BMJ Open Thalamic neural activity and epileptic network analysis using stereoelectroencephalography: a prospective study protocol

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ABSTRACT

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Dr Tomotaka Ishizaki; ishizaki.tomotaka.d8@f.mail. nagoya-u.ac.jp **Introduction** Epilepsy is a prevalent chronic neurological disorder, with approximately one-third of patients experiencing intractable epilepsy, often necessitating surgical intervention. Deep brain stimulation (DBS) of the thalamus has been introduced as a palliative surgical option for seizure control; however, its precise mechanisms remain largely unclear. The thalamus plays a crucial role in coordinating neural networks, both in normal brain function and the propagation of epileptic activity. This study aims to investigate the involvement of the thalamus in epilepsy networks using stereoelectroencephalography (SEEG) to monitor thalamic activity during epileptic seizures in patients with drug-resistant epilepsy.

Methods and analysis This single-arm, non-randomised, prospective, exploratory study will be conducted at Nagoya University Hospital, involving 10 patients undergoing SEEG for presurgical evaluation of drug-resistant epilepsy. Participants must be 18 years or older, have normal cognitive function and provide informed consent. Between 7 and 14 SEEG electrodes, including 2 in the bilateral thalamus, will be implanted in key thalamic nuclei (anterior, dorsomedial, centromedian and pulvinar) using a robotic system. The primary outcome focuses on electroencephalographic findings from the thalamus, emphasising waveform and frequency changes around seizures. Secondary outcomes include postoperative seizure frequency, changes in cognitive function and neuroimaging results. SEEG data will be recorded continuously for 1-2 weeks to capture both ictal and interictal activity. Data analysis will employ t-tests to compare ictal and interictal periods, with p values < 0.05 deemed statistically significant. This study seeks to characterise thalamic spectral and connectivity changes during seizures, identify the thalamic subnuclei involved in seizure propagation and explore their association with seizure outcomes, potentially contributing to future DBS candidate selection. By advancing our understanding of the thalamus in epilepsy networks, this research aims to improve DBS interventions, ultimately enhancing seizure control in patients with intractable epilepsy.

Ethics and dissemination This study was approved by the ethics committee of the Nagoya University Graduate School of Medicine (Approval No. 2024-0044). All participants will provide written informed consent prior to enrolment. The results of this study will be disseminated

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study will employ stereoelectroencephalography (SEEG), a method that allows direct and hightemporal-resolution measurement of thalamic neural activity, providing unique insights into the role of the thalamus in epileptic networks.
- ⇒ The inclusion of electrodes targeting multiple thalamic nuclei, including the anterior, dorsomedial, centromedian and pulvinar, will ensure comprehensive data collection across key regions of interest.
- ⇒ Use of a robotic system for SEEG electrode implantation enhances precision, minimising potential procedural risks and improving reproducibility.
- \Rightarrow The single-arm, uncontrolled design and single-centre settings are limitations of the study.
- ⇒ The small sample size (10 participants) may limit the robustness and generalisability of the findings, though it aligns with the feasibility of SEEG in clinical practice.

through publication in a peer-reviewed journal and presentations at academic conferences. **Trial registration number** jRCT1042240024.

INTRODUCTION

Epilepsy is one of the most common chronic neurological disorders, with a point prevalence of 0.6%.¹ Approximately two-thirds of epilepsy patients achieve seizure control with up to three antiepileptic drugs.² However, the remaining one-third are classified as having intractable epilepsy, and within this group, 10%–20% of patients may require surgical intervention.³ The abnormal brain networks involved in epilepsy are broadly divided into two categories: epileptogenic networks, which generate seizures, and propagation networks, which spread epileptic activity to various brain regions.⁴

Historically, epilepsy surgery focused on resecting the brain regions containing the epileptogenic network in order to eliminate the source of seizures. In recent years, however, surgical strategies have evolved to include palliative approaches aimed at inhibiting seizures by modulating the entire abnormal network involved in epilepsy. This method, known as neuromodulation, adjusts the functioning of the network rather than targeting a specific region for removal.⁵

One form of neuromodulation is deep brain stimulation (DBS), a surgical treatment that suppresses epileptic seizures by delivering electrical stimulation to specific nuclei in the bilateral thalamus. Although DBS is considered a palliative technique, it has shown favourable outcomes in reducing seizure frequency.^{6 7} Despite its clinical success, the exact mechanism by which DBS exerts its effects on epilepsy remains unclear.⁸ Consequently, there is a challenge in determining preoperatively which patients are suitable candidates for DBS before surgery.

The thalamus is a crucial deep subcortical region that acts as a command centre, coordinating neural networks across the brain. Much of what is known about thalamic function has been elucidated through animal experiments. However, due to the central location of the thalamus within the human brain, recording neural activity using conventional electrophysiological methods is challenging. Imaging techniques such as MRI, which are frequently used in recent neural activity studies, are limited by their inability to capture the rapid, millisecond-scale changes in neural activity. Consequently, research into human thalamic function remains technically demanding, and many aspects are still poorly understood.

A recent scoping review by Gadot *et al*^p summarised prior reports on thalamic stereoelectroencephalography (SEEG) in epilepsy surgery. The review highlighted that most studies have been retrospective and descriptive in nature and have typically focused on single thalamic nuclei such as the anterior (ANT) or centromedian (CM) nuclei. Prospective investigations evaluating multiple thalamic subnuclei using standardised protocols are lacking. The present study addresses this gap by systematically recording thalamic activity from four nuclei (ANT, CM, dorsomedial (DM) and pulvinar nuclei) in a prospective manner, aiming to expand the current understanding of the thalamocortical involvement in focal epilepsy.

Under these conditions, SEEG is the only method that allows direct electrophysiological measurement of human thalamic neural activity.¹⁰ SEEG is typically performed as part of preoperative evaluation for patients with refractory epilepsy. Since implanting electrodes in the human brain solely for research purposes is not ethically permissible, we perform thalamic SEEG only in patients who meet clinical indications for invasive monitoring. In such cases, thalamic activity is assessed using electrodes originally planned for clinical purposes, by slightly extending their trajectories. This approach allows us to gain clinically meaningful information, such as evaluating potential candidacy for thalamic DBS, while also obtaining research data with informed consent. Based on previous research on epilepsy networks,¹¹ we hypothesised that DBS targeting the thalamus may play a role in regulating the propagation network within the broader epileptic network. We proposed that analysing electroencephalography (EEG) data obtained through thalamic SEEG could help clarify the timing and network characteristics of thalamic involvement in seizures. This, in turn, could lead to a better understanding of the mechanisms underlying seizure generation and propagation and aid in identifying appropriate DBS candidates, which would be highly valuable in clinical practice. Additionally, the thalamic neural activity captured through SEEG could provide insights into the physiological role of the human thalamus.

The aims of this study are threefold. First, we aim to clarify the role of the thalamus in epileptic networks by characterising the electrophysiological features of thalamic SEEG signals during ictal and interictal periods. Specifically, we will examine changes in the electrophysiological features of frequency-specific spectral power and functional connectivity between thalamic nuclei and cortical regions, particularly those involved in seizure onset and early propagation. Second, we seek to explore whether particular thalamic subnuclei-including the ANT, CM, DM and pulvinar nuclei-exhibit distinctive activation patterns during seizures. This exploratory analysis aims to generate hypotheses for future research regarding optimal DBS targeting, although definitive validation is beyond the scope of the present study. Although this study does not include a DBS intervention, our findings may help generate hypotheses about nucleus-specific roles in seizure dynamics. Third, we aim to investigate whether these specific thalamic electrophysiological features correlate with seizure semiology and postoperative seizure outcomes. This analysis seeks to clarify how thalamic network dynamics relate to clinical manifestations and surgical prognosis in focal epilepsy.

METHODS AND ANALYSIS Study design

This single-arm, non-randomised, non-controlled, prospective study is being conducted at Nagoya University Hospital. Data will be collected exclusively in Japan, with part of the data analysis performed at Nagoya Medical Center. The study schedule and workflow are detailed in table 1 and figure 1. Recruitment will be completed by 31 March 2026.

Eligibility criteria and informed consent

Participants in this study will be adult patients (18 years or older) with drug-resistant focal epilepsy undergoing SEEG as part of presurgical evaluation. Eligible participants must meet the clinical indication for invasive evaluation due to inconclusive findings from non-invasive assessments (such as MRI and scalp EEG) and the need for further localisation of seizure onset zones. The selection criteria are as follows: individuals with drug-resistant

Timepoint	Enrollment SEEG			SEEG (day)					Epilepsy surgery (day)					
	-3month	-2	0	1	3	7	8	30	-2	0	1	3	6	1 yea
Enrollment:														
Eligibility screen	Х													
Informed consent	Х													
Interventions:														
Electrodes implantation			Х											
Electrodes removal						Х								
Epilepsy surgery										Х				
Assessments:														
СТ		Х	Х	Х			Х				Х	Х		
MRI		Х											Х	Х
Neuropsychological test		Х				Х			Х					Х
Cortical Stimulation Functional Mapping							Х							
EEG monitoring			Х	Х	Х									
Primary outcome								Х						
Secondary outcome								Х						Х

epilepsy for whom standard surgical treatment is planned. In cases where non-invasive evaluations (eg, scalp EEG, MRI, seizure semiology) fail to localise the epileptogenic zone, SEEG is clinically indicated. Among such patients, if clinical evaluation or prior literature suggests possible thalamic involvement, and if the patient may be a candidate for thalamic DBS, the SEEG trajectory may be extended to include the thalamus. In selected patients, thalamic SEEG is clinically justified when the findings may inform not only seizure localisation but also potential consideration for thalamic DBS, which is available at our centre as a treatment option for drug-resistant epilepsy. Importantly, these thalamic recordings are obtained using electrodes already scheduled for clinical purposes, and no electrodes are inserted solely for research. Participants must be able to understand the study explanation and provide informed consent (age 18 or older, with an MMSE score of 24 or higher). Exclusion criteria include patients under 18 years of age, as the procedure is invasive and requires personal consent rather than that of a parent or guardian.

Other exclusions include individuals with significant cognitive impairment or those who do not meet the criteria for standard treatment. The intervention will be conducted by a qualified neurosurgeon who specialises in epilepsy.

Potential participants will be selected from patients visiting Nagoya University Hospital for whom SEEG is planned as part of standard epilepsy treatment. After a clinical research physician assesses each candidate against the inclusion and exclusion criteria, the patient and their family will be fully informed of the study's purpose, methods, risks and benefits. Those meeting the eligibility criteria will sign two copies of the consent form, one retained by the researcher and one by the patient. Participants retain the right to refuse participation without any disadvantage.

The consent form will also confirm the potential use of data from this study for future yet unspecified research. Data will not be shared with other research institutions except Nagoya University, though temporary collaboration with external institutions for data analysis may occur, as specified in the consent form. An example of the participant consent form is provided in online supplemental file 1.

Clinical assessments

On enrolment in this study, a clinical research physician will collect information from participants including age, sex, types of epilepsy, medical history, current medication and duration of disease.

Interventions

The patient is fitted with a Leksell frame under general anaesthesia, and intraoperative CT imaging is performed to integrate the images with the preoperative MRI used for planning. A robotic arm (Neuromate, Renishaw, UK) is used to insert SEEG depth electrodes into the intracranial region according to the preoperative plan. The SEEG electrodes, manufactured by Unique Medical (Japan), are approved under pharmaceutical law and covered by health insurance for epilepsy treatment. These electrodes

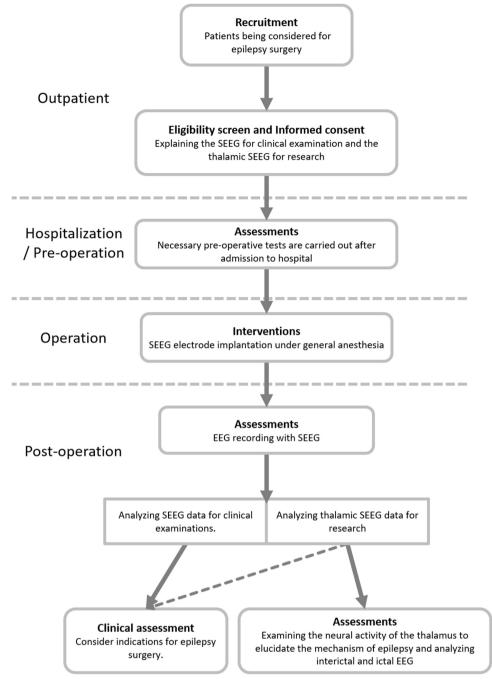


Figure 1 Study workflow. EEG, electroencephalography; SEEG, stereoelectroencephalography.

have demonstrated good reliability and have extensive clinical experience.

As part of the standard SEEG procedure for presurgical evaluation, a total of 7–14 electrodes are implanted, as recommended by guidelines. In selected patients, where thalamic involvement in the epileptic network is suspected based on clinical evaluation and prior literature, and when thalamic DBS may be considered a potential treatment option, two of the clinically indicated electrodes are planned to reach the bilateral thalamus by extending their trajectories. These electrodes are not inserted solely for research purposes but are incorporated into the clinical electrode plan. The thalamic data obtained may also be used for research analysis, based on written informed consent obtained from each participant.

The thalamic targets in this study include the ANT, CM, DM and pulvinar nuclei. The DM nucleus was selected due to its extensive anatomical and functional connectivity with the medial and orbital prefrontal cortices as well as with limbic structures such as the hippocampus and amygdala. These regions are frequently implicated in seizure propagation, particularly in temporal lobe epilepsy. Previous studies have shown that electrical stimulation of the DM nucleus can activate these critical cortical and limbic areas,¹² supporting its inclusion as an exploratory recording site in our investigation.

EEG monitoring will last between 1 and 2 weeks during the period of electrode placement. The package insert states that the electrodes can be used for up to 4 weeks.

The specific thalamic nuclei targeted in each patient will be determined on a case-by-case basis by the epilepsy surgery team. The decision will be based on clinical hypotheses derived from seizure semiology, imaging and non-invasive EEG and may vary depending on individual anatomical and safety considerations. Not all four nuclei will be implanted in every case; rather, electrode placement will be optimised based on clinical relevance and risk assessment. The thalamic electrodes are not planned as independent trajectories. Instead, they are based on clinically necessary electrode paths intended for cortical or subcortical targets, with their depth extended to reach the thalamus. This adjustment will be carefully made during preoperative planning with attention to anatomical safety and clinical utility.

Compliance with the protocol is ensured by the principal investigator, who will oversee all treatments in accordance with the study protocol. If the research leads to death or severe complications, an efficacy and safety evaluation committee will be established to determine whether to continue, modify or discontinue the study. The committee's recommendation to discontinue the research will serve as the discontinuation criterion.

In the event of harm to participants, no treatments will be prohibited, and all appropriate treatments will be allowed. Participants are also covered by clinical research insurance, which provides compensation for health issues, including death or disability, arising from this study.

Outcomes

The primary outcome is the EEG findings (waveform and frequency) observed in the thalamus before and after an epileptic seizure. Thalamic EEG data will be considered appropriate if more than 60% of the total recorded data reflects evaluable neural activity, compared with the electrodes in other areas recorded at the same time.

The secondary outcomes include (1) thalamic EEG findings, functional connectivity and the epileptogenicity index (EI) during rest and task conditions, (2) postoperative seizure outcomes following SEEG recording, (3) higher brain function and ((4) radiological imaging. These outcomes will be evaluated as follows. (1) Thalamic EEG findings (waveform and frequency data) during rest and task conditions will be analysed using the same criteria as the primary outcome. Functional connectivity will be assessed between all implanted SEEG contacts, including cortical, thalamic and other subcortical structures (eg, hippocampus, amygdala), using frequency band-specific power envelope correlations and phase-based coherence measures. Analyses will be conducted across standard frequency bands, including delta (1-4Hz), theta (4-8Hz), alpha (8-13Hz), beta (13-30Hz), low gamma (30–50 Hz), high gamma (50–80 Hz), ripple (80–250 Hz) and fast ripple (250-500 Hz) bands. Changes in thalamic spectral power (eg, low/high gamma, ripple bands) will

be compared between ictal and interictal states, and their relationship to seizure onset and propagation zones will be analysed. (2) Seizure outcomes will be assessed using the Engel classification 1 year after surgery (either resective surgery or DBS), if surgery is performed based on SEEG findings. (3) Cognitive function will be evaluated both preoperatively during SEEG evaluation and 1 year after surgery using the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV) and the Wechsler Memory Scale-Revised (WMS-R). (4) Radiological findings will be recorded and evaluated accordingly.

Sample size

The expected number of participants is 10. Based on previous SEEG studies, several ictal EEG recordings are typically captured over 7 days of monitoring. With 10 participants, statistical analysis of interictal EEGs corresponding to 50–100 ictal EEGs can be performed. This sample size was selected as it is feasible within the research period. Given the number of SEEG procedures performed annually at Nagoya University Hospital, the indication for thalamic SEEG, and an estimated consent rate of 80%, it is expected that 10 participants can be enrolled over the planned 2-year enrolment period.

Data collection and management

Missing data will not be supplemented, and no judgements will be made regarding data abnormality; all data will be included in the analysis. On study termination, EEG data and medical record data collected up to that point will be used for analysis.

All data will be stored on a hard disk and kept in a secure, locked warehouse. EEG data and other information collected in the study will be stored for 10 years after study completion, provided the patient agrees. If new analytical methods are developed in the future for the same research purpose, the data may be reanalysed after obtaining approval from the bioethics review committee. Special precautions will be taken to prevent any leakage of personal information. Once the storage period has ended, paper documents will be shredded, and electronic data will be permanently deleted using appropriate deletion software.

At the time of participant registration, all personally identifiable information, including medical record numbers, names and dates of birth, will be removed and a unique research registration ID will be assigned to each participant. No identifiable information will be shared with external organisations. Principal investigators from collaborating research institutions will securely store reference tables linking research registration IDs with predeidentified data in a locked bookcase. Information collected from participants will be recorded in the case report form and used as the source data for the study.

This study is registered with the Japan Registry of Clinical Trials (jRCT1042240024, https://jrct.niph.go.jp/ latest-detail/jRCT1042240024). On study completion, the full protocol, data and analysis results will be available from the corresponding author on reasonable request. jRCT is an approved member of the Primary Registry Network of WHO ICTRP.

Statistical methods

For determination of the primary outcome, spectral power and the EI will be calculated across multiple frequency bands (eg, theta, beta, gamma, ripple) and compared between ictal and interictal segments using paired or unpaired t-tests, depending on data structure. Functional connectivity measures, including coherence and phase-locking values, will be evaluated between all implanted SEEG contacts, including cortical, thalamic and other deep brain structures (eg, hippocampus, amygdala), where applicable. These analyses will be conducted across all standard frequency bands. Secondary outcomes will be analysed as follows. (1) EEG activity during rest and task conditions will be compared using paired t-tests for spectral power and connectivity measures. (2) Associations between EEG parameters (eg, power, connectivity, EI) and clinical outcomes, such as seizure control (Engel classification at 1 year) and cognitive function (WAIS-IV and WMS-R scores), will be assessed using Pearson's or Spearman's correlation coefficients, as appropriate. (3) Radiological findings will be analysed descriptively.

All statistical analyses will be performed with a two-tailed significance level set at p<0.05. P values will be rounded to the third decimal place; values of 0.000 will be reported as '<0.001', and values of 1.000 will be reported as '>0.999'.

Oversight and monitoring

Nagoya University will serve as the coordinating centre for this research, with data analysis and management conducted at both Nagoya University and Nagoya Medical Center. Two researchers from Nagoya University will monitor the data. Their responsibilities include verifying patient eligibility, ensuring written informed consent, confirming protocol compliance and validating the accuracy of registered data. Monitoring will be conducted under the supervision of a monitoring manager and will include the following items: (1) appropriateness of the study start-up procedures; (2) participant registration status; (3) participant eligibility; (4) implementation method of the informed consent explanation and storage status of the consent form; (5) compliance with the study implementation plan; (6) verification of the case report form and source documents and (7) implementation of study procedures during and after the study.

A potential adverse event in this study is cerebral haemorrhage. Adverse events will be systematically collected during hospitalisation using physical examination records, clinical tests and radiographic image data from the electronic medical record. All adverse events will be documented throughout the study, from admission to discharge. A serious adverse event is defined as death or persistent, significant disability or incapacity requiring hospitalisation or the prolongation of existing hospitalisation. All serious adverse events and other adverse events will be recorded in the final report. The investigator will promptly report any serious adverse events related to the study to the principal investigator. The principal investigator will then report these events to the hospital director and the relevant authorities.

Any changes to the protocol will be registered with the Japan Registry of Clinical Trials (jRCT) after review and approval by the Institutional Review Board (IRB) at Nagoya University Hospital. All relevant updates will be shared among researchers.

Patient and public involvement

We did not have pre-existing relationships with any particular patient groups relevant to this project. Patients did not contribute to the formulation of the research question, the determination of outcome measures or the design and execution of the study. However, we plan to involve patients and the public in the dissemination phase after study completion. Specifically, we intend to organise patient education seminars, release public reports through the hospital, and collaborate with patient advocacy groups to communicate the clinical significance of thalamic SEEG and epilepsy surgery options.

ETHICS AND DISSEMINATION

This study was approved by the ethics committee of the Nagoya University Graduate School of Medicine (No. 2024-0044) and was registered at the jRCT on 9 May 2024 (jRCT 1042240024). Written informed consent will be obtained from all participants. All procedures will adhere to relevant guidelines and regulations. The results of this study will be submitted for publication in a peer-reviewed academic journal and presented at medical conferences both domestically and internationally.

Study status

This manuscript is based on a study protocol (version 1.1, last updated on 5 April 2024). Participant recruitment began on 9 May 2024 and the first patient was recruited on 16 July 2024. Recruitment will be completed by 31 March 2026.

DISCUSSION

In this study, we plan to implant electrodes targeting the ANT, DM, CM and pulvinar nuclei of the thalamus, which have not been precisely identified in previous research. We aim to obtain detailed neural activity recordings from these thalamic nuclei. Although prior studies have explored the relationship between these nuclei and higher brain functions, as well as epilepsy networks, these investigations primarily used indirect methods such as functional MRI¹³ and magnetoencephalography.¹¹ However, these modalities offer only indirect assessments of neural activity, whereas SEEG provides superior temporal and spatial resolution through direct recordings.

By analysing neural activity from electrodes inserted into each thalamic nucleus (ANT, CM, DM and pulvinar), we may be able to demonstrate therapeutic effects in thalamic nuclei that have not traditionally been targeted for epilepsy treatment. In particular, the DM nucleus was selected because of its established connections with prefrontal cortical regions (eg, medial and orbital frontal areas) and limbic structures (eg, hippocampus and amygdala), which are key components of epileptic propagation networks. Previous studies have demonstrated that stimulation of the DM nucleus can modulate activity in these areas,¹² suggesting that the DM nucleus may play an under-recognised role in seizure dynamics. Recording from the DM may thus help to clarify thalamocortical contributions to seizure generation and propagation. Furthermore, by assessing the synchrony between the neural activity in these thalamic nuclei and other regions within the epileptic network, we may be able to predict the efficacy of DBS in patients who are candidates for surgery.

Additionally, in this study, electrodes will be implanted not only in the affected thalamic regions but also in the healthy side of the thalamus, allowing us to record physiological thalamic neural activity. This will enable us to clarify the fundamental role of the thalamus in brain networks. Traditionally viewed as a relay nucleus, recent research on subcortical structures has revealed that the thalamus plays a more active role in physiological neural processes.^{14 15} Our study will also aim to capture physiological thalamic activity and further elucidate the brain networks centred on the thalamus. In addition, by correlating thalamic neural activity patterns with seizure semiology and postoperative outcomes, we aim to better define the clinical relevance of thalamocortical network involvement in epilepsy.

It has been reported that the EI, which reflects the contribution of ictal EEG obtained by SEEG to the epileptic network, is effective for estimating epileptogenic zones.¹⁶⁻¹⁸ A high EI suggests that the region is strongly involved in the epilepsy network. If the EI of the thalamus can be analysed using thalamic SEEG, the effectiveness of thalamic DBS may be evaluated preoperatively. Currently, it can take several months to a year after surgery to confirm the effects of thalamic DBS, making it challenging to assess its efficacy early on. However, if it becomes possible to predict DBS effects in advance based on thalamic neural activity obtained from SEEG, this would hold significant clinical value. Although thalamic SEEG does not directly result in immediate intervention, the data may contribute to surgical planning, particularly in evaluating suitability for future thalamic DBS. This provides potential indirect clinical benefit to participants. However, it must be emphasised that our study is exploratory in nature. While we aim to analyse activation patterns across multiple thalamic subnuclei, the findings are intended to generate hypotheses regarding potential DBS targets, rather than to definitively identify optimal nuclei for stimulation. Without direct therapeutic

interventions such as DBS and subsequent outcome validation, conclusions about clinical efficacy remain speculative. These limitations are inherent to the study design and should be carefully considered when interpreting the results.

The most common complication associated with SEEG is cerebral haemorrhage, with an incidence rate of approximately 1%–2%. Symptomatic cases are rare, but this complication requires careful consideration when performing SEEG.¹⁰ Regarding the safety of thalamic SEEG, previous studies have not reported thalamic haemorrhage or oedema.⁹ Based on these reports, we believe that the risks and burdens to participants in this study will be comparable to those of conventional SEEG, as the electrodes will only be inserted into the thalamus using standard implantation techniques. Additionally, we will carefully consider the angle and location of electrode placement to further minimise risks.

This study has several methodological limitations. First, the small sample size may reduce the statistical power and limit the generalisability of the findings. Second, the single-arm, uncontrolled design and single-centre settings are limitations of the study. Third, the electrode placement and thalamic nucleus selection may vary slightly between participants, which could influence data consistency. Lastly, some exploratory analyses may not yield definitive conclusions but are intended to generate hypotheses for future research. In particular, we recognise that variability in epileptogenic zones across patients may lead to heterogeneity in thalamic involvement. To address this, we plan to stratify analyses based on the location of the seizure onset zone (eg, temporal vs frontal lobe epilepsy) identified during SEEG. However, the small sample size (n=10) may restrict the feasibility of subgroup analyses, and any findings from such analyses will be interpreted as exploratory.

Contributors TI: conceptualisation; data curation; formal analysis; funding acquisition; investigation; methodology (equal); project administration (equal); resources (lead); visualisation; writing–original draft. SM: project administration (equal); resources (lead); supervision (equal); validation. SY: resources (supporting). TS: resources (supporting). MH: resources (supporting). YI: resources (supporting). TT: resources (supporting). RS: supervision (equal). TI is responsible for the overall content as guarantor. No professional medical writing support was used in the preparation of this manuscript. All authors reviewed the manuscript.

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