD. NPI measured 7 days pre-ECT and 7 days after completing the ECT course as the primary outcome. The results have yet to be published.

https://doi.org/10.1017/S104161022300039X Published online by Cambridge University Press

Ongoing clinical trials

Two ongoing clinical trials were included in this systematic review. One trial **(Clinicaltrails. Gov, National Library of Medicine (U.S.), 2021–2024)** studies ECT for agitation in Alzheimer's dementia/major NCD (AD) (ECT-AD) with an estimated completion date of March 2023. The Primary Outcome Measure is CMAI. The total score will be collected after study completion in about 13 months. Another ongoing clinical trial **(Clinicaltrials. Gov, National Library of Medicine (U.S.), 2024–2027)** studies the utility of ECT to treat Alzheimer's disease (ECTAD) with an estimated completion date of January 2024. The primary outcome measure is change in cognition measured by the individual change between the initial and final MMSE within a time frame of 27 weeks. The results of these two ongoing trials are not yet reported.

Discussion

Agitation and aggression in demented patients may be due to numerous conditions (psychosis, disorientation, confusion, sensory loss, etc.). Behavioral disturbances may also be secondary to mood disorders, and the diagnosis of depression may be quite difficult in such patients (Grant and Mohan, 2001b). The etiology of behavioral disturbances in neurocognitive disorder is poorly understood. These may be due to abnormalities of neurotransmission, especially GABAergic and dopaminergic dysfunction, cholinergic and serotonergic deficiency, and noradrenergic hyperactivity, which further promotes agitation and aggression (Aksay *et al.*, 2014). It has been postulated that ECT may mediate its beneficial effects through its known enhancement of GABAergic transmission and inhibition.

Our systematic review indicates that, to date, there are three RCTs, one observational, and one single-group trial for using ECT in individuals with dementia/major NCD. Current evidence from 41 nonrandomized studies reported symptomatic benefits from ECT in individuals with dementia/major NCD, including depression, mania, yelling and screaming agitation, and a combination of these symptoms. Multiple case reports, case series, and retrospective studies suggest that of all the modalities, including behavioral strategies and antipsychotics, ECT remains the most effective, rapidly acting, and safe method for treating mood symptoms in patients with dementia/major NCD.

Notably, there were significant reductions in behavioral disturbances with ECT. One study showed significant reductions in behavioral disturbances by the third, and most participants dramatically improved by the ninth ECT session (Acharya *et al.*, 2015). Although transient post-ECT confusion may be more significant in depressed patients with dementia/major NCD, the treatment course is reported to be well tolerated overall. Performing neurocognitive testing pre- and post-ECT sessions in patients with dementia/major NCD would help evaluate them effectively (Berman *et al.*, 2008).

The strengths of this systematic review include using guidelines from PRISMA and a literature search from five major databases, including case reports, case series, retrospective case–control studies, retrospective chart reviews, and clinical trials only. Limitations of this review are that there is no measure of heterogeneity, and several studies were underpowered and had short treatment duration. Studies (Sackeim *et al.*, 2008) suggest that ECT can significantly impact cardiac health, particularly in the elderly, where receiving ECT had a higher risk of adverse cardiovascular events, such as arrhythmias, heart attacks, and even death, compared to younger patients. ECT increases heart rate, blood pressure, and oxygen demand and acts like a treadmill test for the heart. Patients at risk of cardiovascular disease or with a history of heart conditions may experience complications from ECT.

Conclusion

Current evidence from a systematic review of 46 studies indicates that ECT is beneficial in specific individuals with dementia/major NCD and behavioral symptoms. Still, sometimes adverse events may limit its use in these vulnerable individuals. Although ECT is useful for treating agitation and aggression for a short period, no data suggest when the treatment should be initiated and which patients would benefit the most. Even though it is not FDA-approved for treating agitation in patients with dementia/major NCD, it can be preferred as a treatment option to alleviate the behavioral symptoms. Providing adequate, comprehensive, and timely information about risks and benefits associated with ECT treatment will provide insight to the patient's family and allow the healthcare professionals to act in the patient's best interest.

Acknowledgements

We would like to acknowledge Dr. Silpa Balachandran, MD, and Dr. Sujan Barua, MD, for initial contribution of the study, and data collection.

Conflict of interest

The authors have no conflicts of interest to declare.

https://doi.org/10.1017/S104161022300039X Published online by Cambridge University Press

Source of funding

Dr. Youssef discloses that in the last 5 years, he received research support from the National Institute of Health (NIH), the Department of Veteran Affairs, the Department of Defense, and research support but not salary support from MECTA Corporation, Vistagen, and Merck. He receives royalties from Elsevier Publishing. The opinions or assertions contained herein are the private views of the authors. They are not to be construed as reflecting views of the US government or the Department of Defense. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Description of authors' roles

Anil Bachu, MD, conceived and designed the study, collected the data, contributed to the systematic review of literature, wrote the manuscript, edited the manuscript, and oversaw and coordinated the workflow with other authors.

Vijaya Padma Kotapati, MD, collected and updated the data, contributed to the systematic review of literature, wrote the manuscript, and revised/edited the manuscript.

Tejasvi Kainth, MD, collected and updated the data, contributed to the systematic review of literature, wrote the manuscript, and revised/edited the manuscript.

Rikin Patel, MD, updated the data collection, contributed to the systematic review of literature, wrote the manuscript, and revised and edited the manuscript.

Nagy A. Youssef, MD, Ph.D., provided the final edits and corrections, and oversaw and coordinated the workflow with other authors.

Rajesh R. Tampi, MD, MS, DFAPA, DFAAGP, conceived and designed the study, provided the revisions and corrections, oversaw and coordinated the workflow with other authors, and provided expert-level guidance and final approval of the study.

References

Acharya, D. *et al.* (2015). Safety and utility of acute electroconvulsive therapy for agitation and aggression in Dementia/Major NCD. *International Journal of Geriatric Psychiatry*, 30, 265–273.

Aksay, S. S. *et al.* (2014). Severe agitation in severe early-onset Alzheimer's disease resolves with ECT. *Neuropsychiatric Disease and Treatment*, 10, 2147.

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition: DSM-5*. Washington, DC: American Psychiatric Publishing.

Amison, T. and Foster, A. (2005). Electroconvulsive therapy in a middle-aged adult with cortical atrophy. *The Journal of ECT*, 21, 122–124.

Arrsland, D. and Odberg, S. (1996). Electroconvulsive therapy of depression in Alzheimer's disease. A case presentation of acute and maintenance electroconvulsive therapy. *Nordic Journal of Psychiatry*, 50, 169–173.

Bang, J. *et al.* (2008). ECT treatment for two cases of Dementia/Major NCD-related pathological yelling. *The Journal of Neuropsychiatry and Clinical Neurosciences*, 20, 379–380.

Berman, R. M. *et al.* (2008). Subjective evaluation of the therapeutic and cognitive effects of electroconvulsive therapy. *Brain Stimulation*, 1, 16–26.

Bhat, R. S. *et al.* (2004). ECT-donepezil interaction: a single case report. *International Journal of Geriatric Psychiatry*, 19, 594–595.

Borisovskaya, A. *et al.* (2014). Electroconvulsive therapy for frontotemporal Dementia/Major NCD with comorbid major depressive disorder. *The Journal of ECT*, 30, 45–46.

Burton, M. C. *et al.* (2017). Use of electroconvulsive therapy in Dementia/Major NCD-related agitation: a case series. *The Journal of ECT*, 33, 286–289. https://doi.org/10.1097/yct.0000000000000432

Carlyle, W. *et al.* (1991). ECT: an effective treatment in the screaming demented patient. *Journal of the American Geriatrics Society*, 39, 637–637.

Cerejeira, J. *et al.* (2012). Behavioral and psychological symptoms of Dementia/Major NCD. *Frontiers in Neurology*, 3, 73–73. https://doi.org/10.3389/fneur.2012.00073

Fàzzari, G. *et al.* (2009). Improvement of cognition in a patient with Cotard's delusions and frontotemporal atrophy receiving electroconvulsive therapy (ECT) for depression. *International Psychogeriatrics*, 21, 600–603.

Forester, B. P. *et al.* (2019). Electroconvulsive therapy for the treatment of acute agitation and aggression in Alzheimer's Dementia/Major NCD (ECT-AD). *The American Journal of Geriatric Psychiatry*, 27, S166–S167. https://doi.org/10.1016/j.jagp.2019.01.077

Grant, J. and Mohan, S. (2001a). Treatment of agitation and aggression in four demented patients using ECT. *The Journal of ECT*, 17, 205–209. https://doi.org/10.1097/00124509-200109000-00012

Grant, J. E. and Mohan, S. N. (2001b). Treatment of agitation and aggression in four demented patients using ECT. *The Journal of ECT*, 17, 205–209.

Hausner, L. *et al.* (2011). Efficacy and cognitive side effects of electroconvulsive therapy (ECT) in depressed elderly inpatients with coexisting mild cognitive impairment or Dementia/Major NCD. *The Journal of Clinical Psychiatry*, 72, 91–97. https://doi.org/10.4088/JCP.10m05973gry

Hermida, A. P. *et al.* (2020a). Treatment parameters and rationale for the use of electroconvulsive therapy for the management of treatment-refractory agitation in Alzheimer's disease. *The American Journal of Geriatric Psychiatry*, 28, S144–S145. https://doi.org/10.1016/j.jagp.2020.01.177

Hermida, A. P. *et al.* (2020b). Efficacy and safety of ECT for behavioral and psychological symptoms of Dementia/Major NCD (BPSD): a retrospective chart review. *The American*

Journal of Geriatric Psychiatry, 28, 157–163. https://doi.org/10.1016/j.jagp.2019.09.008

Hermida, A. P. *et al.* (2022). Ultrabrief right unilateral electroconvulsive therapy for the treatment of the neuropsychiatric symptoms of Dementia/Major NCD with Lewy bodies. *The Journal of ECT*, 38, 39–44. https://doi.org/10.1097/yct.0000000000000809

Holmberg, S. K. *et al.* (1996). Efficacy of ECT for agitation in Dementia/Major NCD: a case report. *The American Journal of Geriatric Psychiatry*, 4, 330–334.

Isserles, M. *et al.* (2017). Clinical effectiveness and tolerability of electroconvulsive therapy in patients with neuropsychiatric symptoms of Dementia/Major NCD. *Journal of Alzheimer's Disease*, 57, 45–51. https://doi.org/10.3233/jad-161000

Janjua, A. U. *et al.* (2019). Successful use of electroconvulsive therapy for the treatment of neuropsychiatric manifestations of Dementia/Major NCD with Lewy bodies. *The American Journal of Geriatric Psychiatry*, 27, S136–S137. https://doi.org/10.1016/j.jagp.2019.01.043

Katagai, H. *et al.* (2007). Effective electroconvulsive therapy in a 92-year-old Dementia/Major NCD patient with psychotic feature. *Psychiatry and Clinical Neurosciences*, 61, 568–570.

Lau, T. E. *et al.* (2017). The treatment of disruptive vocalization in dementia/major NCD (behavioral and psychological symptoms of Dementia/Major NCD) with electroconvulsive therapy: a case series. *The Journal of ECT*, 33, e9–e13. https://doi.org/10.1097/yct.0000000000000373

Lenzer, J. (2005). FDA warns about using antipsychotic drugs for dementia. BMJ (Clinical research ed.), 330(7497), 922. https://doi.org/10.1136/bmj.330.7497.922-c

Liang, R. *et al.* (1988). ECT in the treatment of mixed depression and Dementia/Major NCD. *The British Journal of Psychiatry*, 152, 281–284.

Mcdonald, W. M. and Thompson, T. R. (2001). Treatment of mania in Dementia/Major NCD with electroconvulsive therapy. *Psychopharmacology Bulletin*, 35, 72–82.

National Library of Medicine (U.S.). (November 2016-May 2020). Safety and Efficacy of Electroconvulsive Therapy (ECT) for Behavioural and Psychological Symptoms of Dementia (BPSD) (ECTBPSD). Identifier NCT02969499. https://clinicaltrials.gov/ct2/show/record/NCT02969499.

National Library of Medicine (U.S.). (January 28, 2021-March 2024). Electroconvulsive Therapy (ECT) for Agitation in Dementia (AD) (ECT-AD). Identifier NCT03926520. https://clinicaltrials.gov/ct2/show/record/NCT03926520.

National Library of Medicine (U.S.). (December 2024-January 2027). Electroconvulsive Therapy for Treatment of Alzheimer's Disease (ECTAD). Identifier NCT02438202. https://clinicaltrials.gov/ct2/show/study/NCT02438202.

Nelson, J. P. and Rosenberg, D. R. (1991). ECT treatment of demented elderly patients with major depression: a retrospective study of efficacy and safety. *The Journal of ECT*, 7, 157–165.

Page, M. J. *et al.* (2021). The PRISMA. 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*, 372, n71. https://doi.org/10.1136/bmj.n71

Perry, G. F. (1983). ECT for Dementia/Major NCD and catatonia. *The Journal of Clinical Psychiatry*, 44, 117. http://europepmc.org/abstract/MED/6833192

Rasmussen, K. G. *et al.* (2003). Electroconvulsive therapy for patients with major depression and probable Lewy body Dementia/Major NCD. *The Journal of ECT*, 19, 103–109.

Roccaforte, W. H. *et al.* (2000). ECT for screaming in Dementia/Major NCD. *The American Journal of Geriatric Psychiatry*, 8, 177–177.

Rodríguez-Sosa, J. T. *et al.* (2013). Electroconvusive therapy in Dementia/Major NCD. *Actas Españolas de Psiquiatría*, 41, 204–207.

Sackeim, H. A. *et al.* (2008). Effects of pulse width and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *Brain Stimulation*, 1, 71–83. https://doi.org/10.1016/j.brs.2008.03.001

Selvadurai, M. I. *et al.* (2018). Efficacy and safety of maintenance electroconvulsive therapy for sustaining resolution of severe aggression in a major neurocognitive disorder. *BMJ Case Report*, 2018, bcr2017222100. https://doi.org/10.1136/bcr-2017-222100

Sutor, B. and Rasmussen, K. G. (2008). Electroconvulsive therapy for agitation in Alzheimer disease: a case series. *The Journal of ECT*, 24, 239–241.

Suzuki, K. *et al.* (2009). A case of catatonia resembling frontotemporal Dementia/Major NCD and resolved with electroconvulsive therapy. *The World Journal of Biological Psychiatry*, 10, 245–247.

Takahashi, S. *et al.* (2009). Depression associated with Dementia/Major NCD with Lewy bodies (DLB) and the effect of somatotherapy. *Psychogeriatrics*, 9, 56–61.

Testad, I. *et al.* (2007). Prevalence and correlates of disruptive behavior in patients in Norwegian nursing homes. *International Journal of Geriatric Psychiatry*, 22, 916–921.

Ujkaj, M. *et al.* (2012). Safety and efficacy of electroconvulsive therapy for the treatment of agitation and aggression in patients with Dementia/Major NCD. *The American Journal of Geriatric Psychiatry*, 20, 61–72.

Weintraub, D. and Lippmann, S. B. (2001). ECT for major depression and mania with advanced Dementia/Major NCD. *The Journal of ECT*, 17, 65–67.

Wu, Q. *et al.* (2010a). ECT treatment for two cases of Dementia/Major NCD-related aggressive behavior. *The Journal of Neuropsychiatry and Clinical Neurosciences*, 22, 247.e10–247.e11.

Wu, Q. *et al.* (2010b). ECT treatment for two cases of Dementia/Major NCD-related aggressive behavior. *The Journal of Neuropsychiatry and Clinical Neurosciences*, 22, E10–E11. https://doi.org/10.1176/jnp.2010.22.2.247.e10

Zhang, Q. E. *et al.* (2016). Demographic and clinical profile of patients with Dementia/Major NCD receiving electroconvulsive therapy: a case-control study. *The Journal of ECT*, 32, 183–186. https://doi.org/10.1097/yct.0000000000000314

Zink, M. *et al.* (2002). Electroconvulsive therapy in a patient receiving rivastigmine. *The Journal of ECT*, 18, 162–164.

https://doi.org/10.1017/S104161022300039X Published online by Cambridge University Press