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RESEARCH ARTICLE

# Comparative effectiveness clinical trial of magnetic seizure therapy and electroconvulsive therapy in major depressive disorder

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**BACKGROUND:** Magnetic seizure therapy (MST) has demonstrated fewer cognitive side effects than electroconvulsive therapy (ECT) in antidepressant efficacy trials. However, there are no effectiveness trials examining antidepressant efficacy and cognitive side effects against ECT. The aims of this study were to evaluate the comparative effectiveness of MST vs ECT in major depressive disorder (MDD), and compare the cognitive side effects of MST and ECT.

**METHODS:** In this open-label study, patients were assigned to either ECT or high-dose MST twice a week for 5 sessions based on the clinician's and the patient's decision-making. Efficacy was primarily assessed by the Hamilton Depression Rating Scale-21 (HAMD-21); cognitive side effects were assessed by time to reorientation (TRO) and cognitive battery.

**RESULTS:** Sixty patients were enrolled. Efficacy was similar between those assigned to MST (n = 30) and ECT (n = 30). Post-treatment HAMD-21 mean scores were 12.33 after MST, 12.80 after bitemporal (BT) ECT (n = 15), and 27.93 after right unilateral (RUL) ECT (n = 15). Magnetic seizure therapy had a significantly faster TRO of 1.8 minutes (standard deviation [SD] = 0.37) compared with ECT (RUL: 18.9 minutes [SD = 8.25]; BT: 50.2 minutes [SD = 5.89]) and had fewer cognitive side effects.

**CONCLUSIONS:** Magnetic seizure therapy was effective for the treatment of MDD in real-world clinical care, with fewer cognitive side effects than ECT. Future studies are warranted to replicate these findings.

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# INTRODUCTION

Major depressive disorder (MDD) has the highest lifetime prevalence of any major psychiatric disorder in the United States and worldwide.[1,2] Electroconvulsive therapy (ECT) has been established as a viable treatment for MDD, especially in patients who do not respond to traditional antidepressant medications.[3,4] However, its cognitive side effects have been well documented.[5-9]

Magnetic seizure therapy (MST) is an alternative treatment that produces a more focal seizure in the brain[10,11]; thus, it has fewer or no cognitive side effects.[8,11,12] A number of clinical trials with parallel design comparing a full course of MST to that of ECT have demonstrated comparable efficacy.[13,14] The sample sizes of these clinical trials ranged from 20 participants[14,15] to 37 participants.[13]

Although there have been randomized efficacy clinical trials that compared MST to ECT, there have been no trials that compare the real-world effectiveness of these treatments. We wanted to address the question: "Will a given therapeutic regimen help my patient at a given point in his or her clinical course?"[16,17] In this open-label trial, patients were assigned to either arm of the study based on the clinician's decision-making in collaboration with the patient, weighing perceived and anticipated effectiveness and the adverse effect profiles of MST vs ECT. For instance, based on prior literature,[8,12] if a patient had an upcoming examination, MST would be prioritized over ECT due to potentially less impact on memory. If speed of response was of utmost importance or there was severe deterioration in functioning, ECT would be preferred. The aims of our study were to: (1) evaluate the comparative effectiveness of MST to that of ECT for patients with MDD guided by real-world clinical decision-making; and (2) compare the cognitive side effects of MST to those of ECT.

# METHODS

This study was a prospective, open-label comparative effectiveness clinical trial.

## Participants

This study was approved by the research ethics committee of the Tanta University Faculty of Medicine and registered per state standards in Egypt prior to recruitment. The study was conducted from June 2013 through October 2015 in the Centre of Psychiatry, Neurology and Neurosurgery, Tanta University (Egypt).

Researchers provided participants with full explanation of the study, including potential risks and benefits, and obtained informed consent prior to study enrollment. Consent was also obtained from the next of kin or closest caregiver of the participants (as is the common practice in this jurisdiction). All patients had the capacity to give informed consent. Patients did not receive financial compensation for their visits.

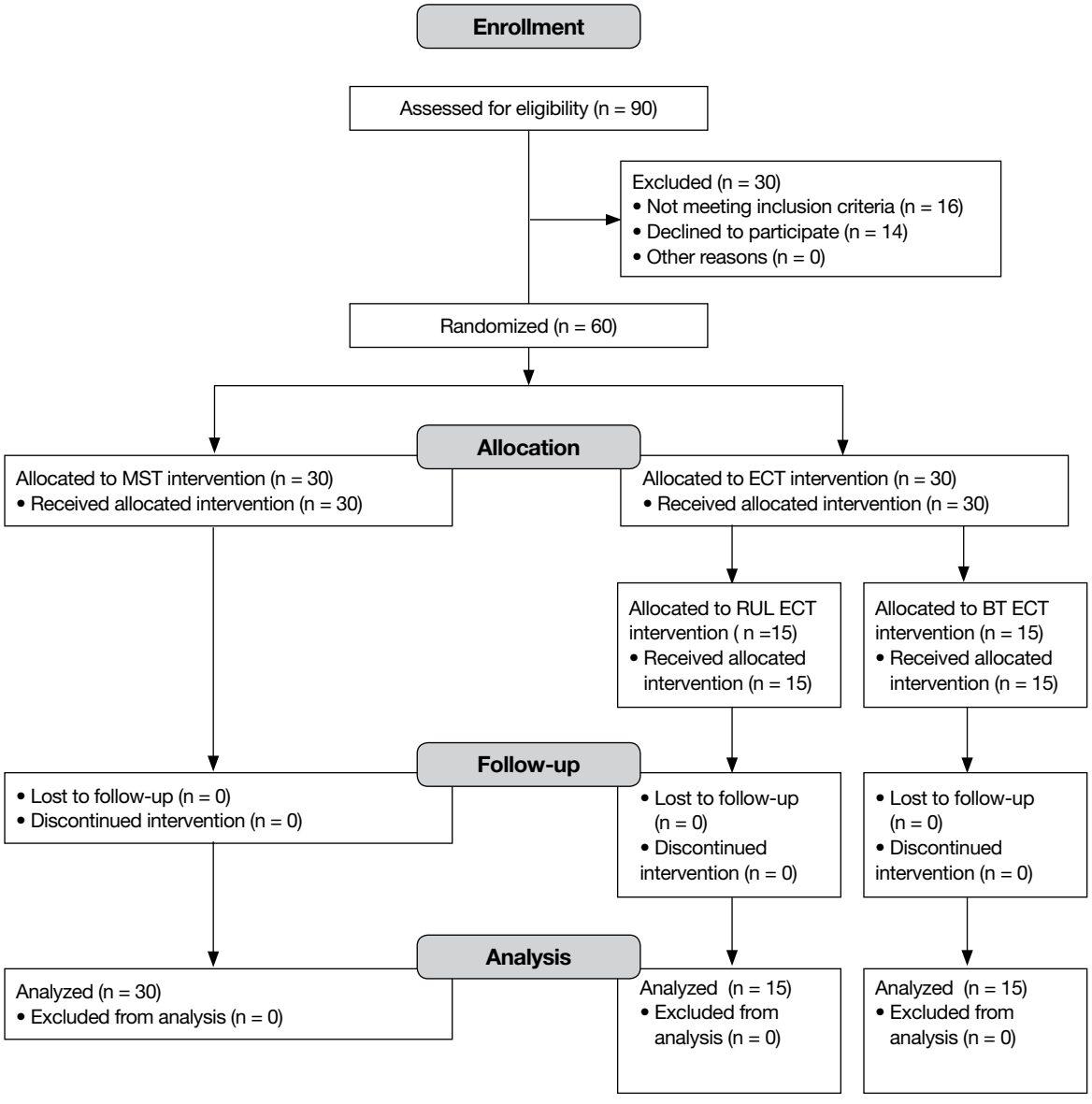
Based on the clinical assessment of the treating clinician and discussion with the patient about clinical factors, such as a need for speed of remission and higher severity (ECT) or higher risk of anticipated cognitive side effects (MST), patients were treated with either MST or ECT. This was done to be more representative of decision-making in real-life clinical situations and of the role MST could play within the clinical treatment armamentarium. The investigators of this study wanted to control for course duration, and thus all patients during the study enrollment completed 5 sessions (over 2.5 weeks) of either MST or ECT. The decision to administer 5 sessions was based on the standard of care at the institution. None of the patients were asked to stop taking their antidepressant medications. Some patients stopped taking medications on their own and were only included if they stopped the medications 6 weeks prior to enrollment. Other patients had never been treated with medications.

## Eligibility

Patients who were first clinically indicated for ECT were considered for enrollment in this study. These clinical indications included: (1) severe depression, (2) presence of suicidal ideation, (3) presence of psychotic symptoms, (4) refusal of feeding, or (5) urgent need for rapid and safe recovery.

After establishing that the patient had 1 of these clinical indications and the capacity to consent, each participant was assessed for the following additional inclusion criteria: (1) patients with MDD who had either never received antidepressant treatment or had chosen to discontinue antidepressants for at least 6 weeks prior to enrollment (as is commonly done in routine clinical care in this jurisdiction due to negative views of psychotropic medications); and (2) male or female patients age 18 to 65. Exclusion criteria were: (1) dementia, (2) delirium, (3) history of significant head trauma, (4) neurologic

**FIGURE**
**CONSORT diagram**




BT: bitemporal; CONSORT: consolidated standards of reporting trials; ECT: electroconvulsive therapy; MST: magnetic seizure therapy; RUL: right unilateral.

disorders (eg, epilepsy, stroke, multiple sclerosis), (5) substance dependence, (6) a comorbid psychiatric disorder, (7) patients who had previously received ECT or transcranial magnetic stimulation, (8) current unstable or serious medical illness (eg, myocardial infarction), (9) pregnancy, (10) presence of implanted electronic devices (eg, cardiac pacemaker, cochlear implants), and (11) inability to participate in clinical and neuropsychological testing.

## Clinical assessments

All participants underwent psychiatric and physical examinations and had their medical history recorded. The Mini International Neuropsychiatric Interview

**TABLE 1**
**Participants' demographic and clinical characteristics**

| Variable | Statistic | MST (n = 30) | ECT | | *P* |
|---|---|---|---|---|---|
| | | | BT (n = 15) | RUL (n = 15) | |
| Age | Mean (SD) | 39.07 (12.85) | 38.80 (14.0) | 39.60 (12.32) | NS |
| Female | N (%) | 17 (56.7%) | 8 (53.3%) | 5 (33.3%) | NS |
| Age of onset | Mean (SD) | 23.93 (8.17) | 25.47 (9.33) | 30.20 (10.52) | NS |
| Family history of depression | N (%) | 13 (43.3%) | 5 (33.3%) | 3 (20.0%) | NS |
| Number of depressive episodes | Mean (SD) | 8.67 (5.35) | 7.47 (6.60) | 6.07 (4.27) | NS |
| Length of current depressive episode (months) | Mean (SD) | 7.73 (5.66) | 6.00 (5.41) | 5.73 (4.03) | NS |
| Presence of psychotic symptoms | N (%) | 11 (36.7%) | 4 (26.7%) | 2 (13.3%) | NS |
| Presence of suicide ideation | N (%) | 13 (43.3%) | 5 (33.3%) | 0 (0.0%) | .006 |

BT: bitemporal; ECT: electroconvulsive therapy; MST: magnetic seizure therapy; NS: not significant; RUL: right unilateral; SD: standard deviation.

Plus (MINI Plus) Arabic version, translated by Ghanem et al[18] from Sheehan et al,[19] was used as a structured diagnostic interview for the diagnosis of a current depressive episode of MDD, according to DSM-IV-TR. Baseline and endpoint assessments of efficacy of treatment included the Hamilton Depression Rating Scale-21 (HAMD-21)[20] and the Beck Depression Inventory (BDI).[21,22]

## Cognitive assessments

The time to reorientation (TRO) was measured after the patient's recovery immediately after the procedure as the primary cognitive outcome. Recovery was defined as the time when patients could breathe independently after anesthesia.[14] A stopwatch was used to measure recovery time. Time to reorientation was defined as the time it took for a patient to recall 4 of the following 5 items: name, date of birth, age, place, and day of the week.[23] A stopwatch was used for accurate calculation of time elapsed between independent respiration and the ability to recall 4 of the 5 items. Patients were interrogated as soon as spontaneous respiration was observed.

Other neuropsychological testing was conducted 4 hours after MST/ECT treatment to ensure full recovery from anesthesia.[14] The rationale for conducting the cognitive testing on the same day of the session and 4 hours after the last session was that patients are less likely to return for cognitive testing on another day (and thus were assessed on the day of treatment to reduce missing data). The measures employed included 3 subtests from the Wechsler Memory Scale–Revised: Information/Orientation (orientation), Verbal Paired Associates I (immediate recall), and Verbal Paired Associates II (delayed recall); and the Wisconsin Card Sorting Test 64-card version (executive function [ie, concentration, planning, organization]). These tests were used to assess for cognitive side effects. They were administered before and after the first session, and were repeated after the third and fifth sessions. Alternate forms of the tests were used at baseline and post-treatment, if available, as a precautionary measure to reduce practice effects.[24]

Assessment of subjective side effects was performed by clinical interview and by using the Columbia ECT subjective side effects schedule.[25]

## ECT administration

Before patients received ECT, a thorough evaluation was performed to ensure safe administration of anesthetics and appropriateness for ECT, including a complete medical history, physical examination, and routine laboratory tests (blood glucose, complete metabolic panel, electrocardiogram [ECG], and any clinically indicated test based on the clinical condition). Right unilateral (RUL) ECT or bitemporal (BT) ECT was performed using a Thymatron IV device (Somatics LLC., USA). Heart rate, blood pressure, $O_2$ saturation, and ECG were monitored during the procedure. A bite-block was inserted prior to seizure elicitation to protect the patient's teeth as per standard of care. The ECT stimulus used was brief pulse

**TABLE 2**
**Time to reorientation after 1, 3, and 5 sessions**

| | | | ECT | | | |
|---|---|---|---|---|---|---|
| | Statistic | MST (n = 30) | BT (n = 15) | RUL (n = 15) | F | *P*[a] |
| After Session 1 (minutes) | Mean (SD) | 1.82 (0.36) | 49.27 (5.82) | 18.77 (8.23) | 449.94 | <.001 |
| After Session 3 (minutes) | Mean (SD) | 1.78 (0.37) | 49.68 (5.82) | 18.87 (8.23) | 458.48 | <.001 |
| After Session 5 (minutes) | Mean (SD) | 1.83 (0.37) | 50.75 (5.95) | 19.01 (8.27) | 467.71 | <.001 |

[a]*P* value for ANOVA with repeated measures.

ANOVA: analysis of variance; BT: bitemporal; ECT: electroconvulsive therapy; MST: magnetic seizure therapy; RUL: right unilateral; SD: standard deviation.

(0.5 msec), with age-based dosing as per the standard of the institution. In age-based dosing, the % Energy was set to age for RUL ECT and to half-age for BT ECT, as described by Petrides and Fink.[26] Treatments were applied twice a week.

## MST administration

For MST, preparation and pretreatment evaluation were conducted in the same way as ECT. Moreover, to protect hearing and minimize exposure to the high-decibel noise of the MST device, staff and patients wore earplugs during MST sessions. As is a standard protective measure for ECT, a bite-block was inserted immediately prior to seizure elicitation to protect the patient's teeth (it was noted, however, that MST did not produce the marked jaw contraction as typically seen with ECT). The temperature in the ECT suite, where MST was also performed, was maintained below 30°C for the proper operation of the MST device (the MST stimulus would stop if the temperature rose to this level) using air conditioning that was 3 times more powerful than necessary for the room area. The coil was removed from the patient's head immediately after the 10-second stimulation, because the coil can become hot. High-dose MST (HD-MST) was given using a Magstim Theta device (Magstim Company Limited, Whitfield, Wales, UK). Magnetic seizure therapy was given by using a circular coil with 100% maximal output of the device, which was constant, with a pulse frequency of 100 Hz and train duration of 10 seconds. These parameters were based on prior MST studies.[7,23] The center of the circular MST coil was positioned over the vertex (halfway point from the nasion to the inion at the sagittal plane).[23] Vertex stimulation was chosen because past MST studies suggested it for reliable seizure induction[7,14] and to avoid the possibility of failure of seizure induction by frontal stimulation.[23]

Because prior research showed minimal to no cognitive side effects from MST, and to maximize the robustness of the antidepressant effects of MST, we decided to conduct MST without titration of the seizure threshold at the first treatment by immediately using HD-MST at twice weekly sessions (as per the routine in this institution). There were no requirements for minimum seizure duration for either MST or ECT.

## Anesthesia

All patients underwent general anesthesia, and followed the same anesthesia protocol regardless of treatment arm. Atropine was given 2 minutes before anesthesia induction. Anesthesia was induced using IV propofol (1.0 to 1.5 mg/kg). The muscle relaxant used was IV succinylcholine (0.5 to 1.0 mg/kg), which was administered 1 minute after the anesthetic agent. Patients were ventilated with 100% $O_2$; vital signs were monitored from the time of anesthetic administration until the return of spontaneous respiration. Doses of atropine, propofol, and succinylcholine were held constant across the 5 study sessions.

## EEG acquisition and ictal monitoring

Seizure expression was monitored by bilateral frontomastoid EEG and inspection of motor manifestations.

## Statistical analysis

The data were visualized and assessed for normality of distribution. For the normally distributed data, comparison between the 2 groups was done using independent *t* test, whereas analysis of variance (ANOVA) was used for comparison between >2 groups. Paired

**TABLE 3A**
**Subtest scores from the Wechsler Memory Scale–Revised: Baseline and after 1, 3, and 5 sessions**

| | | | ECT | | |
|---|---|---|---|---|---|
| | Statistic | MST (n = 30) | BT (n = 15) | RUL (n = 15) | F ($P^a$) |
| Baseline | Mean (SD) | 13.83 (0.38) | 13.87 (0.35) | 13.93 (0.26) | 0.417 (.66) |
| After Session 1 | Mean (SD)<br>$P_{Base}$ | 14.00 (0.00)<br>.023 | 13.20 (0.68)<br><.001 | 13.67 (0.49)<br>.041 | 18.886<br>(<.001) |
| After Session 3 | Mean (SD)<br>$P_{Base}$ | 14.00 (0.00)<br>.023 | 12.27 (0.70)<br><.001 | 13.73 (0.46)<br>.082 | 89.92<br>(<.001) |
| After Session 5 | Mean (SD)<br>$P_{Base}$ | 14.00 (0.00)<br>.023 | 10.93 (1.03)<br><.001 | 12.87 (0.92)<br><.001 | 100.65<br>(<.001) |
| **Verbal Paired Associates I** | | | | | |
| Baseline | Mean (SD) | 18.17 (1.32) | 18.73 (1.44) | 18.53 (1.55) | 0.901 (.41) |
| After Session 1 | Mean (SD)<br>$P_{Base}$ | 19.27 (1.34)<br><.001 | 17.33 (1.35)<br><.001 | 18.33 (1.29)<br>.082 | 10.862<br>(<.001) |
| After Session 3 | Mean (SD)<br>$P_{Base}$ | 21.47 (1.07)<br><.001 | 16.53 (0.74)<br><.001 | 18.33 (1.68)<br>.189 | 94.95<br>(<.001) |
| After Session 5 | Mean (SD)<br>$P_{Base}$ | 23.53 (0.63)<br><.001 | 14.87 (1.19)<br><.001 | 18.33 (1.68)<br>.271 | 327.77<br>(<.001) |
| **Verbal Paired Associates II** | | | | | |
| Baseline | Mean (SD) | 6.57 (0.50) | 6.73 (0.46) | 6.80 (0.41) | 1.421 (.250) |
| After Session 1 | Mean (SD)<br>$P_{Base}$ | 7.20 (0.41)<br><.001 | 5.87 (0.35)<br><.001 | 6.80 (0.41)<br>-- | 56.787<br>(<.001) |
| After Session 3 | Mean (SD)<br>$P_{Base}$ | 7.83 (0.38)<br><.001 | 5.20 (0.68)<br><.001 | 6.73 (0.46)<br>0.334 | 147.56<br>(<.001) |
| After Session 5 | Mean (SD)<br>$P_{Base}$ | 7.93 (0.25)<br><.001 | 4.40 (0.83)<br><.001 | 6.80 (0.41)<br>-- | 256.63<br>(<.001) |

[a]*P* value for ANOVA with repeated measures.

ANOVA: analysis of variance; BT: bitemporal; ECT: electroconvulsive therapy; MST: magnetic seizure therapy; RUL: right unilateral; SD: standard deviation.

*t* test was used to analyze the paired data. Comparison between different periods was performed using ANOVA with repeated measures and using Bonferroni correction. Significance was set at the 0.05 level. SPSS version 20.0 was used for the statistical analyses.

# RESULTS

## Demographic and clinical characteristics

Data from the total sample includes 60 participants (30 males and 30 females) whose ages ranged from 22 to 61 (demographic and clinical characteristics are summarized in TABLE 1). Thirty patients received MST, and 30 patients received ECT (15 received RUL and 15 BT) (FIGURE). There were no problems in inducing seizures in any of the groups.

## Cognitive outcomes

In the MST group, the mean TRO after the first session was 1.82 (±0.36) minutes, and the mean TRO was 1.81 (±0.37) minutes in subsequent sessions. The BT-ECT group yielded a mean TRO of 49.27 (±5.82) minutes after the first session and mean of 50.22 (±5.89) minutes in subsequent sessions. The RUL-ECT group yielded a mean TRO of 18.77 (±8.23) minutes in the first session and 18.94 (±8.25) minutes in subsequent sessions (TABLE 2). For all sessions, the difference was statistically significant between the MST and BT-ECT groups ($P \leq .001$) and statistically significant between the MST and RUL-ECT groups ($P \leq .001$).

The Information/Orientation subtest of the Wechsler Memory Scale was performed to measure the patients' level of orientation. Baseline scores between groups were not statistically significant; scores among patients in the

**TABLE 3B**
**Correct response scores from the Wisconsin Card Sorting Test: Baseline and after 1, 3, and 5 sessions**

| | | | ECT | | |
|---|---|---|---|---|---|
| | Statistic | MST (n = 30) | BT (n = 15) | RUL (n = 15) | F (*P*[a]) |
| Baseline | Mean (SD) | 46.53 (3.29) | 47.27 (3.58) | 47.80 (3.23) | 0.764 (.470) |
| After Session 1 | Mean (SD) | 49.63 (2.03) | 45.07 (3.53) | 47.20 (3.28) | 13.976 |
| | *P*Base | <.001 | <.001 | <.001 | (<.001) |
| After Session 3 | Mean (SD) | 51.93 (1.28) | 42.73 (4.40) | 46.73 (3.56) | 51.604 |
| | *P*Base | <.001 | <.001 | .001 | (<.001) |
| After Session 5 | Mean (SD) | 56.63 (2.36) | 37.87 (3.38) | 43.80 (3.67) | 224.40 |
| | *P*Base | <.001 | <.001 | <.001 | (<.001) |

[a]*P* value for ANOVA with repeated measures.

ANOVA: analysis of variance; BT: bitemporal; ECT: electroconvulsive therapy; MST: magnetic seizure therapy; RUL: right unilateral; SD: standard deviation.

MST group improved from 13.83 to an average of 14.00 after treatment (on a scale of 0 to 14, mean increase of 0.17 points) (TABLE 3A). Scores among patients in the BT-ECT group decreased from 13.87 (±0.35) at baseline to 10.93 (±1.03) after treatment (mean reduction of 3.04 points), while scores among those in the RUL-ECT group decreased from 13.93 (±0.26) to 12.87 (±0.92) (mean reduction of 1.06 points). Among patients who underwent MST, no deterioration in orientation was observed.

The Verbal Paired Associates II subtest of the Wechsler Memory Scale was performed to measure delayed recall. Baseline scores between groups were not statistically significant (TABLE 3A). Scores among patients in the MST group improved from a baseline mean of 6.57 (±0.50) to 7.93 (±0.25) after treatment (mean increase of 1.36 points). Scores among patients in the BT-ECT group decreased from 6.73 (±0.46) at baseline to 4.40 (±0.83) after treatment (mean reduction of 2.33 points), while scores among those in the RUL-ECT group remained unchanged at 6.40 (±0.41) points. Among patients who underwent MST, no deterioration in verbal memory (delayed recall) was observed.

The Wisconsin Card Sorting Test (64-card version) was performed to measure executive functioning. Baseline scores between groups were not statistically significant (TABLE 3B). Patients in the MST group showed an improvement in score, from 46.53 (±3.29) at baseline to 56.63 (±2.36) post-treatment (mean increase of 10.1 points). Patients in the BT-ECT group had decreased scores post-treatment, from 47.27 (±3.58) at baseline to 37.87 (±3.38) after treatment (mean reduction of 9.3 points), while patients in the RUL-ECT group had a less pronounced decrease in scores from 47.80 (±3.23) at baseline to 43.80 (±3.67) post-treatment (mean reduction of 4.0 points).

Although there was significant advantage to MST on cognitive scales of Wechsler Memory Scale and Wisconsin Card Sorting Test 4 hours after session, it is difficult to ascertain whether these differences would persist with long-term follow-up.

## Depression outcomes

***Pre/post comparisons*** **(TABLE 4).** Participants' HAMD-21 scores improved by a mean of 24.3 points in those who received MST, 23.3 points in those who received BT ECT, and 6.5 points in those who received RUL ECT. The differences in improvement were not statistically significant between MST and BT ECT, but were statistically significant between MST and RUL ECT. The differences in baseline HAMD-21 scores were not statistically significant between groups (TABLE 4).

The differences in baseline BDI scores were not statistically significant between the 3 groups. Participants' BDI depression scores were reduced by a mean of 31.0 points in those who received MST, 29.7 points in those who received BT ECT, and 11.8 points in those who received RUL ECT.

***Comparison between intervention groups.*** The mean HAMD-21 score after treatment in the MST group was 12.33 (± 4.97), compared with 12.80 (±4.86) in the BT-ECT group and 27.93 (±2.02) in the RUL-ECT group. The difference between the MST and BT-ECT groups was not statistically significant ($P$ = .739) and but was statistically significant between the MST and

**TABLE 4**
**Baseline and post-treatment clinical assessments for depression**

| Assessment | Statistic | MST (n = 30) | ECT | | F | *P*[a] |
|---|---|---|---|---|---|---|
| | | | BT (n = 15) | RUL (n = 15) | | |
| HAMD-21 baseline | Mean (SD) | 36.63 (3.57) | 36.07 (3.26) | 34.40 (3.68) | 2.024 | .142 |
| HAMD-21 post-treatment | Mean (SD) | 12.33 (4.97) | 12.80 (4.86) | 27.93 (2.02) | 69.33 | <.001 |
| Response to treatment | N (%) | 27 (90%) | 13 (86.6%) | 5 (33.3%) | | |
| BDI baseline | Mean (SD) | 45.87 (4.08) | 44.67 (3.04) | 43.73 (3.20) | 1.818 | .172 |
| BDI post-treatment | Mean (SD) | 14.87 (5.10) | 14.93 (5.09) | 31.93 (1.75) | 80.35 | <.001 |

[a]*P* value for ANOVA with repeated measures.

ANOVA: analysis of variance; BDI: Beck Depression Inventory; BT: bitemporal; ECT: electroconvulsive therapy; HAMD-21: Hamilton Depression Rating Scale-21; MST: magnetic seizure therapy; RUL: right unilateral; SD: standard deviation.

RUL-ECT groups ($P \leq .001$), which conservatively suggests a similar effectiveness between the MST and ECT groups.

The mean BDI score after treatment in the MST group was 14.87 (±5.10), compared with 14.93 (±5.09) in the BT-ECT group and 31.93 (±1.75) in the RUL-ECT group. The difference between the MST and BT-ECT groups was not statistically significant ($P = .963$) but was statistically significant between MST and RUL-ECT groups ($P \leq .001$).

Regarding subjective side effects, body ache was reported by 1 patient in the MST group, 6 patients in the BT-ECT group, and 2 patients in the RUL-ECT group. After the first session of therapy, headache was reported by 6 patients in the BT-ECT group, 1 patient in the RUL-ECT group, and no patients in the MST group. Also after the first session, memory problems were not reported by any patients in any group. In subsequent sessions, memory problems were reported by none of the patients in the MST group, 43.4% of the BT-ECT group, and 10.0% of the RUL-ECT group.

## DISCUSSION

This study examined the comparative effectiveness of MST and ECT. The study found both therapies were equally effective in treating MDD. Magnetic seizure therapy was associated with fewer cognitive side effects, including a significantly faster TRO when compared with ECT.

Regarding the efficacy of MST, statistically significant differences were found between mean baseline HAMD-21 scores compared with post-MST scores. This demonstrates a significant antidepressant effect of MST in patients with MDD, which has been observed in previous studies.[7,14,15,27]

Our study found a faster TRO following MST compared with ECT; this measurement has demonstrated to be a strong predictor of memory side effects in follow-up in prior studies,[28-30] and is commonly used in clinical seizure therapy trials to predict long-term cognitive side effects.[23,31-35] Our results are consistent with previous studies that employed similar criteria and methods for collecting TRO data. Among these are a trial that measured a mean TRO across all sessions of 1.38 minutes.[7] Another study reported a mean TRO of 2.27 minutes in MST and 8.35 minutes in ECT ($P = .01$),[14] which was corroborated by a later study that reported a mean TRO of 2.08 minutes in MST and 7.72 minutes in ECT ($P = .008$).[10]

Regarding other cognitive tests, there was an advantage for MST over ECT, but because these tests were not done with long-term follow-up, the clinical significance of these results should be interpreted with caution.

Based on our criteria for clinical effectiveness, MST was measured to be nearly as effective as BT-ECT and at least as effective as RUL-ECT in this comparative

effectiveness study. This finding varies from earlier efficacy trials comparing MST with ECT. It should also be noted that earlier trials used a lower frequency[15] or an earlier model of the device than what was employed in our study. Recent studies using HD-MST devices have found no difference in effectiveness between MST and RUL-ECT.[14] However, this needs further replication.

These data are in concurrence with previous investigations, suggesting similar improvement of MST on various versions of the HAMD[7,15,27,36] compared with ECT.[14,36]

Several clinical trials have demonstrated fewer or no cognitive side effects of MST compared with RUL-ECT. Although there is still work to be done to establish the efficacy and effectiveness of MST compared with ECT, several clinical trials have already been conducted to examine efficacy of MST in depression. However, no prior studies have examined the real-world effectiveness of MST vs ECT. Thus, this study has filled this gap by examining the effectiveness of utilizing clinical decision-making in stratifying patients to either ECT or MST and the outcomes of that decision on real-world treatment situations.

### Limitations

Our study has several limitations, including: (1) the clinical trial was not randomized or blinded (open-label); (2) long-term effectiveness of MST in patients with MDD was not examined; (3) although the sample size of our study was comparable with that of earlier clinical trials of MST, it still was not large enough, especially regarding real-world clinical effectiveness, considering that our study included 3 groups, and the 2 ECT groups containing only 15 patients each; (4) performing the cognitive assessments at 4 hours may not reflect the long-term cognitive side effects. Thus, the clinical advantage based on these cognitive tests should be interpreted with caution. This is especially the case if cognitive side effects from MST improve faster than ECT, although data regarding this are not yet clear. However, TRO is a good predictor of longer-term cognitive side effects.[37] Also, the results of fewer cognitive side effects in MST compared with ECT are in agreement with prior studies.

This study represents the first study in the direction of comparative effectiveness spectrum.[16,17] Despite not being randomized to simulate real-word decision-making, this study matched age and gender and these variables were equally distributed between groups. It is also the largest study to date comparing MST vs ECT. It was a medication-free trial, which is common in real-world practice in this center and jurisdiction. This can be seen as a less generalizable practice in some other centers around the world; however, one strength is that these data provide for the first time an unaltered measure of the effectiveness of MST vs ECT without the confounding effect of medication on either the antidepressant response or seizure threshold.

## CONCLUSIONS

In this comparative effectiveness trial, MST was efficacious in treating patients with MDD, and possibly produced fewer cognitive side effects than ECT. Magnetic seizure therapy was feasible and safe in this population, and may have better chances of effectiveness when clinicians stratify patients based on need by weighing the protection of cognition and the speed and certainty of treatment response.

Larger comparative effectiveness studies are needed to replicate these findings. In addition, future studies are needed to optimize MST electrode placement and parameters. ■

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REFERENCES

1. Lepine JP, Briley M. The increasing burden of depression. Neuropsychiatr Dis Treat. 2011;7(suppl 1): 3-7.
2. Kessler RC, Berglund P, Demler O, et al; National Comorbidity Survey Replication. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA. 2003; 289:3095-3105.
3. Kellner CH, Greenberg RM, Murrough JW, et al. ECT in treatment-resistant depression. Am J Psychiatry. 2012;169:1238-1244.
4. Kraus C, Kadriu B, Lanzenberger R, et al. Prognosis and improved outcomes in major depression: a review. Transl Psychiatry. 2019;9:127.
5. Calev A, Nigal D, Shapira B, et al. Early and long-term effects of electroconvulsive therapy and depression on memory and other cognitive functions. J Nerv Ment Dis. 1991;179:526-533.
6. Daskalakis ZJ, Dimitrova J, McClintock SM, et al. Magnetic seizure therapy (MST) for major depressive disorder. Neuropsychopharmacology. 2020;45:276-282.
7. Fitzgerald PB, Hoy KE, Herring SE, et al. Pilot study of the clinical and cognitive effects of high-frequency magnetic seizure therapy in major depressive disorder. Depress Anxiety. 2013;30:129-136.
8. Polster JD, Kayser S, Bewernick BH, et al. Effects of electroconvulsive therapy and magnetic seizure therapy on acute memory retrieval. J ECT. 2015;31:13-19.
9. McClintock SM, Choi J, Deng ZD, et al. Multifactorial determinants of the neurocognitive effects of electroconvulsive therapy. J ECT. 2014;30:165-176.
10. Kayser S, Bewernick BH, Hurlemann R, et al. Comparable seizure characteristics in magnetic seizure therapy and electroconvulsive therapy for major depression. Eur Neuropsychopharmacol. 2013;23: 1541-1550.
11. Deng ZD, Lisanby SH, Peterchev AV. Effect of anatomical variability on neural stimulation strength and focality in electroconvulsive therapy (ECT) and magnetic seizure therapy (MST). Conf Proc IEEE Eng Med Biol Soc. 2009;2009:682-688.
12. McClintock SM, Tirmizi O, Chansard M, et al. A systematic review of the neurocognitive effects of magnetic seizure therapy. Int Rev Psychiatry. 2011; 23:413-423.
13. Fitzgerald PB, Hoy KE, Elliot D, et al. A pilot study of the comparative efficacy of 100 Hz magnetic seizure therapy and electroconvulsive therapy in persistent depression. Depress Anxiety. 2018;35:393-401.
14. Kayser S, Bewernick BH, Grubert C, et al. Antidepressant effects, of magnetic seizure therapy and electroconvulsive therapy, in treatment-resistant depression. J Psychiatr Res. 2011;45:569-576.
15. White PF, Amos Q, Zhang Y, et al. Anesthetic considerations for magnetic seizure therapy: a novel therapy for severe depression. Anesth Analg. 2006;103: 76-80, table of contents.
16. Lin CH, Huang CJ, Chen CC. ECT has greater efficacy than fluoxetine in alleviating the burden of illness for patients with major depressive disorder: a Taiwanese pooled analysis. Int J Neuropsychopharmacol. 2018;21:63-72.
17. Singal AG, Higgins PD, Waljee AK. A primer on effectiveness and efficacy trials. Clin Transl Gastroenterol. 2014;5:e45. doi: 10.1038/ctg.2013.13.
18. Ghanem MH, Ibrahim M, El Behairy A, et al. Mini International Neuropsychiatric Interview for children/ adolescents (MINI Kid); Arabic version. Cairo, Egypt: Department of Neuropsychiatry, Ain Shams University; 1999.
19. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998;59(suppl 20):22-33; quiz 34-57.
20. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960;23:56-62.
21. Beck AT, Steer RA, Ranieri WF. Scale for suicide ideation: psychometric properties of a self-report version. J Clin Psychol. 1988;44:499-505.
22. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. Arch Gen Psychiatry. 1961; 4:561-571.
23. Kirov G, Ebmeier KP, Scott AI, et al. Quick recovery of orientation after magnetic seizure therapy for major depressive disorder. Br J Psychiatry. 2008;193: 152-155.
24. Benedict RH, Zgaljardic DJ. Practice effects during repeated administrations of memory tests with and without alternate forms. J Clin Exp Neuropsychol. 1998; 20:339-352.
25. Sackeim HA, Decina P, Portnoy S, et al. Studies of dosage, seizure threshold, and seizure duration in ECT. Biol Psychiatry. 1987;22:249-268.
26. Petrides G, Fink M. The "half-age" stimulation strategy for ECT dosing. Convuls Ther. 1996;12: 138-146.
27. Kayser S, Bewernick BH, Matusch A, et al. Magnetic seizure therapy in treatment-resistant depression: clinical, neuropsychological and metabolic effects. Psychol Med. 2015;45:1073-1092.
28. Martin DM, Gálvez V, Loo CK. Predicting retrograde autobiographical memory changes following electroconvulsive therapy: relationships between individual, treatment, and early clinical factors. Int J Neuropsychopharmacol. 2015;18:pyv067. doi: 10.1093/ ijnp/pyv067.
29. Sobin C, Sackeim HA, Prudic J, et al. Predictors of retrograde amnesia following ECT. Am J Psychiatry. 1995;152:995-1001.
30. Sackeim HA, Luber B, Moeller JR, et al. Electrophysiological correlates of the adverse cognitive effects of electroconvulsive therapy. J ECT. 2000; 16:110-120.
31. Youssef NA, Ravilla D, Patel C, et al. Magnitude of reduction and speed of remission of suicidality for low amplitude seizure therapy (LAP-ST) compared to standard right unilateral electroconvulsive therapy: a pilot double-blinded randomized clinical trial. Brain Sci. 2019;9:99.
32. Youssef NA, Sidhom E. Feasibility, safety, and preliminary efficacy of low amplitude seizure therapy (LAP-ST): a proof of concept clinical trial in man. J Affect Disord. 2017;222:1-6.
33. Lisanby SH, Luber B, Schlaepfer TE, et al. Safety and feasibility of magnetic seizure therapy (MST) in major depression: randomized within-subject comparison with electroconvulsive therapy. Neuropsychopharmacology. 2003;28:1852-1865.
34. Kellner CH, Husain MM, Knapp RG, et al; CORE/ PRIDE Work Group. Right unilateral ultrabrief pulse ECT in geriatric depression: phase 1 of the PRIDE study. Am J Psychiatry. 2016;173:1101-1109.
35. Sahlem GL, McCall WV, Short EB, et al. A two-site, open-label, non-randomized trial comparing focal electrically-administered seizure therapy (FEAST) and right unilateral ultrabrief pulse electroconvulsive therapy (RUL-UBP ECT). Brain Stimul. 2020;13:1416-1425.
36. Wani A, Trevino K, Marnell P, et al. Advances in brain stimulation for depression. Ann Clin Psychiatry. 2013;25:217-224.
37. Tripathi C, Khan B, Youssef NA. Need for standardization of measurement of time to reorientation as a predictor of cognitive adverse effects of electroconvulsive therapy. J ECT. 2020. doi: 10.1097/ YCT.0000000000000703.

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