Assessing the impact of MR-guided focused ultrasound thalamotomy on brain activity and connectivity in patients with essential tremor

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OBJECTIVE Although magnetic resonance–guided focused ultrasound (MRgFUS) at the ventral intermediate (VIM) thalamic nucleus is a novel and effective treatment for medication-refractory essential tremor (ET), it is unclear how the ablation lesion affects functional activity. The current study sought to evaluate the functional impact of MRgFUS thalamotomy in patients with ET, as well as to investigate the relationship between neuronal activity changes and tremor control.

METHODS This study included 30 patients with ET who underwent MRgFUS thalamotomy with a 6-month follow-up involving MRI and clinical tremor rating. Additional sex- and age-matched healthy people were recruited for the healthy control group. The fractional amplitude of low-frequency fluctuation (fALFF) and regional homogeneity were used to identify functional alteration regions of interest (ROIs). To investigate changes after treatment, ROI- and seed-based functional connectivity (FC) analyses were performed.

RESULTS Patients with ET had significantly increased fALFF in the right postcentral gyrus (PoCG; ROI 1), regional homogeneity in the left PoCG (ROI 2), and regional homogeneity in the right PoCG (ROI 3, cluster-level p value family-wise error [pFWE] < 0.05), which were recovered and normalized at 6 months after MRgFUS thalamotomy. FCs between ROI 2 and the right supramarginal gyrus, ROI 2 and the right superior parietal gyrus, and ROI 3 and the left precentral gyrus were also found to be increased after treatment (cluster-level pFWE < 0.05). Furthermore, changes in fALFF, regional homogeneity, and FC values were significantly correlated with tremor relief (p < 0.05). Preoperative FC strengths were found to be inversely related to the postoperative tremor control ratio (p < 0.05).

CONCLUSIONS In patients with ET, the VIM lesion of MRgFUS thalamotomy resulted in symptom-related regional functional recovery associated with sensorimotor and attention networks. Preoperative FC strengths may reflect the postoperative tremor control ratio, implying that this metric could be a useful neuroimaging biomarker for predicting symptom relief in patients with ET following thalamotomy.

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KEYWORDS magnetic resonance–guided focused ultrasound; essential tremor; resting-state functional MRI; fALFF; regional homogeneity; functional connectivity
Researchers due to its potential for widespread clinical application. It was discovered that MRgFUS thalamotomy caused long-term and symptom-related changes in the effective connectivity of the dentate nucleus within the motor circuit.3 According to Jang and colleagues, there was a significant perturbation in the motor network as well as transient changes in the entire brain network after MRgFUS.4 Moreover, MRgFUS thalamotomy also has an effect on structural architecture. A diffusion tensor imaging study identified long-term white matter damage around the ablation core, indicating that tremor pathogenesis may be linked to the dentatorubro-thalamo-cortical pathway.5 In a recent study, a U-shaped MRgFUS-sensitive subnetwork was identified among structural networks, which was associated not only with clinical parameters but also with a robust gene signature of dopaminergic activity.6 Further understanding the impact of MRgFUS on the brain is critical for assessing and analyzing the benefits and risks of MRgFUS thalamotomy, which merits further investigation.

Resting-state functional MRI (rs-fMRI) is a noninvasive imaging modality that offers a variety of perspectives for abnormal regional and global functional measures for pathological mechanisms. An rs-fMRI study found that patients with ET had significantly lower fractional amplitude of low-frequency fluctuation (fALFF) values in the basal ganglia, inferior orbitofrontal gyrus, and insula when compared with healthy controls (HCs).7 In patients with ET, regional homogeneity was found to be decreased in the anterior bilateral cerebellar lobe, bilateral thalamus, and insular lobe, but increased in the bilateral prefrontal cortex, parietal lobe, and primary motor cortex.8 Regional rs-fMRI signal connectivity reflects complex polysynaptic interactions and helps with clinical diagnosis and prediction.9 A ventral intermediate (VIM) seed-based functional connectivity (FC) analysis of patients with ET revealed decreased FC in the cerebellum but increased FC in the motor cortex, indicating the involvement of the motor cortex–cerebellar circuit in the pathogenesis of tremor.10 Resting-state fMRI studies are also widely used in MRgFUS thalamotomy. Spontaneous neural activity in visual areas was found to be associated with tremor improvement in patients with Parkinson’s disease using MRgFUS thalamotomy, implying the involvement of specific visuomotor networks in tremor relief.11 Pre-therapeutic FCs between tractography-based VIM and ipsilateral sensorimotor cortex, subthalamic nucleus, and the visual area were found to be positively correlated with tremor control.12

As a result, we collected longitudinal rs-fMRI data from patients with ET to investigate the characteristics of brain functional alteration after MRgFUS. First, we measured the local brain activity metrics (fALFF and regional homogeneity) to explore significant functional changes at 6 months after MRgFUS thalamotomy. Because characterizing the functional connectome may provide insight into the brain remodeling induced by MRgFUS thalamotomy, we conducted a region of interest (ROI)– and seed–based FC analysis to investigate alterations in functional networks at 6 months postoperatively. Finally, we assessed the relationship between these rs-fMRI features and tremor improvement.

Methods
Experimental Design and Participants

We performed a clinical trial to determine the feasibility and safety of MRgFUS thalamotomy in ET. This study was registered with the ClinicalTrials.gov database (https://clinicaltrials.gov; registration no. NCT04570046). The goal of the trial was to investigate effective imaging biomarkers and longitudinal changes in brain functional activity in patients with movement disorders who underwent MRgFUS VIM thalamotomy. The Ethics Committee of PLA General Hospital approved this study, and all patients and their families were fully informed and signed an informed consent form prior to the operation. The diagnosis of ET was determined by the experienced neurologist specializing in movement disorders. Inclusion criteria were consistent with previous studies, meaning patients had severe tremor (Clinical Rating Scale for Tremor [CRST] score ≥ 2 for habitual hand/arm posture or intentional tremor) and disability (≥ 2 points on any of the 8 items in the CRST disability section).13 Exclusion criteria included patients with brain disorders such as cerebrovascular disease; brain tumors; epilepsy; other neurodegenerative diseases; psychiatric disorders with impaired cognitive function; contraindications to MRI; treatment with deep brain stimulation; stereotactic ablation; Botox injections in the arm, neck, or face within 5 months before baseline; skull density ratio (SDR) ≤ 0.35; head displacement > 3 mm; and/or angular rotation > 3° during MRI.

This study included 30 patients with medication-refractory ET who were treated with unilateral MRgFUS thalamotomy. MR images were obtained preoperatively as well as 1 day, 1 week, 1 month, 3 months, and 6 months after MRgFUS thalamotomy. Tremor was assessed preoperatively as well as 1 and 6 months postoperatively. As a result, 30 patients were successfully treated with MRgFUS and completed pre- and postoperative 6-month follow-up, with 17 completing all follow-up evaluations. Furthermore, 30 age- and sex-matched HCs were recruited.

MRgFUS Thalamotomy and Tremor Assessment

MRgFUS thalamotomy was performed in a 3-T MRI suite (GE Discovery 750, GE Healthcare) using the ExAblate Neuro focused ultrasound system (InSightec), with a hemispheric helmet and 1024-element phased-array transducer. Details of the MRgFUS thalamotomy procedure can be found in previous studies.2 A stereotactic frame was used to secure the patient’s head to the treatment device, and a flexible silicone membrane was stretched around the patient’s head. Low-power sonication was used for the initial target ablation, and once the final target was determined, the energy was increased so that the target tissue ablation temperature reached approximately 55°C–60°C. During MRgFUS thalamotomy, the target was adjusted based on real-time patient feedback.

Tremor performance was evaluated preoperatively and 1 and 6 months postoperatively using the CRST, which was divided into three parts: part A, involving tremor location and severity; part B, involving performance of specific motor tasks; and part C, functional disability due to tremor. The hand tremor score (range 0–32) was...
calculated by combining the treated hand’s CRST part A (three items: resting, postural, and action; 0–4 possible score on each item) and CRST part B (five tasks: handwriting, drawing [3 tasks], and pouring; 0–4 possible score on each item), with higher scores reflecting more severe tremor. The postoperative tremor control ratio was calculated as: (baseline clinical scale scores – postoperative 6-month clinical scale scores)/baseline clinical scale scores × 100%.

MRI Data Acquisition and Preprocessing

All MRI data were collected using a 3-T MRI system (GE Discovery 750). To keep the patient’s head still, thick foam paddings were secured, and earplugs were used to reduce scanner noise. Each patient was instructed to relax and lie quietly, with eyes closed but awake, without thinking about anything else. The echo-planar imaging sequence was applied to collect resting-state functional images using the following parameters: TE 30 msec, TR 2000 msec, flip angle 90°, field of view 240 × 240 mm², 64 × 64 matrix, slice thickness 3.5 mm, slice gap 0.5 mm, and 36 slices. We collected 180 volumes for approximately 6 minutes. The aforementioned sequences were reviewed independently by two senior radiologists (J.L., Y.X.), and the quality of all MR images was carefully examined.

RESTplus software (version 1.24) was used to preprocess images. Briefly, preprocessing consisted of the following steps: 1) the DICOM images were converted to NIfTI format; 2) the top 10 time points were removed; 3) the remaining images were subjected to slice timing and head motion correction; 4) all rs-fMR images were spatially normalized with the standard Montreal Neurological Institute (MNI) space; and 5) spatial smoothing was performed using a 6 × 6 × 6-mm full width at half maximum (FWHM) Gaussian kernel. Image smoothing was performed in the fALFF calculations and FC analysis, but not in the regional homogeneity calculations. The final linear trend removal and nuisance covariate regression were performed with nuisance variables such as Friston 24-parameter correction, white matter signal, and CSF signal. The bandpass filtering frequency range was 0.01–0.08 Hz.

Regional Functional Activity Metrics and Analysis

Among the regional functional metrics, fALFF is a sensitive and specific approach that measures the magnitude of regional activity amplitude to reflect the intensity of local brain activity.15 Regional homogeneity reflects the synchronization of local brain activity by calculating Kendall’s coefficient concordance of the time series between one voxel and the adjacent voxels.16 RESTplus software (version 1.24) was used to calculate these metrics. To obtain the power spectrum, the preprocessed time series is transformed into the frequency domain using the fast Fourier transform. At each frequency in the power spectrum, the square root of the power spectrum was computed. Finally, fALFF was obtained by calculating the ratio of the power spectrum in the 0.01- to 0.08-Hz range to the power spectrum over the entire frequency range, providing a more accurate method for detecting spontaneous brain activity. Next, the calculated regional homogeneity values were smoothed with a 6-mm FWHM Gaussian kernel. Finally, z-standardized fALFF and regional homogeneity values were calculated.

A paired-sample Student t-test was performed using SPM12 software to identify brain regions with significant alterations in fALFF and regional homogeneity 6 months postoperatively compared with preoperatively in ET. The significance level was set at 0.001 for voxels and 0.05 for clusters, with family-wise error (FWE) correction. The fALFF and regional homogeneity values were extracted from cluster regions at ET baseline and 6 months postoperatively, as well as from HCs. A two-sample independent t-test was used to compare the differences in these brain regions between patients with ET and HCs. One-way repeated-measures ANOVA was used to investigate dynamic changes in fALFF and regional homogeneity values at six consecutive time points for patients who completed all MRI follow-up evaluations. A post hoc paired Student t-test with Bonferroni correction was performed for five comparisons (α = 0.05). Pearson correlation coefficients were applied to assess the relationship between the alteration in fALFF and regional homogeneity and the changes in tremor scores. The statistical significance level was set at p < 0.05.

FC Reconstruction and Analysis

FC was defined as the correlation of time series between brain areas measured by the Pearson correlation coefficient, reflecting the temporal coherence between brain areas.17 The RESTplus toolkit was used to build FC. ROIs were defined as brain regions with significant alterations in fALFF and regional homogeneity values at 6 months postoperatively, with a total of three ROIs.

As in previous studies,18 we chose 16 brain regions associated with motor networks for ROI-wise FC analysis. To generate the FC matrix, we calculated Pearson correlation coefficients between each of the three ROIs and motor-related brain regions. Based on fALFF and regional homogeneity results, the correlation coefficients between the mean time series signals of each ROI and the whole-brain voxel signals were calculated to obtain the correlation maps. Finally, the correlation coefficients were converted to z values using a Fisher transform. A paired-sample Student t-test was used to identify brain regions with significant FC changes in patients with ET (ROI-based, p < 0.05 after Bonferroni correction; seed-based, voxel-wise p < 0.001, cluster-level pFWE < 0.05). A two-sample independent t-test was used to examine the FC strength difference between patients with ET and HCs. Pearson correlation coefficients were used to identify tremor-sensitive FC (p < 0.05).

Results

After a successful 6-month follow-up, the data of 30 medication-resistant patients with ET were ultimately collected. The mean age (± SD) of the patients was 61.97 ± 10.77 years (range 30–76 years), with a mean disease duration of 18 years. All patients underwent ablation of the left VIM nuclei. Demographic and clinical characteristics are shown in Table 1. Tremors were eliminated imme-
The paired t-test revealed one cluster (ROI 1) in the right postcentral gyrus (PoCG) with significantly increased fALFF at 6 months postoperatively compared with the preoperative baseline value, with a voxel p value threshold of 0.001 and a cluster pFWE value threshold of 0.05 (Table 3, Fig. 1C). Alteration in the fALFF value in ROI 1 was negatively correlated with changes in tremor scores during the pre- and postoperative 6-month periods (hand tremor score, \( r = -0.57 \); CRST-A score, \( r = -0.63 \); CRST-B score, \( r = -0.53 \); CRST-C score, \( r = -0.60 \); CRST total score, \( r = -0.63 \); all \( p < 0.01 \) (Fig. 1D).

At baseline, the fALFF value in ROI 1 in patients with ET was significantly lower compared with the value in HCs (HCs vs ET baseline: \( t = 4.13, p < 0.001 \)), which was dramatically recovered by MRgFUS thalamotomy (HC vs ET at 6 months: \( t = 2.41, p < 0.05 \) (Fig. 1E)). Furthermore, longitudinal analysis of 17 patients who completed all MRI follow-up evaluations showed fluctuations in fALFF values in ROI 1. Post hoc tests revealed significant differences between pre- and postoperative values at multiple time points, including 1 day, 1 week, 3 months, and 6 months postoperatively (\( F = 9.43, p < 0.01 \) (Fig. 1F).

**Altered Regional Homogeneity in Patients With ET After MRgFUS Thalamotomy**

A paired t-test with a voxel p value threshold of 0.001 and a cluster pFWE value threshold of 0.05 revealed two clusters in the left PoCG (referred to as ROI 2) and right PoCG (referred to as ROI 3) with significantly higher regional homogeneity at 6 months postoperatively compared with baseline (Table 3, Fig. 2A). A significant negative correlation was found between the alterations in regional homogeneity values in ROIs 2 and 3 and changes in tremor scores preoperatively and 6 months postoperatively (ROI 2: hand tremor score, \( r = -0.40 \); CRST-A score, \( r = -0.54 \); CRST-B score, \( r = -0.45 \); CRST-C score, \( r = -0.42 \); CRST total score, \( r = -0.50 \); ROI 3: hand tremor score, \( r = -0.44 \); CRST-A score, \( r = -0.57 \); CRST-B score, \( r = -0.46 \); CRST-C score, \( r = -0.46 \); CRST total score, \( r = -0.53 \); all \( p < 0.01 \) (Fig. 2B and C).

Regional homogeneity values in ROIs 2 and 3 were significantly lower at ET baseline compared with HCs (ROI 2: HC vs ET at baseline, \( t = 2.14, p < 0.05 \); ROI 3: HC vs ET at baseline, \( t = 3.41, p < 0.01 \)), but significantly improved at 6 months postoperatively (ROI 2: HC vs ET at 6 months, \( t = 1.22, p = 0.23 \); ROI 3: HC vs ET at 6 months, \( t = 1.37, p = 0.18 \) (Fig. 2D and E). Longitudinal follow-up revealed fluctuations in regional homogeneity values for ROIs 2 and 3, with significant differences at 1 week and 6 months postoperatively compared with preoperative values (ROI 2: \( F = 5.33, p < 0.01 \); ROI 3: \( F = 3.58, p < 0.05 \) (Fig. 2F and G).

**Altered FC in Patients With ET After MRgFUS Thalamotomy**

We used an ROI-based FC analysis to investigate the connections between three ROIs and 16 motor network-related brain regions. There was no significant alteration in FCs after Bonferroni correction. With three ROIs as the seed points, the FC strengths between ROI 2 of the left PoCG and the right supramarginal gyrus (SMG; left PoCG–right SMG), ROI 2 of the left PoCG and the right superior parietal gyrus (SPG; left PoCG–right SPG), and ROI 3 of the right PoCG and the left precentral gyrus (PreCG; right PoCG–left PreCG) were increased at 6...
FIG. 1. Tremor improvement and altered fALFF in patients with ET after MRgFUS thalamotomy. **A** and **B**: Bar graphs of hand tremor (A) and CRST total (B) scores before (base) and 1 and 6 months after treatment. **C**: Brain regions with significant alteration in fALFF at 6 months postoperatively. **D**: The alteration of fALFF was negatively correlated with changes in tremor scores. **E**: Graph of the difference in fALFF of ROI 1 between HCs and patients with ET before and 6 months after thalamotomy. **F**: Graph of the dynamic changes of fALFF in ROI 1. *p < 0.05; **p < 0.01; ***p < 0.001. 1d = 1 day; 1m = 1 month; 1w = 1 week.

| TABLE 3. Brain regions with fALFF and regional homogeneity alterations in patients with ET at 6 months after MRgFUS thalamotomy compared with baseline |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Peak MNI Coordinate Region      | Side            | Cluster Size (voxels) | MNI Coordinate (mm) | Peak-Level t Value | Cluster-Level pFWE |
| fALFF                           |                 |                  |                  |                  |                  |
| PoCG (ROI 1)                    | Rt              | 371              | 54               | -3               | 27              | 5.98            | <0.001*         |
| Regional homogeneity            |                 |                  |                  |                  |                  |
| PoCG (ROI 2)                    | Lt              | 72               | -39              | -27              | 48              | 4.29            | 0.033           |
| PoCG (ROI 3)                    | Rt              | 410              | 42               | -18              | 33              | 6.59            | <0.001*         |

* Cluster-level pFWE < 0.05 when voxel-level threshold was p < 0.001.
months postoperatively (cluster-level $p_{FWE} < 0.05$) (Table 4, Fig. 3A–C), which recovered relative to the HCs (HC vs ET baseline, all $p < 0.05$; HC vs ET at 6 months, all $p > 0.05$) (Fig. 3D–F). Importantly, these alterations in FCs were negatively correlated with changes in tremor scores, including left PoCG–right SMG (hand tremor score, $r = -0.24$; CRST-A score, $r = -0.28$; CRST-C score, $r = -0.32$; CRST total score, $r = -0.27$; all $p < 0.05$), left PoCG–right SPG (hand tremor score, $r = -0.42$; CRST-B score, $r = -0.36$; CRST-C score, $r = -0.39$; CRST total score, $r = -0.37$; all $p < 0.05$), and right PoCG–left PreCG (hand tremor score, $r = -0.35$; CRST-A score, $r = -0.42$; CRST-B score, $r = -0.36$; CRST-C score, $r = -0.39$; CRST total score, $r = -0.39$; all $p < 0.05$) (Fig. 4).

Preoperative FCs of the left PoCG–right SMG, left PoCG–right SPG, and right PoCG–left PreCG were negatively correlated with the ratio of alterations in right hand tremor score and CRST-B score (hand tremor score: left PoCG–right SMG, $r = -0.42$; left PoCG–right SPG, $r = -0.39$; right PoCG–left PreCG, $r = -0.39$; CRST-B score: left PoCG–right SMG, $r = -0.37$; left PoCG–right SPG, $r = -0.39$; right PoCG–left PreCG, $r = -0.33$; all $p < 0.05$) (Fig. 4).
TABLE 4. Brain regions with seed-based FC alterations in patients with ET at 6 months after MRgFUS thalamotomy compared with baseline

<table>
<thead>
<tr>
<th>ROI</th>
<th>Peak MNI Coordinate Region</th>
<th>Side</th>
<th>Cluster Size (voxels)</th>
<th>MNI Coordinate (mm)</th>
<th>Peak-Level t Value</th>
<th>Cluster-Level pFWE</th>
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<td>ROI 2</td>
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<td>201</td>
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<td>5.44</td>
<td>&lt;0.001*</td>
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<tr>
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<td>Rt</td>
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<tr>
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<td>Lt</td>
<td>88</td>
<td>x=-33 y=-18 z=48</td>
<td>5.47</td>
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</table>

* Cluster-level pFWE < 0.05 when voxel-level threshold was p < 0.001.

FIG. 3. Altered FC in patients with ET after MRgFUS thalamotomy. A–C: FC strengths were elevated at 6 months postoperatively. D–F: Graphs showing the differences in FCs between HCs and patients with ET before and 6 months after thalamotomy. G–I: Graphs showing a negative correlation between alterations of FCs and changes in tremor scores. *p < 0.05; **p < 0.01; ***p < 0.001. ns = not significant (p > 0.05); PoCG.L = left PoCG; PoCG.R = right PoCG; PreCG.L = left PreCG; SMG.R = right SMG; SPG.R = right SPG.
Discussion

In the current study, we found that fALFF and regional homogeneity alteration features in patients with ET undergoing MRgFUS thalamotomy were primarily located in the PoCG. It is well known that the PoCG plays an important role in ET modulation via the cerebello-thalamocortical circuit.\textsuperscript{19,20} The PoCG showed abnormally robust synchronization of local neural activities, implying spatiotemporal inconsistency.\textsuperscript{21} Benito-León et al. found that the global functional efficiency in ET was disrupted with higher local efficiency and clustering coefficient in the right PoCG.\textsuperscript{22} Functional remodeling of the PoCG was frequently reported after thalamotomy, which is consistent with our findings. Passive wrist movement–induced activation in the PoCG was inhibited after VIM thalamotomy in patients with ET, possibly due to disruption of thalamocortical pathways.\textsuperscript{23} According to an H\textsubscript{2}\textsuperscript{15}O PET motor activation study, thalamotomy suppressed activation of the PoCG, lateral premotor cortex, and parietal area during hand movement.\textsuperscript{24} Unlike enhanced regional homogeneity in bilateral PoCG, increased fALFF was limited in the PoCG contralateral to the ablated lesion. We speculated that this result was due to hemispheric interactions, and that VIM ablation affected the balance of hemispheric activation, resulting in compensatory activation of the contralateral cortex. Similar cases have been observed in stroke research, in which an ischemic lesion caused a shift in activation balance to the unaffected hemisphere and promoted activation of the contralateral motor network.\textsuperscript{25–27} In our study, we found additional enhanced FC of the right PoCG–left PreCG, confirming the interhemispheric interaction. The alteration in lateralization caused by a brain lesion required further investigation.

However, no significant changes in thalamic functional activity were discovered. There are several reasons to consider for this finding. First, it is possible that the ablated lesion was so small that the functional alteration in the thalamus was too subtle to detect. Second, because the resolution of a typical rs-fMRI study may not be able to detect the activity signals of different nuclei within the thalamus, current rs-fMRI was insensitive to small subcortical structures.\textsuperscript{28} Finally, microelectrode detection revealed that thalamic neurons did not exhibit tremor frequency activity during rest, explaining the lack of altered thalamic activity in the resting state.\textsuperscript{29}

Pathophysiological changes in ET could involve various corticocortical pathways.\textsuperscript{30} Nicoletti et al. has reported that the FC between the somatosensory cortex and the parietal areas (both the SPG and SMG) in patients with ET was involved in tremor onset.\textsuperscript{31} Moreover, longitudinal observation after thalamotomy also suggested a reorganization of the dorsal attention and salience networks.\textsuperscript{32} Interestingly, we found that tremor-related FCs of left PoCG–right SMG and left PoCG–right SPG were elevated after MRgFUS, implying that the pathological corticocortical pathway had been restored. Furthermore, previous studies have shown that pre-therapeutic FC was a powerful fMRI predictor of tremor relief after thalamotomy.\textsuperscript{12,33} In our study, preoperative FCs of left PoCG–right SMG, left PoCG–right SPG, and right PoCG–left PreCG were also found to be negatively correlated with postoperative tremor score alteration ratios, including hand tremor score and CRST-B score. This finding suggests that preoperative FC can predict postoperative improvements in hand tremor and specific functional activities such as writing, pouring, and drawing. Together, our findings suggest a reorganization of the sen-
sorimotor and attention networks following thalamotomy, which could be used as a neuroimaging marker to predict patient prognosis.

Limitations of the Study

Some limitations of the study still exist. First, we only explored the alteration in functional brain activity at 6 months after thalamotomy, but the study lacked longer-term exploration of brain activity. Second, because some patients did not complete all follow-up evaluations, the sample size was relatively small in comparison with larger imaging cohorts. The imbalance in the number of male and female participants was a final limitation, with males outnumbering females.

Conclusions

We attempted to determine the effect of MRgFUS thalamotomy on functional remodeling. We found that an MRgFUS thalamotomy-induced focal Vim lesion affects and normalizes areas associated with sensorimotor and attentional networks. Importantly, the restoration of the fMRI metrics in these brain regions was negatively correlated with tremor relief. It was also revealed that preoperative FCs of left PoCG—right SMG, left PoCG—right SPG, and right PoCG—left PreCG were negatively correlated with tremor improvement, suggesting that this could be a valid fMRI predictor of tremor response after thalamotomy.

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References


**Disclosures**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**Author Contributions**

Conception and design: Lou, Lu, Lin, Pan. Acquisition of data: Kang, Bian, Zhou. Analysis and interpretation of data: Lu, Lin, Xiong, Deng. Drafting the article: Lu. Critically revising the article: Lou, Lu, Lin. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Lou. Statistical analysis: Lu, Lin, Xiong, Wang. Administrative/technical/material support: Lou, Pan. Study supervision: Lou, Lin, Wang, Pan. MR-guided focused ultrasound thalamotomy: Zhou, Pan.

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