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Continuation and Maintenance Electroconvulsive Therapy for Mood Disorders: Review of the Literature

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Key Words
Electroconvulsive therapy · Continuation electroconvulsive therapy · Maintenance electroconvulsive therapy · Mood disorders · Review

Abstract
Background: Electroconvulsive therapy (ECT) is a highly effective treatment for mood disorders. Continuation ECT (C-ECT) and maintenance ECT (M-ECT) are required for many patients suffering from severe and recurrent forms of mood disorders. This is a review of the literature regarding C- and M-ECT. ***Methods:*** We conducted a computerized search using the words continuation ECT, maintenance ECT, depression, mania, bipolar disorder and mood disorders. We report on all articles published in the English language from 1998 to 2009. ***Results:*** We identified 32 reports. There were 24 case reports and retrospective reviews on 284 patients. Two of these reports included comparison groups, and 1 had a prospective follow-up in a subset of subjects. There were 6 prospective naturalistic studies and 2 randomized controlled trials. ***Conclusions:*** C-ECT and M-ECT are valuable treatment modalities to prevent relapse and recurrence of mood disorders in patients who have responded to an index course of ECT. C-ECT and M-ECT are underused and insufficiently studied despite positive clinical experience of more than 70 years. Studies which are currently under way should allow more definitive recommendations regarding the choice, frequency and duration of C-ECT and M-ECT following acute ECT.

Introduction

More than 70 years since its introduction, electroconvulsive therapy (ECT) remains the most effective somatic treatment in psychiatry, with unsurpassed efficacy and remarkable safety. ECT is effective for various conditions and is a viable treatment option when pharmacotherapy and psychotherapy have failed, when affective, psychotic or catatonic symptoms are present, and when rapid relief

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of symptoms is required because of suicide risk or deterioration of medical conditions [1–6]. ECT is most commonly used for the treatment of severe depression, but is also effective for the treatment of manic or mixed episodes [7–9].

Many patients with mood disorders, for which treatment with ECT is indicated, suffer from conditions that are chronic and recurrent in nature. Continuation therapy after remission of an acute episode of a mood disorder is considered to be the standard of practice in modern psychiatry [10]. Following successful treatment with acute ECT, continuation therapy is of particular importance, as these patients frequently have the most severe, recurrent and treatment-resistant illness. A study by Sackeim et al. [11] demonstrated that the relapse rate of patients with unipolar depression who remit after an acute course of ECT is extremely high if there is no active treatment after the last ECT. Patients who received placebo relapsed at a rate of 84% within 6 months after acute ECT. Patients who received monotherapy with the tricyclic antidepressant nortriptyline relapsed at a rate of 60%, and those receiving combination therapy consisting of nortriptyline and lithium relapsed at a rate of 39%. These results underscore the need for aggressive preventative approaches to sustain the clinical benefits of acute treatment.

When ECT is used for the treatment of an acute episode, it is reasonable to consider continuation ECT (C-ECT) or maintenance (M-ECT) to prevent relapse of the current episode or recurrence of a new episode. The term 'continuation ECT' (C-ECT) and 'maintenance ECT' (M-ECT) are frequently used interchangeably and indiscriminately across the mood disorder treatment continuum. For the purpose of this report, we will use the following definitions: an *index/acute course* is the initial series of treatments given for the purpose of relieving acute symptoms of the illness. *C-ECT* is a course that begins after the index course, lasts up to 6 months, and is designed to prevent relapse of the episode (return of the symptoms to full syndromal criteria before the end of the natural duration of the illness). *M-ECT* is a course that begins after the end of C-ECT and is intended to prevent recurrence of an episode (a new episode).

The practice of C-ECT and M-ECT has been documented almost since the introduction of ECT by Cerletti and Bini in 1938 [12, 13]. However, it has not always been widely implemented in clinical practice during the psychotropic medication era of modern psychiatry. The development of antipsychotic and antidepressant medications in the 1950s created the belief that ECT had been superseded, and the practice of ECT declined dramatically. This period, which lasted until the early 1970s, was characterized by the polemics of the antipsychiatry movement which attacked psychiatry in general and ECT in particular [14]. ECT, despite its decline in numbers, was never abandoned, as many patients did not respond to medications and psychotherapy. However, the negative climate prompted many psychiatrists to recommend as few treatments as possible, often limiting the number of ECT treatments to the absolute minimum to achieve improvement of acute symptoms, thus automatically excluding C-ECT and M-ECT from their armamentarium. In 1974, the American Psychiatric Association (APA) appointed a Task Force to study and report on '[ECT] legislative issues, consent, indications for its use and possible increasing use ...' [15]. The Task Force reported that there was a role for ECT in the treatment of depression, intractable mania and treatment-resistant schizophrenia [15]. There was no particular mention of C-ECT in that report, yet interest in the practice of ECT was restimulated.

A survey of practice by Kramer [16] conducted in 1986 revealed that many psychiatrists were treating their most treatment-resistant patients with C-ECT. C-ECT was first mentioned in the 1990 APA Task Force report [17]. The third and latest APA Task Force Report (2001) [3] established the indications for C-ECT and M-ECT for patients who responded to an acute ECT course when one of the following has occurred:

(1) pharmacotherapy alone has not been effective in treating index episodes or in preventing relapse or recurrence;
(2) pharmacotherapy cannot be safely administered, or
(3) the patient prefers treatment with ECT and the patient or surrogate consentor agrees to the patient's receiving C-ECT. The patient must be capable, with the assistance of others, of complying with the treatment plan.

The Association for Convulsive Therapy (ACT), a professional society of ECT clinicians and researchers, created a task force that recommended guidelines for the practice of ambulatory ECT [18]. As most C-ECT and M-ECT is performed on an outpatient basis, the majority of these guidelines are applicable and should facilitate this practice. Nevertheless, as we pointed out in an earlier review [19], there is little early systematic research on C-ECT and M-ECT. Many case reports and several studies appeared in the literature until 1965, attesting to the utility of ECT courses given beyond the point of acute treatment [20]. Inherent weaknesses of these studies, as in most of the psychiatric literature of that era, include the use of heterogeneous populations and weak methodology.

One would have expected a much greater number of research publications on C-ECT and M-ECT over the course of more than 7 decades, especially considering the almost unanimously positive attestations of the reports. This lack of literature between 1965 and 1985 reflects, besides the decline in the use of ECT, the fact that C-ECT is underused and that research resources directed to the study of ECT are limited. One cannot underestimate the effects of the negative public environment regarding ECT on scientific thinking and directions of scientific research. The stigma against ECT is perpetrated even by professionals, as evidenced by the National Institute for Clinical Excellence (NICE) report in the UK, which disputed the utility of C-ECT and M-ECT in its 'Guidance on the Use of Electroconvulsive Therapy' [21], despite positive recommendations from the APA Task Force on ECT and protest from British psychiatrists [22–24]. We responded to this report with a paper in the *Journal of ECT* [25] which documents the logical inconsistencies in the flawed British report.

With the renewal of interest in ECT, more reports about C-ECT were published during the last two decades. These studies reconfirm the benefits of ECT given beyond the index course. Unfortunately, most of these reports are retrospective and describe only a small number of patients. Prolonging remission after successful acute treatment with ECT remains an important clinical challenge. If C-ECT is implemented, common clinical practice includes a taper and then treatments spaced out at gradually increasing intervals. However, there is a dearth of guidance about the optimal frequency of C-ECT, concurrent pharmacotherapy and the overall tolerability of C-ECT.

At the time of our earlier review in 1997, C-ECT and M-ECT were not often considered as options. However, newer research and experience have established C-ECT and M-ECT as important tools for relapse prevention in patients who have responded to ECT for the treatment of an acute episode of a mood disorder. The aim of this report is to review the literature on C-ECT and M-ECT after 1997 and to delineate evidence-based guidelines for its safe and effective practice.

Methods

A PubMed search was conducted using the words 'continuation ECT', 'maintenance ECT', 'depression', 'mania', 'bipolar disorder' and 'mood disorders'. We report on all articles published in the English language from 1998 to 2009.

Results

We identified 32 reports. There were 24 case reports and retrospective reviews on 284 patients. Two of these reports included comparison groups, and 1 had a prospective follow-up component in a subset of subjects. Table 1 summarizes the published retrospective studies and case reports on C-ECT and M-ECT. There were 6 prospective naturalistic studies and 2 randomized controlled trials (RCTs). Table 2 summarizes the published literature on prospective studies. Of note, there are several reports that examine the use of C-ECT and M-ECT in various other disorders, such as schizophrenia and schizoaffective disorder, Parkinson's disease and autism, that are beyond the scope of this review and are not included here [26–34].

Most published studies are positive with regards to the efficacy and safety of C-ECT and M-ECT in mood disorders. As in our earlier review, the majority of these studies are uncontrolled prospective or retrospective studies, or case reports. However, a major addition to the literature is the National Institute of Mental Health (NIMH) funded multicenter RCT conducted by the Consortium for Research on ECT (CORE) [65]. This is the first large RTC to compare the relative efficacy of C-ECT to a combination pharmacotherapy regimen. In this well-designed study, 531 patients with unipolar major depressive disorder (with and without psychotic features) were enrolled into the acute ECT phase. ECT was performed with bifrontotemporal electrode placement at 1.5 times the determined seizure threshold. Of those patients 341 met remission criteria after an average of 6.8 ECT. After an interim week without additional treatment, 201 patients were enrolled into the continuation phase of the study and were randomized to receive 6 months of C-ECT or continuation pharmacotherapy (C-PHARM). C-ECT was given at a predetermined fixed schedule with 4 weekly treatments the first month, followed by 4 biweekly treatments for 2 months and 2 monthly treatments for a total of 10 ECT in 6 months. Patients in this arm received no psychotropic medications except for lorazepam or diphenhydramine on an as-needed basis. C-PHARM consisted of the combination of lithium and nortriptyline and patients were evaluated at the same interval as in the C-ECT arm. The relapse rates at 6 months did not differ statistically between the two arms – 37.1% for C-ECT and 31.6% for C-PHARM – and were comparable to those reported in the similarly designed study by Sackeim et al. [11] for the combination of lithium and nortriptyline (39%), and far better than those reported for nortriptyline

Table 1. Retrospective studies and case reports on C-ECT effectiveness and tolerability (1998–2009)

Author	Design	Diagnostic criteria	Subjects, n	C-ECT type/ duration/interval	Medication	Outcome/comments
Bonds et al. [35] (1998)	case report	BD	1	BL/10 months/variable, then monthly	haloperidol for 6 of 10 months, then no psychotropic medication	Psychotic depression, remained in remission. 'No adverse medical complications and minimal cognitive side effects'. Outpatient C-ECT cost-effective relative to 1-year comparison period of acute courses of ECT and hospitalizations.
Gupta et al. [36] (1998)	case report	BD	1	BL/unspecified/unspecified	lithium (0.77 mEq/l at 2nd C-ECT) and diphenhydramine	'Mood and affect were much improved'. 'No delirium or other complications noted'. No self-report decline in memory as measured by the SSMQ.
Kramer [37] (1999a)	case report	BD	1	BL/3 years/individualized to target at-risk seasonal biological pattern	lithium and clonazepam PRN	C-ECT effective in maintaining euthymia for long periods of time. Reduced hospitalizations relative to 4-year comparison period with pharmacotherapy alone. 'Memory loss was minimal.'
Kramer [38] (1999b)	retrospective review of a university ECT service	MDD, BD, depression + Axis II diagnosis, depression + PD	53	'most patients ... BL'/ 6 months – 4 years/variable	unspecified	18 of 24 patients with MDD experienced sustained improvement, 3 patients w/comorbid anxiety disorder had 'only partial response' even after more frequent C-ECT, 3 of 9 BD patients 'remained much improved', 7 of 9 had 'partial improvement', 1 of 10 patients with Axis II 'remained much improved', 6 of 10 patients with Axis II had a 'partial response,' PD patients had decrease in motor symptoms, '... no medical problems, other than headache and transient memory complaints'.
Gagne et al. [39] (2000)	retrospective review vs. matched pharmacotherapy control group	MDD, BD	C-ECT + C-PHARM = 29 C-PHARM = 29	unilateral = 8; BL = 19 crossover = 2/unspecified/'... generally ... weekly for the first month, every 2 weeks for the following month, and then monthly'.	various medications	Following acute ECT, C-ECT + medication superior to med. alone in preventing relapse ('... cumulative probability of surviving without relapse ... 93% compared to 52% at year 2; 73% compared to 18% at year 5. Mean survival times were 6.9 years for the continuation ECT patients and 2.7 years for the antidepressant-alone patients.')
Chanpattana [40] (2000)	case report	BD, manic episode	1	BL/18 months/variable	clozapine	C-ECT + clozapine 'resulted in remission over an 18-month period.' The patient returned to his normal life and continued his academic studies.'
Stewart [41] (2000)	case report	MDD	1	BL/8 months/'every 6 weeks'	lithium (level around 0.7 mEq/l)	Age 78. 'Depressive symptoms remain in complete remission after 8 months.'
Fox [42] (2001)	case report	MDD	3	2 BL 1 unknown/variable, >18 months/variable	various medications	Lifetime frequency, severity, and duration of relapse diminished by C-ECT, 'no medical complications', 'subjective complaints of memory impairment were common'. At 5–8 weeks after last C-ECT, 2 patients scored 29/30 on MMSE.
Kho [43] (2002)	case report	RCBD	1	BL and unilateral/>1 year/ 4 weeks	lithium added (0.8 mmol/l)	Age 79, C-ECT improved mood stability 'without ill effect to her (frail) physical condition', lithium alone not sufficient for mood stability. After 51 ECTs, MMSE 13/30.
Russell et al. [44] (2003)	retrospective review	MDD, BD	38	BT (85%); RUL (12%); BF (3%)/27.8 months (mean); 12–61 months (range)/variable	various medications	'... sustained initial post-index ECT depression ratings and even a slight drop over time, improved functional status, and no cognitive deterioration' (as measured by the MMSE, $HRSD_{24}$, GAF). Reduced hospital days relative to comparison period of 1 year w/out C-ECT.
Vaidya et al. [45] (2003)	retrospective review	BD	12	large majority received BL/2 weeks to 7 years/ variable	various medications in 8 patients	Reduced number of hospitalizations for all patients relative to comparative period (of unspecified length) w/o C-ECT. 4 patients continued to receive CECT at the time of publication; C-ECT stopped in 1 patient due to nonresponse, 1 due to memory problems, 5 due to patient preference, and 1 due to PVCs and arrhythmia.
Tsao et al. [46] (2004)	case report	BD, manic episode	1	BL/>4 months/every 2 weeks	unspecified	C-ECT effective in maintaining euthymia after resolution of acute manic episodes. C-ECT stopped due to patient preference. Relapse into mania 1 month later, ECT re-started.
Wijkstra and Nolen [47] (2005)	case report	MDD, w/psychotic features	1	BL/6 years 2 months/ variable (range: weekly – monthly)	oxazepam (20 mg/d) or zolpidem (7.5 mg/d)	C-ECT effective ($HRSD_{17}$ <10 at 66 of 70 assessments, <5 at 55 of 70 assessments), reduced number of hospitalizations compared to 4-year pre-C-ECT period, no cognitive deterioration as measured by patient report and MMSE.

Table 1 (continued)

Author	Design	Diagnostic criteria	Subjects, n	C-ECT type/ duration/interval	Medication	Outcome/comments
Abraham et al. [48] (2006)	retrospective review	depression	18	BF/10.8 months (mean); 8.0 months (SD)/2.6 weeks (mean)	various medications	11% relapse rate, relapse rate higher for patients who were more symptomatic at the end of acute ECT. Severe memory impairment in 5.7% as measured by notes in record.
Suzuki et al. [49] (2006)	case report	MDD, with psychotic features	1	BL/4 years/variable (4 weekly, 10 every 2 weeks, 6 every 3 weeks, 34 every 4 weeks)	milnacipran (75 mg/d)	Age 70. Residual symptoms improved (acute phase end $HRSD_{17}$ = 11 to $HRSD_{17}$ = 3 after 2 years of C-ECT), patient remained remitted ($HRSD_{17}$ = 3), cerebral hypoperfusion resolved, no adverse effects (acute phase baseline MMSE = 18; after 2.5 years MMSE = 25).
Sienaert and Peuskens [50] (2006)	case report	BD, mixed episode	1	RUL/37 months/variable	haloperidol (5 mg/d)	C-ECT effective in preventing mixed episodes. Cognitive deterioration associated with depressive episode improved and there were no signs of retrograde amnesia as measured by NP battery. 'C-ECT was stopped because of an increasing anesthetic risk due to morbid obesity.' Patient relapsed 3 months after C-ECT was discontinued.
Nascimento et al., (2006) [51]	case report	BD, manic episode	1	BT/16 months/variable	no medication	Age 45. No manic or depressive episodes, MMSE scores above 29, no subjective treatment-related complaints.
Yero et al. [52] (2006)	case report	BD, PSAS	2	BT and BF/9 months and unknown/variable	valproic acid and paroxetine	Both patients experienced remission from mood disorder and PSAS.
Balke and Varma [53] (2007)	case report	MDD and possible PD	1	unspecified/6 years/ monthly and bimonthly	unspecified	Age 78. Long-term C-ECT effective and did not cause cognitive impairment (MMSE score range 25/30 to 28/30). 'Over the years, successful maintenances ECT has helped her to continue to live independently ...'
Bozkurt et al. [54] (2007)	case report	psychotic depression in a pregnant patient	1	BL/15 weeks/variable (3 weekly, 3 monthly)	no medication	C-ECT effective (HSRD = 3 after 3 weekly C-ECT), no complications except for pelvic pain and transient fetal arrhythmias.
Zisselman et al. [55] (2007)	case report	MDD w/psychotic features, BD w/moderate mental retardation	2	BL/several years/weekly	various medications	Weekly C-ECT for extended periods effective and well tolerated, with attempts to increase the interval between treatments unsuccessful.
Gupta et al. [56] (2008)	retrospective review w/matched control group (acute ECT w/out C-ECT)	MDD	C-ECT = 19 no C-ECT = 19	BL and RUL/range 18–329 weeks/2.5 weeks (mean)	unspecified	C-ECT phase showed within-group reduction in mean admission rates compared to pre-ECT period (mean 1.00 admissions/year in 2-year pre-ECT period, to 0.316 admissions/year during C-ECT, to 0.2555 admissions/year in post-C-ECT. Bed occupancy was signifycantly lower for C-ECT compared to control group ($p < 0.001$).
Odeberg et al. [57] (2008)	retrospective review	MDD, BD	41	BL and RUL/>4 months/ variable (2-week interval common)	various medications	Over 6-year comparison period (3 years before and after C-ECT + medication). 'The total number of hospital days was reduced by 76%, and the numbers of hospitalized patients and hospitalizations were both reduced by 64%.'
O'Connor et al. [58] (2009)	retrospective review	elderly patients, MDD, BD	54	laterality varied/varied/ varied; '... started with weekly ... to fortnightly ... to monthly.'	various medications	Over 4-year comparison period (2 years before and after C-ECT), number of hospital admissions and length of stay declined. '... admissions were halved in number and quartered in duration.' 'Most patients had no recorded adverse event.' '... 8 instances of memory loss or confusion ... resolved safely.'

MDD = Major depressive disorder; BD = bipolar disorder; PD = Parkinson's disease; RCBD = rapid cycling bipolar disorder; PSAS = persistent sexual arousal syndrome; BL = bilateral; BF = bifrontal; RUL = right unilateral; C-PHARM = continuation pharmacotherapy; HRSD = Hamilton rating scale for depression; MMSE = Mini mental state examination; GAF = global assessment of functioning; PVC = premature ventricular contraction; SD = standard deviation; SSMQ = Squire subjective memory questionnaire.

Table 2. Prospective studies on the efficacy/effectiveness and tolerability of C-ECT (1998–2009)

Author	Design	Diagnostic criteria	Subjects, n	C-ECT type/ duration/interval	Medication	Outcome/comments
Wijkstra et al. [59] (2000)	prospective naturalistic study	MDD	12	BL/6 months/variable ('between once/week and once /3–4 weeks)	no medication	50% remained remitted, $HRSD_{17} < 4$, 6 of 12 relapsed and required hospitalization. 'No drop-outs.'
Swoboda et al. [60] (2001)	prospective comparison w/matched pharmacotherapy control group	MDD, BD	13 13	BL and unilateral/9.61 months (mean); 2–24 months (range)/ variable, '... usually weekly ... bi-weekly to monthly sessions'.	various pharmacotherapy	Post C-ECT MMSE = 28.52 (mean); control group MMSE = 27.66 (mean). M-ECT stopped due to: cognitive-related issues for 2 patients and hypertension for 1 patient. These data include scores from 8 patients with SAD. C-ECT + medication reduced hospitalization by 77% compared to 46% with pharmacotherapy alone, at 12 months.
Datto et al. [61] (2001)	prospective naturalistic pilot study using telephone assessments to detect cognitive impairment	MDD, BD, organic mood disorder	16	BL and RUL/6 months minimum/2.92 weeks (mean); 0.966 (SD)	uncontrolled and unspecified pharmacotherapy	Overall tolerability of ECT supported. 1 patient experienced cognitive impairment that persisted the day after C-ECT but resolved 1 week later as measured by a telephone cognitive battery. 'One of nine tests (verbal fluency category) showed group level effects, with decrements in performance the day after a treatment.' 'Many of these patients noted the most significant negative effect on their cognition occurs the day of their treatment.'
Rami-Gonzalez et al. [62] (2003)	prospective matched comparison	MDD, in remission for at least 3 months	C-ECT = 11 C-PHARM = 11	BL/27.2 months (mean); 17.7 (SD)/ 52.7 days (mean); 16.8 (SD)	various medications (in both groups)	C-ECT frontal function significantly impaired on 4/5 tests compared to depressed controls who never had ECT. C-ECT short-term memory scores lower; long-term memory characterized as normal. C-ECT MMSE = 27.5 (mean)/HRSD = 3.5 (mean); C-PHARM MMSE = 28.2 (mean); HRSD = 2.5 (mean).
Vothknecht et al. [63] (2003)	prospective naturalistic comparison	MDD, BD	C-ECT = 9 C-PHARM = 13	BL and RUL/65 weeks (mean); 16–161 (range)/2.2 weeks (mean); 0.9–4.4 (range)	'psychotropic medication was discontinued if possible' for C-ECT group mixed pharmacotherapy in C-PHARM group	Following acute ECT and then 6 months of continuation treatment, C-ECT cognition comparable to C-PHARM as measured by NP battery. After 6 months, 'cognitive function remained stable throughout' C-ECT 'with an average duration of 65 weeks'. Depression scores stabilized in both groups, with a trend to further improvement in C-ECT group. At end of follow-up period, more patients in C-PHARM relapsed compared to C-ECT.
Rami et al. [64] (2004)	prospective comparison	MDD, BD	C-ECT = 14 C-PHARM control = 8	BL/1 year/36.85 days (mean); 14.41 (SD); 15–60 days (range)	all C-ECT patients also had C-PHARM of unspecified type C-PHARM medication unspecified	Cognitive tolerability of M-ECT supported as measured by NP battery and compared to C-PHARM control group (no ECT). Baseline C-ECT means: HRSD = 3.8; MMSE = 28.0; 1 year M-ECT retest means: HRSD = 3.2; MMSE = 28.90.
Kellner et al. [65] (2006)	randomized controlled trial	MDD	C-ECT = 89 C-PHARM = 95	BT/6 months/fixed schedule (4 weekly, 8 biweekly, 2 monthly)	C-ECT: lorazepam and diphenhydramine as needed in both arms C-PHARM: Li + nortriptyline	After acute ECT, similar efficacy and tolerability in 6-month period for C-ECT and C-PHARM. Relapse rates 37.1% for C-ECT; 31.6% for C-PHARM. Drop-out rates 16.8% C-ECT; 22.1% C-PHARM. No difference in cognitive side effects as measured by the MMSE.
Odeberg et al. [57] (2008)	partial prospective naturalistic follow-up (following retrospective review, see table 1)	MDD, BD	16	BL and RUL/ >4 months/variable (2-week interval common)	various medications	Subset of patients assessed at follow-up interview mean time-point: 15 months; range: 4–29 months and 87% were in remission (defined as MADRS <10 & CGI <2). C-ECT ongoing in 56% of patients.

Table 2 (continued)

Author	Design	Diagnostic criteria	Subjects, n	C-ECT type/ duration/interval	Medication	Outcome/comments
Navarro et al. [66] (2008)	randomized controlled trial	elderly patients, MDD w/psychotic features	C-ECT = 16 C-PHARM = 17	BL/2 years weekly for 4 weeks, every 2 weeks for 1 month, monthly	nortriptyline/ nortriptyline and risperidone for 10 weeks, then nortriptyline alone	After acute ECT + nortriptyline, 'the risk of relapse/recurrence was 8-fold higher during the first year of follow-up in the patient subgroup treated w/o C-ECT.' 'No significant differences were found in the subscores on the UKU, in the UKU global score, or in mean changes in ECG intervals, heart rate, or diastolic and systolic blood pressure.' Changes in MMSE score also not significant.

MDD = Major depressive disorder; BD = bipolar disorder; BL = bilateral; RUL = right unilateral; C-PHARM = continuation pharmacotherapy; HRSD = Hamilton rating scale for depression; MMSE = Mini mental state examination; CGI = Clinical global impression; NP = neuropsychological; MADRS = Montgomery-Åsberg depression rating scale; UKU = Udvalg for kliniske undersøgelser side effect rating scale; SAD = schizoaffective disorder; SD = standard deviation.

monotherapy (60%) and placebo (84%). There were no memory outcome differences between unrelapsed recipients of C-ECT and C-PHARM at six months as determined by an extensive neuropsychological battery [67]. The authors concluded that memory effects should have only a small role in the choice between C-ECT and C-PHARM. These results confirmed the value of C-ECT for relapse prevention in patients with depression successfully treated with ECT. However, with over one-third of patients in even the most effective arm of both RCTs relapsing during the 6 months of continuation treatment, it is clear that neither C-ECT nor combination pharmacotherapy alone represents the last word on post-acute-ECT prolongation of remission [11, 65].

In an effort to improve the rates of sustained remission after completion of a successful acute course of ECT, clinicians and investigators are turning to more intensive follow-up interventions. For example, in a relatively small prospective, single-blind study, Navarro et al. [66] randomized 33 elderly patients with psychotic depression responsive to an acute course of ECT to receive either C-ECT plus nortriptyline, or nortriptyline alone, both arms combined with risperidone, for 10 weeks. They report that after successful acute ECT, 'the risk of relapse/recurrence was eightfold higher during the first year of follow-up in the patient subgroup treated without C-ECT'. They also report no differences in tolerability between groups.

As listed in table 1, a growing number of uncontrolled studies report positive outcomes using the combination of C-ECT and medications. Thus, the reasonable next step in C-ECT research is to test in a controlled fashion whether the combination of C-ECT and C-PHARM may improve remission rates beyond those seen with either intervention alone. For example, the CORE group has embarked on a multicenter study, Prolonging Remission in Depressed Elderly (PRIDE), to test this hypothesis. This study will compare, over a 6-month period, the relative efficacy of lithium and venlafaxine versus lithium, venlafaxine, and continuation ECT in geriatric depression.

C-ECT/M-ECT Frequency and Duration

We lack established guidelines with regard to frequency and duration of C-ECT. The guidelines used for continuation pharmacotherapies, as well as common sense, would call for a duration of C-ECT at least equal to the expected natural course of the episode of illness. In the case of major depression and bipolar disorder, this duration should be at least 8–20 weeks. Typically, C-ECT courses for depression last from 2 to 6 months. Longer courses of treatment and M-ECT are indicated for patients with more severe, recurrent and treatment-resistant forms of depression. In these cases, M-ECT should be administered at the minimum frequency necessary to prevent relapse. The APA Task Force calls for reevaluation of the necessity of treatment at least every 6 months, taking into consideration both beneficial and adverse effects.

In clinical practice, psychiatrists often follow one of three types of schedules: (1) a tapered schedule that usually starts with weekly treatments for 2–4 weeks, followed by a gradual decrease in the frequency to once per month,

(2) a fixed-interval schedule with treatments every 1–4 weeks, and (3) an 'as-needed' approach with 1–2 treatments each time there are signs of relapse [18, 19].

However, the question of optimum frequency and duration of C-ECT has not been studied systematically. The PRIDE study C-ECT arm features an initial fixed, tapered treatment schedule (with 4 ECT treatments in the first month) followed by a treatment algorithm based on individual patient symptomatology [68]. Patients are given 0, 1, or 2 treatments each week based on a comprehensive algorithm that takes into account changes in the Hamilton Rating Scale for Depression – 24 items ($HRSD_{24}$) scores at the previous and current assessments, and readjusts for baseline $HSRD_{24}$ score. This approach seeks to treat residual symptoms early in the continuation treatment course and to treat the reemergence of symptoms before full syndromal relapse, in order to improve long-term outcome.

Risks

The risks of C-ECT are similar to those of the index treatment. It should be noted that most C-ECT treatments are given in an outpatient setting and thus may only be appropriate for certain patients. This situation creates the need for very cooperative and reliable patients, who will follow the 'nothing by mouth after midnight' instructions, and who have a strong support system that will provide care and transportation after each treatment. Patients should not be allowed to drive home nor for 24 h after a treatment.

Some patients (especially the elderly) may remain confused for longer periods after ECT. In such cases, the risk of falls is substantial. Caregivers should be educated about this specific risk, and provide adequate supervision.

As C-ECT treatments are given less frequently than in the index course, cognitive difficulties are shorter lasting and not cumulative as in index courses. Several cases of patients who received many treatments over years without problems have been reported. In an earlier report by Barnes et al. [69], a 74-year-old patient who received more than 400 treatments did not show any signs of progressive cognitive deterioration. In the CORE C-ECT study, patients who received C-ECT did not differ in cognitive side effects from the C-PHARM group. The drop-out rates due to treatment side effects was slightly higher for the medication group (21–17%), but the difference did not reach statistical significance [65].

Technical Issues

Anesthesia

The same treatment techniques as used in the index course are applied in C-ECT. Anesthetic medications and dosages remain the same, unless a change in the patient's general health or the use of concurrent medications dictates a different approach. Posttreatment evaluation includes assessment of orientation, alertness, gait and vital signs. When reoriented, with stable gait and vital signs, patients are allowed to leave the treatment facility.

Concurrent Medications

The efficacy of combination C-ECT and antidepressant medications for relapse prevention in mood disorders has not been studied systematically. However, nearly all of the published literature on C-ECT cites the use of combined C-ECT with medications. Navarro et al. [66] combined nortriptyline with acute and continuation ECT in a sample of elderly depressed patients, and found the combination to be safe and effective in decreasing post-acute ECT relapse.

Safety concerns are the same in any ECT course. Some clinicians advise patients to discontinue all psychotropic medications other than antipsychotic agents, 1–2 days prior to each C-ECT and then continue with regular dosing after treatment [70]. However, a recent study [71] reports the safe use of nortriptyline or venlafaxine during an acute course of ECT. Interestingly, concurrent pharmacotherapy enhanced efficacy rates up to 15% compared to ECT alone in that study.

The role of concurrent use of mood stabilizers and C-ECT is also unknown. Caution should be used when lithium is prescribed in parallel with C-ECT because of the reported increased risk of confusion and cognitive impairment [70]. It is recommended that serum levels be kept lower than usual full therapeutic concentrations at the time of ECT. Patients should be instructed not to take any lithium the day before and the morning of ECT. Anticonvulsants should be avoided as they increase the seizure threshold and may make the elicitation of a seizure during ECT difficult. Benzodiazepines may interfere with the efficacy of the treatment [72]. Practitioners should consider the use of shorter-acting benzodiazepines such as lorazepam, or reversing benzodiazepines with flumazenil at the time of ECT [73].

Systemic medications should be continued. Specific attention should be given to concurrent use and (possible dosage changes) of nonpsychiatric medications that may affect treatment parameters, e.g. seizure duration or sei-

zure threshold. Agents such as β-blockers and lidocaine may interfere with seizure induction or duration, while calcium-channel blockers, antiepileptics and some analgesics may increase seizure threshold. Theophylline has been associated with prolonged seizures [70]. Insulin-dependent patients may need dosage and time of dosage adjustments on the days of treatment.

Electrode Placement and Electrical Dosage

The optimum electrode placement for C-ECT has not been studied. Most studies report bilateral (bifrontotemporal) placement, but some use right unilateral placement. There are no studies comparing the efficacy and safety of different placements in the continuation and maintenance phases. Commonly, the technique that was effective in the index course is used in C-ECT or M-ECT [74]. It is noteworthy that concerns about cognitive impairment that may have guided the choice of electrode placement during the index course may not be as relevant during C-ECT. Since the treatments during C-ECT are given less frequently, there is usually ample time between treatments to allow for cognitive recovery. The CORE C-ECT study, which was performed with bilateral ECT during both index and continuation phases, showed no major differences between the ECT group and the pharmacotherapy group in outcome or adverse effects, thus suggesting that bilateral ECT is a viable option in C-ECT.

Optimal electrical doses for use during C-ECT have also not been studied. Because of the infrequent schedule, the seizure threshold changes little or decreases between treatments, in contrast to the rise in seizure threshold typically observed during an index course of ECT. Clinicians should try to adjust electrical dosages to avoid unnecessary overstimulation and unwanted cognitive side effects.

Interim Evaluations

No specific examinations are required before the initiation of a C-ECT course, provided that these were performed before the onset of the index course. However, given the fact that outpatients are not under continuous direct medical observation between treatments, an interval psychiatric and medical history should be obtained before each treatment. Physical complaints and findings, especially those pertaining to systems at risk with ECT (i.e. cardiovascular, central nervous and musculoskeletal systems), should be evaluated before each treatment.

The APA Task Force and the ACT Task Force on ambulatory ECT recommend the performance of a physical examination, laboratory tests (including hematocrit, hemoglobin and serum electrolytes) every 6 months in patients undergoing C-ECT and M-ECT [3, 18].

Special Instructions

Patients should be instructed not to eat or drink anything for at least 8 h prior to each treatment. Although reliable outpatients may come for treatment alone, a family member or other reliable caregiver should take them home. Adequate supervision should be provided for several hours after treatment and for longer periods if there is a prior history of prolonged postictal confusion. Some patients may need to miss a day of work. It is prudent that instructions are given to the patients and caregivers in writing.

Consent

A new informed-consent form should be signed before the beginning of C-ECT. This consent form should reflect the particularities of the treatment and should be renewed according to state and local laws and institutional policies. When such laws and policies are vague, it is recommended that renewal of consent be done at least every 12 treatments or 6 months, whichever occurs first [3].

Cost

In an article not included in the tables, Aziz et al. [75] conducted a cost-utility analysis of M-ECT compared to maintenance pharmacotherapy in depressed elderly patients. This sophisticated analysis took both objective and subjective reports of the disease into consideration, and adjusted for quantitative (number of years) and qualitative (quality of years) factors. These authors found that M-ECT yielded a significantly higher number of 'quality-adjusted life years' compared to C-PHARM (11.43 vs. 7.55, respectively), and at much lower cost per year (USD24,616 vs. 57,762). Other published reports support ECT as a cost-effective treatment modality in the continuation and maintenance phases [35, 76].

Conclusions

C-ECT and M-ECT are valuable treatment modalities to prevent relapse and recurrence of mood disorders in patients who have responded to an index course of ECT. C-ECT and M-ECT are underused and insufficiently studied despite positive clinical experience of more than 70 years.

There are now adequate controlled data to conclude that without active treatment following an acute course of ECT, the short-term relapse rate is unacceptably high. It is still unknown whether there are features of the underlying disorder or the initial ECT course that influence the relapse rate or the response to subsequent continuation and maintenance treatment.

As we have shown in this review, both medications (particularly the combination of antidepressants and mood stabilizers) and ECT are effective as continuation and maintenance interventions following ECT-induced remission. Further research is necessary to identify which approach is better for a given individual, and to explore methods of enhancing the still inadequate protection against relapse provided by either option. For example, current research is seeking to assess the role of combined antidepressant pharmacotherapy plus ECT in both acute and continuation phases of treatment. Individualized C-ECT and M-ECT schedules are also under study, using the patient's weekly depression rating to determine the number (if any) of treatments to be delivered during the maintenance phase [68].

Thus, studies that are currently under way should allow more definitive recommendations regarding the choice, frequency and duration of continuation and maintenance treatment following acute ECT. This knowledge will enable the field to move closer to the goals of personalizing treatment and reducing the burden of depression and other serious mental disorders.

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