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**Systematic Review**

# Evaluation of functional magnetic resonance imaging in the identification of presurgical epileptic zones comparison between conventional and advanced techniques in patients with drug-refractory epilepsy: a systematic review

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## ABSTRACT

Drug-refractory epilepsy (DRE) is a significant clinical challenge when conventional treatments are ineffective. Localization of epileptic zones is essential for successful surgery but conventional techniques such as scalp EEG, PET and structural MRI are usually ineffective, particularly in MRI-negative cases. Functional MRI (fMRI) has emerged as a valuable tool for presurgical assessment by offering information on seizure networks and functional connectivity. This systematic review evaluates the efficacy of traditional and novel fMRI methods in identifying epileptogenic areas and enhancing surgical outcomes. Traditional fMRI with task-based paradigms assists in mapping cerebral functions but is constrained by patient compliance and inability to detect deeply seated foci. Novel techniques like resting-state fMRI (rs-fMRI) EEG-fMRI fusion and analysis aided by AI provide greater spatial and temporal resolution for better epileptic network localisation. These methods are of use for MRI-negative patients and those patients with motor or cognitive deficits. Advanced fMRI techniques, though, require a lot of computational power and skill which can limit their application. Through consideration of the literature, this paper indicates the advantages and limitations of each technique and emphasizes the value of the integration of multiple methods to enhance presurgical planning. The results indicate that improved fMRI techniques have the potential to increase the success of surgery and enhance patients' quality of life with DRE. The research should further improve these techniques so that they are more accessible and feasible for use in clinics.

**Keywords:** Epilepsy, Refractory, Magnetic resonance imaging, Presurgical evaluation, Electroencephalography, Artificial intelligence

## INTRODUCTION

Drug-refractory epilepsy (DRE) affects about 30% of epilepsy patients who do not respond to at least two well-chosen and well-tolerated antiepileptic drugs.[1] Persistent seizures reduce quality of life and increase the risk of sudden unexpected death in epilepsy (SUDEP). Managing DRE is difficult since patients often need alternative treatments and surgical resection is considered as an effective option for cases with a well-defined epileptic focus.[2] Successful surgery depends on accurate localization of epileptic zone and it includes the seizure onset zone (SOZ), symptomatogenic zone and functional areas that must be preserved.

Conventional methods like scalp electroencephalography (EEG), positron emission tomography (PET) and structural magnetic resonance imaging (MRI) may not always identify the epileptogenic zone in MRI-negative cases.[3]

Advanced imaging is necessary in such cases. Functional magnetic resonance imaging (fMRI), a key non-invasive tool, can analyze seizure networks and functional connectivity changes.[4] Resting-state fMRI (rs-fMRI) and task-based fMRI help map abnormal neural activity and track seizure propagation pathways to improve surgical planning.[5]

This review is conducted to evaluate conventional and advanced fMRI techniques for presurgical assessment in DRE. We aim to compare their accuracy in localization and their impact on surgical success. We aim to identify benefits, limitations, and clinical uses of fMRI in epilepsy surgery and we seek to optimize presurgical evaluation protocols and improve patient outcomes.[6]

## METHODS

The systematic review investigates the position of traditional and advanced fMRI methods in presurgical epilepsy assessment. It contrasts the clinical utility limitations and efficacy of these methods in detecting epileptogenic regions and eloquent cortical areas. This section discusses the inclusion criteria, data extraction procedure, and analytical structure utilized to combine results from the literature.

### *Inclusion and exclusion criteria*

We included peer-reviewed studies published between 2019 and 2024 that investigate the use of fMRI in presurgical epilepsy evaluation and we focused on studies that examine conventional fMRI task-based fMRI or advanced fMRI techniques such as resting-state fMRI, EEG-fMRI DTI integration and AI-driven analysis.

Studies must provide comparative data on sensitivity, specificity, spatial and temporal resolution and clinical utility. They must address the limitations and challenges of fMRI in presurgical planning and include patients with drug-resistant epilepsy or MRI-negative epilepsy.

Studies that lack a comparative analysis between conventional and advanced fMRI techniques, focus solely on non-epilepsy applications of fMRI, or are case reports, editorials or reviews without original data are excluded.

### *Data extraction and synthesis*

Data extraction involves selecting relevant studies, including randomized controlled trials, observational studies, and meta-analyses. Key parameters include technique-specific outcomes such as sensitivity, specificity, spatial and temporal resolution, and patient compliance requirements.

Clinical utility is evaluated by measuring accuracy in localizing epileptogenic zones, integration with other modalities such as EEG, PET and MEG, and impact on surgical outcomes.

Limitations such as motion artifacts, computational complexity, and applicability in pediatric or cognitively impaired populations are also assessed. Extracted data are synthesized into a comparative framework that highlights the strengths and weaknesses of conventional and advanced fMRI techniques. Tables and figures summarize findings including comparisons of spatial resolution sensitivity and clinical utility.

### *Analytical framework*

A narrative synthesis approach is used with quantitative analysis where applicable. Key themes include efficacy in epileptogenic zone localization, integration with multimodal imaging, patient-specific challenges, and computational limitations. Advanced fMRI techniques particularly resting-state fMRI and AI-driven analysis demonstrate superior accuracy in identifying epileptic networks compared to conventional task-based fMRI.

The combination of fMRI with EEG, PET, or DTI enhances localization accuracy especially in MRI-negative cases. Conventional fMRI's reliance on patient cooperation limits its utility in pediatric and cognitively impaired populations while advanced techniques such as resting-state fMRI offer greater adaptability. Although advanced fMRI techniques improve accuracy, they require significant computational resources and expertise, which limits widespread clinical adoption.

### *Conventional fMRI techniques in presurgical evaluation*

Functional magnetic resonance imaging (fMRI) is an essential tool in the presurgical evaluation of epilepsy. It helps clinicians map eloquent cortex regions and identify epileptogenic zones. The blood oxygen level dependent (BOLD) contrast mechanism forms the basis of conventional fMRI. It detects changes in oxygenation levels that correspond to neural activity.[7]

This enables non-invasive functional mapping and it is crucial for preserving language motor and sensory functions during epilepsy surgery. Activation-based mapping is another core technique in conventional fMRI where patients perform specific tasks during scanning to identify functional regions.[8]

This process is useful for localizing brain areas responsible for essential functions but its ability to detect seizure foci is limited since it primarily captures interictal activity rather than ictal events. Conventional fMRI has limitations in sensitivity and specificity when identifying epileptogenic zones as previous studies show that while fMRI can detect functional alterations in epileptic networks but, it is often less precise than other imaging modalities like positron emission tomography (PET) or single-photon emission computed tomography (SPECT) by Redjal et al.

A major advantage of fMRI is its ability to reliably localize eloquent cortex regions which ensures neurosurgeons avoid damaging critical functional areas during surgery. This is important in temporal lobe epilepsy (TLE) where preserving memory and language function is crucial by Chilappa et al. Comparing conventional fMRI with other neuroimaging techniques reveals key differences. PET and SPECT assess metabolic and perfusion patterns. They are often more specific in identifying seizure onset zones when structural MRI findings are negative, as Redjal et al, have suggested.

EEG-fMRI combines electrophysiological and hemodynamic data which provides better insight into the spatiotemporal dynamics of epilepsy networks as per Sala Padró 2024 research. EEG-fMRI is not always available due to technical complexity and cost, and this makes conventional fMRI a more accessible option in many clinical settings. Multimodal imaging has been proposed to improve presurgical evaluation. Combining fMRI with PET, MEG (magnetoencephalography) or diffusion tensor imaging (DTI) provides us a more comprehensive picture of structural and functional abnormalities.[7]

Although it has advantages, traditional fMRI is hindered by technical and clinical problems. Motion artifacts compromise signal integrity and cause false-positive or false-negative findings.[9] This problem is especially concerning in children and mentally impaired patients who have difficulty staying motionless during scanning. Patient compliance factors also occur with those who cannot finish task-based paradigms that decrease functional maps' reliability.[8]

In addition, difficulty lies in how deep-seated epileptic foci like in the mesial temporal lobe insula or the subcortical brain regions are difficult to map.[7] BOLD signals are superior in cortical zones. Therefore, routine fMRI tends to work less well with detecting seizure foci deep inside the brain. This requires the application of ancillary imaging methods such as PET or intracranial EEG.[8]

### *Advanced fMRI techniques in presurgical evaluation*

Functional magnetic resonance imaging (fMRI) is considered as an indispensable tool in the presurgical evaluation of drug-resistant epilepsy (DRE). Traditional methods such as electroencephalography (EEG) and structural MRI often fall short in localizing epileptic foci with sufficient precision in cases where no visible lesion is detected.Advanced fMRI techniques including resting-state fMRI (rs-fMRI), task-based fMRI, diffusion tensor imaging (DTI), integration EEG-fMRI and artificial intelligence (AI)-driven analysis have improved our ability to delineate epileptogenic zones and optimize surgical planning by Desale et al.

These modalities enhance spatial and functional resolution which improve connectivity analysis and facilitate real-time multimodal integration, ultimately increasing the success rate of epilepsy surgery. Resting-state fMRI (rs-fMRI) identifies functional networks in the brain by analyzing spontaneous fluctuations in the blood oxygen level-dependent (BOLD) signal while the patient is at rest. Unlike task-based fMRI which requires active participation, rs-fMRI is useful for patients with cognitive or motor impairments and the technique measures functional connectivity by assessing temporal correlations between different brain regions, helping to identify disruptions associated with epilepsy by Ellsay et al. In DRE rs-fMRI plays a critical role in seizure network mapping since changes in functional connectivity usually spread beyond the seizure onset zone (SOZ).

It has been shown that epileptogenic areas have aberrant connectivity patterns in the default mode network (DMN) and thalamocortical circuits to gain important information about the underlying mechanisms of seizure spread rs-fMRI can be combined with DTI and EEG to improve localization precision especially in MRI-negative epilepsy.

Task-based fMRI (tb-fMRI) can measure neural activation induced by a precise motor or cognitive task to identify eloquent cortical areas that should be spared from damage during surgery. New developments in tb-fMRI include the application of more advanced paradigms like language understanding, semantic processing, and intricate motor coordination tasks that provide higher accuracy in localizing functional areas as proposed by Chaulagain et al.[10]

This is applicable in temporal lobe epilepsy (TLE) in which seizures tend to interfere with language and memory processing. It has been demonstrated that more sophisticated tb-fMRI paradigms provide more accurate localization through decreased false positives and discriminating between epileptic activity and normal functional areas based on Redjal et al. 2025 studies.[11]

Combining high-field MRI with tb-fMRI adds better spatial resolution to ensure that resection planning avoids postoperative neurological deficits as much as possible.

Diffusion tensor imaging (DTI) is a specialized MRI technique that maps white matter tracts by analyzing water diffusion patterns, and in epilepsy, DTI provides crucial insights into structural connectivity, revealing microstructural abnormalities in pathways affected by seizures. Combining DTI with fMRI has been shown to significantly improve presurgical planning by offering both functional and structural perspectives of seizure networks, as Redjal et al and Ziu et al stated.[11] DTI is valuable in assessing the integrity of white matter tracts in patients with TLE where disruption of the fornix and corpus callosum can influence seizure propagation and cognitive outcomes. Integrating fMRI-DTI data helps neurosurgeons tailor resection strategies by identifying critical fiber tracts that should be preserved to maintain cognitive and motor function as stated by Sala Padró 2024.[9] EEG-fMRI is a hybrid technique which combines high temporal resolution of EEG with the superior spatial resolution of fMRI and this integration allows for the real-time localization of seizure onset zones and the characterization of both ictal (seizure-related) and interictal (between seizures) activity. A key advantage of

EEG-fMRI is its ability to detect deep-seated epileptogenic foci that are not easily accessible through scalp EEG. Ferri et al, previous studies have shown that EEG-fMRI can provide comprehensive insights about the seizure propagation networks by identifying distant but functionally connected brain regions involved in seizure activity.[12,13]

This capability is useful for cases where standard imaging methods yield inconclusive results. Furthermore, EEG-fMRI has been successfully applied in presurgical evaluations to distinguish primary seizure foci from secondary activation sites, ensuring more targeted surgical interventions.[11]

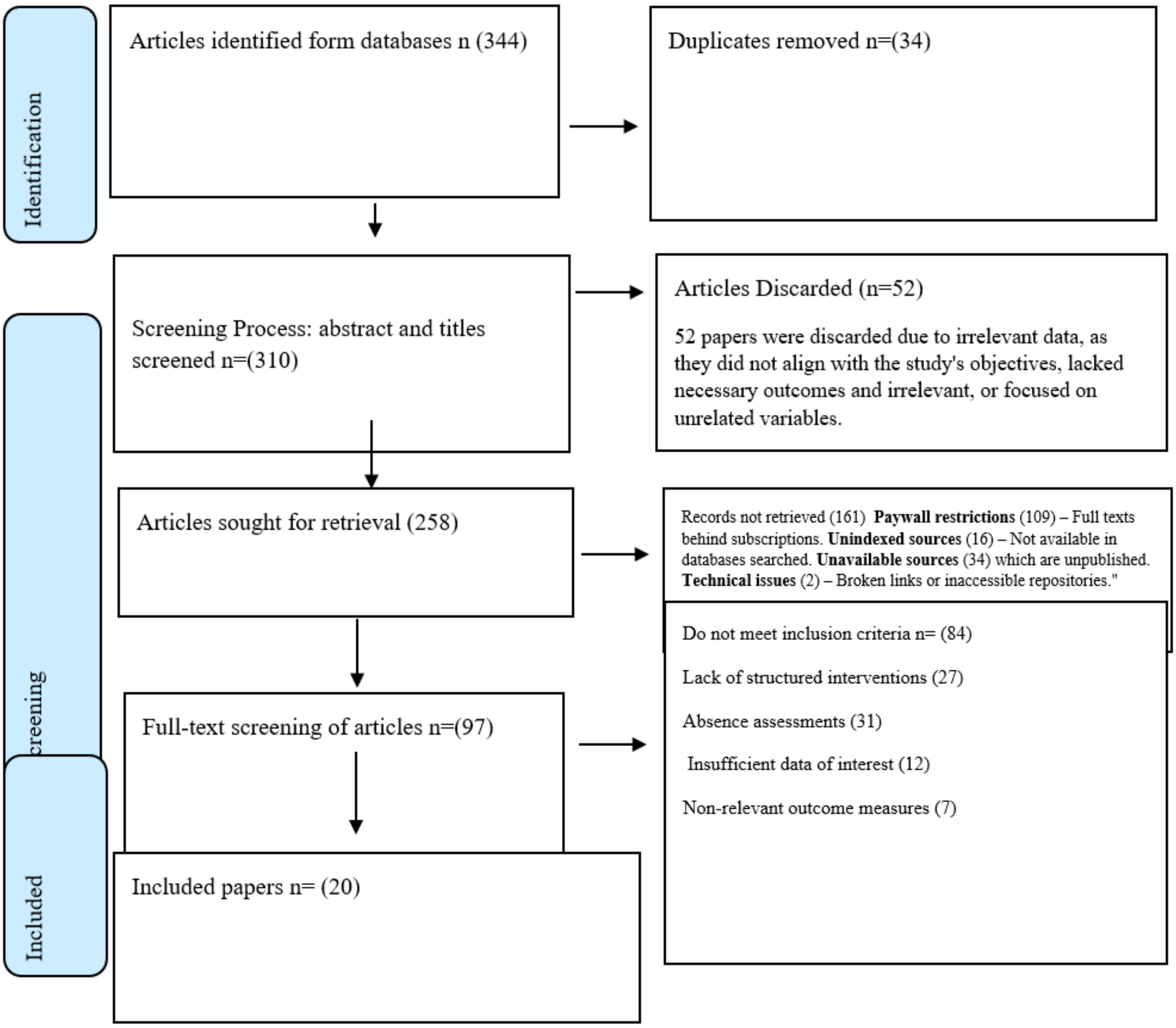


**Figure 1: PRISMA of included studies.**

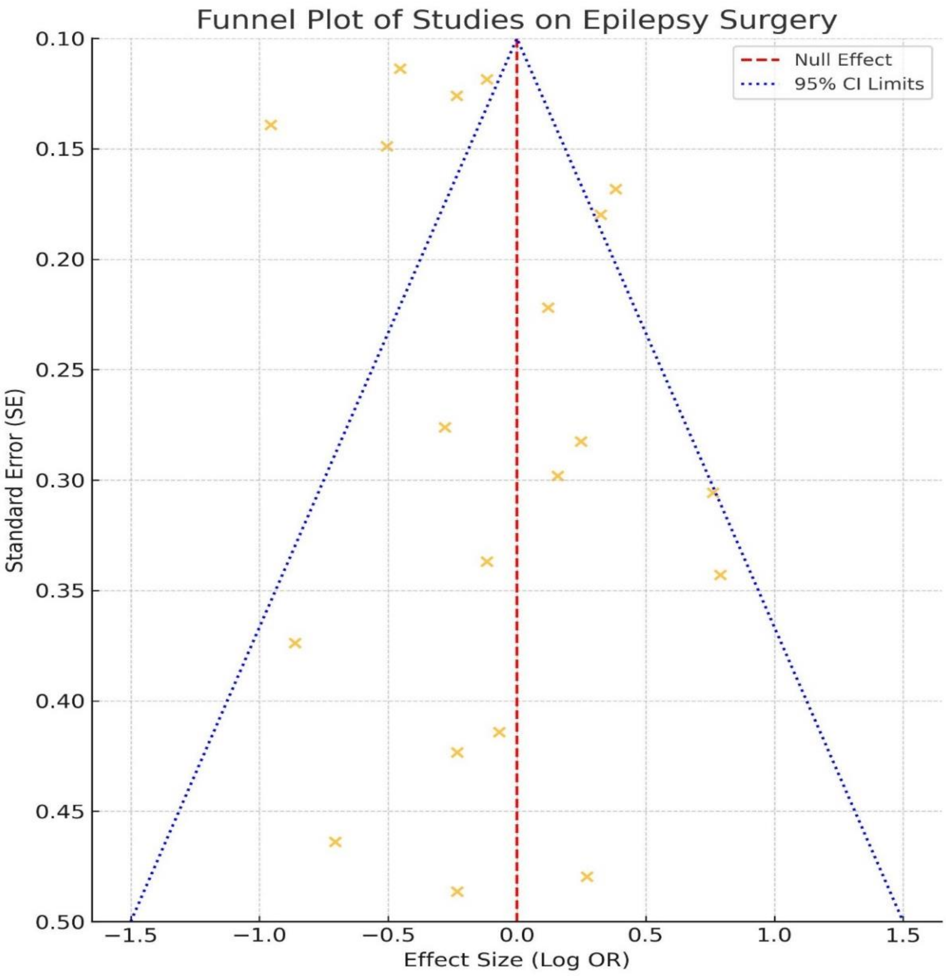


**Figure 2: Funnel plot of included studies.**

Artificial intelligence (AI) and machine learning (ML) have transformed the analysis of fMRI by enabling automation of data processing and enhanced diagnostic accuracy. AI models can examine large fMRI datasets for faint patterns linked to epileptic activity which can be missed under normal manual interpretation.[12] Deep learning algorithms, in particular, have been shown to perform better than others at discovering aberrant patterns of functional connectivity and surgical outcome prediction, according to Desale et al, in 2024.[11]

AI-powered fMRI analysis minimizes inter-rater differences, increases reproducibility, and speeds up the diagnostic process leading to better clinical decision-making. In addition, AI models can fuse imaging data from more than one modality like EEG DTI and PET to create a more complete representation of epilepsy networks.[12] Presurgical planning using AI has also been found to improve the accuracy of epileptogenic zone localization, minimizing the chances of failed surgeries. Recent studies show that advanced functional magnetic resonance imaging fMRI techniques are superior to conventional methods in presurgical epilepsy evaluations for drug-refractory epilepsy. Conventional MRI-based approaches often fail to detect epileptic foci in MRI-negative patients. This limits their use in guiding surgical interventions. Resting-state fMRI rs-fMRI improves epileptic zone localization by mapping abnormal connectivity patterns in seizure-prone networks as shown by Shi et al Guo et al, found that integrating 18F-FDG PET with MRI improves seizure outcome predictions in patients with inconclusive MRI findings.[15,16] Carrette et al, demonstrated that magnetic source imaging MSI enhances preoperative evaluations by improving functional mapping of epileptic zones.[17]

Baumgartner et al, supported multimodal approaches combining neurophysiology with fMRI to improve surgical outcomes.[18] Paranathala et al, 2023 showed that high-resolution fMRI provides better localization accuracy than conventional methods, reducing the risk of postoperative neurological deficits.[19] A 2024 study by Sala Padró introduced new presurgical biomarkers for temporal lobe epilepsy TLE reinforcing the value of network-based imaging techniques in epilepsy management.[20] These findings suggest that while conventional MRI remains essential, advanced fMRI techniques significantly improve presurgical evaluation accuracy and increase the likelihood of successful surgery.

**Table 1: Comparative analysis of conventional vs. advanced FMRI techniques in identifying presurgical epileptic zones.**

| Parameter | Conventional fMRI (task-based fMRI, TB-fMRI) | Advanced fMRI (resting-state fMRI, AI, and machine learning-based analysis) |
|---|---|---|
| **Underlying principle** | TB-fMRI identifies activation in specific brain regions by analyzing blood oxygen level-dependent (BOLD) signals during task performance. | Advanced techniques use resting-state networks, graph theory, and AI-based modeling to analyze spontaneous neuronal activity independent of tasks. |
| **Spatial resolution** | Moderate (3–5 mm) due to reliance on task-based responses and susceptibility to motion artifacts. | Higher (1–3 mm) due to advanced denoising, improved spatial modeling, and high-resolution acquisition protocols. |
| **Temporal resolution** | Limited by block/task design (typically 2–3 seconds per volume), affecting the ability to track dynamic changes in seizure propagation. | Enhanced with dynamic functional connectivity analysis, allowing near-real-time tracking of epileptiform network alterations. |
| **Identification of epileptic networks** | Primarily localizes eloquent cortex regions rather than epileptic networks, requiring additional modalities for precise mapping. | More accurate due to the ability to capture interictal and ictal activity patterns, even in non-cooperative patients. |
| **Dependency on patient cooperation** | High–requires active participation in tasks (e.g., language, motor, or memory tasks), which may be challenging in pediatric or cognitively impaired patients. | Low–does not rely on patient compliance, making it suitable for those with impaired cognitive or motor functions. |
| **Sensitivity in detecting epileptic zones** | Moderate–only identifies task-related activation and may miss broader epileptic networks. | Higher–resting-state connectivity analysis detects abnormalities across the epileptogenic network, improving localization of seizure onset zones. |
| **Specificity in identifying false-positive regions** | Moderate–task-related hemodynamic responses may lead to false activations due to unrelated functional activity. | Higher–advanced machine learning models distinguish pathological connectivity from normal resting-state fluctuations, reducing false positives. |
| **Integration with Other Modalities (EEG, PET, MEG, SPECT)** | Commonly combined with EEG-fMRI, but suffers from limited spatial precision when correlating with EEG spikes. | Stronger multimodal integration with EEG, PET, and MEG, improving the accuracy of epileptogenic focus localization. |
| **Clinical utility in presurgical planning** | Provides supplementary information for cortical mapping but often insufficient alone for surgical decision-making. | More effective in identifying resectable regions by capturing complex networks associated with seizure propagation. |
| **Utility in cases with no apparent structural abnormalities On MRI (MRI-negative epilepsy)** | Limited–depends on task performance and may fail in cases where no structural lesions are visible. | More effective–can identify subtle network-level dysfunctions in MRI-negative epilepsy cases, aiding in resection planning. |
| **Computational complexity and processing time** | Moderate-standard fMRI processing pipelines require relatively simpler analyses. | High–involves complex computational models, AI-driven classification, and network-based connectivity analysis, requiring advanced expertise. |
| **Limitations** | Susceptible to motion artifacts and task-related variability. Cannot capture seizure dynamics outside of task paradigms. Limited applicability in cognitively impaired patients. | Computationally intensive, requiring substantial processing power and expertise. Higher cost and longer analysis time. Interpretation requires specialized training in network neuroscience. |

## CONCLUSION

Functional magnetic resonance imaging (fMRI) is an important tool in presurgical assessment for drug-refractory epilepsy (DRE), providing useful information about epileptic networks and functional connectivity. Standard task-based fMRI is still a valuable tool for functional mapping, but its dependence on patient compliance and poor sensitivity in the detection of deep-seated foci limits its use. Sophisticated methods, such as resting-state fMRI, EEG-fMRI fusion, and machine learning-based analysis, improve localization precision, especially in MRI-negative patients and individuals with cognitive or motor disabilities.

These methods offer enhanced spatial and temporal resolution, enhancing the accuracy of epileptic zone localization and outcomes of surgery. Yet, they are beset with issues such as computational burden, technical skill demands, and limited clinical availability, thus preventing widespread implementation. This systematic review highlights the requirement for multimodal imaging strategies involving the integration of traditional and advanced methods to maximize presurgical evaluation. Refinement of these methodologies, increased standardization, and increased clinical feasibility should be areas of future study to maximize surgical success and quality of life for patients in the management of DRE.

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