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Cardiovascular Effects of High-Frequency Magnetic Seizure Therapy Compared With Electroconvulsive Therapy

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Background: Magnetic seizure therapy (MST) is a novel convulsive therapy that has been shown to have antidepressant efficacy comparable to electroconvulsive therapy (ECT) with fewer cognitive side effects. However, the cardiovascular (CVS) effects of high frequency MST in comparison to ECT have not been investigated.

Materials and Methods: Forty-five patients with depression received 6 treatment sessions of 100 Hz MST versus 6 bifrontal ECT treatments in a nonrandomized comparative clinical design. Data on CVS function including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and rate pressure product (RPP) were collected at baseline (T0), after the induction of anesthesia but before the electrical stimulation (T1), during convulsion (T2), 2 minutes after cessation of motor seizure (T3), 5 minutes after cessation of motor seizure (T4), and 10 minutes after cessation of motor seizure (T5). Comparisons were made with baseline data and between MST and ECT groups.

Results: There were statistically significant elevations in the maximum HR, SBP, DBP, and RPP in patients receiving ECT compared with MST both in the initial and sixth treatments (all $P < 0.05$). Particularly, at T2, the ECT group had significantly higher HR, SBP, DBP, and RPP than those in MST group both in initial and sixth treatment (all $P < 0.001$). At the sixth treatment, the ECT group had significantly higher SBP, DBP, and RPP during the treatment than in the MST group (all $P < 0.001$).

Limitations: The anesthetic choices for this study may limit the generalizability of our findings. The sample size was relatively small.

Conclusions: Compared with ECT, high-frequency MST has fewer CVS side effects and may be a safer option for depression patients with CVS disorders.

Key Words: magnetic seizure therapy, electroconvulsive therapy, cardiovascular effects

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Electroconvulsive therapy (ECT) is the most efficacious treatment for depression, which does not respond to antidepressant therapy.[1] Electroconvulsive therapy has long been known to affect the autonomic nervous system,[2,3] and it may lead to transient blood pressure elevation or even an acute hypertensive crisis or tachycardia.[4,5] Previous studies suggested that the cardiovascular (CVS) effects of ECT were related to the generalized convulsion induced by ECT in the cerebral cortex, especially hypothalamus, striatum, and hippocampus areas.[6,7] Some studies suggested that greater hemodynamic response (eg, increase in HR and BP) during ECT is associated with greater therapeutic benefits.[8] Other studies suggested that there was no correlation of hemodynamic impact and antidepressant efficacy of ECT.[9,10]

Magnetic seizure therapy (MST) is a promising alternative to ECT with similar antidepressant efficacy and fewer cognitive effects relative to ECT.[11–17] Previous studies have shown that the magnetoelectric field of MST stimulates the cortex more focally than the ECT stimulus and depolarizes neurons resulting in a secondary electric field to induce seizure activity.[18,19] Studies also demonstrated that MST stimulation over the vertex could reliably induce seizures and result in a quicker recovery of orientation relative to ECT.[20,21]

It is known that partial and generalized seizures alter autonomic function during ictal, postictal, and interictal states.[22] All aspects of autonomic function can be affected, including the parasympathetic, sympathetic, and adrenal medullary systems. Ictal autonomic changes can cause physiological changes involving the CVS, respiratory, gastrointestinal, and other systems. Sinus tachycardia can occur in more than 85% of complex partial and tonic-clonic seizures.[23]

To our knowledge, there were only 2 published studies comparing CVS effects between ECT and MST. An early (2009) nonhuman study involving 24 rhesus monkeys found significant differences in HR changes in the immediate poststimulus, ictal and postictal epochs between animals receiving MST and ECT. The ECT group showed significantly more tachycardia than MST or sham in both the ictal and postictal periods. This study also found that HR increased by 25% in the ECT and 8% in MST groups, respectively.[24]

Another clinical study[25] examined CVS function in 20 case-matched depressed patients receiving MST or ECT. This study demonstrated that patients receiving 50 Hz MST required significantly lower doses of nicardipine than patients in the ECT group. One limitation of this study is that the investigators did not demonstrate significant differences in HR or mean arterial blood pressure. Another limitation of this study was that the MST stimulation was suboptimal (i.e., 50 Hz for 8 seconds), and the efficacy of MST was significantly less than the ECT group. The MST stimulator maximal output currently used in clinical practice is 100 Hz for 10 seconds.[26] This study examines the CVS effects of 100 Hz MST versus ECT at comparable levels of cerebral stimulation.

METHODS AND MATERIALS

Study Design and Participants

The study used a rater-blinded, nonrandomized comparative design. Eligible patients were offered either MST or ECT treatment in addition to medication treatment. The patient's physician and the patient or their legal guardians decided which arm (MST

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or ECT) to enter for the clinical trial. The data analyzers and clinical assessors were blind to the patients' group assignment. This study was approved by the Ethics Committee of Beijing Anding Hospital, Capital Medical University. All participants or their legal guardians provided written informed consent before entering the study. The trial was registered in the Chinese Clinical Trial Register (ChiCTR-ONN-17010740) on February 27, 2017.

Fifty-two patients, aged 18 to 60 years were enrolled at Beijing Anding Hospital, Capital Medical University (Beijing, China), from July 2016 to November 2018. The inclusion criteria were as follows: met the diagnostic criteria for a major depressive episode (including both major depressive disorder and bipolar disorder type II, depressed phase) based on assessments using the Structured Clinical *Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*,[27] 17-item Hamilton Depression Rating Scale score (HAMD-17) of 17 or greater[28]; consented to convulsive therapy as recommended by the patient's physician. The exclusion criteria included comorbid axis I psychiatric disorders (eg, current substance abuse or dependence and dementia). Exclusion criteria included unstable medical conditions, pregnancy, being on antiepileptic medications and a known history of allergies to propofol or succinylcholine.

Antidepressants were allowed but the medications had to be kept unchanged for 1 week prior to and during the study. Benzodiazepines were not allowed 12 hours before the first MST/ECT treatment.

CVS Measurements

Pulse oximetry and electrocardiograms monitored heart rate (HR), systolic blood pressure (SBP), and DBP using the Nihon bedside monitor, PVM-2701 (Nihon Kohden Corp., Japan). Heart rate, SBP, and DBP were recorded at 6 time points: before induction of anesthesia (baseline, T0), after the induction of anesthesia but before electrical stimulation (T1), during convulsion (T2), 2 minutes after cessation of motor seizure (T3), 5 minutes after cessation of motor seizure (T4), and 10 minutes after cessation of motor seizure (T5). The CVS measurements at T2 were conducted immediately after the MST or ECT stimulation was administered.[9] The rate pressure product (RPP) was calculated as the product of HR and SBP, and is considered a measure of the energy consumption of the cardiac workload.[9]

MST Treatment and ECT Treatment

Magnetic seizure therapy was conducted using a Magstim device (Magstim Co., Whitland, Carmarthenshire, Wales, UK). The diameter of the stimulation coil was 130 mm. The position of the coil was centered over central zero (Cz) according to the international standard 10 to 20 electroencephalogram system, the vertex of the patients' head.[29] The stimulation frequency was 100 Hz, with 100% maximum stimulator output, and the duration time was 10 seconds.[30–32] Electroconvulsive therapy was administered using a brief-pulse constant current device (Somatics Thymatron, Venice, FL) with a bifrontal electrode placement. The maximum stimulus output was 200 joules. The dosage was determined using the half-age method.[33]

All patients were administered atropine 0.5 mg IV before the induction of anesthesia using propofol (1.5 mg/kg) IV. Succinylcholine (male, 0.5 mg/kg; female, 0.4 mg/kg, IV) was administered for muscle relaxation.

Statistical Analysis

The statistical analysis was performed using the SPSS software (version 25.0, SPSS Inc., USA). Statistical significance was set at the level of 0.05, 2-tailed. Quantitative data were shown as mean ± SD. χ^2 Tests were used in qualitative data analysis. Repeated-measures analysis of variance (ANOVA) was used to compare the mean differences in CVS measures (HR, SBP, DBP, and RPP) between MST and ECT groups with 6 within-subjects factors (T0, T1, T2, T3, T4, T5 as independent variables). In addition, a Bonferroni correction was applied to reduce the type I error due to multiple testing.[34]

RESULTS

Participants

A total of 52 patients were assessed for eligibility in this study. Six patients failed to meet the inclusion criteria (HAMD<17) and were excluded. One patient was excluded due to probable cerebral hemorrhage. Forty-five right-handed patients with depressive episodes (28 met the criteria of major depressive disorder, 17 met the diagnosis of bipolar disorder, type II, depressed phase) participated in the study. Eighteen received MST and 27 received ECT. All participants completed the entire study protocol. The demographics and clinical characteristics of the participants are summarized in Table 1. There were no significant differences in the baseline demographics and clinical variables between 2 groups (all $df = 43$, $P > 0.05$).

Changes of CVS Parameters Before and After the Initial and Sixth Treatment in MST and ECT Groups

The patients received 6 treatment sessions and CVS data was evaluated on the first and sixth treatments. Hear rate, SBP, DBP, and RPP at 6 time points (T0, T1, T2, T3, T4, T5) within and between MST and ECT groups were compared, as shown in Table 2. Compared with baseline data (T0), changes in all CVS parameters were significant both in MST and ECT groups (all $P < 0.001$). There were statistically significant time × treatment effects for HR ($F = 16.052$, $df = 40$, $P < 0.001$), SBP ($F = 2.754$, $df = 40$, $P = 0.033$), and RPP ($F = 15.277$, $df = 40$, $P < 0.001$) between MST and ECT groups at first treatment. At the sixth treatment, there were also statistically significant time × treatment effects for HR ($F = 9.882$, $df = 40$, $P < 0.001$), SBP ($F = 9.742$, $df = 40$, $P < 0.001$), DBP ($F = 8.111$, $df = 40$, $P < 0.001$), and RPP ($F = 12.207$, $df = 40$, $P < 0.001$) between MST and ECT groups.

To further illustrate the pattern of the changes in CVS measures, the CVS data were plotted over 6 time points as shown in Figure 1. The independent *t* test was used to analyze the difference of HR, SBP, DBP, and RPP at fixed time points (T0, T1, T2, T3, T4, T5) between MST and ECT groups in post hoc analysis. In the first treatment, the ECT group had significantly higher HR ($t = -4.084$, $df = 43$, $P < 0.001$), SBP ($t = -2.580$, $df = 43$, $P = 0.013$), DBP ($t = -2.850$, $df = 43$, $P = 0.007$), and RPP ($t = -5.008$, $df = 43$, $P < 0.001$) than those in MST group at T2. During the seizure (T2), HR, SBP, DBP, and RPP reached their peak values. At T2, the ECT group had significantly higher HR, SBP and RPP than those in the MST group ($t = -4.084$, $df = 43$, $P < 0.001$ for HR; $t = -2.580$, $df = 43$, $P = 0.013$ for SBP; $t = -5.008$, $df = 43$, $P < 0.001$ for RPP). Heart rate, SBP, and DBP decreased after the seizure. There were no significant differences in HR, SBP, DBP, and RPP at T3, T4, and T5 between MST and ECT groups. In the sixth session, HR, SBP, DBP, and RPP reached peak values at T2 in both groups. The ECT group had significantly higher HR, SBP, DBP, and RPP than the MST group ($t = -4.524$, $df = 43$, $P < 0.001$ for HR; $t = -3.442$, $df = 43$, $P = 0.001$ for SBP; $t = -3.218$, $df = 43$, $P = 0.002$ for DBP; $t = -5.794$, $df = 43$, $P < 0.001$ for RPP). At T3, there were significant differences in SBP, DBP, and RPP ($t = -5.942$, $df = 43$, $P < 0.001$ for SBP, $t = -3.941$, $df = 43$, $P < 0.001$ for DBP, $t = -3.878$, $df = 43$, $P < 0.001$ for RPP) between the 2 groups.

TABLE 1. Demographic and Clinical Characteristics in ECT and MST Groups

Characteristics	ECT (n = 27)	MST (n = 18)	t/χ^2	df	P
Diagnosis (n)				43	
MDD (n)	17	11	0.016		0.900
BP-II (n)	10	7			
Sex				43	
Male, n (%)	5 (18.52%)	2 (11.11%)	0.063		0.801
Female, n (%)	22 (81.48%)	16 (88.89%)			
Age (mean ± SD), y	32.78 ± 8.84	29.00 ± 8.32	−1.437	43	0.158
Age of onset (mean ± SD), y	24.96 ± 7.90	24.72 ± 6.86	−1.420	43	0.163
Duration of the illness (mean ± SD), y	4.47 ± 5.42	3.77 ± 3.77	−0.474	43	0.638
No. hospitalization (times; mean ± SD)	1.63 ± 1.18	1.39 ± 0.61	−0.795	43	0.431
Years of education (mean ± SD)	13.00 ± 3.41	13.11 ± 3.10	0.111	43	0.912
Family history of mental disorders, n (%)	12 (44.44%)	9 (50%)	0.134	43	0.714
History of suicide ideation/attempts, n (%)	21 (77.78%)	15 (83.33%)	0.006	43	0.939
Current medications				43	
SSRIs, n (%)	19 (70.37%)	13 (68.42%)	0.018		0.893
Antipsychotic medications, n (%)	13 (48.15%)	10 (55.56%)	0.237		0.626
Mood stabilizers, n (%)	10 (37.04%)	7 (38.89%)	0.016		0.900
HAMD-17 total score (mean ± SD)	26.81 ± 5.91	27.39 ± 7.31	0.290	43	0.773
Concomitant medical conditions			8.672	43	0.468
Hypertension, n (%)	1 (50.00)	1 (50.00)			
Sinus tachycardia, n (%)	0 (0.00)	2 (100.00)			
Other conditions, n (%)	7 (87.50)	1 (12.50)			
Medication for medical conditions				43	
Antiarrhythmics, n (%)	1 (33.30)	2 (66.70)	0.952		0.329
Antianemic, n (%)	1 (50.00)	1 (50.00)	0.087		0.768
Antihypertensives, n (%)	1 (50.00)	1 (50.00)	0.087		0.768

MDD indicates major depressive disorder; BPII, bipolar disorder, type II; SSRIs, Selective Serotonin Reuptake Inhibitors.

Other conditions include: Mammitis, Anemia, Chronic Gastritis, Sinusitis, Colpitis, Postabortion.

There were also significant differences in RPP at T4 (t = −2.924, df = 43, P = 0.005) and T5 (t = −3.581, df = 43, P = 0.001). Cardiovascular changes recovered more rapidly in the MST group than the ECT group at the sixth treatment. The differences between ECT and MST have increased over the course of treatments.

To investigate the time-point that HR, SBP, DBP, and RPP returned to baseline, the values at T3, T4, T5 were compared with T0. In the MST group, there were no significant differences in SBP at T3 and DBP at T5 compared with T0. However, there were still significant differences in HR and RPP at T5 compared with T0 (t = −5.080, df = 43, P < 0.001 for HR; t = −4.225, df = 43, P = 0.001 for RPP). In the ECT group, compared with T0, there were no significant differences in SBP at T5. There were significant differences in DBP, HR, and RPP at T5 compared with T0 (t = −3.405, df = 43, P = 0.002 for DBP; t = −8.505, df = 43, P < 0.001 for HR; t = −7.098, df = 43, P < 0.001 for RPP).

The results showed that in the MST group, 2 minutes after the motor seizure ended the SBP returned to baseline, while the ECT group did not return to baseline until 10 minutes after the seizure was initiated. Diastolic blood pressure returned to baseline 10 minutes after the motor seizure in the MST treatment, and it did not return to baseline in the ECT group. Heart rate and RPP did not return to baseline level within 10 minutes after the motor seizure in both groups.

Motor Seizures Duration

In the initial treatment, the motor seizure duration was 40.00 ± 25.18 seconds for MST and 50.48 ± 21.03 seconds for ECT patients, with no significant differences between the 2 groups (t = −1.153, df = 43, P = 0.138). There were no significant differences in motor seizure durations for treatments 2, and 3 between the 2 treatment groups. The average seizure durations for treatments 4, 5, and 6 were significantly longer in the ECT group than the MST group (F = 7.651, df = 43, P = 0.008).

CVS Effect in Patients With Hypertension

Two patients had preexisting hypertension, one was in the MST group and the other patient was in the ECT group. Their blood pressure was managed with oral antihypertensive medications (one patient was on nifedipine and metoprolol and the other on captopril). Both patients took their antihypertensive medications the mornings of their treatments, and no cardiac medications were administered during the procedures.

DISCUSSION

The overall changes in HR, SBP, DBP, and RPP in the MST and ECT groups were similar, although there were significantly fewer CVS effects in the MST group. The CVS parameters in the MST patients also returned to baseline more quickly than patients receiving ECT. These findings may have important clinical implications and MST may be a safer option for patients with preexisting CVS disorders. This is the first study to compare the CVS side effects of ECT and high-frequency MST.

Significant differences in CVS measures were observed in the MST and ECT groups. During the seizure, HR, SBP, DBP

TABLE 2. Comparison of Cardiovascular Parameters in Different Time Points Between MST and ECT Groups (Mean ± SD) of the First and Sixth Session

		T0	T1	T2	T3	T4	T5	*Df*	Time		Time × Treatment	
Factors	**Group**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**		***F***	***P***	***F***	***P***
HR	1st MST	77.00 ± 13.32	96.72 ± 15.34	112.61 ± 19.34*	104.11 ± 12.20	96.39 ± 14.44	94.00 ± 13.50	40	81.965	<0.001†	16.052	<0.001†
	1st ECT	75.67 ± 15.47	87.19 ± 13.68	146.44 ± 31.33	100.59 ± 22.44	95.63 ± 15.30	100.93 ± 12.93					
	6th MST	74.83 ± 11.08	89.11 ± 12.51	108.06 ± 35.28*	85.72 ± 13.72	82.28 ± 13.88	80.67 ± 11.46*	40	33.42	<0.001†	9.882	<0.001†
	6th ECT	74.74 ± 14.07	84.67 ± 15.28	146.67 ± 22.07	93.11 ± 17.79	91.52 ± 13.42	96.15 ± 13.94					
SBP	1st MST	118.83 ± 14.486	116.22 ± 12.52	122.61 ± 15.80*	125.28 ± 17.78	119.94 ± 13.97	119.72 ± 12.55	40	11.856	<0.001†	2.754	0.033†
	1st ECT	118.52 ± 14.44	112.07 ± 12.32	133.67 ± 12.83	130.37 ± 16.50	124.07 ± 13.46	120.52 ± 12.59					
	6th MST	115.56 ± 14.55	113.89 ± 11.38	121.33 ± 13.29*	111.33 ± 10.94*	115.44 ± 10.25	114.61 ± 8.75	40	10.129	<0.001†	9.742	<0.001†
	6th ECT	115.85 ± 10.42	110.00 ± 8.45	143.19 ± 24.59	135.96 ± 16.87	122.26 ± 10.39	117.74 ± 11.31					
DBP	1st MST	73.56 ± 12.98	73.78 ± 10.85	80.78 ± 7.92†	81.28 ± 16.53	78.78 ± 11.58	79.33 ± 10.93	40	11.531	<0.001†	1.007	0.401
	1st ECT	72.93 ± 10.95	69.59 ± 10.58	82.74 ± 15.77	83.93 ± 14.74	79.67 ± 11.07	79.70 ± 11.91					
	6th MST	73.44 ± 10.65	70.22 ± 9.24	73.22 ± 14.58*	66.94 ± 9.03*	71.61 ± 10.96	71.33 ± 8.18	40	8.257	<0.001†	8.111	<0.001†
	6th ECT	71.96 ± 9.34	67.77 ± 8.87	89.81 ± 18.17	84.00 ± 16.71	77.54 ± 9.53	76.00 ± 10.78					
RPP	1st MST	9205.06 ± 2553.53	11302.22 ± 1597.72	13813.28 ± 3707.94*	13065.00 ± 2572.90	11564.67 ± 2501.18	11255.78 ± 2458.64	40	64.902	<0.001†	15.277	<0.001†
	1st ECT	8949.41 ± 1386.69	9736.41 ± 1322.14	19595.11 ± 4912.02	13212.07 ± 2725.71	11836.89 ± 2396.98	12179.37 ± 2395.10					
	6th MST	8705.22 ± 2048.96	10150.44 ± 1710.26	12952.33 ± 3406.19*	9571.67 ± 1901.32*	9510.89 ± 1848.29*	9267.11 ± 1620.41*	40	25.531	<0.001†	12.207	<0.001†
	6th ECT	8656.30 ± 1830.07	9299.93 ± 1715.27	21079.22 ± 5249.65	12671.44 ± 3008.32	11197.67 ± 1926.53	11338.63 ± 2064.29					

Repeated-measures ANOVA was conducted. Bonferroni correction was used for multiple comparisons.

*Significant difference in *t* test.

†Significant difference in ANOVA.

Time points represent as: baseline (T0), immediately after the induction of anesthesia but before electrical stimulation (T1), during convulsion (T2), 2 minutes after cessation of motor seizure (T3), 5 minutes after cessation of motor seizure (T4) and 10 minutes after cessation of motor seizure (T5).

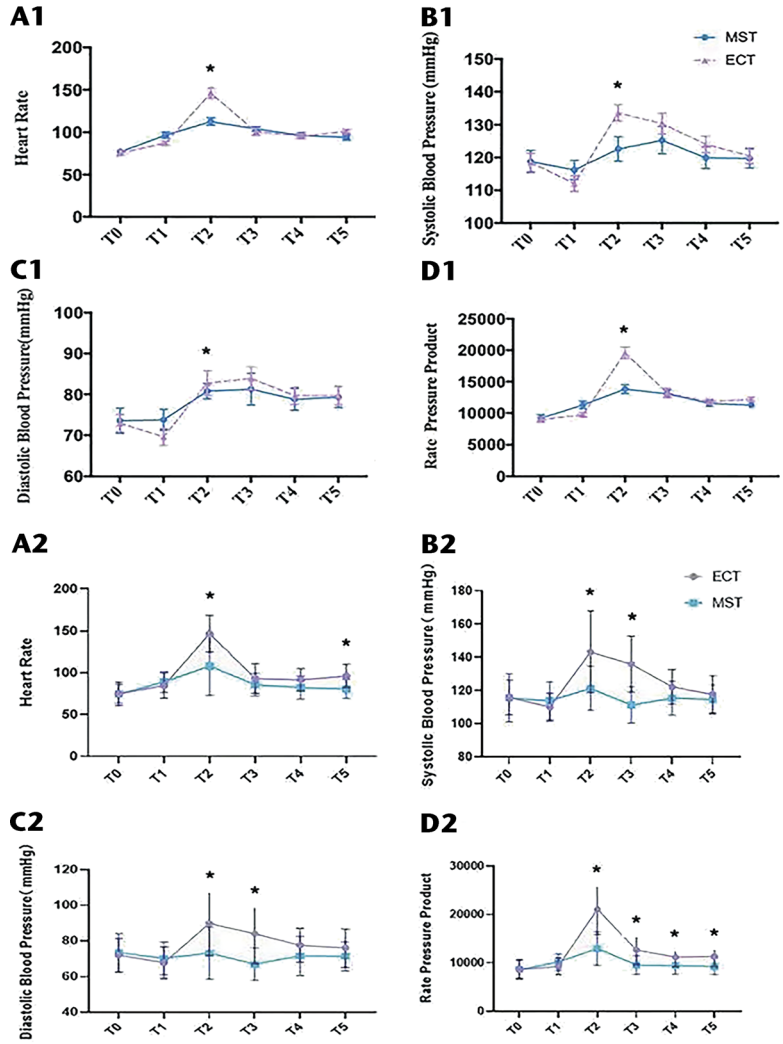

FIGURE 1. Comparison in cardiovascular parameters between MST and ECT groups at first treatment and sixth treatment. (A1) HR at first treatment, (B1) SBP at first treatment, (C1) DBP at first treatment, (D1) RPP at first treatment. (A2) HR at sixth treatment, (B2) SBP at sixth treatment, (C2) DBP at sixth treatment, (D2) RPP at sixth treatment. Time points represent as: baseline (T0), immediately after the induction of anesthesia but before electrical stimulation (T1), during convulsion (T2), 2 minutes after cessation of motor seizure (T3), 5 minutes after cessation of motor seizure (T4) and 10 minutes after cessation of motor seizure (T5). All comparisons were between MST and ECT groups using Student *t* test. Bonferroni correction was used for multiple comparisons. **P* < 0.0084(0.05/6) (after Bonferroni *P* value correction). full color online

and RPP increased and reached peak values. The ECT group had significantly higher HR, SBP, DBP, and RPP than the MST group. Heart rate, SBP, DBP, and RPP decreased after the motor seizure stopped. The CVS parameters returned to baseline 10 minutes after the motor seizure stopped in MST group, and the parameters in the ECT group did not return to baseline level at that time point. Our findings are consistent with 2 previous studies, which showed that MST resulted in significantly less sympathetic and parasympathetic response than ECT.[24,25] Rowny et al[24] monitored HR in 24 rhesus monkeys, which were randomly assigned to receive 6 weeks of daily treatment with ECT, MST or anesthesia-alone sham. They found that HR increased by 25% and 8% in the ECT and MST conditions, respectively. In a clinical study involving 20 case-matched patients, White et al[25] found that, compared with patient receiving ECT, patients receiving 50 Hz MST required a smaller dose of nicardipine, and they also had a decrease in MAP and HR at the 2-minute and 3-minute time intervals after MST. The study did not demonstrate significant differences in HR or MAP, with the exception of the late postictal period. Similar to ECT, MST is associated with an acute hyperdynamic response after application of the magnetic stimulus. The magnitude of the acute hemodynamic response after application of the magnetic stimulus was smaller than the hyperdynamic response after the electrical stimulus. However, the differences in the poststimulus MAP values were probably related to the use of smaller doses of nicardipine and the more rapid recovery of cognitive functioning in the MST (versus ECT) group. Our study further confirmed that CVS effects were significantly less with 100 Hz MST than bifrontal ECT despite the comparable motor seizure durations in both groups.

This differential physiological responses between MST and ECT are consistent with stimulus from MST having a cortical focus of stimulation with less impact on deeper brain structures implicated in cardiac control relative to ECT.[24] Bifrontal ECT stimulates the frontal lobes directly and other deep brain regions, such as the thalamus, indirectly due to the generalized seizure

induced by ECT. The seizure induced by MST is more focal and stimulates primarily the cerebral cortex and affects the CVS center through anatomical links and functional connections.[7,24] A computational simulation study demonstrated the restricted electric field strength and spatial distribution of MST compared with ECT.[35]

Animal studies[36] have found that ECT induced CVS effects (e.g., tachycardia, hypertension and cardiac arrhythmias) occur via the hypothalamus. Less marked CVS effects after MST relative to ECT are probably the result of a reduced electrical current through specific brain regions.[37] Supratentorial and cortical brain areas, such as the insula, amygdala, hippocampus, thalamus, and cingulate gyrus, are closely involved in the control of CVS functions. Electrically induced seizures are associated with prominent alterations of autonomic function. It remains unclear to what extent the autonomic dysfunction is due to direct cerebral effects following seizure activity, or due to indirect 'peripheral' effects. This is clearly an area that warrants further research.

The increased SBP and DBP during the seizure returned to baseline within 10 minutes after seizure stopped in MST group, but not in the ECT group. We cannot say for certain when the ECT induced increases in CVS variables returned to baseline as our monitoring did not extend beyond the ECT session in this study. Previous studies have shown that the hemodynamic effects of ECT may last for approximately 10 minutes.[38]

The CVS responses in ECT have been reported to be associated with the release of catecholamine in ECT.[39] Pretreatment with the α2-adrenergic agonists dexmedetomidine produced significant amelioration of CVS response to ECT without affecting the seizure duration.[40] Previous study has shown that repeated electroconvulsive shocks in the locus coeruleus increase burst activity of norepinephrine neurons.[41] Therefore, ECT may cause a short-term rise in catecholamine and which diminishes over 24 hours. Different neural networks may be activated depending on the seizure propagation.[42] Today, there are no studies available to examine the effects of MST on catecholamines. Compared with ECT, MST is believed to only stimulate focal superficial cerebral cortex,[37] and it may induce a generalized seizure through anatomical links and functional connections, which is less likely to affect locus coeruleus in the deep brain area.[24] We speculate that the catecholamine changes induced by MST were of decreased intensity and shorter than seizures induced by ECT. Our study found that, comparing with the first treatment, the CVS changes in the MST group recovered more rapidly than the ECT group at the sixth treatment. It appears that the differences in CVS measures between ECT and MST increased over the course of treatments, a finding that has not been reported before. We speculate this may be due to the different cumulative effects of ECT and MST on catecholamine and brain functional connections. Exploring the relationship of CVS effects with catecholamine changes induced by MST and ECT may shed light on the mechanism in future.

In summary, in this comparative study, we found that the CVS effects of 100 Hz MST were significantly less compared with ECT and some of the ictal changes in hemodynamic parameters were quicker to return to baseline in MST group. This suggests that MST may be an alternative, safer option for patients with CVS disorders, especially elderly patients.

Limitations

Notably, the anesthetic choices for this study may limit the generalizability of our findings: first, the study routinely administered atropine, which would block parasympathetic activation and affect CVS measures. Although bifrontal ECT likely has the lowest incidence of this effect, anticholinergic blockade nonetheless negates any modulating effect on HR and blood pressure in the early ictal and postictal phases of ECT treatment.[4] Second, propofol may have decreased the CVS response to ECT compared with other induction agents.[43] The interaction between CVS responses and anesthetic choices and dosing are of importance, because recovery of orientation may occur prior to recovery from paralysis triggering a late sympathetic reaction. There were several other limitations in our study. The patient groups were not randomized to the MST and ECT treatment group, although the assessors and data analyzers were blind to the group assignment. The stimulation sites for MST (vertex) and ECT (bifrontal) were different, which might have contributed to the group differences, as different sites of stimulation may affect different regions. This is an area that warrants further investigation. Furthermore, most of the important patient variables at baseline appear evenly distributed in the 2 groups. The sample size was relatively small, and larger sample size studies are warranted to validate our findings. Longer observation and more time points may be needed to understand when the changed parameters will return to baseline. The motor seizure activity instead of electroencephalogram monitoring to determine the seizure duration in both groups, and the latter would likely provide more accurate data. Checking neurotransmitters or their metabolites levels may help understand the mechanisms of CVS effects of both ECT and MST.

REFERENCES

1. UK ECT Review Group. Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. *Lancet*. 2003;361:799–808.
2. Gravenstein JS, Anton AH, Wiener SM, et al. Catecholamine and cardiovascular response to electro-convulsion therapy in man. *Br J Anaesth*. 1965;37:833–839.
3. Mann JJ, Manevitz AZ, Chen JS, et al. Acute effects of single and repeated electroconvulsive therapy on plasma catecholamines and blood pressure in major depressive disorder. *Psychiatry Res*. 1990;34:127–137.
4. Stewart PT, Loo CK, MacPherson R, et al. The effect of electrode placement and pulsewidth on asystole and bradycardia during the electroconvulsive therapy stimulus. *Int J Neuropsychopharmacol*. 2011; 14:585–594.
5. Nagler J. Heart rate changes during electroconvulsive therapy. *Ann General Psychiatry*. 2013;12:19.
6. Landau AM, Chakravarty MM, Clark CM, et al. Electroconvulsive therapy alters dopamine signaling in the striatum of non-human primates. *Neuropsychopharmacology*. 2011;36:511–518.
7. Hageman I, Nielsen M, Wortwein G, et al. Electroconvulsive stimulations prevent stress-induced morphological changes in the hippocampus. *Stress*. 2008;11:282–289.
8. Phutane VH, Thirthalli J, Muralidharan K, et al. Double-blind randomized controlled study showing symptomatic and cognitive superiority of bifrontal over bitemporal electrode placement during electroconvulsive therapy for schizophrenia. *Brain Stimul*. 2013;6:210–217.
9. Abhishekh HA, Anusha M, Thirthalli J, et al. Cardiovascular responses are similar in bifrontal and bitemporal ECT. *J ECT*. 2012;28:194.
10. Jurek L, Dorey JM, Nourredine M, et al. Impact of vascular risk factors on clinical outcome in elderly patients with depression receiving electroconvulsive therapy. *J Affect Disord*. 2021;279:308–315.
11. Kayser S, Bewernick BH, Soehle M, et al. Degree of postictal suppression depends on seizure induction time in magnetic seizure therapy and electroconvulsive therapy. *J ECT*. 2017;33:167–175.
12. 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.

13. Farzan F, Atluri S, Mei Y, et al. Brain temporal complexity in explaining the therapeutic and cognitive effects of seizure therapy. *Brain*. 2017;140:1011–1025.
14. 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.
15. Kayser S, Bewernick BH, Wagner S, et al. Effects of magnetic seizure therapy on anterograde and retrograde amnesia in treatment-resistant depression. *Depress Anxiety*. 2020;37:125–133.
16. 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.
17. Wang J, Vila-Rodriguez F, Ge R, et al. Accelerated magnetic seizure therapy (aMST) for treatment of major depressive disorder: a pilot study. *J Affect Disord*. 2020;264:215–220.
18. Barker AT, Jalinous R, Freeston IL. Non-invasive magnetic stimulation of human motor cortex. *Lancet*. 1985;1:1106–1107.
19. George MS, Lisanby SH, Sackeim HA. Transcranial magnetic stimulation: applications in neuropsychiatry. *Arch Gen Psychiatry*. 1999;56:300–311.
20. 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.
21. Zhang J, Ren Y, Jiang W, et al. Shorter recovery times and better cognitive function-a comparative pilot study of magnetic seizure therapy and electroconvulsive therapy in patients with depressive episodes. *Brain Behav*. 2020;10:e01900.
22. Devinsky O. Effects of seizures on autonomic and cardiovascular function. *Epilepsy Curr*. 2004;4:43–46.
23. Opherk C, Coromilas J, Hirsch LJ. Heart rate and EKG changes in 102 seizures: analysis of influencing factors. *Epilepsy Res*. 2002;52:117–127.
24. Rowny SB, Cycowicz YM, McClintock SM, et al. Differential heart rate response to magnetic seizure therapy (MST) relative to electroconvulsive therapy: a nonhuman primate model. *NeuroImage*. 2009;47:1086–1091.
25. 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.
26. 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.
27. First MB, Spitzer RL, Gibbon ML, Williams JBW. Structured clinical interview for DSM-IV-TR Axis I Disorders, Research Version, Non-patient Edition. 2002.
28. A Rating Scale for Depression. *J Neurol Neurosurg Psych*. 1960;23:56–62.
29. Klem GH, Lüders HO, Jasper HH, et al. The ten-twenty electrode system of the international federation. The International Federation of Clinical Neurophysiology. *Electroencephalogr Clin Neurophysiol Suppl*. 1999;52:3–6.
30. Cretaz E, Brunoni AR, Lafer B. Magnetic seizure therapy for unipolar and bipolar depression: a systematic review. *Neural Plast*. 2015;2015:521398.
31. Milev RV, Giacobbe P, Kennedy SH, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 4. Neurostimulation Treatments. *Can J Psychiatr*. 2016;61:561–575.
32. de Sousa RT, Zanetti MV, Brunoni AR, et al. Challenging treatment-resistant major depressive disorder: a roadmap for improved therapeutics. *Curr Neuropharmacol*. 2015;13:616–635.
33. Petrides G, Fink M. The "half-age" stimulation strategy for ECT dosing. *Convuls Ther*. 1996;12:138–146.
34. Holm S. A simple sequentially rejective multiple test procedure. *Scand Stat Theory Appl*. 1979;6:65–70.
35. Lee WH, Lisanby SH, Laine AF, et al. Comparison of electric field strength and spatial distribution of electroconvulsive therapy and magnetic seizure therapy in a realistic human head model. *Eur Psychiatry*. 2016;36:55–64.
36. Welch CA, Drop LJ. Cardiovascular effects of ECT. *Convuls Ther*. 1989; 5:35–43.
37. Deng ZD, Lisanby SH, Peterchev AV. Electric field strength and focality in electroconvulsive therapy and magnetic seizure therapy: a finite element simulation study. *J Neural Eng*. 2011;8:016007.
38. Aydogan MS, Yücel A, Begec Z, et al. The hemodynamic effects of dexmedetomidine and esmolol in electroconvulsive therapy: a retrospective comparison. *J ECT*. 2013;29:308–311.
39. Castelli I, Steiner LA, Kaufmann MA, et al. Comparative effects of esmolol and labetalol to attenuate hyperdynamic states after electroconvulsive therapy. *Anesth Analg*. 1995;80:557–561.
40. Parikh DA, Garg SN, Dalvi NP, et al. Outcome of four pretreatment regimes on hemodynamics during electroconvulsive therapy: a double-blind randomized controlled crossover trial. *Ann Card Anaesth*. 2017;20:93–99.
41. Tsen P, El Mansari M, Blier P. Effects of repeated electroconvulsive shocks on catecholamine systems: electrophysiological studies in the rat brain. *Synapse*. 2013;67:716–727.
42. Ito M, Hatta K, Usui C, et al. Urine catecholamine levels are not influenced by electroconvulsive therapy in depression or schizophrenia over the long term. *Psychiatry Clin Neurosci*. 2012;66:602–610.
43. Rasmussen KG. Propofol for ECT anesthesia a review of the literature. *J ECT*. 2014;30:210–215.