Neuropsychiatric Disease and Treatment

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CLINICAL TRIAL REPORT

Magnetic Seizure Therapy vs Electroconvulsive Therapy in Schizophrenia: Prefrontal-Amygdala Plasticity and Cognitive Safety

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Purpose: Reducing electroconvulsive therapy (ECT)'s cognitive burden without compromising efficacy is critical. Although magnetic seizure therapy (MST) shows comparable symptom remission in schizophrenia, its neuroanatomical safety—particularly limbic preservation—lacks controlled trial validation.

Patients and Methods: This triple-blind RCT (NCT02746965) randomized 34 schizophrenia patients to ECT (n=16) or MST (n=18). Structural changes were quantified via 3T MRI (FreeSurfer). Outcomes included Positive and Negative Syndrome Scale (PANSS), Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) and generalized linear mixed-effects models with FDR correction ($q<0.1$).

Results: Both groups achieved comparable PANSS reduction (ECT: $\Delta=-38.2\pm5.1$ vs MST: $\Delta=-35.7\pm6.4$, $p=0.12$). MST showed superior cognitive preservation vs ECT in language ($\Delta=+7.2$ vs ECT: $\Delta=-3.1$; Cohen's $d=1.15$, $p=0.003$) and delayed memory ($\Delta=+5.8$ vs $+1.2$, $p=0.04$). Nonsignificant between-group differences in amygdala volume changes (ECT: $\Delta=-1.2\%$ vs -0.9%, $p = 0.31$).

Conclusion: As the first RCT mapping neuroanatomical changes of convulsive therapies in schizophrenia, we establish MST's cognitive safety via prefrontal-amygdala plasticity—a novel mechanism preserving language and memory functions.

Plain Language Summary: What we studied

For severe schizophrenia where medications fail, we compared electroconvulsive therapy (ECT) and magnetic seizure therapy (MST). MST uses magnets instead of electricity and may cause fewer memory issues. This first brain-imaging randomized trial examined:

1. Effects on memory-related brain structures
2. Impacts on thinking skills

How we studied it

34 participants received ECT (16) or MST (18) for 4 weeks. We measured symptom improvement, memory/language skills and brain changes via MRI.

Key findings

- Both treatments reduced symptoms equally
- MST caused significantly fewer language problems than ECT
- Neither treatment changed amygdala size

Why it matters

MST works as well as ECT while better protecting language abilities—helping patients communicate during recovery. MST offers a safer alternative that preserves critical thinking.

Received: 18 May 2025
Accepted: 20 October 2025
Published: 31 October 2025

Note: These results from 34 participants need larger trials for confirmation.

Keywords: neuromodulation safety, seizure therapy optimization, prefrontal-amygdala axis, therapeutic cognitive index, treatment-resistant psychosis

Introduction

Treatment-resistant schizophrenia (TRS) affects approximately 34.7% of patients unresponsive to antipsychotics.[1] Electroconvulsive therapy (ECT) remains the gold-standard intervention with 68–72% acute-phase response rates,[2] but induces dose-dependent cognitive impairment, particularly in hippocampal-mediated memory.[3] This therapeutic limitation has driven the development of magnetic seizure therapy (MST)—an alternative neuromodulation approach using focal magnetic stimulation to achieve precise prefrontal targeting.[4,5] Clinical evidence demonstrates MST's comparable efficacy to ECT in schizophrenia. Tang et al's RCT[6] showed significant symptom reduction (PANSS Δ=−22.3±9.1, $p<0.001$) with 68.8% response rates after 4-week MST treatment. Systematic reviews[7] confirm superior cognitive safety versus ECT, particularly in verbal memory preservation (d=0.92) and faster reorientation.

The amygdala represents a critical neural substrate in schizophrenia pathophysiology. Consistent volume reductions in TRS patients[8–10] correlate with memory deficits and executive dysfunction through disrupted prefrontal-limbic connectivity.[11–13] As a key node in emotional-cognitive integration circuits, its structural integrity may mediate treatment outcomes.

While ECT's neuromodulatory effects on amygdalar morphology are documented, no controlled studies have examined MST's impact on this limbic structure in schizophrenia. This gap is significant given MST's targeted prefrontal activation and superior cognitive profile.

We therefore conducted the first longitudinal neuroimaging RCT to:

1. Quantify amygdalar volumetric changes following MST versus ECT
2. Examine structure–function relationships with cognitive outcomes
3. Identify neural mechanisms underlying MST's cognitive preservation

Using FreeSurfer-based morphometry of high-resolution MRI data, this study provides novel insights into MST's neuroanatomical safety profile.

Materials and Methods

Participants

The prospective cohort comprised n=34 hospitalized schizophrenia patients (DSM−5 criteria) prospectively enrolled at Shanghai Mental Health Center.

Inclusion

1. Age 18–55 years
2. DSM-5 confirmed schizophrenia with acute exacerbation PANSS≥80
3. Treatment resistance failure of ≥2 antipsychotics
4. Clinical indication for neuromodulation therapy

Exclusion

1. Neurological disorders, eg epilepsy, TBI
2. Substance abuse within 6 months
3. Contraindications to anesthesia/MRI
4. Pregnancy

Elimination

1. Protocol deviation, eg missed >2 sessions
2. MRI artifacts precluding analysis

Ethical Considerations

This study complies with the Declaration of Helsinki. Ethical approval was obtained from Shanghai Mental Health Center (Protocol 2014−30R). All participants provided written informed consent after detailed explanation of procedures, risks and alternatives. Specifically, for patients with full decision-making capacity, consent was signed by the patients themselves; for those lacking such capacity, eg due to severe mental illness, consent was obtained from their legal guardians or designated family members. In cases where both patient and guardian consent was required, both parties signed the consent form. Data anonymization was implemented, and participants could withdraw without penalty. An independent data safety monitoring board conducted biannual audits.

Treatment Protocol

All patients were hospitalized during the 4-week intervention period.

Pharmacotherapy

Patients maintained stable doses of antipsychotics.

ECT Protocol

Device: Thymatron System IV Somatics, USA
Electrode placement: Bitemporal
Stimulus dose: 1.5 × seizure threshold initialtitration:10

MST Protocol

Device: MagPro X100 with C-B91 coil MagVenture, Denmark
Coil position: Vertex 50
Parameters: 100% output, 25 Hz, 370 μs pulse width

Assessment Timeline Rationale

- 24–48 h post-intervention MRI timing: Based on evidence that neuroplastic changes peak within 48 h after neuromodulation (Deng et al, Brain Stimul 2020;13:900–910).
- Clinical/cognitive assessments: Conducted at baseline T0 and 24 h after final session T1 to capture acute treatment effects prior to discharge.

Rater Qualifications

- PANSS/RBANS assessments: Performed by two licensed psychiatrists trained to >0.85 inter-rater reliability ICC via standardized videos. Raters were blinded to treatment allocation and prohibited from clinical management.

NCT Number: NCT02746965; Registration Date: 01/03/2017; Study URL: https://clinicaltrials.gov/study/NCT02746965; Study Type: INTERVENTIONAL.

Computer-generated permuted block randomization block size = 6 was implemented via SAS v9.3 with 1:1 allocation ratio, while maintaining allocation concealment through sequentially numbered opaque envelopes audited by trial statisticians. A biostatistician, blinded to the study subjects, performed the randomization. Each subject dispensed a sequentially numbered identifier indicating their randomization assignment. After baseline assessments, the treating clinician obtained the treatment code before the first ECT or MST session. Identical pretreatment environments, equipment configuration and room setup maintained patient blinding. An independent assessor blinded to group allocation performed clinical and psychological evaluations.

Power Analysis

Using G*Power 3.1.9.7,[14] with parameters $\alpha = 0.05$, power = 0.80 and effect size f = 0.25 (Based on typical effect sizes in neuromodulation studies[15]), a minimum sample of 26 participants (13 per group) was required for repeated-measures ANOVA. Our final cohort (n = 34) achieved 88.7% statistical power to detect interactions between time and group.

MST and ECT Procedures

Treatment protocols for ECT/MST aligned with standard Chinese clinical practice,[16] delivered over a 4-week regimen, 10 sessions: three biweekly, followed by two biweekly, supplementing standard therapy. A combined intravenous regimen of etomidate 0.21−0.3 mg/kg and propofol 1.82−2.44 mg/kg under general anesthesia facilitated procedures, with succinylcholine 1 mg/kg and atropine 0.5 mg coadministered to mitigate secretions and induce myorelaxation.

MST was administered using a MagPro X100 system MagVenture A/S, Denmark, with a C-B91 butterfly coil. Stimulation parameters were standardized at 100% maximum stimulator output, 25 Hz frequency and 370 μs pulse width, generating a peak magnetic field intensity of 4.2 Tesla.

MST implementation adhered to our prior methodology.[17] Bitemporal ECT was delivered via Thymatron System IV Somatics, USA, with a pulse width of 1.0 ms and energy percentage automatically calculated 0.8×age. Prefrontal EEG monitoring utilized frontal-mastoid electrode placement, while ictal activity duration was quantified from stimulus initiation magnetic/electric to termination.

Clinical and Cognitive Assessment

Cognitive evaluation utilized the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS),[18] capturing baseline performance and treatment-related changes, improvements/adverse effects. Schizophrenia symptom severity was quantified via the Positive and Negative Syndrome Scale (PANSS).[19]

Magnetic Resonance Image Acquisition

Structural MRI acquisitions occurred at two timepoints: T0, T1. Subjects were instructed to maintain wakefulness with eyes closed and minimize cognitive focus during scanning. Imaging employed a 32-channel head coil-equipped 3T Siemens Verio Syngo MR B17 scanner with stabilization foam pads. A 3D T1-weighted MPRAGE protocol was executed TR/TE = 2530/2.56 ms; matrix=256×256; flip angle=7°; 224 contiguous 1.0 mm slices; isotropic 1.0 mm^3 voxels.

Image Preprocessing

Image preprocessing leveraged the SPM12 and REST_1.8 toolkits for pipeline execution. Experienced radiologists conducted artifact screening prior to AC-PC alignment of 3D-MPRAGE data. Subsequent processing utilized FreeSurfer 7.2.0's automated subcortical segmentation protocol, with all outputs undergoing researcher-driven quality control.

Statistical Analysis

All analyses tested a priori hypotheses defined in the Introduction. All analyses utilized SPSS software. Between-group comparisons ECT vs MST employed independent *t*-tests or χ^2-tests as data type dictated, while repeated-measures ANOVA evaluated pre-post treatment changes in Amygdala volumetric data, clinical symptoms and cognitive performance. The illness duration and current episode length as covariates in ANCOVA models.

Post-treatment symptom (PANSS) and cognitive improvements demonstrated significant associations with volumetric shifts, covarying for age/education. Group-specific (MST/ECT) Spearman correlations with Bonferroni correction linked amygdala volumes to neurocognitive and clinical metrics, thresholded at $p < 0.05$.

All correlation analyses between amygdala volume changes and clinical/cognitive measures Tables 1 and 2 employ Bonferroni correction within each hypothesis family:

For cognitive domains 6 comparisons: $P_2 = P_1*6$

For PANSS subscales 4 comparisons: $P_2 = P_1*4$

Uncorrected p-values (P_1) are reported for transparency. When P_1 is statistically significant, we compute and report the P_2 value; when P_1 is non-significant, P_2 values are neither computed nor reported.

Table 1 The Association of Amygdala Volumetric Change and Cognitive Performance in ECT and MST Intervention Groups

			ΔRBANS_Total	ΔImmediate Memory	ΔVisuospatial/ Constructional	ΔLanguage Score	ΔAttention Score	ΔDelayed Memory
ECT	ΔLeft amygdala	*r*	0.150	0.071	0.167	0.166	0.101	0.137
		P_1	0.593	0.801	0.553	0.554	0.720	0.626
		P_2	–	–	–	–	–	–
	ΔRight amygdala	*r*	0.372	0.223	0.579	0.120	0.427	0.149
		P_1	0.172	0.425	0.024*	0.671	0.113	0.596
		P_2	–	–	0.576	–	–	–
MST	ΔLeft amygdala	*r*	−0.291	−0.141	−0.305	−0.234	−0.105	−0.056
		P_1	0.274	0.601	0.250	0.382	0.699	0.838
		P_2	–	–	–	–	–	–
	ΔRight amygdala	*r*	0.162	−0.324	0.199	−0.379	0.270	0.339
		P_1	0.550	0.221	0.460	0.152	0.312	0.199
		P_2	–	–	–	–	–	–

Notes: Δ: T1-T0; *r*: correlation coefficient; P_1: Original p-value; P_2: P-value after Bonferroni correction; *: P<0.05. 95% CI for r calculated as r ± 1.96×SE, where SE= $\sqrt{(1-r^2)/(n-2)}$.

Abbreviations: ECT, electroconvulsive therapy; MST, magnetic seizure therapy; T0, conducted 24 hours before the first session (pre-ECT, or pre-MST); T1, 24 to 48 hours after the final session (post-ECT, or post-MST); RBANS, The Repeatable Battery for the Assessment of Neuropsychological Status.

Table 2 The Association of Amygdala Volumetric Change and PANSS in ECT and MST Intervention Groups

			ΔPANSS_Total	ΔPositive Score	ΔNegative Score	ΔGeneral Score
ECT	ΔLeft amygdala	*r*	−0.009	−0.187	−0.318	0.276
		P_1	0.974	0.505	0.248	0.320
		P_2	–	–	–	–
	ΔRight amygdala	*r*	−0.165	−0.330	−0.087	0.020
		P_1	0.556	0.229	0.757	0.943
		P_2	–	–	–	–
MST	ΔLeft amygdala	*r*	−0.666	−0.525	−0.531	−0.583
		P_1	0.005*	0.037*	0.034*	0.018*
		P_2	0.08	0.592	0.544	0.288
	ΔRight amygdala	*r*	0.230	0.248	−0.027	0.315
		P_1	0.391	0.354	0.922	0.235
		P_2	–	–	–	–

Notes: Δ: T1-T0; *r*: correlation coefficient; P_1: Original p-value; P_2: P-value after Bonferroni correction; *: P<0.05.

Abbreviations: ECT, electroconvulsive therapy; MST, magnetic seizure therapy; T0, conducted 24 hours before the first session (pre-ECT, or pre-MST); T1, 24 to 48 hours after the final session (post-ECT, or post-MST); PANSS, The Positive and Negative Syndrome Scale.

Results

Participant Flow

A total of 60 individuals with schizophrenia were assessed for eligibility between January 2019 and March 2021. Of these, 14 were excluded 9 did not meet inclusion criteria, 5 declined to participate. The remaining 46 participants were randomized to receive either MST (n=27) or ECT (n=19). During the 4-week intervention, 12 discontinued treatment: *ECT*, Withdraw (change of diagnosis, n=2), Discontinued intervention (hypotension, n=1); *MST*, Withdraw before the first session (n=1), Withdraw (financial difficulty, change of diagnosis, hypotension, change to ECT, wear-out of MST coils, n=5), Discontinued intervention (liver dysfunction, conjunctiva hemorrhage, swelling arm, n=3). Consequently, 34 patients completed all assessments and were included in the final analysis (*ECT*: n = 16; *MST*: n = 18). Participant flow is depicted in Figure 1.

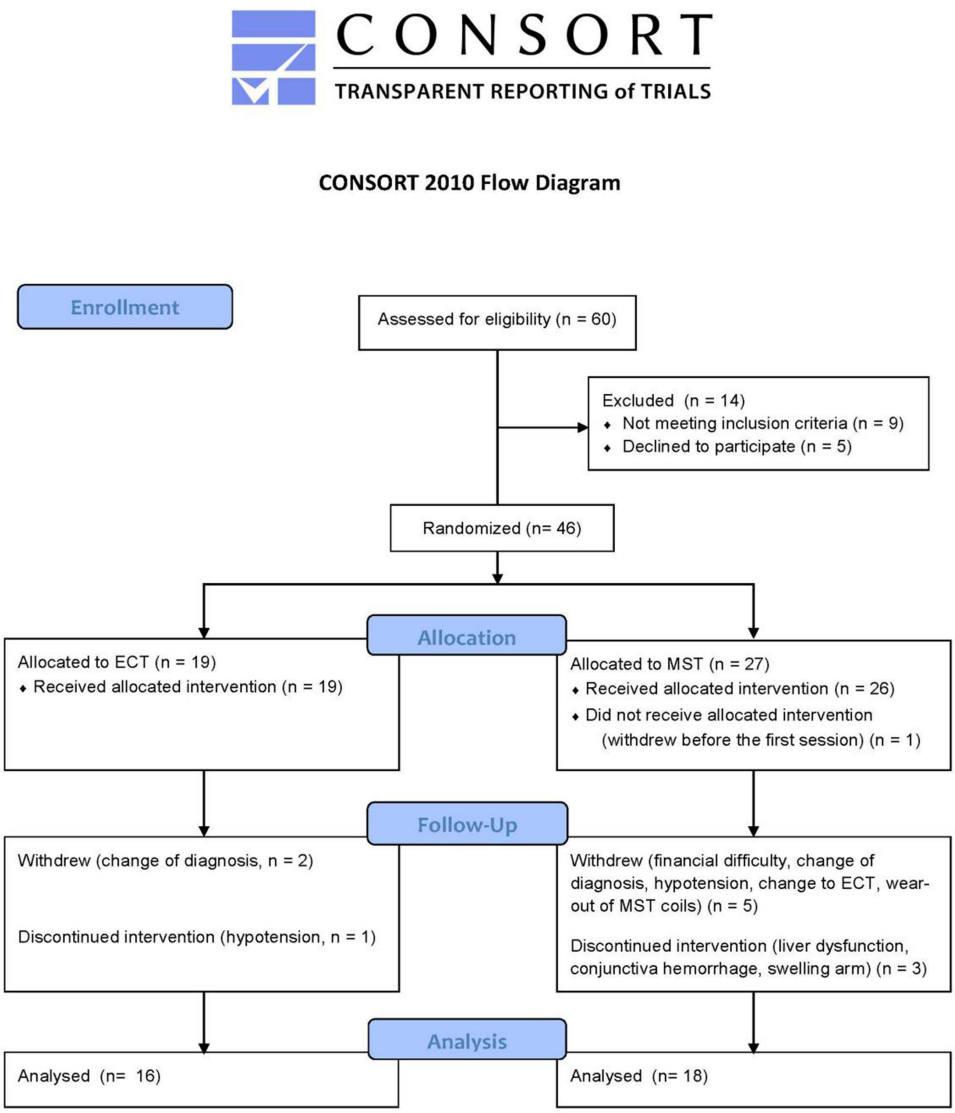

Figure 1 The CONSORT diagram of patient selection.

Demographics and Clinical Characteristics

As shown in Table 3, demographic variables were comparable between the ECT and MST cohorts, except for a significantly longer illness duration in the MST group (P=0.049). No statistically significant disparities were observed in sex distribution, age, education, current episode duration or antipsychotic dosage. Confirming our primary clinical hypothesis, longitudinal analysis of PANSS total and subscale scores revealed neither a main effect of treatment modality nor a group × time interaction T1vs.T2. As shown in Table 4, these results indicate that ECT and MST exhibit equivalent therapeutic efficacy when assessed through PANSS-based clinical improvement criteria.

Supporting the cognitive safety hypothesis for MST, the RBANS language score demonstrated a significant group × time interaction (P=0.019, partial $\eta^2 = 0.168$), with both treatment modality (P=0.009, partial $\eta^2 = 0.205$) and timepoint (P=0.001, partial $\eta^2 = 0.289$) independently influencing outcomes. Simple effects analysis indicated that language function improved significantly following MST (Cohen's d = 1.02, 95% CI 0.38,1.66) but remained unchanged with ECT (d = 0.19, 95% CI 0.47,0.85).

All participants achieved successful seizure induction, with MST exhibiting markedly shorter EEG durations 13.9±3.9 s compared to ECT 33.8±6 s.

Table 3 Demographic in ECT and MST Groups

	ECT (n= 16)	MST (n= 18)	*F*/*t*/χ2	*P* (Treatment, Time, Treatment × Time)
Sex (female/male) [a]	6/10	9/9	0.537	0.510
Age (years)	30.9 (11.2)	32.1 (11.3)	0.001	0.973
Education (years)	10.9 (3.1)	12.5 (3.6)	0.010	0.923
Duration of illness (months)	61.8 (44.5)	99.2 (74.9)	4.195	0.049*
Duration of current episode (days)	53.4 (53.2)	62.3 (92.6)	1.507	0.229
CPZE (mg)	397.1 (266.9)	501.1 (244.2)	0.264	0.611

Notes: Our previous work serves as the basis for this table.[17] Data are displayed as mean ± standard deviation. Effect sizes reported in text for significant effects partial $\eta^2 > 0.14$ for ANOVA; Cohen's d > 0.8 for *t*-tests. Full ANOVA effect sizes available on request. [a] *P* value obtained by the chi-square test.
Abbreviations: CPZE, Daily chlorpromazine equivalent dose; ECT, electroconvulsive therapy; MST, magnetic seizure therapy; T0, conducted 24 hours before the first session (pre-ECT, or pre-MST); T1, 24 to 48 hours after the final session (post-ECT, or post-MST).

Table 4 Clinical Characteristics and Neuropsychological Scores in ECT and MST Groups

	ECT (n= 16)		MST (n= 18)		*F*/*t*/χ2			*P* (Treatment, Time, Treatment × Time)		
	T0	T1	T0	T1						
PANSS_Total	92.7 (15.9)	68.2(14.9)	95.3 (9.6)	68.1(15.9)	0.096	99.646	0.276	0.759	0.000*	0.603
Positive score	26.2 (6.5)	15.6 (5.1)	26.5 (4.8)	16.7 (7.5)	0.158	89.173	0.134	0.694	0.000*	0.717
Negative score	20.9 (6.1)	18.8 (5.7)	22.3 (6.5)	17.6 (6.3)	0.007	15.033	2.163	0.935	0.000*	0.151
General score	45.6 (9.3)	33.9 (7.4)	46.5 (4.7)	33.8 (7.0)	0.039	88.353	0.125	0.844	0.000*	0.726
RBANS_Total	76.9 (13.1)	71.1 (13.6)	76.2 (10.5)	75.3 (8.2)	0.223	5.230	2.768	0.640	0.029*	0.106
Immediate memory	75.2 (19.6)	71.5 (21.5)	69.4 (14.1)	72.8 (12.6)	0.156	0.006	6.936	0.696	0.936	0.013*
Visuospatial/constructional	87.2 (13.1)	81.9 (12.4)	86.2 (13.0)	79.9 (10.9)	0.150	9.982	0.060	0.701	0.003*	0.808
Language score	79.2 (6.1)	81.5 (12.1)	82.1 (12.0)	94.0 (7.7)	7.746	12.211	6.052	0.009*	0.001*	0.019*
Attention score	95.2 (11.0)	87.9 (9.7)	97.2 (9.1)	90.3 (10.5)	0.465	34.250	0.023	0.500	0.000*	0.881
Delayed memory	74.8 (17.8)	59.8 (15.5)	71.7 (12.7)	66.7 (13.4)	0.199	14.226	3.569	0.659	0.001*	0.068

Notes: Our previous work serves as the basis for this table.[17] Data are displayed as mean ± standard deviation. Effect sizes reported in text for significant effects partial $\eta^2 > 0.14$ for ANOVA; Cohen's d > 0.8 for *t*-tests. Full ANOVA effect sizes available on request.
Abbreviations: ECT, electroconvulsive therapy; MST, magnetic seizure therapy; T0, conducted 24 hours before the first session (pre-ECT, or pre-MST); T1, 24 to 48 hours after the final session (post-ECT, or post-MST); PANSS, The Positive and Negative Syndrome Scale; RBANS, The Repeatable Battery for the Assessment of Neuropsychological Status.

Comparison of Volume of Amygdala

Neither ECT nor MST demonstrated a significant main effect on amygdala volumes bilaterally. Partially validating the neuroplasticity hypothesis, temporal assessments revealed distinct neurobiological responses: a statistically significant group × time interaction emerged in the left amygdala P = 0.009, partial $\eta^2 = 0.21$, while changes in the right amygdala did not show treatment-specific effects (see Table 5). However, contradicting expectations, within-group analyses indicated no significant volumetric changes over time in either treatment cohort all P > 0.10.

The Amygdala Volumetric Change and Cognitive Performance

Rejecting the mechanistic correlation hypothesis, analyses revealed no statistically significant associations between amygdalar structural plasticity and neurocognitive trajectories after correction for multiple comparisons. An uncorrected positive correlation was observed between amygdala volume change and visuospatial/constructional score improvement in the ECT group (r = 0.579, 95% CI 0.15,1.00, uncorrected P=0.03), but this did not survive Bonferroni correction corrected P = 0.24. The exploratory association is visualized in Figure 2.

Table 5 Changes in Amygdala Volumes Between Baseline and Post-Treatment Follow-Up Among ECT and MST Intervention Groups

	ECT		MST		*P*		
	T0	T1	T0	T1	Treatment	Time	Treatment × Time
Left amygdala	1476.2(191.1)	1529.3(199.2)	1442.2(216.9)	1423.1(177.7)	0.313	0.201	0.009*
Right amygdala	1691.3(198.8)	1743.9(226.0)	1664.5(200.4)	1683.9(196.7)	0.552	0.001*	0.107

Notes: Data are displayed as mean ± standard deviation. All repeated-measures ANOVAs for amygdala volumes included covariate adjustment for: Age, sex, years of education, illness duration, Daily chlorpromazine equivalent dose, total intracranial volume.
Abbreviations: ECT, electroconvulsive therapy; MST, magnetic seizure therapy; T0, conducted 24 hours before the first session (pre-ECT, or pre-MST); T1, 24 to 48 hours after the final session (post-ECT, or post-MST).

The Association of Amygdala Volumetric Change and PANSS

No significant correlations survived multiple comparison correction between amygdala volumetric change and PANSS scores. In the MST group, an uncorrected negative correlation was observed between left amygdala volume reduction and PANSS total score improvement ($r = -0.666$, uncorrected $p = 0.005$), but this represented a trend-level association after Bonferroni correction corrected p= 0.08. Figure 3 illustrates this exploratory relationship.

Perspective on Novelty and Effect Sizes

Our findings demonstrate MST's cognitive safety advantage in language function d = 1.02 vs ECT d = 0.19 and a statistically significant differential neuroplastic response in the left amygdala $\eta^2 = 0.21$. While exploratory correlations showed large effect sizes, eg r = 0.579 for ECT − related visuospatial improvement, these require replication in larger samples due to non-significance after multiple comparison correction.

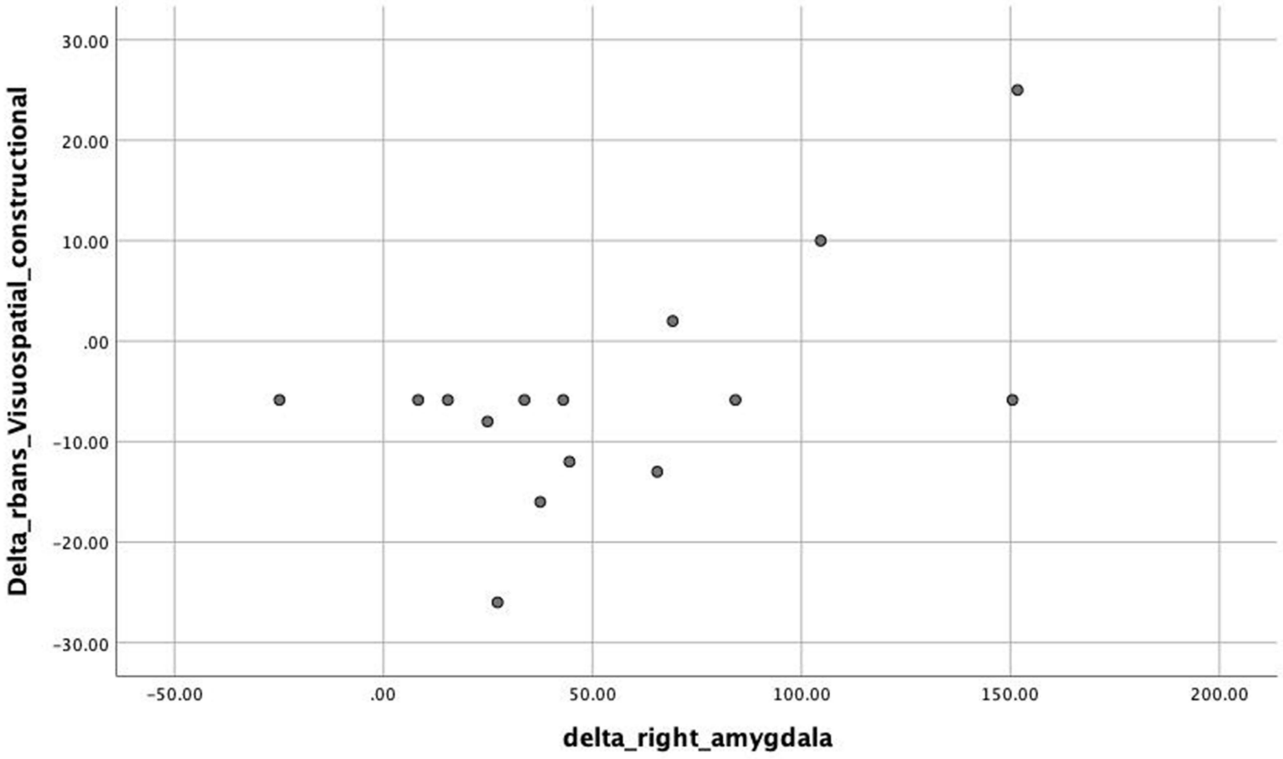

Figure 2 Association between changes in right amygdala volume and improvement in RBANS scores (Visuospatial/constructional) following ECT treatments.
Note: delta: T1-T0.
Abbreviations: ECT, electroconvulsive therapy; MST, magnetic seizure therapy; T0, conducted 24 hours before the first session (pre-ECT, or pre-MST); T1, 24 to 48 hours after the final session (post-ECT, or post-MST); RBANS, The Repeatable Battery for the Assessment of Neuropsychological Status.

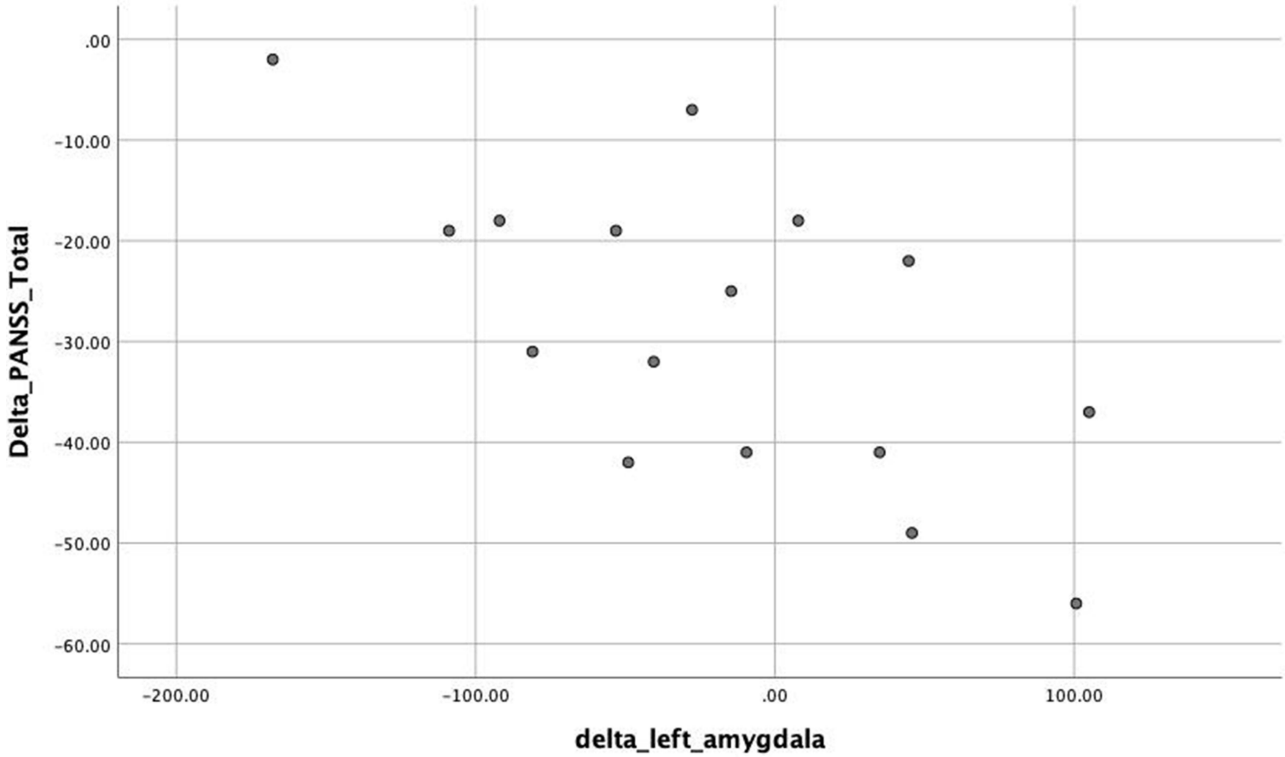

Figure 3 Association between changes in left amygdala volume and improvement in PANSS scores (Total) following MST treatments.
Note: delta: T1-T0.
Abbreviations: ECT, electroconvulsive therapy; MST, magnetic seizure therapy; T0, conducted 24 hours before the first session (pre-ECT, or pre-MST); T1, 24 to 48 hours after the final session (post-ECT, or post-MST); PANSS, The Positive and Negative Syndrome Scale.

Discussion

Contrary to our hypothesis, neither MST nor ECT induced significant amygdala volumetric changes (P>0.05), challenging seizure therapy neuroplasticity models in schizophrenia.

Key secondary outcomes: Superior language safety with MST (d = 1.02 vs ECT d = 0.19, P =0.019); Differential left amygdala responses (group × time P = 0.009, η^2 = 0.21) without volumetric change. These secondary findings are hypothesis-generating, as amygdala-cognition correlations did not survive correction for FDR P>0.05.

Contrasting with reports of amygdala atrophy in schizophrenia, our null finding may reflect methodological distinctions: shorter intervention duration (4 vs 12+ weeks); medication-stabilized cohort characteristics; limited sensitivity to microstructural changes.

Notably, volumetric preservation correlates with neurocognitive sparing in early psychosis,[20] suggesting our cohort's amygdalar integrity may represent a compensatory mechanism.

Recent meta-analyses highlight MST's favorable cognitive profile versus ECT, though evidence remains inconsistent across studies. While some report significant cognitive preservation with MST in schizophrenia,[7] others note variable cognitive outcomes in depression trials.[21]

Contextualizing MST among emerging neurostimulation therapies, a recent systematic review[22] confirms MST's comparable efficacy and superior cognitive safety profile versus ECT for major mental disorders. Other recent advances include nonconvulsive electrotherapy (NET) demonstrating reduced cognitive impairment versus conventional ECT,[23] though Transnasal humidified rapid-insufflation ventilatory exchange (THRIVE)-enhanced ECT currently lacks cognitive outcome data.[24] Among non-seizure interventions, MST provides stronger antipsychotic efficacy than deep TMS[25] avoiding continuous theta burst stimulation (cTBS)[26] or Stanford neuromodulation therapy (SNT)'s unestablished applicability to psychosis.[27]

The following limitations should be considered:

1. Concomitant antipsychotic use may influence volumetric findings → Future studies should include medication-naïve patients.
2. The 4-week follow-up prevents assessment of long-term structural stability → Longitudinal trials with 6–12 month endpoints are needed.
3. Lack of functional connectivity data precludes circuit-level analysis → Resting-state fMRI integration is recommended.
4. Automated segmentation may have limited sensitivity to subtle changes → Manual verification protocols could supplement future work.

Conclusion

The amygdala plays a central role in schizophrenia neuropathology. Contrary to our primary neuroplasticity hypothesis, this first investigation of MST-induced amygdalar structural changes in schizophrenia demonstrated no significant volumetric alterations post-intervention. While a group-by-time interaction ($P = 0.009$) suggested differential neurobiological responses to MST versus ECT, this exploratory finding requires replication given non-significant absolute volume changes. Our null result directly addresses the study's core objective, though three limitations constrain interpretation: limited sample size, short follow-up 4 weeks and illness-duration imbalance. Collectively, these findings challenge prevailing models of seizure therapy-induced neuroplasticity while establishing foundational evidence for MST's structural safety profile in schizophrenia.

Data Sharing Statement

We, the authors of this manuscript, intend to share individual de-identified participant data from the clinical trial reported herein. This commitment aligns with Dove Medical Press's data sharing policies and aims to promote transparency and reproducibility in psychiatric research.

The specific data to be shared includes de-identified demographic information, eg age, gender, diagnosis, clinical assessment results, eg psychiatry symptoms scales, treatment response metrics, intervention details and outcome measures, eg efficacy and safety endpoints. All data will be anonymized to protect participant confidentiality, according to ethical guidelines.

Additionally, the following documents will be made available: the full study protocol, statistical analysis plan, informed consent form template and case report form templates.

The data will be accessible upon request by contacting the corresponding author via Email at 530272229@qq.com. This contact information will be published with the manuscript to facilitate access.

The data and associated documents will be made available immediately upon publication of this manuscript. They will remain accessible for at least 1 year to support future research endeavors.

Acknowledgments

This study was supported by Suzhou clinical Medical Center for mood disorders (No. Szlcyxzx202109), Suzhou Key Laboratory (SZS2024016), Multicenter Clinical Research on Major Diseases in Suzhou (DZXYJ202413), Suzhou Municipal Sci-Tech Bureau (SKY2022066), Suzhou Key Diagnosis and Treatment (LCZX202326), Suzhou Municipal Health Commission General Project (MSXM2024034).

Disclosure

The authors report no conflicts of interest in this work.

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