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Deep Brain Stimulation Therapy for Drug-Resistant Epilepsy: Present and Future Perspectives

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Drug-resistant epilepsy (DRE) remains a formidable clinical challenge, affecting nearly 30-40% of patients despite optimized pharmacotherapy. In patients for whom resective surgery is contraindicated or poses unacceptable risks, neuromodulatory therapies-most notably deep brain stimulation (DBS)-have emerged as viable and reversible treatment options. This narrative review critically examines the current applications of DBS for DRE, with a focus on major targets including the anterior thalamic nucleus, centromedian nucleus, hippocampus, and emerging targets such as the pulvinar. We provide an in-depth discussion of the therapeutic mechanisms underlying DBS-from local cellular inhibition and desynchronization to widespread network modulation and neuroplasticity induction-and review the latest advances in sensing technologies, patient-specific connectivity mapping, and closed loop stimulation paradigms. In addition to integrating data from randomized controlled trials, long-term observational studies, and advanced imaging investigations, we discuss limitations, persistent challenges, and future research directions that will guide clinical decision-making and optimize therapeutic outcomes. **(2025;15:33-41)**

Key words: Deep brain stimulation, Drug resistant epilepsy, Anterior thalamic nucleus, Centromdeian nucleus, Hippocampal, Pulvinar

Introduction

Epilepsy is a complex and heterogeneous neurological disorder that affects roughly 1% of the global population. Despite significant advances in antiepileptic drug development and pharmacotherapy, an estimated 30-40% of patients continue to experience seizures that remain refractory to medical treatment.[1,2] This drug-resistant epilepsy (DRE) not only imposes a substantial burden on individuals in terms of quality of life and cognitive function but also poses serious social and economic challenges. For many patients, traditional resective surgery is not a feasible option due to multifocal seizure onset zones, involvement of eloquent cortical areas, or the presence of widespread epileptogenic networks. These limitations have spurred the development of neuromodulatory therapies as alternative strategies to control seizure activity.

Deep brain stimulation (DBS) has emerged as a promising neuromodulation technique for DRE. Unlike resective procedures, DBS offers a non-destructive and titratable intervention that can be fine-tuned to individual patient needs. The development of DBS for epilepsy has been driven largely by landmark clinical trials such as the SANTE trial, which demonstrated not only the short-term efficacy but also the long-term benefits of anterior thalamic nucleus (ATN) stimulation.[2] Since that seminal work, the field has expanded to include additional targets-such as the centromedian nucleus (CM) and the hippocampus-as well as emerging regions like the pulvinar.[1,3,4]

The evolution of DBS for epilepsy has paralleled advances in imaging, electrophysiology, and computational modeling. These developments have allowed for more precise targeting, improved understanding of underlying mechanisms, and the eventual integration of patient-specific biomarkers into treatment planning.[5,6] In addition, the advent of closed-loop systems-devices capable of real-time neural sensing and adaptive stimulation-has opened new avenues for personalized neuromodulation, potentially leading to enhanced seizure control and minimized side effects.[7-9]

Literature selection methodology

This narrative review was conducted using a systematic approach to literature identification and selection. We performed comprehensive searches in PubMed, Embase, and the Cochrane Library databases for articles published between January 2000 and December 2023. Search terms included combinations of "deep brain stimulation", "DBS", "neuromodulation", "drug-resistant epilepsy", "refractory epilepsy", "anterior thalamic nucleus", "centromedian nucleus", "hippocampus", and "pulvinar". We prioritized randomized controlled trials, prospective cohort studies, systematic reviews, and meta-analyses, but also included relevant retrospective studies, case series, and mechanistic investigations to provide comprehensive coverage of the field. Additional relevant articles were identified through reference lists of selected publications. We focused on studies reporting clinical outcomes, mechanisms of action, imaging correlates, and emerging technologies in DBS for epilepsy. Articles were selected based on their methodological quality, relevance to current clinical practice, and contribution to understanding therapeutic mechanisms.

Mechanism of therapeutic action of DBS

The clinical efficacy of DBS in epilepsy is underpinned by a series of mechanisms that operate across multiple scales-from molecular and cellular events to large-scale network modulation. A thorough understanding of these processes is essential to appreciate how DBS exerts its therapeutic effects and how ongoing technological advances might further refine these interventions.

Cellular and molecular effects

At the most fundamental level, DBS exerts its influence through the modulation of neuronal excitability. High-frequency stimulation, typically delivered in the range of 130-145 Hz, has been shown to induce what is known as a "functional lesion". This effect is characterized by the hyperpolarization of neurons in the vicinity of the stimulating electrode, which in turn reduces abnormal burst firing and suppresses the local generation of epileptiform discharges.[10,11] Experimental studies using both *in vitro* slice preparations and *in vivo* animal models have demonstrated that high-frequency stimulation can dampen pathological local field potentials (LFPs), particularly those in the gamma frequency band-a range often implicated in the generation and propagation of seizures.[10]

Beyond these immediate effects, chronic DBS appears to induce longer-term neuroplastic changes. Repeated stimulation may lead to alterations in neurotransmitter dynamics, including shifts in the balance between gamma-aminobutyric acid and glutamate. These neurotransmitter changes may contribute to the stabilization of hyperexcitable circuits. Moreover, evidence suggests that chronic stimulation can upregulate the expression of neuroprotective genes and modulate inflammatory pathways, potentially creating a more resilient neural environment less prone to seizure generation.[12,13]

Network-level modulation

While the local effects of DBS are significant, a growing body of evidence highlights the importance of network-level modulation in achieving clinical efficacy. Epilepsy is increasingly recognized as a disorder of distributed neural networks rather than a purely focal phenomenon. In this context, DBS may act not only at the site of stimulation but also by altering the dynamics of interconnected brain regions. For instance, stimulation of the ATN is thought to disrupt the epileptogenic limbic circuitry by desynchronizing abnormal interactions between the thalamus and the hippocampus.[14,15] Functional imaging studies have provided compelling evidence that ATN DBS can alter activity patterns in distant cortical areas, suggesting that the therapeutic benefit extends well beyond the immediate vicinity of the electrode.[15]

Diffusion tensor imaging (DTI) studies have further illuminated the relationship between structural connectivity and clinical outcomes. By mapping the volume of tissue activated (VTA) during stimulation, researchers have demonstrated that the efficacy of DBS is highly dependent on the integrity and configuration of underlying white matter tracts. In particular, the degree of connectivity between the stimulated region and areas such as the medial prefrontal and cingulate cortices has been shown to correlate with improved seizure control.[14,16-18] This network-level perspective underscores the potential of DBS not only as a localized treatment but also to "reset" the aberrant connectivity patterns that facilitate seizure propagation.

Similar network-level effects have been observed with CM and hippocampal deep brain stimulation (Hip-DBS). In generalized epilepsies and refractory status epilepticus, CM stimulation has been shown to modulate thalamo-cortical circuits, leading to widespread desynchronization of pathological activity.[16,19,20] Hippocampal stimulation, on the other hand, may act by directly inhibiting the primary seizure focus while simultaneously modulating hippocampal-cortical interactions.[21-23] These findings collectively suggest that effective DBS may require a nuanced understanding of individual network architectures, thereby paving the way for personalized neuromodulatory strategies.

Modulation of aperiodic neural activity

Recent advances in neurophysiological monitoring have allowed researchers to dissect LFPs into their oscillatory and aperiodic components. Traditionally, emphasis has been placed on the role of oscillatory activity-such as theta, alpha, and gamma rhythms-in normal and pathological brain function. However, emerging data indicate that the non-oscillatory, or aperiodic, component of the LFP may also be a critical determinant of neuronal excitability and seizure susceptibility. Changes in the slope of the flicker noise (1/f) aperiodic component have been observed during both interictal and ictal periods, and these alterations appear to correlate with the efficacy of DBS.[10] In practical terms, modulation of aperiodic activity could serve as a novel biomarker for assessing the therapeutic impact of DBS. By monitoring these changes in real time, clinicians may be able to fine-tune stimulation parameters more precisely, thereby enhancing efficacy while minimizing side effects. The integration of such biomarkers into closed-loop systems is an area of intense research, with the goal of developing adaptive DBS strategies that respond dynamically to fluctuations in neural activity.[10,24]

Closed-loop versus open-loop dynamics

Traditionally, DBS has been delivered using an open-loop system, in which stimulation is provided continuously or according to a predetermined schedule, regardless of the patient's moment-to-moment neural state. While this approach has yielded substantial benefits, it does not account for the dynamic nature of epileptogenic networks. In contrast, closed-loop systems-exemplified by responsive neurostimulation-continuously monitor neural activity and adjust stimulation parameters in real time.[24,25]

The promise of closed-loop systems lies in their potential to provide stimulation only when needed, based on specific electrophysiological triggers. This targeted approach not only improves therapeutic efficacy by synchronizing stimulation with the onset of abnormal activity but also reduces the overall stimulation burden, potentially limiting side effects. Comparative studies have suggested that while the fundamental mechanism of action may be similar between open- and closed-loop systems (i.e., modulation of network connectivity), closed-loop approaches offer a refined, adaptive means to maintain seizure control.[7,25] As computational algorithms and sensing technologies continue to advance, the integration of closed-loop systems is expected to become increasingly prevalent in the clinical management of DRE.

Target-specific clinical characteristics & therapeutic efficacy

The clinical application of DBS for epilepsy is characterized by the selection of distinct neural targets, each with its own therapeutic profile and technical challenges. In this section, we detail the clinical trends associated with stimulation of the ATN, CM, and hippocampus, as well as emerging targets that may expand the therapeutic landscape.

ATN DBS

ATN DBS remains the most extensively studied and widely applied target in the management of focal epilepsies. The seminal SANTE trial provided robust evidence of its efficacy, with an initial median seizure reduction of approximately 40.4% observed during a blinded phase.[26] These findings underscore the potential of ATN DBS as a durable treatment modality for patients who are not candidates for resective surgery.

In addition to the direct antiepileptic effects, ATN stimulation appears to modulate cognitive and neuropsychological functions. Several studies have reported improvements in executive function, verbal memory, and word fluency, which are believed to arise from the modulation of the fronto-limbic network and the Papez circuit.[27,28] This dual impact-reducing seizure burden while potentially enhancing cognitive performance-positions ATN DBS as a uniquely attractive option for patients with DRE, particularly those for whom preservation or improvement of cognitive function is a priority.

Optimal targeting of the ATN is critical to achieving these outcomes. Advanced imaging techniques, including high-resolution magnetic resonance image and DTI, have been instrumental in refining electrode placement.[5,29] Detailed computational models suggest that even slight deviations in electrode position (on the order of 2-3 mm) can lead to significant differences in clinical efficacy.[5] Recent electrophysiological studies have further highlighted the importance of acute gamma suppression and chronic theta modulation as biomarkers of effective stimulation.[30] These insights are guiding the development of individualized treatment protocols that leverage patient-specific connectivity maps to optimize electrode placement and stimulation parameters.

CM DBS

Centromedian nucleus DBS has been primarily explored in the

context of generalized epilepsies, including lennox-gastaut syndrome (LGS) and cases of refractory status epilepticus. Clinical trials have shown that CM DBS can yield seizure reductions in the range of 70-73% in carefully selected patient cohorts.[31-33] In one controlled trial, patients with generalized epilepsy demonstrated more robust improvements compared to those with focal frontal lobe epilepsy, highlighting the target-specific nature of DBS effects.[33]

The therapeutic rationale for CM stimulation is rooted in its strategic position within thalamo-cortical circuits. The CM nucleus is intricately connected with widespread cortical areas, including the anterior cingulate and frontal cortices, which play a crucial role in the generation and propagation of seizures in generalized epilepsy.[34,35] Functional imaging studies have confirmed that stimulation of the CM nucleus leads to significant alterations in thalamo-cortical dynamics, promoting a state of desynchronization that appears to underlie its antiepileptic effects.[36,37] Although effective in reducing seizure frequency in generalized epilepsies, its impact on focal epilepsies is comparatively less pronounced.[33,38] This differential efficacy is thought to stem from the distinct patterns of seizure propagation inherent to focal versus generalized epilepsies.

The unique position of the CM within both corticothalamic and striatothalamic circuits may explain its particular efficacy in LGS and other epilepsies characterized by tonic seizures. A recent study by Warren et al.[36] employed connectivity-based segmentation to identify optimal stimulation sites within the CM, revealing that electrodes with stronger connections to supplementary motor areas achieved superior outcomes in LGS patients. This finding suggests that patient-specific targeting based on individual connectivity profiles may further enhance the efficacy of CM stimulation, particularly in complex epilepsy syndromes.

Hip-DBS

Hip-DBS has been primarily indicated for patients with mesial temporal lobe epilepsy (MTLE), particularly in cases where mesial temporal sclerosis is evident. The hippocampus, with its intricate architecture and pivotal role in memory processing, presents both opportunities and challenges for neuromodulation.

One of the major challenges in Hip-DBS is the precise targeting of the epileptogenic zone. The complex cytoarchitecture of the hippocampus necessitates the use of advanced imaging and patient-specific modeling techniques to ensure accurate electrode placement.[39] In parallel, electrophysiological biomarkers-such as interictal spike rates and distinctive theta/gamma power profiles-have been identified as predictors of clinical success, providing a quantitative framework for assessing treatment response.[7,40] Unlike resective surgery, which often carries the risk of postoperative memory impairment, Hip-DBS has been associated with preserved-and in some cases improved-cognitive performance.[21,41,42]

Despite the promising outcomes of hippocampal DBS, there remains significant variability in cognitive outcomes across studies. While some investigations report cognitive improvement or preservation following hippocampal stimulation, others have yielded more neutral results. This discrepancy may be attributed to several factors. First, the specific region targeted within the hippocampal formation (e.g., anterior versus posterior) can significantly impact cognitive networks differentially.[41,42] Second, baseline characteristics-including the presence of pre-existing hippocampal sclerosis, duration of epilepsy, and laterality of seizure onset-may influence cognitive trajectories. Wang et al.[41] demonstrated that patients with shorter disease duration and less structural pathology showed more favorable cognitive outcomes. Third, stimulation parameters vary considerably between studies, with higher frequencies (>130 Hz) potentially offering superior seizure control but at the expense of more pronounced effects on memory networks.[21,23] These factors highlight the need for standardized protocols and patient-specific approaches to optimize both seizure control and cognitive outcomes.

Emerging targets: pulvinar nucleus of thalamus

Recent research efforts have begun to explore additional thalamic nuclei as potential targets for DBS, particularly in cases of multifocal or posteriorly dominant epilepsy. Among these, the pulvinar nucleus has emerged as a promising candidate.[3,4,43,44] The pulvinar is characterized by its extensive connectivity to occipital and parietal cortices-regions that are increasingly recognized for their involvement in complex seizure networks.[45]

Mechanistically, pulvinar stimulation may function differently than other thalamic targets. While ATN stimulation primarily modulates the Papez circuit and limbic connectivity, the pulvinar's involvement in visual and attentional processing networks suggests a distinct mechanism of action. Filipescu et al.[44] demonstrated that pulvinar stimulation modulates alpha and gamma oscillations in posterior cortical regions, potentially disrupting the synchronization patterns necessary for seizure propagation. This electrophysiological profile makes the pulvinar a compelling complementary target to ATN or CM stimulation in patients with multifocal epilepsy involving posterior regions. Preliminary case series have reported bilateral pulvinar re-

sponsive neurostimulation with seizure reductions ranging from 25% to 100%, suggesting that stimulation of this nucleus could offer significant benefits for select patients.[3,4,44]

However, pulvinar stimulation presents several notable evidence gaps. First, the current literature consists primarily of small case series with heterogeneous patient populations, limiting generalizability. Second, the optimal placement within the pulvinar's extensive territory remains undefined, with some studies targeting the anterior pulvinar and others the lateral or medial regions.[3,44] This anatomical variability may account for inconsistent outcomes. Third, the vast majority of pulvinar studies employ responsive neurostimulation rather than continuous stimulation, making direct comparisons with other thalamic targets challenging. Controlled trials with standardized targeting and stimulation protocols are essential to establish the pulvinar's definitive role in the DBS armamentarium for epilepsy, particularly for patients with occipital and parietal lobe seizures that respond poorly to conventional targets.

Long-term outcomes of DBS for DRE

Long-term outcome data are crucial in evaluating the sustained efficacy and safety of DBS for DRE. Over the past decade, multiple studies have provided insights into how DBS performs over extended periods, highlighting both its benefits and limitations.

ATN DBS

The long-term efficacy of ATN DBS has been well documented in several longitudinal studies. In the SANTE trial, for example, patients followed for over 5 years exhibited a median seizure reduction of approximately 69%, with some individuals achieving reductions as high as 75% over 7 years.[2,27] These outcomes are complemented by high retention rates; reports indicate that nearly 72.4% of patients remain on therapy after 11 years, with discontinuations primarily occurring due to unsatisfactory results rather than adverse effects.[27] Beyond seizure control, ATN DBS has demonstrated potential cognitive benefits. Improvements in executive function, verbal memory, and overall cognitive processing have been reported, which may be attributed to the modulation of key networks such as the Papez circuit.[27,28] Importantly, the majority of adverse events associated with ATN DBS occur during the early postoperative period, with complications such as implant site pain and transient memory disturbances being relatively common but generally self-limiting.[1,2,27,28] Serious complications remain rare, reinforcing the overall safety profile of this intervention over the long term.

CM DBS

The long-term outcomes of CM DBS have been evaluated primarily in the context of generalized epilepsies, particularly in patients with LGS. Clinical trials, including the ESTEL trial, have reported that approximately 50% of patients achieve a $\geq$50% reduction in seizure frequency within the initial months following implantation.[37] Longer-term follow-up studies, spanning up to 18 months, have confirmed that the mean seizure reduction can reach as high as 68%, with particularly notable improvements in patients with LGS.[19,46] Despite these encouraging results, the efficacy of CM DBS appears to be more variable when applied to focal epilepsies. This variability is likely a consequence of the distinct seizure propagation mechanisms inherent to focal versus generalized epilepsy. Nonetheless, imaging studies have provided evidence that the modulation of thalamo-cortical circuits via CM DBS correlates with clinical improvements, suggesting that further refinements in targeting and stimulation parameters could potentially enhance outcomes for a broader patient population.[34,36,47]

Hip-DBS

Hip-DBS has shown particularly impressive long-term outcomes in patients with MTLE. A few studies have demonstrated median seizure frequency reductions of 50-66% for focal aware seizures and up to 91% for focal impaired awareness seizures.[21,23] Extended follow-up periods-spanning several years-indicate that a significant majority of patients (often exceeding 80%) maintain a clinically meaningful reduction in seizure frequency, with a subset achieving periods of complete seizure freedom.[21,23] An additional advantage of Hip-DBS is its favorable cognitive profile. Unlike traditional resective surgery, which carries a high risk of postoperative memory impairment, hippocampal stimulation has been associated with preserved-and in some cases improved-cognitive performance.[21] This memory-sparing effect is a critical consideration when weighing the risks and benefits of different therapeutic modalities in epilepsy.

Collectively, these long-term outcome data underscore the potential of DBS as a durable treatment for DRE. However, the variability in outcomes across different targets and patient subgroups also highlights the need for ongoing research to refine patient selection criteria and optimize stimulation protocols (Table 1).

Table 1. Comparative clinical characteristics of major DBS targets for drug-resistant epilepsy

Feature	Anterior thalamic nucleus	Centromedian thalamic nucleus	Hippocampus
Primary indication	Focal epilepsy; temporal/frontal lobe seizures[1,2,26,27]	Generalized epilepsy; lennox-gastaut syndrome (LGS); tonic seizures[31-33,37]	Mesial temporal lobe epilepsy; mesial temporal sclerosis[21,23]
Mechanism	Modulation of the Papez circuit and limbic network	Influences thalamocortical and sensorimotor networks	Direct inhibition at the seizure focus; modulation of hippocampal-cortical connectivity
Seizure reduction	69-75% (long-term)[2,27,28]	50-70% (LGS), >90% for electrographic seizures[19,37]	66-91% (focal seizures)[21,23,42]
Seizure freedom rate	13.8-24.1%[2,27]	20-30%[31,33,37]	~20%[21,41]
Retention rate	72.4% (11 years)[2,27]	68% (18 months)[37]	86.7% (57 months)[21,23]
Cognitive effects	Improved verbal memory and executive function[27,28]	No significant cognitive impairment[31]	Memory-sparing; potential improvements in spatial memory[21,41,42]
Limitations	May not be effective for posterior onset seizures[2,27]	Less effective in focal epilepsy[33,38]	Requires precise targeting; less effective in seizures with primary motor semiology[21,39]

Data compiled from referenced clinical studies and meta-analyses. Seizure reduction percentages represent median values from long-term follow-up studies. Retention rates indicate the percentage of patients continuing therapy at the specified follow-up duration.
DBS, deep brain stimulation.

Limitations and unmet needs

Despite the significant strides made in the application of DBS for drug-resistant epilepsy, several limitations and unmet needs persist that warrant further investigation.

One of the foremost challenges is the inherent heterogeneity of epilepsy itself. Variations in etiology, seizure semiology, and underlying structural pathology make it difficult to predict which patients will derive the greatest benefit from DBS.[1,6,7] Although promising electrophysiological biomarkers-such as interictal spike rate and spectral power profiles-have been identified, their translation into routine clinical practice remains in its infancy. Further research is needed to validate these biomarkers across diverse patient populations and to develop standardized protocols for their integration into treatment planning.[48]

Another critical challenge lies in the precision of electrode targeting and the optimization of stimulation parameters. The therapeutic efficacy of DBS is highly dependent on the accurate placement of electrodes within the intended target nucleus. Even minimal deviations in electrode positioning can result in suboptimal stimulation and reduced clinical benefit.[5,36,39] Current programming of DBS devices is largely empirical, and there is a pressing need for advanced imaging modalities and computational models to standardize electrode placement and parameter selection. The development of patient-specific VTA models and improved diffusion imaging techniques are promising steps in this direction, yet further refinement is required to ensure consistent clinical outcomes.

Moreover, modern DBS devices equipped with chronic sensing capabilities generate vast amounts of data that remain largely underutilized. While these data have the potential to provide invaluable insights into the dynamics of epileptogenic networks, current analytical methods are insufficient to extract clinically actionable information. The development of sophisticated, data-driven algorithms for real-time analysis and adaptive programming is essential to fully leverage the capabilities of these devices.[10,49]

Closed-loop DBS systems, while promising, also face several challenges. The optimal detection algorithms and thresholds for triggering stimulation remain topics of ongoing debate, and the integration of individualized electrophysiologic signatures into these systems is not yet standardized.[49,50] Additionally, the long-term reliability and battery life of closed-loop devices require further improvement before these systems can be widely adopted in clinical practice.

Finally, the integration of network-based targeting into routine clinical workflows represents a significant unmet need. Although research has clearly demonstrated that patient-specific structural connectivity plays a critical role in determining DBS outcomes, translating these findings into everyday clinical practice remains challenging.[22,39,49] Large-scale, multicenter trials are necessary to validate the use of connectivity-based targeting and to develop standardized guidelines that can be adopted across institutions.

Future perspectives and emerging trends

Looking forward, the field of DBS for DRE is poised for transformative advances that promise to enhance the precision, efficacy, and adaptability of neuromodulatory therapies.

One of the most exciting avenues is the development of personalized, closed-loop DBS systems. Future devices are expected to incorporate advanced real-time sensing capabilities, combined with machine learning algorithms that adjust stimulation parameters based on individualized neural signatures.[49,51] This adaptive approach holds the potential to further improve seizure control by delivering stimulation only when it is needed, thereby reducing side effects and prolonging device longevity.

Another promising trend lies in the integration of advanced imaging and tractography into the treatment planning process. High-resolution diffusion imaging and individualized tractography are already being used to map the complex networks involved in seizure propagation.[16,40,52] As these techniques become more refined, they will enable clinicians to identify the most critical nodes within a patient's epileptogenic network, thereby guiding electrode placement and optimizing stimulation parameters. Such network-based approaches may eventually lead to the development of multi-target stimulation strategies that address the distributed nature of epilepsy more effectively than single-target interventions.

Additionally, there is growing interest in exploring non-invasive and minimally invasive alternatives to traditional DBS. Techniques such as repetitive transcranial magnetic stimulation and closed-loop vagus nerve stimulation are being actively investigated as potential adjuncts or alternatives for patients who may not be ideal candidates for invasive procedures.[53,54] While these approaches are still in the early stages of development, they offer the promise of reduced procedural risks and increased patient acceptance.

Finally, the future of DBS for DRE will likely be shaped by collaborative, multicenter research efforts. Large-scale clinical trials and international consortia will be essential to validate emerging technologies and to develop standardized protocols that can be implemented across diverse clinical settings.

Conclusion

DBS has firmly established itself as a transformative approach in the management of drug-resistant epilepsy. Over the past decade, extensive research has demonstrated that DBS can achieve sustained, clinically meaningful reductions in seizure frequency across a variety of targets-including the ATN, CM, and hippocampus. The multifaceted mechanisms of action-ranging from cellular inhibition and modulation of neurotransmitter dynamics to the desynchronization of large-scale neural networks-underscore the complexity and potential of this therapeutic modality.

In summary, DBS represents not only a significant advancement in the treatment of DRE but also a platform for the development of innovative, network-based neuromodulatory therapies. By addressing current limitations and embracing emerging technologies, the future of DBS is poised to deliver even greater improvements in seizure control and quality of life for patients with refractory epilepsy.

Conflicts of Interest

None.

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