Continuation Magnetic Seizure Therapy for Treatment-Resistant Unipolar or Bipolar Depression

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ABSTRACT

Objective: Electroconvulsive therapy (ECT) is highly effective for treatment-resistant depression (TRD) but may be associated with adverse cognitive effects. Magnetic seizure therapy (MST) is a promising alternative convulsive treatment with a safer cognitive profile. Although there is emerging evidence for the efficacy of MST for TRD as an acute treatment, there are no published studies of continuation MST for the prevention of relapse.

Methods: Patients with TRD with a *DSM-IV* diagnosis of major depressive disorder or bipolar disorder who met response criteria after acute MST were offered continuation MST in a prospective, open-label trial between February 2012 and June 2019. They received 12 continuation MST sessions with decreasing frequency over the course of 6 months, with additional booster sessions if their depression symptoms started to worsen. The primary outcome was relapse of depression or psychiatric hospitalization. Secondary outcomes included relapse of suicidal ideation and neurocognitive outcomes.

Results: Thirty participants completing at least one assessment during continuation MST were included in the analysis; 10 (33.3%) relapsed, with no significant differences in survival distributions between unipolar and bipolar groups ($\chi^2 = 0.3$, $P = .58$). Mean (SD) survival time was 18.6 (1.6) weeks. All 17 participants who achieved resolution of baseline suicidality after acute MST remained free of suicidality during the continuation phase. Except for improvement in verbal fluency, neurocognitive test scores did not change during continuation MST.

Conclusions: During 6 months of continuation MST, two-thirds of participants sustained improvements in depressive symptoms without any adverse cognitive effects. Future studies of continuation MST are warranted, particularly in comparison to ECT.

Trial Registration: ClinicalTrials.gov identifier: NCT01596608

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Treatment-resistant depression (TRD) is common in major depressive disorder (MDD) and bipolar disorder (BD).[1,2] Although many pharmacologic and psychotherapeutic strategies have been proposed for TRD, there is a paucity of evidence-based interventions.[3] Electroconvulsive therapy (ECT) has consistently demonstrated effectiveness for TRD, with remission rates estimated between 50% and 80%.[4] However, common barriers include the fear of adverse cognitive effects (particularly memory loss) and negative stigma associated with this treatment.[4,5] Magnetic seizure therapy (MST) is a novel convulsive brain stimulation treatment; early evidence suggests it is as effective as ECT but has fewer adverse cognitive effects.[6–9] MST induces generalized seizures using high-frequency, high-intensity transcranial magnetic stimulation and, in contrast to ECT, is unaffected by impedance from the scalp or the skull.[10] MST produces a more focal field of stimulation with relative sparing of deeper brain structures such as the hippocampus thought to be involved in memory and other cognitive functions.[10,11]

Despite relatively high rates of remission with acute ECT, sustaining remission remains a challenge. In the Consortium for Research in ECT (CORE) multisite study,[12] after achievement of remission from ECT, the relapse rate was 84% after 6 months in the absence of any continuation treatment. Continuation pharmacotherapy reduced relapse rates to 39% with nortriptyline and lithium.[12] In another study,[13] relapse rates did not differ between lithium and nortriptyline or ECT during 6 months of continuation treatment, with approximately half of participants sustaining remission. Two smaller randomized controlled trials (RCTs) of continuation and maintenance ECT plus pharmacotherapy versus pharmacotherapy alone[14,15] showed superiority of ECT plus pharmacotherapy. A 2013 meta-analysis[16] estimated the 6-month relapse rate with continuation ECT to be 37.2%. In the most recent multicenter Prolonging Remission in Depressed Elderly (PRIDE) trial,[17] continuation ECT plus

Clinical Points

- Emerging research demonstrates that magnetic seizure therapy (MST) is effective for treatment-resistant depression (TRD) and does not produce adverse cognitive effects. However, how to prevent relapse after a successful course of acute MST is unknown.
- Open-label continuation MST over 6 months, with booster treatments if clinically indicated, successfully prevented relapse of depressive symptoms in two-thirds of a sample with TRD, and there were no significant cognitive changes.

pharmacotherapy (venlafaxine and lithium) was superior to pharmacotherapy alone.

Published studies of MST have focused on the acute phase of treatment. In one study,[18] half of 18 MST responders relapsed when they were followed for 6 months without any continuation. Thus, it is important to develop strategies to prevent relapse after a successful course of acute MST. To our knowledge, no study of continuation MST has been reported. We report on the results of 6-month continuation MST in an open-label clinical trial of MST for TRD in MDD or BD.

METHOD

Study Design

Continuation MST was provided to patients who had completed an acute course of MST and met response or remission criteria as described in detail elsewhere.[19,20] Between February 2012 and June 2019, MST was provided in a prospective, open-label, single-arm clinical trial for patients with treatment-resistant unipolar and bipolar depression (ClinicalTrials.gov identifier: NCT01596608) at a tertiary-care psychiatric hospital in Toronto, Canada. All participants provided written informed consent. The study protocol was approved by the Research Ethics Board, in accordance with the Declaration of Helsinki. In the acute phase, MST was delivered 2 to 3 times per week for up to 24 sessions or until remission of depression.[19,20] Response was defined as ≥ 50% reduction from baseline score on the 24-item Hamilton Depression Rating Scale ($HDRS_{24}$)[21] on two consecutive ratings; remission was defined as an $HDRS_{24}$ score of ≤ 10 and ≥ 60% reduction from baseline on two consecutive ratings. Participants whose depression responded or remitted were offered continuation MST for up to 24 weeks (6 months) or until relapse of their depression. Relapse criteria were defined as (*a*) a score ≥ 21 on the $HDRS_{24}$ and nonresponse to booster treatments, (*b*) one score ≥ 21 on the $HDRS_{24}$ and dropout from the study, (*c*) psychiatric hospitalization, or (*d*) switch to hypomania/mania. Nonresponse to booster treatments was defined as being unable to reach the participant's response cutoff again, which was a 50% reduction from baseline on the $HDRS_{24}$. The primary outcome for this MST continuation trial study was relapse rate. Secondary outcomes were reorientation times, neurocognitive function, and suicidality.

Participants

Patients were eligible for MST if they (1) had a *DSM-IV* diagnosis of a major depressive episode in the context of MDD or BD as confirmed by the Structured Clinical Interview for *DSM-IV*,[22] (2) were referred for ECT, (3) were 18 to 85 years old, and (4) had an $HDRS_{24}$ score of ≥ 21, indicating moderate to severe symptom severity. Exclusion criteria included unstable physical or neurologic condition; being currently pregnant or lactating; not being eligible for general anesthesia; having a cardiac pacemaker, cochlear implant, implanted electronic device, or nonelectric metallic implant; taking a benzodiazepine medication at a dosage higher than 2 mg/d of lorazepam or equivalent; taking an anticonvulsant medication; active substance misuse or dependence within the preceding 3 months; a diagnosis of delirium, dementia, or another cognitive disorder secondary to a medical condition; other significant neuropsychiatric comorbidity; a history of suicide attempt within the preceding 6 months; or a diagnosis of antisocial or borderline personality disorder confirmed by the Structured Clinical Interview for *DSM-IV-TR* Axis II Personality Disorders.[23] Participants could continue all of their current medications, and they were instructed not to make any changes during the study.

Clinical Measures

Demographic variables, medication history, and information on clinical course were collected at baseline. Treatment resistance was quantified using the Antidepressant Treatment History Form (ATHF).[24] The $HDRS_{24}$ was administered at sessions 3, 6, 9, and 12, corresponding to weeks 2, 7, 14, and 24 of the continuation phase. An $HDRS_{24}$ assessment was also done after completion of MST booster if required. In addition, data from the Quick Inventory of Depressive Symptomatology–Self Report (QIDS-SR)[25] were collected from the participant prior to every session. If the QIDS-SR score was ≥ 10, additional $HDRS_{24}$ assessments were immediately scheduled.

Scheduled assessments at sessions 3, 6, 9, and 12 included the Beck Scale for Suicidal Ideation (SSI)[26] and the Young Mania Rating Scale.[27] We examined the effect of continuation MST on preventing reoccurrence of suicidality in participants who presented with suicidality at baseline (ie, SSI score > 0) and experienced a full resolution with acute MST (ie, SSI score = 0).

Neurocognitive Measures

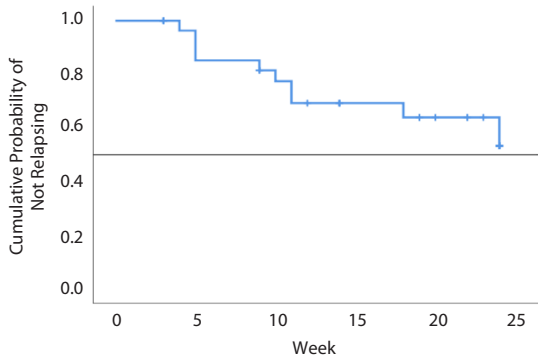
A neurocognitive test battery was performed after the 24-week course of continuation MST. Post-continuation scores were compared with baseline scores obtained prior to acute MST, which have been previously reported.[19,20] Tests included the Autobiographical Memory Inventory–Short Form (AMI-SF),[28] the Montreal Cognitive Assessment (MoCA),[29] Trail Making Test B,[30] Stroop Color and Word Test,[31] the Controlled Oral Word Association Test (COWAT),[32] and the MATRICS Consensus Cognitive Battery (consisting of the Brief Assessment of Cognition in Schizophrenia–Symbol Coding, Trail Making Test A,

Table 1. Clinical and Demographic Characteristics of Study Participants (N = 30)[a]

Characteristic	Value
Age, y	47.3 (12.8)
Sex, female/male, n	20/10
Diagnosis, MDD/BD, n	23/7
Education, y	15.8 (2.2)
Age at onset, y	27.1 (14.2)
Duration of current episode, wk	97.4 (107.2)
$HDRS_{24}$ score	
Baseline	28.4 (3.7)
Post-acute	8.5 (3.9)
Frontal HF/MF/LF, n	9/9/8
Vertex HF, n	4
No. of acute MST sessions	10.37 (3.58)
No. of adequate medication trials prior to MST	3.16 (1.80)
Total ATHF Score	11.43 (6.37)

[a]Values are shown as mean (SD) unless otherwise noted.
Abbreviations: ATHF = Antidepressant Treatment History Form, cumulative score for current episode; BD = bipolar disorder; frontal/vertex = MST coil placement; $HDRS_{24}$ = 24-item Hamilton Depression Rating Scale; HF = high frequency; LF = low frequency; MDD = major depressive disorder; MF = medium frequency, MST = magnetic seizure therapy; post-acute = after completion of acute MST, prior to continuation MST.

Figure 1. Kaplan-Meier Survival Curves Showing Proportion of Patients Who Remained Free of Relapse During the 24-Week Continuation MST Treatment Phase



Abbreviation: MST = magnetic seizure therapy.

the Hopkins Verbal Learning Test–Revised, the Wechsler Memory Scale–Spatial Span, Category Fluency Animal Naming, Letter Number Span, Brief Visuospatial Memory Test–Revised, and Neuropsychological Assessment Battery–Mazes).[33] The MoCA was administered after continuation MST sessions 3, 6, 9, and 12. Reorientation time (ability to provide correct personal name, date, age, place, day of the week, and date of birth) was assessed after each MST session.

Continuation MST

Continuation MST was delivered according to a fixed schedule of gradually decreasing frequency from week 0 to week 24: 1 session per week for 4 weeks, then 1 session every 2 weeks for 2 months, then 1 session every 3 weeks for 2 months, and then 1 final session 4 weeks later. Participants were offered booster sessions if their depression began to worsen. If the $HDRS_{24}$ score was above the cutoff score that defined their response or remission, a second $HDRS_{24}$ rating was scheduled shortly thereafter. If this second score remained above the cutoff, the participant was offered 4 booster sessions over the following 2 weeks. If depressive symptoms improved to these cutoffs, the continuation MST schedule resumed from where it was paused when booster sessions were initiated.

The MST and anesthesia procedures have been described in detail elsewhere.[19,20] During the acute phase, different coil placement and stimulation frequencies were tested in 4 consecutive, non-randomized cohorts: prefrontal placement, high frequency (100 Hz); prefrontal placement, medium frequency (50–60 Hz); prefrontal placement, low frequency (25 Hz); and vertex placement, high frequency (100 Hz). The placement and stimulation parameters each participant received in the acute phase were also used in the continuation phase.

Statistical Analysis

The primary outcome was the proportion of participants who had at least one assessment during their continuation MST course not meeting relapse criteria. Kaplan-Meier survival curves for time to relapse were determined for the entire group. The log rank test was used to compare diagnostic subgroups. Censored cases included dropouts at the time of last MST session or at the end of the observation period. We used Cox proportional hazards model with sex, age, diagnosis, stimulus parameter subgroups, ATHF scores, and post-acute $HDRS_{24}$ scores as covariates to explore potential moderators of relapse risk. A repeated-measures analysis of variance (RM-ANOVA) was used to determine differences in neurocognitive performance between baseline, post-acute, and post-continuation time points. Sphericity was tested with the Mauchly test, and the Greenhouse-Geisser correction was used if necessary. When applicable, post hoc tests using Bonferroni corrections were used. Neurocognitive data analysis was limited to participants who completed a post-continuation assessment at week 24, with the exception of the MoCA, which was administered throughout the treatment course, and in this case the last available observation was used. All statistical tests were 2-tailed, with significance set as $\alpha = .05$.

RESULTS

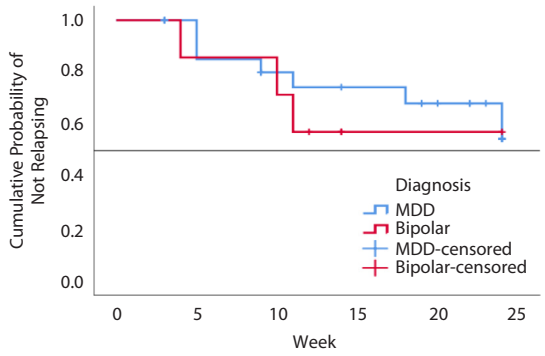
Study Sample Characteristics

Twenty-six participants with MDD and 8 participants with BD completed an adequate trial of acute MST were eligible for continuation MST. One participant refused continuation MST, preferring a less invasive continuation treatment. In total, 33 participants received continuation MST (25 with MDD, 8 with BD), with 30 completing at least 1 clinical assessment included in the analysis (Table 1). Participants represented a severely ill and treatment-resistant population.

Depression Relapse Rates

In 30 participants analyzed, 10 (33.3%) met relapse criteria during the 6-month continuation phase: 7 of 23 (30.4%) with MDD and 3 of 7 (42.9%) with BD. Fifteen (50%) of the 30 participants required booster treatments,

Figure 2. Kaplan-Meier Survival Curves Comparing Proportion of Patients With Bipolar Disorder and Major Depressive Disorder (MDD) Who Remained Free of Relapse During the 24-Week Continuation MST Treatment Phase



Abbreviation: MST = magnetic seizure therapy.

and 1 participant required a second set of booster treatments. Seven of 30 participants (23.3%) dropped out of the continuation trial, for reasons including treatment anxiety (n = 3), worsening mood although not meeting relapse criteria (n = 2), muscle and headache side effects (n = 1), and memory complaints (n = 1). Five (16.7%) had to stop MST due to a device malfunction. One participant with a diagnosis of MDD at baseline experienced a hypomanic episode that was considered as a relapse event. For those who relapsed, the mean (SD) time to relapse was 10.4 (6.9) weeks. Between stimulus parameters, the numbers meeting relapse criteria were 1 of 9 (11.1%) for prefrontal placement, high frequency; 4 of 9 (44.4%) for prefrontal placement, medium frequency; 3 of 8 (37.5%) for prefrontal placement, low frequency; and 2 of 4 (50%) for vertex placement, high frequency.

The Kaplan-Meier survival curve for relapse is shown in Figure 1. Mean (SD) survival time was 18.6 (1.6) weeks. Survival curves with diagnostic subgroups are shown in Figure 2, showing mean (SD) survival times of 17.3 (3.0) weeks for BD and 19.3 (1.8) weeks for MDD; the survival distributions of the two groups did not differ significantly ($\chi^2 = 0.3$, $P = .58$). Cox regression analyses revealed no significant moderating effects on survival time from age, sex, diagnosis, stimulus parameters, post-acute (ie, pre-continuation MST) $HDRS_{24}$ scores, or treatment resistance as per ATHF (Table 2).

Suicidality

Among the participants who completed an adequate course of continuation MST, 28 (23 with MDD and 5 with BD) were identified as being suicidal at baseline (ie, SSI score > 0), and 17 (14 MDD and 3 BD) having complete resolution of their suicidality by the end of the acute MST phase (ie, SSI score = 0). All 17 (100%) sustained resolution of their suicidality (ie, SSI score = 0) by week 24 or last observed score of the continuation phase. Three participants had a transient increase in SSI scores; by the end of the course, their SSI score was back to 0.

Table 2. Survival Analysis Results From Cox Proportional Hazards Regression Model

Variable	Hazard Ratio (95% CI)	*P* Value
Age, y	0.98 (0.91–1.07)	.68
Sex, female/male	2.18 (0.45–10.56)	.33
Stimulation parameters		
Low-front vs med-front	0.89 (0.09–8.41)	.92
Low-front vs hi-front	0.19 (0.01–2.46)	.20
Low-front vs hi-vert	1.82 (0.22–14.96)	.58
Post-acute $HDRS_{24}$ score	1.09 (0.87–1.38)	.45
Diagnosis	1.32 (0.22–7.93)	.76
ATHF	0.91 (0.79–1.06)	.23

Abbreviations: ATHF = Antidepressant Treatment History Form, cumulative score for current episode; $HDRS_{24}$ = 24-item Hamilton Depression Rating Scale; hi-front = high-frequency (100 Hz) frontal placement; hi-vert = high-frequency (100 Hz) vertex placement; low-front = low-frequency (25 Hz) frontal placement; med-front = medium-frequency (50–60 Hz) frontal placement.

Neurocognitive Outcomes

Most neurocognitive tests showed no significant differences across timepoints with a few exceptions (Table 3). In the continuation MST phase, post hoc tests revealed a significant improvement on the COWAT from post-acute to post-continuation assessments. The BVMT total scores showed significant improvement from baseline to post-acute MST. The AMI-SF showed a significant decline from baseline to post-acute MST and from baseline to post-continuation MST, but no significant changes from post-acute to post-continuation MST. There were no significant differences between timepoints for all other neurocognitive measures (Table 3).

Although the AMI-SF showed a significant decrease in scores, we hypothesized that this was primarily due to the effects of time and not due to the effects of MST. To test this hypothesis, an exploratory analysis compared the group receiving continuation MST to a comparator group of 14 participants who completed acute MST but not continuation MST and were also followed for 24 weeks. Mean (SD) score for the comparator group was 50.0 (8.0) at baseline, 40.1 (9.4) post-acute MST, and 38.6 (9.1) at 24 weeks post-MST. A 2-way RM-ANOVA found no significant differences between groups (group × time interaction: $F_{2,26} = 057$, $P = .58$), although there was a significant overall reduction in AMI-SF scores (effect of time: $F_{2,26} = 51.69$, $P < .01$).

Reorientation Time

Mean (SD) reorientation time was 18.6 (16.0) minutes after the first continuation MST session and 14.3 (10.5) minutes after the last session; the difference was not significant.

DISCUSSION

This study is the first clinical trial to assess the clinical effects of continuation MST in the prevention of depression relapse in patients with MDD or BD. Using a schedule with decreasing frequency of MST sessions, with additional booster MST sessions when needed, we observed a relapse rate of 33.3% over a 6-month period. Mean time to relapse

Table 3. Neurocognitive Outcomes[a]

Measure	Baseline Score, Mean (SD)	Post-Acute Score, Mean (SD)	Post-Continuation Score, Mean (SD)	*F*	*P*	Post Hoc Tests Mean Δ (SE)	Post Hoc Tests *P*
TMT-A	33.35 (13.53)	31.63 (16.40)	28.28 (15.17)	2.81	.10		
TMT-B	74.33 (29.85)	72.60 (29.13)	73.78 (46.44)	0.03	.94		
Symbol Coding	57.10 (14.61)	54.95 (11.54)	58.52 (14.57)	1.47	.25		
HVLT-R							
Total	26.57 (5.35)	25.71 (4.05)	26.90 (5.32)	0.81	.45		
Recall	9.10 (3.00)	9.14 (2.59)	9.48 (2.73)	0.40	.67		
Retention	87.24 (20.49)	82.15 (21.07)	88.34 (17.09)	1.11	.34		
Recognition	11.05 (1.20)	10.19 (2.65)	11.29 (0.90)	2.31	.13		
Spatial span forward	9.00 (1.75)	8.95 (1.79)	8.91 (2.02)	0.04	.96		
Spatial span backward	8.00 (2.00)	7.59 (2.06)	8.45 (1.60)	3.17	.05		
LNS	16.05 (4.43)	16.48 (4.30)	16.67 (4.14)	0.49	.61		
Mazes	13.57 (7.46)	14.71 (7.90)	14.24 (8.65)	0.51	.61		
BVMT-R							
Sum	24.10 (5.57)	27.25 (6.03)	24.90 (5.88)	4.20	.02*		
Post-acute – baseline						3.15 (0.94)	.01*
Post-cont – baseline						0.80 (1.19)	1.00
Post-cont – post-acute						−2.350 (1.23)	.22
Learning	4.80 (2.40)	3.80 (1.88)	4.30 (1.38)	1.53	.23		
Recall	9.35 (1.95)	10.15 (1.87)	9.75 (1.89)	1.29	.29		
Retention	92.36 (11.15)	94.98 (8.37)	93.82 (9.66)	0.31	.74		
Recognition	5.58 (0.69)	5.89 (0.32)	5.84 (0.37)	2.04	.14		
COWAT	42.09 (13.27)	38.23 (14.06)	44.68 (15.41)	4.72	.01*		
Post-acute – baseline						−3.86 (2.23)	.29
Post-cont – baseline						2.59 (1.92)	.58
Post-cont – post-acute						6.46 (2.18)	.02*
Categories	23.67 (7.70)	22.38 (7.31)	22.81 (7.67)	0.98	.37		
SCWT	93.45 (23.27)	95.90 (24.95)	97.25 (25.63)	1.30	.28		
SCWT time	111.81 (12.77)	110.24 (14.31)	107.29 (14.83)	2.80	.07		
MoCA	26.42 (3.54)	27.04 (2.18)	27.46 (2.17)	2.18	.13		
AMI-SF	50.73 (6.34)	40.23 (6.52)	38.55 (6.67)	50.60	<.01**		
Post-acute – baseline						−10.50 (1.04)	<.01**
Post-cont – baseline						−12.18 (1.66)	<.01**
Post-cont – post-acute						−1.68 (1.16)	<.48

[a]Statistical significance indicated by *P < .05 and **P < .01.

Abbreviations: AMI-SF = Autobiographical Memory Interview–Short Form; BVMT-R = Brief Visuospatial Memory Test–Revised; Categories = Category Fluency task, Animals subset; COWAT = Controlled Oral Word Association Test; HVLT-R = Hopkins Verbal Learning Test–Revised; LNS = letter number span; Mazes = Mazes test from the Neuropsychological Assessment Battery; MoCA = Montreal Cognitive Assessment; MST = magnetic seizure therapy; post-acute = after completion of acute MST, prior to continuation MST; post-continuation = after completion of continuation MST; SCWT = Stroop Color and Word Test; Symbol Coding = Brief Assessment of Cognition in Schizophrenia Symbol Coding; Trails A/B = Trail Making Test, Form A or B; Spatial span = Spatial span test from the Weschler Memory Scale–Third Edition.

Symbol: Δ = change.

was approximately 18 weeks. This relapse rate appears to be lower than the 50% relapse rate reported in a previous study[34] in patients who received acute MST and were followed for 6 months without continuation treatment. Furthermore, we found a sustained benefit of continuation MST on suicidality, which extends our previous result[35] showing a robust effect of acute MST on suicidality.

The 6-month relapse rate we observed with continuation MST (33.3%) is comparable to the 6-month relapse rates reported in most studies of continuation ECT.[13,16] A lower relapse rate for continuation ECT was reported in the PRIDE study (13.1% in the ECT plus pharmacotherapy arm).[17] The PRIDE study may have provided a slightly more individualized treatment schedule based on when symptoms were beginning to emerge, called the Symptom-Titrated, Algorithm-Based Longitudinal ECT (STABLE) algorithm. All patients in the PRIDE study were also started on adjunctive lithium, which has demonstrated efficacy in relapse prevention,[13] but also may increase risk of delirium when used with ECT.[36] Other factors may be that PRIDE was a study in an older sample, and older age may be associated with a lower relapse risk following ECT.[37] It remains unknown how pharmacotherapy alone compares with continuation MST in the prevention of relapse, and this requires further research. A recent meta-analysis[38] of 5 RCTs reported that continuation ECT plus pharmacotherapy is superior to continuation pharmacotherapy alone.

A Cox proportional hazards model showed no significant contributions to survival from stimulation parameters, diagnosis, sex, age, degree of treatment resistance, or depression symptom severity. However, our sample size may have been insufficient to detect any effects. While no previous studies of predictors of relapse after MST have been published, there are a few studies with ECT. In one report,[37] older age and the number of antidepressant treatment trials prior to ECT were associated with a higher risk of relapse. That study also found no moderating effects of MDD versus BD diagnosis or severity of depression. In other studies,[12,39,40] the degree of treatment resistance quantified by the ATHF predicted relapse after successful acute ECT.

Omori et al[41] conducted a retrospective analysis finding that a smaller number of episodes prior to treatment with ECT and mood-stabilizer medications was associated with lower relapse rates, with no differences between diagnoses. Thus, several reports have replicated the finding that a more severe depressive illness pre-ECT predicts a higher relapse risk post-ECT and that the relapse rates of those with MDD or BD do not differ. Future studies with larger samples will need to assess the predictors of relapse during continuation MST.

Our results showed no significant adverse cognitive effects from continuation MST. There was a significant decrease in score on the AMI-SF from baseline to post-continuation assessments, but not from post-acute to post-continuation, suggesting a decline only during the acute phase. The AMI-SF is a measure of consistency of autobiographical memory recall, which is expected to decay with time (approximately 25%–40%) in healthy populations over a few weeks to months.[42] In an RCT of depressed patients receiving ECT or pharmacotherapy alone for 6 weeks,[43] patients receiving pharmacotherapy alone had a 19.2% decrease in AMI-SF score. This is similar to our study's finding of a 20.6% decrease in score from baseline to post-acute. Thus, the decline we observed was likely due to the effects of time during the first few weeks during the acute MST phase, with stabilization during the continuation MST phase. Future studies with a comparator group are needed. Our supplementary analysis found no significant group differences on the AMI-SF between those who received continuation MST and a separate group of participants who did not. However, this analysis was limited by the absence of randomization, and most had not responded to acute MST. There were significant improvements on the BVMT-R and COWAT, measures of visual learning and verbal fluency, respectively. Both ECT and MST have been found to result in improvements in some cognitive domains, attributed to the improvement in depression.[9] Overall, our results are congruent with results from previous studies showing that MST is cognitively safe.

In conclusion, we present here the first report of continuation MST, showing two-thirds of participants sustained improvements in their depressive symptoms. In our modest sample, we identified no significant moderators of relapse risk among several demographic and clinical variables. Furthermore, resolution of suicidality was sustained during continuation MST, and there were no substantial adverse cognitive effects. Due to our modest sample size, interpretation of these results is limited and requires further validation in larger clinical trials. Other limitations included a lack of blinding and comparator group. Our results are promising and warrant further study given the known high rates of relapse in TRD. Future studies should compare the efficacy of MST relative to ECT, the current standard of convulsive brain stimulation treatments.

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