

Relapse Prevention with Maintenance ECT: State-of-the-Art

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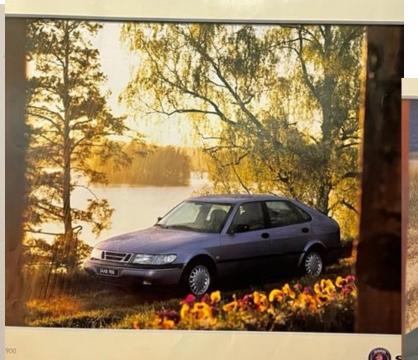
Financial Disclosures

Dr. Charles Kellner:

- Has received grant/research support from the National Institute of Mental Health for ECT research;
- Has received fees from Psychiatric Times for ECT articles;
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- Receives fees from Northwell Health for teaching an ECT course;
- Receives royalties from Cambridge University Press for an ECT textbook;
- Receives fees for expert witness testimony.

Other disclosures







The Enemy Within: NICE, Not Really

Given Meechan *et al.*'s attempt to cite NICE in support of their critique of the two reviews, it seems important to point out that NICE has, for nearly 20 years, been calling for exactly the same thing as the two reviews, i.e. better research that can actually determine whether ECT does work and precisely how unsafe it is:

Further research is urgently required to examine the long-term efficacy and safety of ECT, including its use as a maintenance therapy and its use in particular subgroups who may be at increased risk, for example older people, children and young people, and during pregnancy. ... In addition to the use of appropriately validated psychometric scales, outcome measures should include user perspectives on the impact of ECT, the incidence and impact of important side effects such as cognitive functioning, and mortality. (NICE, 2003)

The Enemy Within: FDA

Similarly, Meechan *et al.*'s claim about FDA endorsement fails to inform readers that the FDA's (2020) regulation code 21(G) states that a notice must be displayed next to ECT machines warning that 'The long term safety and effectiveness of ECT has not been demonstrated.'

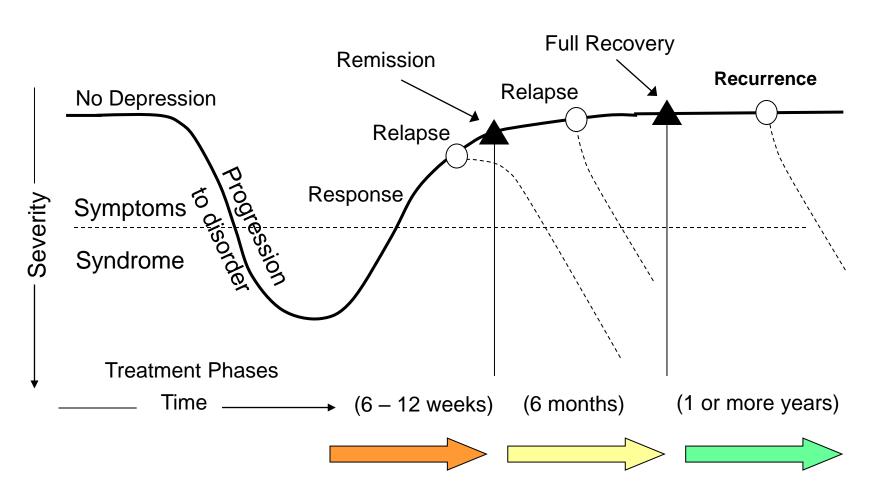
Episodic vs Continuous Illness

- Episodic
 - Unipolar depression
 - Bipolar disorder

Continuous

- Schizophrenia
- Parkinson's Disease
- OCD
- SIB in autism

Three Phases of Treatment



ECT Medical Analogies

Acute (index) ECT is like penicillin for pneumonia

Maintenance ECT is like nitrofurantoin (Macrodantin) for recurrent UTI

Definitions

- **Continuation** ECT given after an episode of depression to *prevent relapse back into the same episode*. Arbitrarily defined as 6 months post remission.
- Maintenance ECT ongoing ECT given to prevent recurrence of a new episode of depression. Arbitrarily defined as after 6 months post remission, can last for years, perhaps indefinitely.
- "C/M ECT"

Post Acute Remission Treatment Options

- No treatment
- rTMS/tDCS
- Psychotherapy
- Medication(s)
- C/M ECT
- C/M ECT plus medication(s)
- C/M ECT plus medication(s) plus psychotherapy

Scholarship in Electroconvulsive Therapy

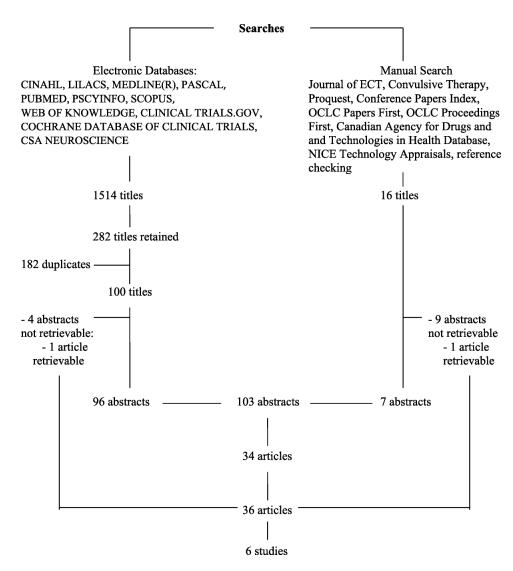
PubMed Citations (as of 16/3/22)

Search Term	# Citations
"Maintenance electroconvulsive therapy"	583
"Maintenance ECT"	484

How Big is the Evidence Base? (since 1990, estimates)

- RCTs before PRIDE
 - n= ~175
- PRIDE
 - n= 64
- Other Studies (e.g. retrospective chart reviews)
 - $n = ^{600}$
- Case Reports
 - $n = ^200$

Brown et al. (2014): Systematic Review of C/M ECT



Brown et al. (2014): Systematic Review

- Four/six studies showed superior effect of C/M ECT over medications alone
- C/M ECT monotherapy less efficacious than C/M ECT + medication
- C/M ECT on a flexible schedule better than fixed

American Journal of Psychiatry, 1957

RESULTS OF FOUR YEARS ACTIVE THERAPY FOR CHRONIC MENTAL PATIENTS AND THE VALUE OF AN INDIVIDUAL MAINTENANCE DOSE OF ECT

GUNTHER E. WOLFF, M.D.1

More than 4 years have passed since we started a more active treatment for our geriatric female mental patients at the Camarillo State Hospital. The *systematic* use of ECT for this type of elderly patient has never been attempted before though some are on record who have received occasional ECT for acute emergencies.

It was our hope to relieve the condition of the most pitiful patients. Some were completely withdrawn, refused to eat, tried to commit suicide or in a most morbid way played with or ate their excrements. Others were destructive to themselves or their surroundings, tearing up their mattresses, banging the doors, screaming at the top of their has convinced us more of the value of ECT in certain cases than our results during the last 4 years. We have been using every method to help our patients. Many have become more cooperative, relaxed and amenable to psychotherapy with tranquillizing drugs. However, quite a number could not maintain their improvement and others continued to be very disturbed, either depressed or hyperactive. They received ECT and the majority have shown improvement which no other therapy had accomplished.

Of 200 patients now on active treatment, 61 are receiving tranquillizing drugs only; 82 are on ECT only; and 57 are on ECT plus tranquillizing drugs.

American Journal of Psychiatry, 1957

• "From my experience of 25 years in internal medicine, I have learned that some diseases will never be cured permanently and that certain patients are able to carry on only by getting a maintenance dose of their medication whether this is digitalis for the chronic cardiac, insulin for the diabetic or B-12 for the pernicious anemic. No doctor would ever dream of discontinuing an established maintenance dose because he would know that he might endanger the health or even the life of his patient. We felt that a similar consideration should be applied to ECT."

Continuation Electroconvulsive Therapy vs Pharmacotherapy for Relapse Prevention in Major Depression

A Multisite Study From the Consortium for Research in Electroconvulsive Therapy (CORE)

Charles H. Kellner, MD; Rebecca G. Knapp, PhD; Georgios Petrides, MD; Teresa A. Rummans, MD; Mustafa M. Husain, MD; Keith Rasmussen, MD; Martina Mueller, PhD; Hilary J. Bernstein, DHA; Kevin O'Connor, MD; Glenn Smith, PhD; Melanie Biggs, PhD; Samuel H. Bailine, MD; Chitra Malur, MD; Eunsil Yim, MS; Shawn McClintock, MS; Shirlene Sampson, MD; Max Fink, MD

Background: Although electroconvulsive therapy (ECT) has been shown to be extremely effective for the acute treatment of major depression, it has never been systematically assessed as a strategy for relapse prevention.

Objective: To evaluate the comparative efficacy of continuation ECT (C-ECT) and the combination of lithium carbonate plus nortriptyline hydrochloride (C-Pharm) in the prevention of depressive relapse.

Design: Multisite, randomized, parallel design, 6-month trial performed from 1997 to 2004.

Setting: Five academic medical centers and their outpatient psychiatry clinics.

Patients: Two hundred one patients with Structured Clinical Interview for DSM-IV-diagnosed unipolar depression who had remitted with a course of bilateral ECT.

Interventions: Random assignment to 2 treatment groups receiving either C-ECT (10 treatments) or C-Pharm for 6 months. Main Outcome Measure: Relapse of depression, compared between the C-ECT and C-Pharm groups.

Results: In the C-ECT group, 37.1% experienced disease relapse, 46.1% continued to have disease remission at the study end, and 16.8% dropped out of the study. In the C-Pharm group, 31.6% experienced disease relapse, 46.3% continued to have disease remission, and 22.1% dropped out of the study. Both Kaplan-Meier and Cox proportional hazards regression analyses indicated no statistically significant differences in overall survival curves and time to relapse for the groups. Mean±SD time to relapse for the C-ECT group was 9.1±7.0 weeks compared with 6.7±4.6 weeks for the C-Pharm group (P=13). Both groups had relapse proportions significantly lower than a historical placebo control from a similarly designed study.

Conclusions: Both C-ECT and C-Pharm were shown to be superior to a historical placebo control, but both had limited efficacy, with more than half of patients either experiencing disease relapse or dropping out of the study. Even more effective strategies for relapse prevention in mood disorders are urgently needed.

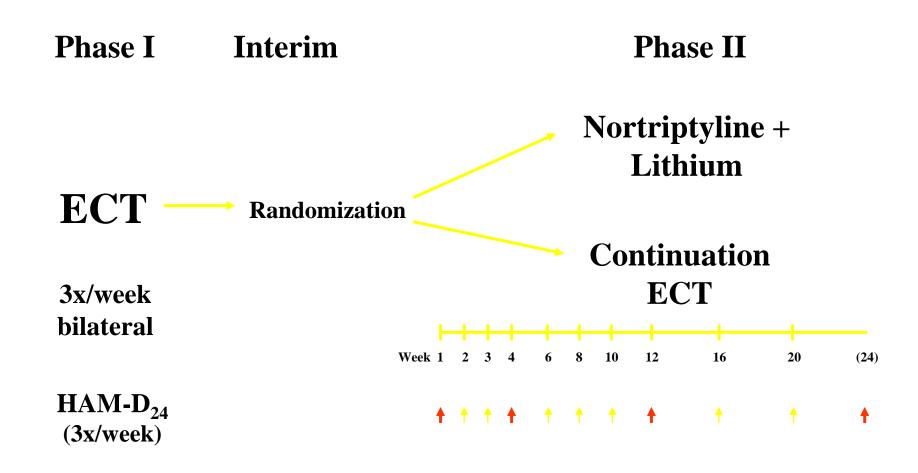
Arch Gen Psychiatry. 2006;63:1337-1344

tion that for most patients, mood dispatients, mood dispatients, mood dispatients, mood dispatients, mood dispersion and researchers have turned their attention from acute treatment strategies to the evaluation of relapse prevention strategies. Electroconvulsive therapy (ECT) has repeatedly been demonstrated as an extremely effective acute treatment

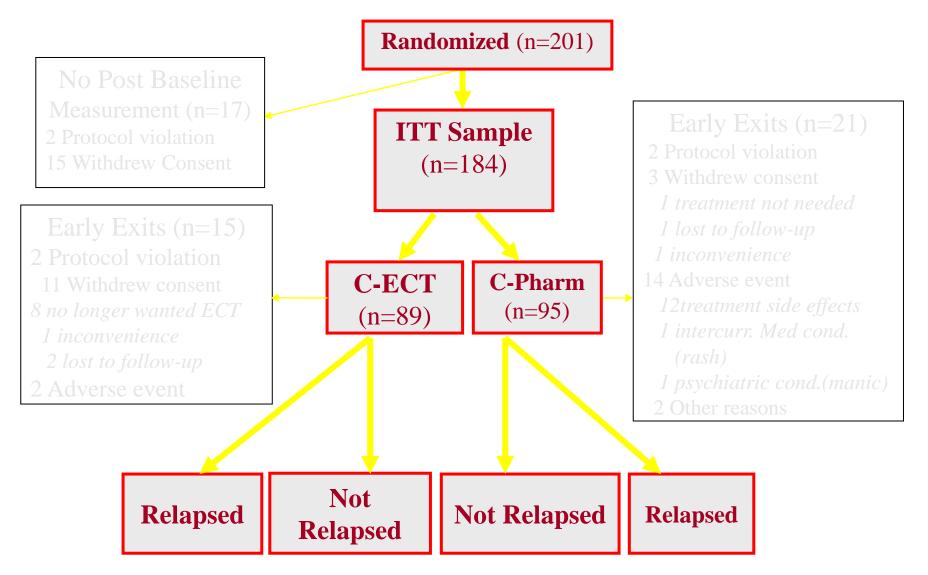
for major depressive episodes. 1-3 It is also used clinically as a continuation and maintenance treatment, despite a lack of well-designed trials to support such use. 1 We evaluated the role of continuation ECT (C-ECT) as a relapse prevention strategy compared with a combination pharmacotherapy (C-Pharm) strategy, lithium carbonate plus nortriptyline hydrochloride, in a multicenter randomized controlled trial. Because treatment options for relapse pre-

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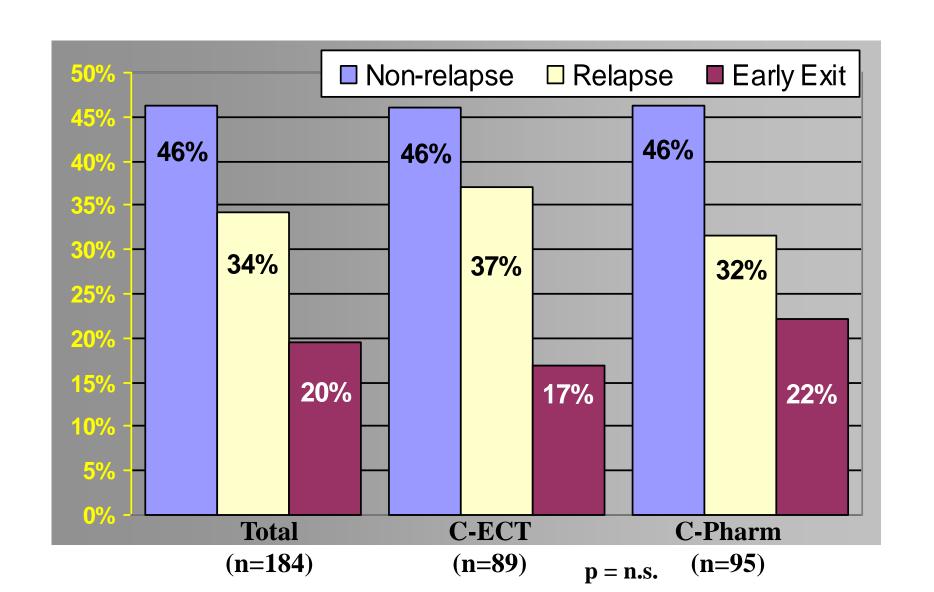
Continuation ECT vs. Pharmacotherapy



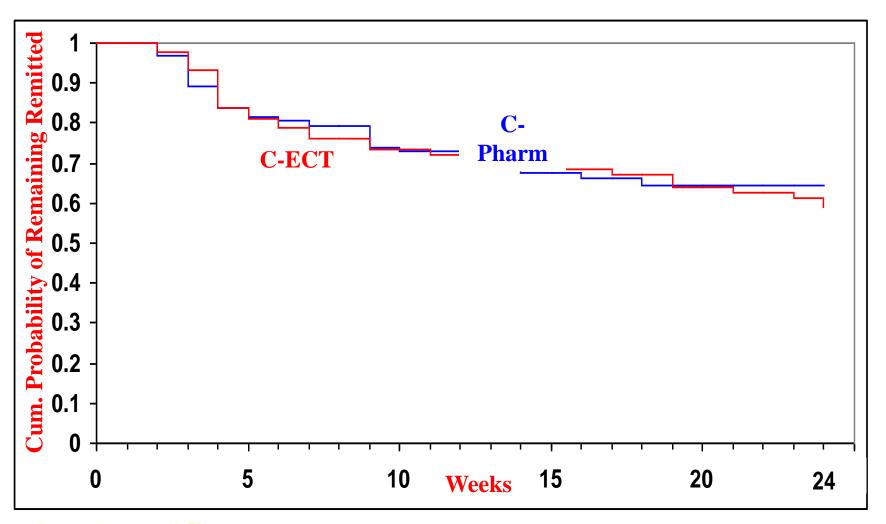
Enrollment Phase II



Relapse Status at 6 Months



Kaplan-Meier Curves for C-ECT and C-Pharm



Logrank test, p=0.59

Conclusion

 Continuation ECT is an effective alternative to pharmacotherapy for relapse prevention.

(Note: this is CECT alone, not combined with medications)

Individualized Continuation Electroconvulsive Therapy and Medication as a Bridge to Relapse Prevention After an Index Course of Electroconvulsive Therapy in Severe Mood Disorders: A Naturalistic 3-Year Cohort Study

Håkan Odeberg, MD,*† Bruce Rodriguez-Silva, MD,† Pirjo Salander, MD,† and Björn Mårtensson, MD, PhD‡

Abstract: Electroconvulsive therapy (ECT) is recognized as an effective acute treatment for mood disorders but is associated with high risk of relapse. To minimize this risk, we introduced as a routine individually tapered continuation ECT with concomitant medication (C-ECT + Med) after an index series in January 2000. In August 2002, a chart review of all patients (n = 41) who had received C-ECT + Med for more than 4 months was carried out. Sixteen patients also participated in an extensive interview. Mean duration of administered C-ECT at follow-up was 1 year, but for most patients (63%), C-ECT had been terminated. For 49% of patients, adjustments between ECT sessions had been made due to early signs of relapse. Two weeks was the most common interval between sessions for patients with ongoing C-ECT. The frequency of lithium-treated patients had increased from 12% before index to 41% during C-ECT. However, the rated response to the drug varied.

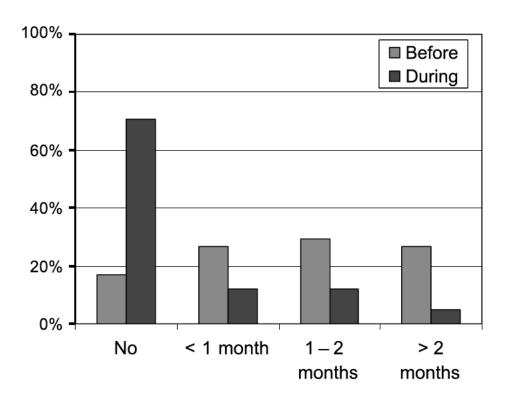
Need for hospital care 3 years before and after the initiation of C-ECT + Med was compared in a second evaluation of the cohort. The number of patients hospitalized, number of admissions, and total days in hospital were all significantly reduced. Hospital days were reduced by 76% (P < 0.001). Three patients with previously cumulative years in hospital are described as case vignettes after 6 years with no or minimal need for further hospitalization. This study supports previous findings that individually tapered C-ECT + Med can maintain initial response to ECT and serve as a bridge to long-term relapse prevention.

Key Words: electroconvulsive therapy, continuation electroconvulsive therapy, continuation pharmacotherapy, mood disorder, relapse prevention

(J ECT 2008;24:183-190)

stopped immediately after remission is achieved. This distinguishes practice of ECT from pharmacological treatment, which is normally continued for stabilization or used eventually for long-term relapse prevention once the patient has responded. To avoid relapse after ECT, psychotropic medication can be introduced during or immediately after the acute treatment series. In early studies with tricyclics alone, this strategy seemed to be rather successful, preventing relapse in approximately 80% of cases. ^{1,2} However, in modern studies, relapse rates of approximately 50% within 6 to 12 months despite intensive pharmacological treatment—have repeatedly been reported, with pre-ECT medication resistance indicating even more unfavorable outcome.^{3–7} In a study by Sackeim et al,⁴ relapse within 1 year after index ECT was 84% on placebo, 60% on nortriptyline alone, and 39% on a combination of nortriptyline and lithium, thus establishing the latter combination as the to-date best proven pharmacological strategy for relapse prevention after acute ECT for major depression.

Continuation ECT (C-ECT) and maintenance ECT are other strategies for relapse prevention after the index series. Maintenance ECT is defined by the American Psychiatric Association as continuation treatment continued beyond 6 months. However, because of the arbitrary character of the distinction between these 2 modalities, the combined term C-ECT has been proposed for the treatments offered to patients whose symptoms are in remission ; this term will be used in this study. Because of the practical difficulties and side effects of maintained initial treatment frequency, C-ECT sessions are typically spaced up to once per month during a period of 2 to 4 months.



Time in hospital

FIGURE 2. Percentage of patients with no hospital days, short-term, intermediate, or long-term hospitalization, 3 years before and during 3 years of C-ECT + Med (n = 41).

Right Unilateral Ultrabrief Pulse ECT in Geriatric Depression: Phase 1 of the PRIDE Study

Charles H. Kellner, M.D., Mustafa M. Husain, M.D., Rebecca G. Knapp, Ph.D., W. Vaughn McCall, M.D., M.S., Georgios Petrides, M.D., Matthew V. Rudorfer, M.D., Robert C. Young, M.D., Shirlene Sampson, M.D., Shawn M. McClintock, Ph.D., Martina Mueller, Ph.D., Joan Prudic, M.D., Robert M. Greenberg, M.D., Richard D. Weiner, M.D., Ph.D., Samuel H. Bailine, M.D., Peter B. Rosenquist, M.D., Ahmad Raza, M.D., Ph.D., Styliani Kaliora, M.D., Vassilios Latoussakis, M.D., Kristen G. Tobias, M.A., Mimi C. Briggs, B.A., Lauren S. Liebman, B.A., Emma T. Geduldig, B.A., Abeba A. Teklehaimanot, M.S., Sarah H. Lisanby, M.D., the CORE/PRIDE Work Group

Objective: The Prolonging Remission in Depressed Elderly (PRIDE) study evaluated the efficacy of right unilateral ultrabrief pulse electroconvulsive therapy (ECT) combined with venlafaxine for the treatment of geriatric depression.

Method: PRIDE was a two-phase multisite study. Phase 1 was an acute course of right unilateral ultrabrief pulse ECT, combined with open-label venlafaxine at seven academic medical centers. In phase 2 (reported separately), patients who had remitted were randomly assigned to receive pharmacotherapy (venlafaxine plus lithium) or pharmacotherapy plus continuation ECT. In phase 1, depressed patients received high-dose ECT (at six times the seizure threshold) three times per week. Venlafaxine was started during the first week of treatment and continued throughout the study. The primary outcome measure was remission, assessed with the 24-item Hamilton Depression Rating Scale (HAM-D), which was administered three times per week. Secondary outcome measures were post-ECT reorientation and safety. Paired t tests

were used to estimate and evaluate the significance of change from baseline in HAM-D scores.

Results: Of 240 patients who entered phase 1 of the study, 172 completed it. Overall, 61.7% (148/240) of all patients met remission criteria, 10.0% (24/240) did not remit, and 28.3% (68/240) dropped out; 70% (169/240) met response criteria. Among those who remitted, the mean decrease in HAM-D score was 24.7 points (95% CI=23.4, 25.9), with a mean final score of 6.2 (SD=2.5) and an average change from baseline of 79%. The mean number of ECT treatments to remission was 7.3 (SD=3.1).

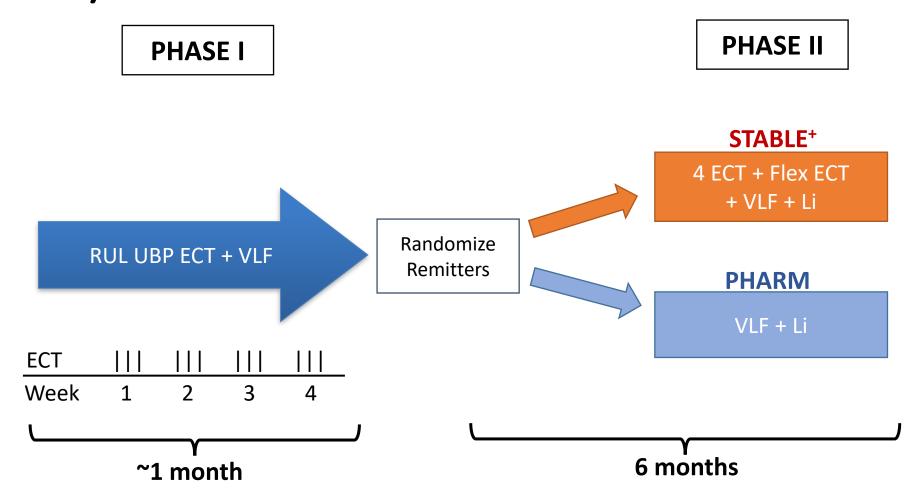
Conclusions: Right unilateral ultrabrief pulse ECT, combined with venlafaxine, is a rapidly acting and highly effective treatment option for depressed geriatric patients, with excellent safety and tolerability. These data add to the evidence base supporting the efficacy of ECT to treat severe depression in elderly patients.

Am J Psychiatry 2016; 173:1101–1109; doi: 10.1176/appi.ajp.2016.15081101

CORE PRIDE Sites



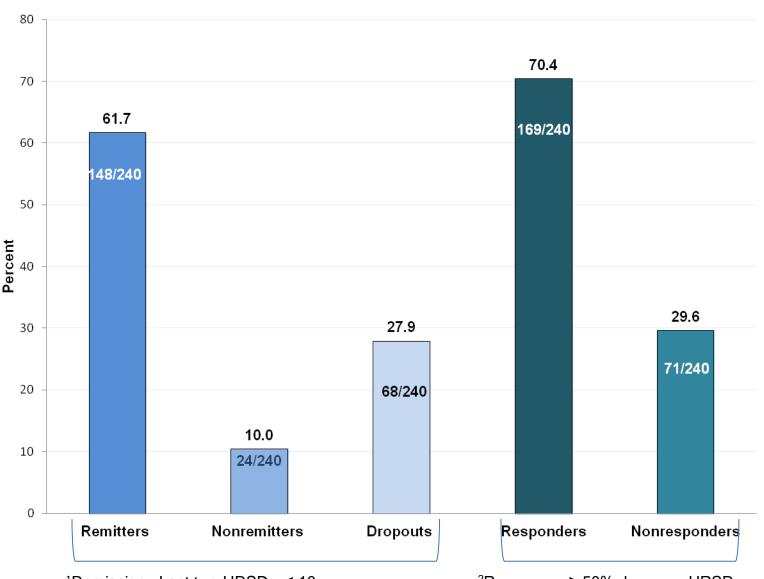
Prolonging Remission in Depressed Elderly (PRIDE)



PRIDE ECT Procedures

- THE STATE OF STATE OF
- Dose Titration (5, 10, 15, 20 %)
- 6x Seizure Threshold RUL (0.25 ms) ECT 3/wk
- Anesthesia
 - Glycopyrrolate (0.2 mg IV) (first procedure only)
 - Methohexital (0.75 mg/kg)
 - Succinylcholine (0.75 mg/kg)
- Adequate seizure ≥15s motor
- Midcourse dose increase if response plateaus

PRIDE Phase I Remission¹ and Response Proportions²



¹Remission: Last two HRSD₂₄ ≤ 10

²Response: ≥ 50% decrease HRSD₂₄ (Baseline - Last)

PRIDE Phase I Conclusions

• RUL-UBP ECT is a viable treatment technique for geriatric depression

RUL-UBP is rapidly acting (including on suicidality)

RUL-UBP is generally well-tolerated

A Novel Strategy for Continuation ECT in Geriatric Depression: Phase 2 of the PRIDE Study

Charles H. Kellner, M.D., Mustafa M. Husain, M.D., Rebecca G. Knapp, Ph.D., W. Vaughn McCall, M.D., M.S., Georgios Petrides, M.D., Matthew V. Rudorfer, M.D., Robert C. Young, M.D., Shirlene Sampson, M.D., Shawn M. McClintock, Ph.D., Martina Mueller, Ph.D., Joan Prudic, M.D., Robert M. Greenberg, M.D., Richard D. Weiner, M.D., Ph.D., Samuel H. Bailine, M.D., Peter B. Rosenquist, M.D., Ahmad Raza, M.D., Ph.D., Styliani Kaliora, M.D., Vassilios Latoussakis, M.D., Kristen G. Tobias, M.A., Mimi C. Briggs, B.A., Lauren S. Liebman, B.A., Emma T. Geduldig, B.A., Abeba A. Teklehaimanot, M.S., Mary Dooley, M.S., Sarah H. Lisanby, M.D., the CORE/PRIDE Work Group

Objective: The randomized phase (phase 2) of the Prolonging Remission in Depressed Elderly (PRIDE) study evaluated the efficacy and tolerability of continuation ECT plus medication compared with medication alone in depressed geriatric patients after a successful course of ECT (phase 1).

Method: PRIDE was a two-phase multisite study. Phase 1 was an acute course of right unilateral ultrabrief pulse ECT, augmented with venlafaxine. Phase 2 compared two randomized treatment arms: a medication only arm (venlafaxine plus lithium, over 24 weeks) and an ECT plus medication arm (four continuation ECT treatments over 1 month, plus additional ECT as needed, using the Symptom-Titrated, Algorithm-Based Longitudinal ECT [STABLE] algorithm, while continuing venlafaxine plus lithium). The intent-to-treat sample comprised 120 remitters from phase 1. The primary efficacy outcome measure was score on the 24-item Hamilton Depression Rating Scale (HAM-D), and the secondary efficacy outcome was score on the Clinical Global Impressions severity scale (CGI-S). Tolerability as measured by neurocognitive performance (reported elsewhere) was assessed using an extensive

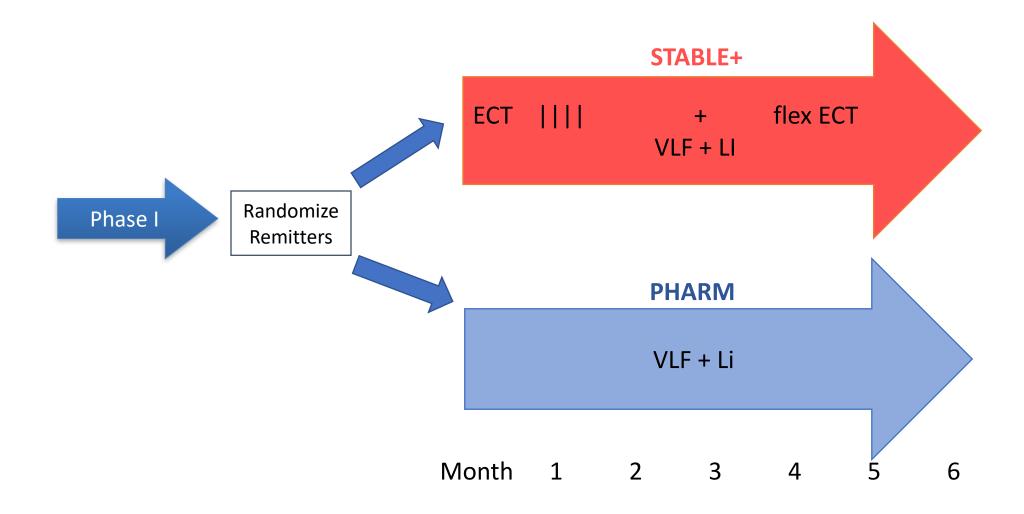
test battery; global cognitive functioning as assessed by the Mini-Mental State Examination (MMSE) is reported here. Longitudinal mixed-effects repeated-measures modeling was used to compare ECT plus medication and medication alone for efficacy and global cognitive function outcomes.

Results: At 24 weeks, the ECT plus medication group had statistically significantly lower HAM-D scores than the medication only group. The difference in adjusted mean HAM-D scores at study end was 4.2 (95% CI=1.6, 6.9). Significantly more patients in the ECT plus medication group were rated "not ill at all" on the CGI-S compared with the medication only group. There was no statistically significant difference between groups in MMSE score.

Conclusions: Additional ECT after remission (here operationalized as four continuation ECT treatments followed by further ECT only as needed) was beneficial in sustaining mood improvement for most patients.

Am J Psychiatry 2016; 173:1110–1118; doi: 10.1176/appi.ajp.2016.16010118

PRIDE Phase II



Symptom-Titrated Algorithm-Based Longitudinal ECT

STABLE

STABLE Algorithm

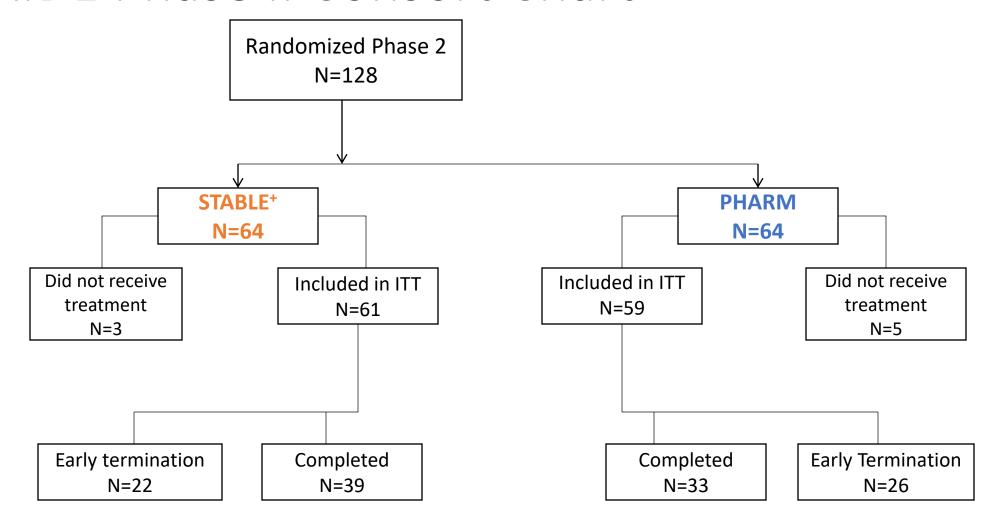
Phase 2: Weeks 1-4: Fixed ECT Schedule: 1 ECT 2-5 days after randomization, 1 ECT 7-12 days after randomization, 1 ECT 14-19 days after randomization, 1 ECT 23-28 after randomization (Total = 4 ECT in one month

Phase 2: Weeks 5-24: Symptom Titrated Schedule

Number ECT per week	Description	Corresponding HAM-D Condition	Relapse potential
0	Current symptomology level very low, or	HAM-D _C ≤ 6, or	Low
	Current symptomology level low to moderate, with only small drift from baseline level, or	$7 \le \text{HAM-D}_{C} \le 12$ and $\text{HAM-D}_{C}\text{-HAM-D}_{B} \le 2$, or	Low
	Last 2 HAM-D in remitted range with flat trajectory (remission stable with less than 2 point change from previous)	7≤HAM-D _C ≤ 10 and 5 ≤HAM-D _P ≤ 10 and (HAM-D _C -HAM-D _P) ≤ 2	Low
2	Current symptomology level very high, or	HAM-D _C ≥ 16, or	High
	Current symptomology level moderate to high, with trajectory increasing rapidly and large drift from baseline	$11 \le \text{HAM-D}_{C} \le 15$, and $(\text{HAM-D}_{C}\text{-HAM-D}_{P}) \ge 3$, and $(\text{HRSD}_{C}\text{-HRSD}_{B}) \ge 8$	High
1	Patients not requiring 0 or 2 received 1 ECT	HAM-D _C intermediate between criteria for "low" or "high" relapse potential	Moderate
Discontinue study	$\text{HAM-D}_{\mathbb{C}}$ and $\text{HAM-D}_{\mathbb{P}} \geq 21$, or patient suicidal, or	patient requires psychiatric hospitalization	

^aHAM-D_B= baseline HAM-D; HAM-D_C=current visit HAM-D; HAM-D_P= previous visit HAM-D (visit preceding current visit)

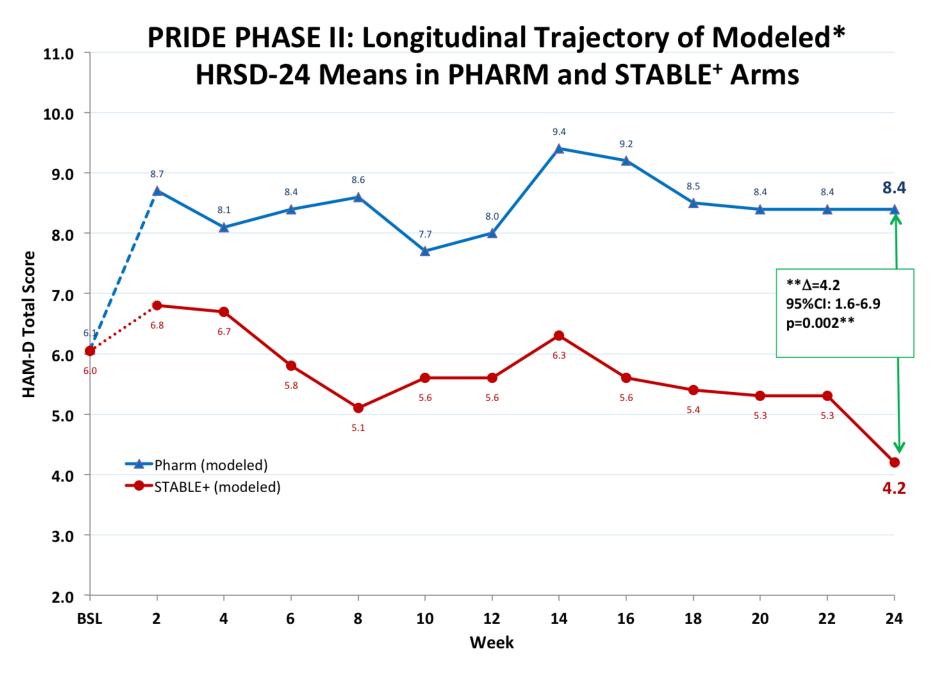
PRIDE Phase II Consort Chart



Li and VLF in Phase II

VLF dose (mean): 192 mg (no difference between arms)

- Li level (mean): 0.53 mEq/l (PHARM)
- Li Level (mean): 0.36 mEq/l (STABLE+)



^{*}Model contains treatment, time, treatment-by-time with HRSD baseline, site, psychosis as adjustment covariables

^{**} Δ=4.2 is difference in baseline, site, psychosis adjusted least squares means for STABLE+ vs PHARM

PRIDE Phase II Results

- At 6 month study endpoint, mean HRSD-24 score for STABLE⁺ = 4.2 vs PHARM = 8.4 (p=0.002)
- CGI-S: odds of being rated "not at all ill" were 5.2 times greater for STABLE⁺ vs PHARM
- Odds of relapsing 1.7 times higher for PHARM vs STABLE⁺
- 34.4% (21/61) of STABLE⁺ patients received at least one additional ECT in weeks 5-24

Relapse* by Treatment Group

• Overall Relapse Rate: 16.7%

• PHARM Relapse Rate: 20.3%

• STABLE⁺ Relapse Rate: 13.1%

^{*}Relapse defined as when a patient was removed from the study for safety because of worsening of MDD requiring alternative treatment (2 consecutive HRSD₂₄ ≥ 21, or patient required psychiatric hospitalization, or patient became suicidal).

PRIDE PHASE II Conclusions

- STABLE⁺ was superior to PHARM in maintaining low depression symptom severity for 6 months after remission
- RUL UBP was safe and well tolerated
- Practitioners should be liberal in prescribing additional ECT past the acute course (taper, continuation/maintenance)
- Aim is to prevent full syndromic relapse and its attendant catastrophic consequences

Clinical Practice Recommendations for Continuation and Maintenance Electroconvulsive Therapy for Depression Outcomes From a Review of the Evidence and a

Outcomes From a Review of the Evidence and a Consensus Workshop Held in Australia in May 2017

Shane P. Gill, FRANZCP*†‡ and Charles H. Kellner, MD§

Objectives: Continuation or maintenance electroconvulsive therapy (ECT) is often provided as a strategy for post-ECT relapse prevention. However, the evidence has been insufficient until recently to produce clear consensus on what best practice maintenance ECT (mECT) should be like in a real world ECT clinical service. The aims of this article are to help fill this gap and to provide a comprehensive set of practical, clinically-based recommendations for ECT clinicians and services.

Methods: A workshop was held at the Royal Australian and New Zealand College of Psychiatry Congress in Adelaide on April 30, 2017. This workshop was hosted by the authors. After a presentation on the state of the evidence, the 30 participants were asked to work in small groups to develop consensus recommendations on different aspects of mECT. These were then collated into one comprehensive set of clinical recommendations for the practice of mECT.

Results: These best practice recommendations are set out below.

Conclusions: These recommendations will assist ECT services and clinicians to provide best practice mECT according to currently available evidence.

Key Words: maintenance ECT, continuation ECT, ECT guidelines, electroconvulsive therapy, best practice ECT, ECT recommendations

(J ECT 2018;00: 00-00)

However, cECT will be used when reporting studies that used this term and provided ECT for 6 months or less after an index course.

High relapse rates after successful ECT have been reported in the literature. In a small naturalistic follow-up study, 12 of 15 patients treated with placebo after a successful course of ECT had relapsed within 6 months.⁴ A larger study of ECT responders managed with treatment as usual after ECT (mostly antidepressant medication) found that 51% had relapsed within 6 months, whereas an earlier prospective follow-up study of ECT remitters, also managed with treatment as usual, found that 64% had relapsed by 6 months. In this same study, the relapse rate for ECT responders who had not achieved full remission was even higher, at 77%. In a study comparing placebo, nortriptyline, and nortriptyline combined with lithium after successful treatment with ECT, relapse rates were 84%, 60%, and 39%, respectively, at 6 months. Although this showed the benefit of continuation pharmacotherapy, and lithium in particular, the absolute relapse rates were still high. In a Consortium for Research in Electroconvulsive Therapy study of mECT, the relapse rates for those who completed the study were 45% for continuation bitemporal ECT alone and 41% for continuation pharmacotherapy alone.⁸

Published ECT manuals include recommendations for con-

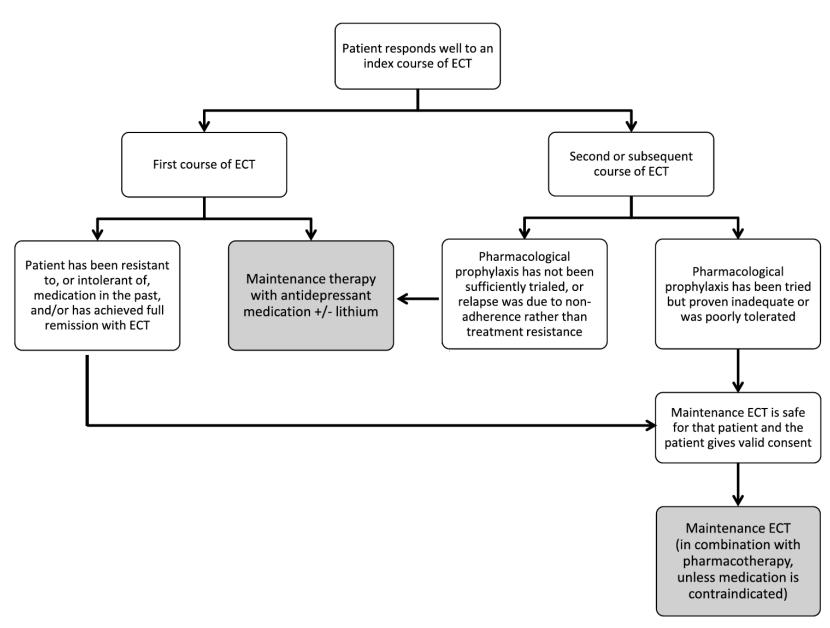


FIGURE 1. Decision flow-chart for mECT.

Best Practice mECT Protocol

Concluding the Index ECT Course

The index course should conclude when the patient achieves remission, or when response plateaus, or if the patient withdraws consent. Ideally, courses of ECT should be concluded by tapering off the ECT frequency, ^{21,22,38,43} which is often referred to as stepdown ECT, for example:

- If the index course was 3 times per week, give 2 ECT in the following week and 1 to 2 further ECT sessions a week apart. ⁴⁴ For inpatients, these may be given as an outpatient after discharge.
- This can then be followed by either mECT or a medication-only relapse prevention strategy (or both), as indicated.

Frequency of mECT Sessions

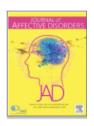
After a taper from the index course, it is appropriate to step down further to approximately every 2 weeks. From here, there is choice to do mECT in either of the following ways:

- At a fixed frequency (eg, monthly);
- Using gradually increasing intervals (eg, to 3 weeks, to monthly, to 2 months, to even 3 months). This may be done over a period of 6 to 12 months;
- Providing rescue ECT treatments based on early signs of relapse, rather than at a predetermined frequency.



Journal of Affective Disorders

Volume 271, 15 June 2020, Pages 109-114



Research paper

Maintenance ECT is associated with sustained improvement in depression symptoms without adverse cognitive effects in a retrospective cohort of 100 patients each receiving 50 or more ECT treatments

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Luccarelli et al., 2020

Highlights

- This study describes a cohort of 100 patients who each received at least 50 electroconvulsive therapy treatments, over a median period of 22 months
- During treatment there was an improvement in depressive symptoms and overall self-reported mental health outcomes which is sustained throughout the study period
- There was no detectable cognitive deficits on the Montreal Cognitive assessment at any point during treatment

Luccarelli et al. Page 11

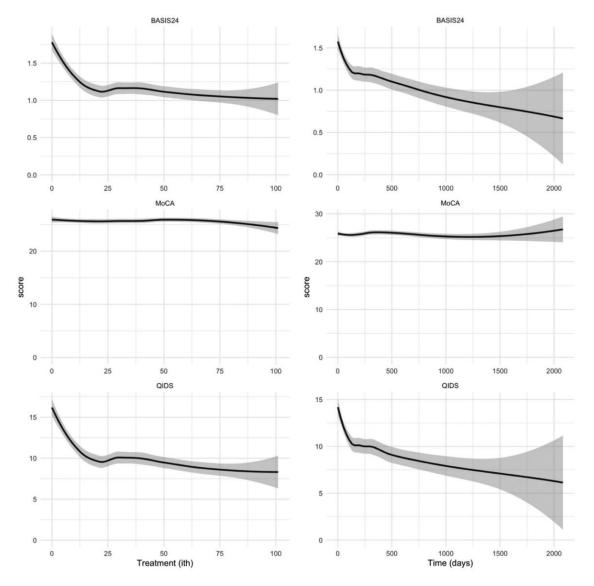


Figure 1: Change in QIDS, BASIS-24, and MoCA with treatment number (left) and time since first treatment in days (right). QIDS and BASIS-24 sharply decline over then first 10 treatments with continued slight decline in QIDS over the remainder of the study period. MoCA scores are unchanged at any point in treatment.

Recurrence After Stopping Maintenance Electroconvulsive Therapy A Retrospective Case Series

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Objectives: Relapses and recurrence remain the greatest risks posed by patients with severe mood disorders after discontinuation of electroconvulsive therapy (ECT). To date, despite a wide range of literature on ECT, little is known about the rate of recurrence of depression after maintenance ECT (mECT) discontinuation specifically. This study sought to address this lacuna, confronting literature data to the results of a retrospective case study. **Methods:** A comprehensive review was conducted, followed by a retrospective analysis of 18 cases of mECT discontinuation between January 2011 and June 2016 involving patients with affective disorders.

Results: The comprehensive review revealed that only 3 studies have assessed recurrence rate after c/mECT discontinuation. In our retrospective analysis, mean (SD) mECT duration was 12.69 (12.16) months. A new mood event (usually a depressive state) was observed in 50% of the cases, and 44% of those recurrences occurred during the first 6 months after discontinuation.

Discussion: Given that high recurrence rates are observed after mECT discontinuation, the authors discuss the advantages of long-term mECT and the choice of concomitant pharmacotherapy for severe and complex affective disorders.

Key Words: electroconvulsive therapy, maintenance, affective disorder, depression, recurrence

(JECT 2020;36: 265–271)

and recurrence, in unipolar,^{4–11} bipolar,^{11–13} or schizoaffective disorders.¹³ Elderly patients seem to be especially good candidates for cECT and mECT, given their efficacy and tolerability in that population,^{14–17} compared with psychotropic drug therapy alone.

According to French guidelines, ¹⁸ cECT is indicated for most patients after the index course of ECT, especially in early relapses despite preventive pharmacotherapy, when antidepressant and mood regulation treatments are contraindicated (or not well tolerated), and if desired by the patient.

In a randomized study of 201 patients with unipolar depressive disorder, Kellner et al¹⁹ showed that pharmacotherapy (nortriptyline + lithium) and cECT were comparably effective for relapse prevention: rates of recurrence at 6 months were 31.6% and 37.1%, respectively. The average (SD) times to relapse were 9.1 (7) weeks in the cECT group and 6.7 (4.6) weeks in the pharmacotherapy group (P = 0.13).

In a large meta-analysis, Jelovac et al²⁰ estimated that 51.1% of patients under continuation pharmacotherapy relapsed within the 12 months after successful initial treatment with ECT, whereas 37.7% relapsed within the first 6 months after ECT. The 6-month relapse rate was similar in patients receiving cECT (37.2%).

The main indications for mECT^{4,18} are lack of sustained remission under pharmacotherapy, recurrence or early relapse despite preventive pharmacotherapy, relapse after treatment disruption in

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ORIGINAL ARTICLE



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Relapse after abrupt discontinuation of maintenance electroconvulsive therapy during the COVID-19 pandemic

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Funding information

Fonds Wetenschappelijk Onderzoek

Abstract

Objective: Maintenance electroconvulsive therapy (M-ECT) is considered an effective relapse prevention strategy in severe mood and psychotic disorders. How long M-ECT should be continued, and what the outcome is after its discontinuation has not been adequately studied. In our tertiary psychiatric hospital, M-ECT treatments were suspended at the start of the COVID-19 pandemic. We aimed to determine the 6-month relapse rate and time to relapse after abrupt discontinuation of M-ECT and to assess the impact of patient and treatment characteristics on the risk of relapse.

Methods: Eighty-one patients whose M-ECT was discontinued abruptly were followed up prospectively for 6 months, or until relapse (i.e., hospital admission, restart of ECT, change of pharmacotherapy, or suicide (attempt)). We used multivariable Cox proportional hazards models to assess the impact of patient and treatment characteristics on the risk of relapse.

Results: Thirty-six patients (44.44%) relapsed within 6 months following abrupt discontinuation of M-ECT. A greater number of previous acute ECT courses, a diagnosis of psychotic disorder (compared with major depressive disorder or bipolar disorder), and a shorter interval between M-ECT treatments at the time of discontinuation were significantly associated with increased risk of relapse.

Conclusion: Almost half of the patients relapsed, similar to the relapse rate after a successful acute course of ECT. Patients with a shorter interval between M-ECT treatments at the time of discontinuation seem to be at increased risk, as well as patients with a diagnosis of psychotic disorder, compared to patients with mood disorders.

KEYWORDS

COVID-19, discontinuation, maintenance electroconvulsive therapy, relapse



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Research paper

Evaluating maintenance electroconvulsive therapy in Bipolar Disorders: 3-year mirror-image study

Santiago Madero ^{a, b, d, e}, Gerard Anmella ^{a, c, d, e, f}, Maria Sagué-Vilavella ^{a, c}, Maria Teresa Pons ^a, Anna Giménez ^{a, c, d, e, f}, Andrea Murru ^{a, c, d, e, f}, Marta Gómez-Ramiro ^{a, b}, Joaquín Gil-Badenes ^{a, b}, José Rios ^{g, h}, Miquel Bioque ^{a, b, d, e, f}, Eduard Vieta ^{a, c, d, e, f}

Antonio Benabarre ^{a, c, d, e, f}

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https://doi.org/10.1016/j.jad.2021.10.052

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Higlights

- The use of <u>mECT</u> reduced the number of psychiatric hospitalizations and hospitalization days in <u>Bipolar Disorder</u>.
- The use of mECT outlines a mood stabilizing effect in Bipolar Disorder.
- This naturalistic study supports the effectiveness of mECT in Bipolar Disorder across several mood states.

DOI: 10.1002/epi4.12294

CONCEPTS AND HYPOTHESES

Epilepsia Open®

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Development of temporal lobe epilepsy during maintenance electroconvulsive therapy: A case of human kindling?

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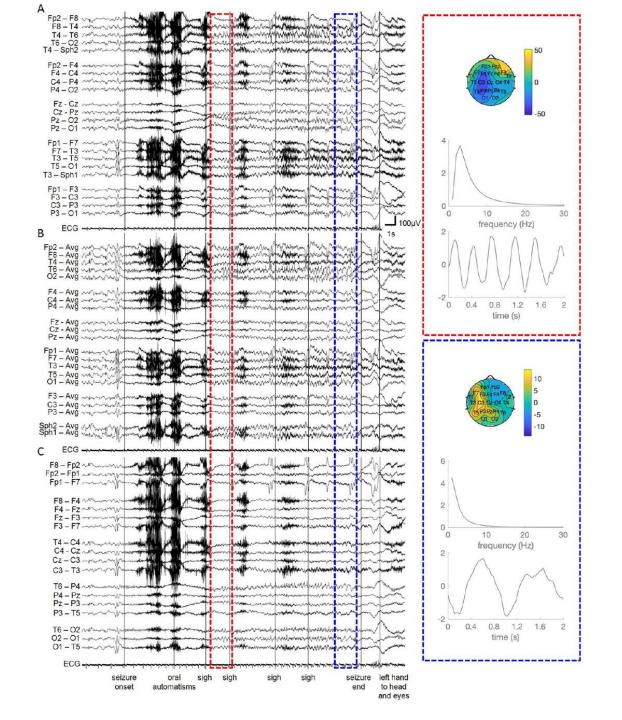
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Summary

We describe a patient with new-onset temporal lobe epilepsy during prolonged maintenance electroconvulsive therapy. We suggest a possible causal relationship with maintenance electroconvulsive therapy through electrical kindling of the temporal lobe.

KEYWORDS

electroconvulsive therapy, kindling, temporal lobe epilepsy



Open Access

3 | DISCUSSION

Published case reports about spontaneous seizures occurring after ECT are rare. Bryson et al and Rasmussen et al have described 5 and 4 patients, respectively, who developed (temporal lobe) epilepsy in the context of maintenance ECT, as in our patient. In Bryson's patients, cessation of ECT led to a clear reduction in the frequency of interictal discharges and no further clinical seizures, even in 2 patients in whom AEDs were not started. 14 The 4 patients of Rasmussen obtained good seizure control after starting AEDs. In 2 of these 4 patients, maintenance ECT was continued or reintroduced without complications. 13 In these 9 cases, the median number of administered ECT sessions at the time of diagnosis was 92 (range 36-348). No cases of developing epilepsy after only a short induction therapy of ECT have been described.

Because epilepsy is not a rare disorder and ECT is widely used, co-occurrence of epilepsy and ECT is insufficient to prove a causal relationship. Still, we suggest a possible causal relationship with ECT in our patient through electrical kindling of the temporal lobe. The

with AEDs, consistent with the progressive nature of kindling epileptogenesis.

4 | CONCLUSION

We describe a patient with new-onset TLE during prolonged maintenance ECT. We suggest a possible causal relationship with maintenance ECT through electrical kindling of the temporal lobe. Development of TLE may be a complication of prolonged maintenance ECT.

ACKNOWLEDGMENTS

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EEG Changes after ECT

The Persistence of Electroconvulsive Therapy-Induced Changes in the Electroencephalogram

RICHARD D. WEINER, M.D., Ph.D.¹

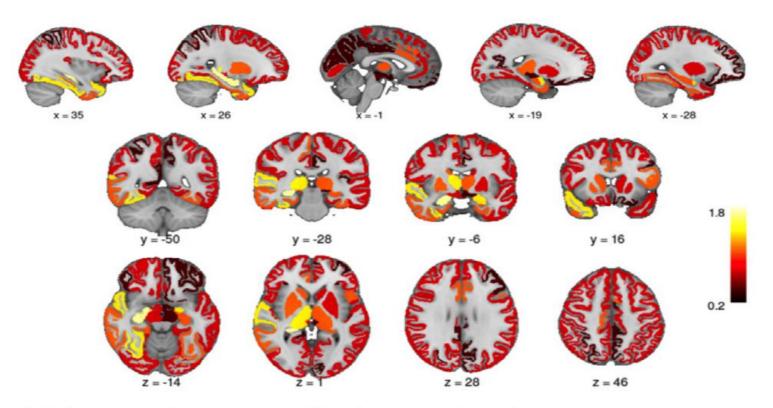
Conclusions

- 1. Generalized EEG slowing, both regular and irregular in morphology, is the most prominent electrophysiological correlate of ECT. It is a nonspecific abnormality consistent with diffuse cortical and subcortical impairment.
- 2. In most cases, by 1 month after completion of a course of ECT, the slowing has returned to baseline levels, although the presence of mild slowing at this time is not uncommon.
- 3. The incidence of increased slowing by 3 months following completion of the ECT treatments is low.
- 4. Both the severity and the persistence of EEG slowing are proportional to the number of ECT treatments received.
- 5. Unilateral ECT typically produces slowing which is maximal over the ipsilateral hemisphere, despite generalization of the evoked seizure activity. It is still unclear whether or not EEG changes are more transient with unilateral than with bilateral ECT.

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Brain Changes Induced by Electroconvulsive Therapy Are Broadly Distributed

Olga Therese Ousdal, Miklos Argyelan, Katherine L. Narr, Christopher Abbott, Benjamin Wade, Mathieu Vandenbulcke, Mikel Urretavizcaya, Indira Tendolkar, Akihiro Takamiya, Max L. Stek,



Volume change, all electrode placements

Lithium in Post-ECT Prophylaxis

- Strong evidence for lithium (plus AD) in post-ECT relapse prevention
- Coppen et al. (1981)
- Sackeim et al. (2001)
- Nordenskjold et al. (2011)
- Prudic et al. (2013)
- Rasmussen (2015) Review
- Lambrichts et al. (2021) Systematic Review and Meta-analysis

C/M ECT Technical Options

Stick with what worked in the acute course

Go to more "powerful" form of ECT

Cognitive issues MUCH less with single treatment spaced weeks apart

EDITORIAL

Maintenance Electroconvulsive Therapy Is Not Acute Electroconvulsive Therapy

Samuel H. Bailine, MD, Sohag N. Sanghani, MD, MPH, and Georgios Petrides, MD

Reviewing our extensive experience of more than 3 decades in our outpatient ECT program, we observed that most of the patients who maintained remission for many years on maintenary have been receiving treatments with maximum US and bilateral placements. This practice did not restreatment strategy or adherence to a theoretic rather a naturalistic evolution determined crease the electrical stimulus and re-treatment short or inadequate seizures and (b) decision cal dose and/or switch from unilateral to be tients regressed prior to the end of schedule who have had their doses increased and the have had very successful maintenance of relections and the complaining or suffering from noticeable cognitions.

In summary, "strongest" treatments during the maintenance period may help decrease the frequency of the treatment and prevent relapses.

In summary, "strongest" treatments during the name period may help decrease the frequency of the treatment and vent relapses. This needs to be tested formally in large random studies. Based on this experience, following a successful coursecute treatments, if possible, a few weekly treatments and the monthly treatments may be given to stabilize the patient, not dissimilar to the STABLE algorithm. ¹³ If maintenance is planned, increasing the intervals between treatments to once a month using the acute treatment parameters is recommended. However, if the

Effects of maintenance

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Sackeim HA. Continuation therapy following ECT: directions for future research. Psychopharmacol Bull. 1994;30:501–521.

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 Lisanby SH, Sampson S, Husain MM, et al. Toward individualized post–electroconvulsive therapy care: piloting the Symptom-Titrated, Algorithm-Based Longitudinal ECT (STABLE) intervention. *J ECT*. 2008; 24:179–182.

How Long to Continue M-ECT?

• "...maintenance ECT, like psychoanalysis, should not be interminably prolonged."

Richard Abrams, *Electroconvulsive Therapy*, 4th ed. 2002

Or can/should it be?

Need to weigh risk of relapse against risk of ongoing treatment.

British Journal of Psychiatry (1985), 147, 203-204

1,250 Electroconvulsive Treatments without Evidence of Brain Injury

*SELECTED STAFF, UNIVERSITY OF LOUISVILLE SCHOOL OF MEDICINE

Since its introduction in the late 1930s, electroconvulsive therapy (ECT) has been an important yet controversial treatment of psychiatric disorders. In spite of being effective in selected circumstances, it has been questioned as an inducer of central nervous system (CNS) damage (Calloway et al, 1977). Animal studies have demonstrated brain injury from electroconvulsive applications (Friedberg, 1977) though the technique utilised was not the same as ECT employed in current psychiatric practice (Frankel, 1977). ECT results in transient memory deficits, but correlation to CNS damage or permanent memory dysfunction has not been confirmed (Fink, 1977, 1982; Frankel, 1977; Frith, 1983; Menken et al, 1979; Squire, 1977; Weeks et al, 1980). The medical community is concerned about these treatments, in spite of the lack of any consensus that they produce brain damage.

This report presents a post-mortem brain study of a patient who received over 1,250 ECTs during a 26-year period. The neuropathological examination was normal.

Absence of Cognitive Impairment After More Than 100 Lifetime ECT Treatments

D.P. Devanand, M.D., Anil K. Verma, M.D., Fughik Tirumalasetti, M.D., and Harold A. Sackeim, Ph.D.

The cognitive function scores and subjective memory complaints of eight patients who had each received more than 100 treatments with bilateral modified sine wave ECT were equivalent to those of matched patients who had never received ECT. The results suggest that patients given many ECT treatments over several courses do not manifest measurable cognitive impairment at long-term follow-up.

(Am J Psychiatry 1991; 148:929-932)

Successful Maintenance Electroconvulsive Therapy for More Than Seven Years

Jaap Wijkstra, MD* and Willem A. Nolen, MD, PhD†

Abstract: We report on a patient with recurrent major depressive episodes with psychotic features who was successfully treated with maintenance electroconvulsive treatment (M-ECT) over a long period without the need for concurrent treatment with an antidepressant or mood stabilizer. She started ECT in 1996 and has received M-ECT for more than 7 years. To date (2005), she has received 244 treatments. After 5 admissions in nearly 4 years, involving 29 months in hospital, she has not needed any further psychiatric admission for 7 1/2 years since the start of the M-ECT. Her depression has been in complete remission for nearly 6 years, with the exception of one mild-to-moderate nonpsychotic depressive episode lasting for 2 months. The patient exhibited slight cognitive deficits but had no subjective complaints before ECT, and her cognitive deficits did not worsen after the initial ECT. Thus M-ECT does not appear to cause cognitive deterioration. M-ECT is being continued on the patient's request.

Key Words: continuance ECT, maintenance ECT, depression

(*J ECT* 2005;21:171–173)

Electroconvulsive therapy: a life course approach for recurrent depressive disorder

Sarah Carney, ¹ Musa Basseer Sami, ² Victoria Clark, ³ Kompancariel Kuruvilla Kuruvilla ⁴

SUMMARY

We describe the case of an 89-year-old woman (deceased) with a 60-year history of recurrent depressive disorder treated with electroconvulsive therapy (ECT). It is estimated that she received up to 400 ECTs over her life course as her symptoms would not respond to oral medication. Despite extensive exposure to ECT, there was only minimal cognitive impairment and an excellent safety record, even in later life, as she became increasingly frail from multiple comorbidities. Over the years, there has been a drive to reduce the frequency of ECT administration. However, this case illustrates how in some patients ECT may be vital for acute episodes of severe depression as well as for maintenance therapy. This case report adds to observational evidence that maintenance ECT may be an underused treatment for recurrent depression and also recommends that greater emphasis be given to incorporating carers' views when planning individualised treatment approaches.

- 19 year old male with first episode psychosis (some mood features, not clear if bipolar disorder or schizophrenia)
- Failed 3 neuroleptic trials
- Remitted after acute course of 8 bilateral ECT
- Acute ECT course tapered for 2 weeks, then stopped

- 69 year old male, unusual "neuropsychiatric" presentation with tremor, delirium, severe depression, visual hallucinations, and catatonic features
- Remitted after acute course of 12 high-dose bilateral ECT
- Relapsed quickly with catatonia
- Maintenance ECT scheduled Q 3 weeks (he and wife would want Q 2 weeks, but schedule does not allow)

- 45 year old male with moderate intellectual disability and autism, atypical bipolar disorder
- Failed medication trials too numerous to count
- When depressed, is regressed and incontinent
- When manic, is violent and unmanageable
- Maintenance ECT scheduled either weekly or Q 2 weeks, indefinitely

- 72 year old female, with > 10 severe episodes of psychotic depression, 6 lifetime hospitalizations, 2 serious suicide attempts
- Well interval between current presentation and prior episode = 4 months
- Remitted after acute course of 12 RUL UBP ECT
- Acute ECT course tapered, maintenance ECT scheduled starting at Q 2 weeks, extended to monthly after 2 months

Conclusions

- C/M ECT works
- Schedule/frequency should be tailored to patient's history of illness
- C/M ECT should be combined with medication(s)
- Lithium has a special place
- Long term M-ECT is typically safe and well tolerated

Aitäh!

Allan H. Ropper, M.D., Editor

Electroconvulsive Therapy

Randall T. Espinoza, M.D., and Charles H. Kellner, M.D.

LECTROCONVULSIVE THERAPY (ECT) HAS BEEN AN ESSENTIAL TREAT- From the Department of Psychiatry and ment for severe mood and psychotic disorders for many decades, and its use is supported by evidence of efficacy and safety.¹⁻³ This brief review discusses current indications for ECT and recent advances in treatment. Over the past 15 years, new treatments — for example, vagus-nerve stimulation, transcranial magnetic stimulation, and intranasal administration of esketamine — have been approved for use in depression. Trials comparing new treatments directly with ECT have been inadequate,^{2,3} and none of these approaches have been considered a replacement for ECT in severely depressed and certain psychotic patients.3,4

Untreated severe depressive and psychotic illnesses are associated with high rates of suicide and hospitalization, prolonged illness, and reductions in productivity and quality of life. Studies have indicated that the use of ECT results in a N Engl | Med 2022;386:667-72. decreased risk of suicide,6 improved functional outcomes7 and quality of life,7,8 and decreased rates of rehospitalization.9-11 In specific populations, ECT can rapidly ameliorate depressive, psychotic, and catatonic symptoms and can decrease suicidal drive. Trials of ECT for major depressive disorder in patients with treatmentresistant depression have shown pooled response rates of 60 to 80% and pooled remission rates of 50 to 60%.^{2,7} High rates of response to ECT have been reported in patients with psychotic depression or catatonia. In a study involving patients with treatment-resistant schizophrenia, ECT efficacy rates ranged from 40 to 70%, 12 and in some Asian countries, the primary indication for ECT is schizophrenia.^{7,9} For example, in an uncontrolled study of treatment-resistant schizophrenia, in which ECT was combined with clozapine, 50% of patients had at least a 40% reduction in symptoms after a course of ECT.13 In patients with bipolar mania and those with mixed mood states (the concurrent presence of manic and depressive symptoms), ECT has led to symptom control within weeks. 14,15

However, a study has shown that ECT has been underused.1 Furthermore, ECT is less accessible to uninsured or underinsured patients and those receiving care in public hospitals than to other patient populations, 16 it has been underused in some large health care systems,¹⁷ it has been limited to inpatient settings,¹⁸ and it is less accessible to minority racial or ethnic groups than to other groups. 19,20 Stigma and lack of knowledge have constrained the use and acceptance of ECT.1,21,22

The contemporary practice of ECT involves induction of brief general anesthesia (typically lasting less than 10 minutes), pharmacologic muscle relaxation, and continuous monitoring of oxygen saturation, blood pressure, and heart rate and rhythm. An electrical charge is delivered to the brain through scalp electrodes, which results in a generalized seizure typically lasting for 20 to 60 seconds. Most patients receive between 6 and 12 treatments spaced over a period of 2 to 4 weeks as an initial course of treatment.

CLINICAL INDICATIONS

In 2018, the Food and Drug Administration (FDA) reclassified ECT devices from class III (high risk) to class II (moderate risk, requiring special controls) for use

N ENGL J MED 386;7 NEJM.ORG FEBRUARY 17, 2022

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Clinical Neuroscience of ECT (CNECT)

Interpreting the ECT literature

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