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EFFECTIVENESS OF DEEP BRAIN STIMULATION (DBS) IN THE ANTERIOR THALAMIC NUCLEUS (ATN) FOR DRUG-RESISTANT EPILEPSY: A COMPREHENSIVE LITERATURE REVIEW

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ABSTRACT

Epilepsy is a chronic neurological disorder causing recurrent seizures and affecting millions globally. Despite standard antiepileptic drug treatment, seizures continued in about one-third of patients. This highlights the need for better treatment options. Deep Brain Stimulation (DBS) has emerged as a promising solution for drug-resistant epilepsy. DBS involves implanting electrodes in specific brain regions to modulate abnormal neural activity. The Anterior Thalamic Nucleus (ATN) is a key target, showing potential to reduce seizures where other therapies have failed. A literature search was conducted from journal articles using databases such as Pubmed, Medline, Google Scholar, Proquest, Embase, SAGE, and Web of Science. The search strategy involved using a set of keywords and their synonyms without any publication date restrictions. We revealed that DBS in the ATN reduced seizure frequency by 40% after three months and by 69% over five years. Despite potential side effects like bleeding, infections, and psychiatric disorders, DBS significantly improves seizure control and patient quality of life. It also shows promise for other neurological conditions. Future advancements in neuroscience could make DBS even more effective. Ongoing research aims to refine treatment parameters and optimize patient outcomes, positioning DBS as a hopeful option for those with drug-resistant epilepsy.

Keywords: anterior thalamic nucleus (ATN); clinical trials; deep brain stimulation (DBS); drug-resistant epilepsy; epilepsy; neuromodulation; quality of life; seizure control; treatment

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INTRODUCTION

Epilepsy is a chronic neurological disorder which is caused by excessive electrical activity in the brain that leads to recurrent seizures, affecting brain function. These seizures can provoke significant impact on the patient's quality of life and increase the risk of mortality. While anti-

epileptic drugs (AEDs) have been the standard treatment for controlling seizures, approximately one-third of epilepsy patients continue to experience seizures despite trying multiple different medications (Li et al., 2017). Consequently, there is a pressing need to explore more effective treatment alternatives.

Patients with drug-resistant epilepsy often face challenges in managing their condition, which can have adverse effects on their overall well-being. Deep Brain Stimulation (DBS) is a surgical procedure which involves placements of small electrodes within the brain to deliver precise electrical stimulation to specific areas involved in epilepsy. One of the targeted regions that has been extensively researched is the Anterior Thalamic Nucleus (ATN). The ATN is a part of the limbic system which plays a crucial role in seizure regulation. It has been shown to be an effective target for DBS in reducing seizure frequency in patients with drug-resistant epilepsy (Xu et al., 2015).

The epidemiological data on epilepsy in Indonesia is limited. Estimates suggest that there are approximately 1.5 million people with epilepsy in Indonesia, with a prevalence of 0.5-0.6% of the population. However, epilepsy prevalence varies worldwide, with the highest numbers reported in Africa and Asia. Incidence rates also vary, with the highest rates observed in infants and young adults. Risk factors for epilepsy include genetic factors, head injuries, brain infections, and other medical conditions (Xu et al., 2015).

Understanding the epidemiology of epilepsy is essential for providing effective healthcare and developing targeted interventions. In Indonesia, the estimated number of epilepsy patients is 1.5 million, accounting for a prevalence of 0.5-0.6% of the total population (Xu et al., 2015). However, the global prevalence of epilepsy varies significantly. The highest prevalence rates are found in regions such as Africa and Asia, suggesting that epilepsy is a global health concern with varying regional impacts. Incidence rates of epilepsy also exhibit variations across age groups, with the highest incidence recorded in infants and young adults. These patterns may be attributed to different risk factors and etiologies associated with epilepsy. Identifying the specific risk factors and causes of epilepsy in different age groups can aid in tailoring treatment approaches and preventive strategies.

Various risk factors contribute to the development of epilepsy. Genetic factors play a significant role, as certain individuals may have a genetic predisposition to epilepsy. Additionally, head injuries resulting from accidents or falls can lead to epilepsy, especially if there is damage to the brain's structures. Brain infections, such as meningitis or encephalitis, are another potential cause of epilepsy. Moreover, individuals with certain medical conditions, such as neurodevelopmental disorders or brain tumors, have a higher risk of developing epilepsy (Xu et al., 2015).

Understanding the epidemiological factors associated with epilepsy provides valuable insights for healthcare planning and resource allocation. It also underscores the need for effective treatment options, particularly for patients who do not respond to conventional anti-epileptic drugs (AEDs). This sets the stage for exploring alternative treatments like DBS targeted at specific brain regions, such as the ATN, which has shown promise in reducing seizures in patients with drug-resistant epilepsy. This study aims to investigate the effectiveness of DBS on the ATN for drug-resistant epilepsy, as well as the epidemiology of epilepsy and the currently available treatments for this condition. The research will also review recent clinical studies and the outcomes of DBS treatment on the ATN. Additionally, it will explore the benefits and risks associated with this treatment and discuss the clinical implications of the

findings. This comprehensive review aims to shed light on the potential that DBS holds for drug-resistant epilepsy.

METHOD

The literature review was conducted by systematically searching multiple reputable databases, including Pubmed, Medline, Google Scholar, Proquest, Embase, SAGE, and Web of Science. The search strategy involved using a set of keywords and their synonyms without any publication date restrictions. The following keywords were used: "anterior thalamic nucleus," "deep brain stimulation," "drug-resistant," and "epilepsy." To ensure the quality and relevance of the selected literature, Only English language original research articles were included in the review. Review articles, case reports, and conference abstracts were excluded. The selected literature had to investigate the use of DBS specifically targeted at the ATN in patients with drug-resistant epilepsy. Studies not meeting this specific focus were excluded. The search results were comprehensively reviewed and assessed for their relevance to the research topic. We found 13 articles in the range of 2015-2022. All selected articles were scrutinized and synthesized into a comprehensive literature review. To ensure the reliability of the review process, it involved a panel of five authors (YASH, BH, CM, BAR, IFR), each independently reviewing the literature. In cases where differences of opinion emerged, they were resolved through discussions involving all authors, with the assistance of a sixth author (AFP) as a mediator when necessary.

While every effort was made to conduct a thorough and unbiased literature review, it is essential to acknowledge potential limitations such as, publication bias, lack of restrictions in publication date may result in the inclusion of older studies, which might not reflect recent advancements in the field and subjectivity despite efforts to minimize subjectivity through discussions and mediation, the review process may still be influenced by individual interpretations and biases of the reviewing authors. Despite these limitations, this methodology aimed to provide a comprehensive and objective overview of the available literature regarding DBS in the treatment of drug-resistant epilepsy, with a specific focus on the ATN. The review process was conducted meticulously to ensure the reliability and credibility of the findings presented in this research article.

RESULTS

Effectiveness of DBS in the ATN for Drug-Resistant Epilepsy

Drug-resistant epilepsy remains a significant challenge for a substantial portion of the global epilepsy population, affecting more than 20% of the estimated 50 million individuals worldwide living with epilepsy. DBS is an effective therapy for drug-resistant epilepsy besides other stimulation therapies such as responsive nerve stimulation (RNS) and vagus nerve stimulation (VNS), DBS has also gained recognition and surgery (Li et al., 2017).

DBS is done by surgically placing small electrodes within the brain to provide controlled electrical stimulation to specific regions implicated in epilepsy. It consists of three main components: lead, extension, and neurostimulator (Li et al., 2017). The lead is a thin electrode that was inserted through small holes in the skull and implanted into the brain. The extension is an insulated wire routed beneath the scalp, neck, and shoulder, connecting to the neurostimulator, or battery, implanted near the collarbone or lower chest (Deep Brain Stimulation, 2019; Pycroft et al., 2018). DBS, as an anti-epileptic therapy, exerts both inhibitory and excitatory effects through neuro-modulation. The stimulation inhibits seizures and raises the seizure threshold. Stimulation in low-frequency has shown promise in restoring normal neuronal electrical activity, while stimulation in high-frequency is more effective in

inhibiting abnormal neuronal activity. Direct stimulation of the epileptogenic zone could alters network excitation and synchronizes nerves without causing functional deficits (Zangiabadi et al., 2019).

DBS targeting the ATN has gained approval for the treatment of refractory epilepsy in Canada, Europe, and Australia. As part of the limbic circuitry, the ATN is connected to the hippocampus (HC) through the mammillothalamic tract and fornix prior to projecting to the neocortex and cingulate cortex. Given the involvement of this circuit in emotional processing and seizure control, high-frequency stimulation of the ATN can inhibit the spread of electrical stimulation to cortical areas. To date, commonly used stimulation parameters are a frequency of ≥100 Hz and a voltage range of 1-10 V for ATN stimulation, ≥130 Hz and 1-5 V for hippocampal and subthalamic nucleus (STN) stimulation, and low-frequency stimulation at 10 Hz or high-frequency at 200 Hz for other brain regions (Li et al., 2017; Bouwens et al., 2018). However, there have been no randomized clinical trials comparing these parameters (Li et al., 2017).

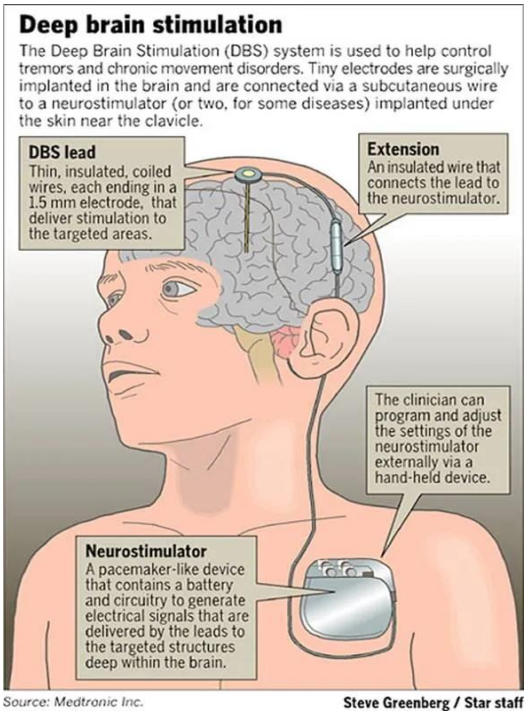

Figure 1. Deep Brain Stimulation (Deep Brain Stimulation, 2019)

According to a review by Li et al, DBS targeting the ATN and HC in drug-resistant epilepsy patients has yielded positive outcomes. From clinical studies, approximately half of all patients experienced improvement, with a decrease in the frequency of seizure ranging from 46% to 90% with ATN DBS and 48% to 95% with hippocampal DBS (Li et al., 2017).
According to a study conducted by Xu Xin, Ling Zhi-Pei, and colleagues involving three drug-resistant epilepsy patients with varying severity levels who received ATN DBS therapy without changes in drug type and dosage after ATN DBS, one patient experienced a 100% reduction in seizures, the second patient saw a 25% reduction, and the third patient experienced a 55% reduction in seizures (Xu et al., 2015).

A literature review by Nasser et al, spanning from 1980 to 2018 and comparing the effectiveness of DBS in the ATN, CMT, HC, basal ganglia, cerebellum, and hypothalamus for drug-resistant epilepsy, recommended ATN DBS over other target areas. However, the review

acknowledged several biases in the literature that may influence outcomes (Zangiabadi et al., 2019). Michael C. H. Li et al reviewed the literature on brain stimulation such as DBS as an important treatment option for drug-resistant epilepsy. Stimulation of the ATN and HC has been shown to reduce the frequency of difficult-to-treat seizures. Approximately three-quarters of patients receiving stimulation in ANT, HC, or the CMT respond with at least 50% seizure reduction. The timing of clinical benefit varies widely, with early lesion effects and sustained stimulation effects playing a role. Side effects are analogous to those reported in DBS therapy and may include movement disorders (dyskinesia), mood disorders, anxiety disorders, and paresthesia. Several factors potentially related to stimulation effectiveness include the absence of structural abnormalities on imaging for ATN and HC stimulation and the electrodes' relative position from the target. Some seizure types or syndromes may respond better to specific targets, such temporal lobe or limbic seizures which respond to ATN stimulation and generalized seizures and Lennox-Gastaut syndrome which respond to CMT stimulation. Large-scale experimental sutdies are needed to further explore different parameters of stimulation, assert indications for DBS, and evaluate predictors of patient response (Li et al., 2017)

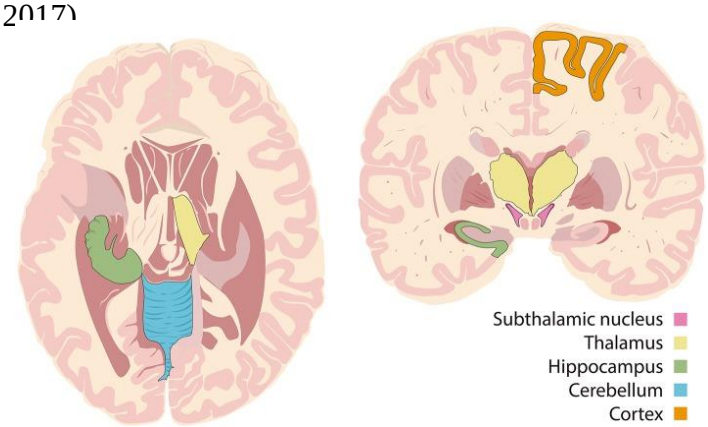

Figure 2. Target location of DBS (Li et al., 2017)

Comparison of DBS results on different targets is presented in the study of Li et al, The study reported in the SANTE (Stimulation of the Anterior Nucleus of Thalamus for Epilepsy) trial, 110 drug-resistant focal seizure patients who received ANT DBS experienced a 40% decrease in the frequency of seizure after 3 months, albeit with reports of memory impairment and depression. After up to 5 years of follow-up, patients showed progressive improvement, with a reduction in seizure frequency of approximately 69% (Salanova et al., 2015). However, a randomized controlled trial conducted by Tellez-Zenteno found an average seizure frequency reduction of only 15%, which was less significant, likely due to therapy duration and a small sample size (Tellez-Zenteno et al., 2006). In 1992, Fisher et al published a double-blinded crossover study following 7 patients with focal and generalized epilepsy. Two of the patients had Lennox-Gastaut syndrome, a severe and refractory epilepsy syndrome, especially in early childhood, typically under the age of 4. Although seizures decreased by 30%, this result failed to reach significance (Fisher et al., 1992). Velasco's study also shown that centromedian thalamic (CMT) stimulation did not significantly decrease total seizure frequency for specific seizure types. However, electroencephalographic (EEG) studies revealed significant reductions in generalized spike-wave and secondary synchrony release, as well as focal spikes in the frontal area (Velasco et al., 2000).

Table 1.
Comparison of DBS results on different targets (Li et al., 2017)

DBS target	RCT	Outcomes during the blinded phase	
		Stimulation compared with baseline	Sham stimulation compared with baseline
ATN	Fisher et al. 2010	40.4% median SR	14.5% median SR
HC	Tellez-Zenteno et al. 2006	26% median SR	49% median SR
	Velasco et al. 2007	40% median SR	0% median SR
	McLachlan et al. 2010	33% mean SR	4% mean SR
	Morrell et al. 2011	3,9% mean SR	17,3% mean SR
CMT	Fisher et al. 1992	30% mean SR	8% mean SR
	Velasco et al. 2000	No statistically significant SR (values not reported)	
CB	Wright et al. 1984	No statistically significant SR (values not reported)	
	Velasco et al. 2005	67% GTC mean SR	7% GTC mean SR
NA	Kowski et al. 2015	48% mean SR	14% mean SR

SR, seizure reduction; ATN, anterior thalamic nucleus; HC, hippocampus; CMT, centromedian nucleus of the thalamus; CB, cerebellum; NA, nucleus accumbens.

Adverse Event of DBS in ATN

Adverse events associated with DBS procedures in the ATN can be categorized into three main groups: complications related to surgery (bleeding, venous infarction, or improper DBS lead placement), complications related to the use of the device (infections, erosion, device fracture, or lead displacement), and complications induced by stimulation (increased seizure frequency or triggering new psychiatric symptoms or exacerbating existing psychiatric comorbidities). The relatively low incidence of adverse events in ATN DBS procedures can be attributed to the fact that these procedures are carried out by experienced functional neurosurgery teams with extensive expertise in DBS for movement disorders and neuropsychiatric conditions (Fenoy et al., 2014).

Table 2.
Adverse events related to ATN DBS

Study	Number of patients	Procedure-related adverse event	Tools-related adverse event	Stimulation-related adverse event	Cognitive and behavioral changes	Emotional changes	Quality of Life
Upton et al, 1987	6	No	No	Some patients underwent euphoric feeling	Behavioral improvement	Improvement on emotional response	n/a
Hodaie et al, 2002	5	No	1 (20%) skin erosion	No	Cognitive improvement	n/a	Improvement
Kerrigan et al, 2004	5	No	1 (20%) re-do because of misplaced location	No	n/a	n/a	n/a
Lee et al, 2006	6	No	1 (16%) infection around IPG	No	3 (50%) cognitive improvemen	n/a	Improvement

					t		
Andrade et al, 2006	8	No	No	1 (12.5%) fatigue	n/a	n/a	n/a
Lim et al, 2007	4	1 (25%) bleeding on frontal region	1 (25%) skin erosion	No	n/a	n/a	n/a
Osorio et al, 2007	4	No	No	No	3 (75%) cognitive improvement	n/a	4 (100%) improvement
Fisher et al, 2010	110	5 (4.5%) asymptomatic bleeding	23 (20.9%) pain in implantation area, 25 (22.7%) paresthesia in implant area, 14 (12.7%) infection, 9 (8.2%) DBS was not located on target, 6 (5.5%) movement of IPG	2 (1.8%) acute transient seizure, 7 (6.4%) epileptic status episode, 2 SUDEP	Long-term improvement in attention and executive function no changes in visual and verbal memory	Improvement in depression and anxiety	110 (100%) improvement
Lee et al, 2012	15	No	1 (6%) infection	No	n/a	n/a	n/a
Piacentino et al, 2015	6	No	No	No	3 (50%) improvement	n/a	2 (33%) improvement

Adverse events related to ATN DBS can be further categorized based on the timing relative to operation: intraoperative, perioperative (less than 2 weeks postoperation), and long-term postoperative (more than 2 weeks postoperation). Common intraoperative complications include vasovagal responses, which developed in 6 patients (0.8%), leading to syncope in 4 patients and cancellation of procedure in 4 cases. One episode resulted in temporary hemiplegia but did not delay the procedure: postoperative CT revealed putaminal and intraventricular hemorrhage (IVH). One patient with procedure cancellation correlated with postoperative CT findings of air in the cavernous sinus. One subcortical infarction and 1 intracerebral hemorrhage (ICH) led to intraoperative hemiparesis, occurring right after the placement of the first lead, necessitating postponement of subsequent case. Hemorrhage was one of the most severe DBS complications: symptomatic ICH occured in 8 patients (1.1%), manifesting as early somnolence in 4 patients and postoperative hemiparesis in 7 patients. Asymptomatic ICH was found on postoperative CT in 4 patients (0.5%). Incidental reports of small IVH in the atrium or occipital horn of the lateral ventricle was also found in 28 patients (3.8%); with 3 of these patients (11% of IVH cases and 0.4% of the total cases) experienced transient postoperative confusion. Two patients (0.3%) experienced tonic-clonic seizures

shortly before microelectrode recording (MER), with negative imaging findings, resulting in cancellation of procedure. Isolated intraoperative issues encompassed 5 cases of anxiety (0.7%), 2 cases of transient confusion (0.3%), and a case of arrhythmia (0.1%), all of which were resolved with small propofol infusions that resolved before MER (Fenoy et al., 2014).

Perioperative complications, occurring ≤2 weeks postoperation, were observed during inpatient stays after stage 1 or upon return to the operating chamber for stage 2 procedures. Most patients complained of transient headaches (31 patients [4.2%]). Confusion, with or without agitation, was another common symptom, and again, all of them were transient; 10 such events were associated with the STN target. Temporary hallucinations developed in 3 patients (0.4%) (Fenoy et al., 2014). Some severe side effects also occurred, primarily within a few hours after the procedure. Thirteen patients (1.7%) experienced hemiplegia with or without a decrease in consciousness, with 8 of them were found having ICH on postoperative CT. There were postoperative CT evidences of 1 cortical infarction (0.1%), 2 (0.3%) subcortical infarctions, and 2 (0.3%) "unclear hypodensities" around the electrode tip, suspected to be edema, resulting in only temporary hemiparesis. Further severe side effects included seizures in 3 patients (0.4%) on postoperative day 1-2 (with normal CT findings) and respiratory distress in 3 patients (0.4%), 2 of whom needed re-intubation due to subsequent aspiration pneumonia (1 patient) and pulmonary edema (1 patient) (Fenoy et al., 2014).

Long-term adverse events are defined as complications occurring more than 2 weeks postoperation. Given the perspective of surgical research, only side effects reported to the neurosurgery clinic were included, with adverse effects caused by temporary programs not included. These adverse events can be classified into wound, hardware, and satisfaction-related complications. Wound complications, notably infections, were the most common with a total of 23 cases (3.1%), with 10 (1.4%) being self-limited and 13 (1.7%) requiring reoperation for debridement and/or device removal. Erosion and dehiscence developed in 2 patients each (0.3%), indicating for surgical debridement (Fenoy et al., 2014).

In another study, there were no reported instances of bleeding or surgery-related fatalities, although two participants experienced temporary seizures induced by stimulation. Other side effects included paresthesia at the site of implantation in 18% of cases, local pain in 11% of cases, and infections in 9% of cases. Memory disturbances and depression were more frequent in the case group compared to the control group. Considering these occurrences, efforts to mitigate adverse events caused by DBS are necessary (Zangiabadi et al., 2019).

DISCUSSION

The first-line therapy for drug-resistant epilepsy is typically resective surgery. However, surgery is contraindicated or ineffective in many cases, in which DBS presents itself as an effective alternative. Alongside other stimulation therapies such as responsive neurostimulation (RNS) and vagus nerve stimulation (VNS), DBS has gained recognition. This study suggests that DBS is highly effective in reducing seizure frequency, controlling seizures, and improving the patient's quality of life.DBS decrease frequency of seizure in half of the patients stimulation on ATN, HC and MCT contributed 50% seizure reduction and there is several factor related to stimulation effectiveness include structural abnormalitiesm position electrodes and type of seizure. DBS on ANT is recommended over other targets.[1,5] Side effects due to DBS can include bleeding, infection, venous infarction, increased frequency of seizures, dyskinesia, and psychiatric symptoms such as mood disorders, anxiety disorders, parathesia (Fenoy et al., 2014).

DBS represents a therapeutic modality with immense potential. Besides its application to drug-resistant epilepsy patients, DBS can also serve as a treatment option for various other neurological disorders. These conditions encompass motor disorders like tremors or dystonia, Parkinson's disease, and neuropsychiatric symptoms such as Obsessive-Compulsive Disorder (OCD) or Tourette's syndrome (Maret-Barrutia et al., 2021; Hariz et al., 2022). With increasing research on DBS, the scope of treatable conditions is expected to expand. Specifically, ANT-DBS has been found to offer significant clinical improvements, especially in reducing the frequency of seizures in patients. This benefit is expected to become even more effective in the future with advancements in neuroscience, particularly neurointervention, allowing for more precise targeting of individual anatomies (Krishna et al., 2016a). While many benefits and advantages of ANT-DBS therapy have been discussed, further research is necessary to evaluate these benefits across a more diverse range of parameters and detailed long-term follow-up outcomes. Such follow-up should not only measure positive aspects of patient improvement but also assess risks, side effects, and complications experienced by individual patients (Doležalová et al., 2019). The reviewed literature has provided numerous considerations regarding ANT-DBS. However, these reviews are not without limitations. More recent follow-up methods are still required, especially for assessing the implant itself, beyond clinical symptoms or electroencephalography, and require contributions from experts in various fields, longer follow-up durations, and larger patient cohorts.

CONCLUSION

In this article, we have explored the effectiveness of DBS in the ATN as a therapy for drug-resistant epilepsy patients. Drug-resistant epilepsy is a challenging disease to treat with the ability to impact a patient's quality of life significantly. In this literature review, we assessed various aspects related to the use of DBS in the ATN, including its effectiveness in reducing seizure frequency, potential complications, and opportunities and recommendations for future research. From the findings of the literature review, it is evident that DBS in the ATN can effectively reduce seizure frequency in drug-resistant epilepsy patients. Clinical studies have shown a significant improvement in reducing seizures, although some side effects such as paresthesia, local pain, and infections may occur. Additionally, some patients reported mood and memory disturbances after DBS.

When considering the implications of this research, several key take-home messages emerge. First and foremost, DBS in the ATN should be recognized as a viable therapeutic option for individuals grappling with drug-resistant epilepsy, particularly when conventional medications and surgical resection prove inadequate or ineffective. The successful implementation of DBS hinges on factors unique to each patient and the precise calibration of stimulation parameters. Tailored treatment plans and vigilant monitoring are pivotal in achieving the most favorable outcomes. It is paramount to balance the potential benefits of DBS against the associated risks and side effects. The process should involve careful patient selection and informed consent to make informed decisions. Efforts to mitigate side effects, such as infection prevention and strategies for addressing mood fluctuations, should be integrated into the treatment strategy to optimize patient well-being and satisfaction.

Moving forward, there are critical avenues for further exploration in the realm of DBS for drug-resistant epilepsy. In-depth, long-term studies are imperative to assess the enduring effects and safety profile of DBS in the ATN. These studies should encompass a larger patient cohort and extended post-implantation monitoring. Continued research should be directed

toward identifying the most effective and well-tolerated stimulation parameters for individual patients, with a focus on minimizing side effects and enhancing seizure control. Advancements in neuroimaging and patient-specific anatomical mapping hold potential for more precise targeting of the ATN, which could significantly improve therapy outcomes. Comparative studies should be undertaken to evaluate DBS in the ATN in relation to other neuromodulation therapies such as VNS and RNS. This comparative analysis can help determine the most suitable approach for specific patient profiles. A comprehensive exploration of the psychosocial impact of DBS, including its effects on mood, memory, and overall quality of life, is essential for delivering holistic care to patients. By embracing these suggestions and advancing research in these areas, we can refine DBS as a treatment option for drug-resistant epilepsy, ultimately enhancing the quality of life for individuals facing the challenges of this condition.

While DBS holds promise as a treatment option for drug-resistant epilepsy, there are several considerations to be mindful of. Proper patient selection, optimal stimulation parameter settings, and long-term monitoring are necessary to optimize therapy outcomes. Furthermore, mitigation efforts need to be undertaken to reduce the risk of potential side effects. Overall, DBS in the ATN represents a promising therapy for drug-resistant epilepsy patients, but further research is required to gain a deeper understanding of long-term side effects and effectiveness. With advancements in neuroscience and medical technology, the opportunities to enhance epilepsy treatment are expanding. Future research should focus on a better understanding of individual anatomy, more precise stimulation parameter settings, and meticulous long-term monitoring to provide the best possible benefits to patients.

REFERENCES

Li, M. C., & Cook, M. J. (2017). Deep brain stimulation for drug-resistant epilepsy. *Epilepsia*, 59(2), 273–290. https://doi.org/10.1111/epi.13964

Xu, X., Ling, Z. P., Mao, Z. Q., Pan, L. S., Cui, Z., & Yu, X. (2015). Clinical study on treatment of drug-resistant epilepsy with deep brain stimulation in bilateral anterior thalamic nuclei. *Chinese Journal of Contemporary Neurology and Neurosurgery*, 15(9), 716–721. https://doi.org/10.3969/j.issn.1672-6731.2015.09.0073.

Deep Brain Stimulation. Neurosurgical Associates of San Antonio. (2019, December 13). https://neurosurgerysa.com/deep-brain-stimulation.

Pycroft, L., Stein, J., & Aziz, T. (2018). Deep Brain Stimulation: An overview of history, methods, and future developments. B*rain and Neuroscience Advances*, 2, 239821281881601. https://doi.org/10.1177/2398212818816017.

Zangiabadi, N., Ladino, L. D., Sina, F., Orozco-Hernández, J. P., Carter, A., & Téllez-Zenteno, J. F. (2019). Deep brain stimulation and drug-resistant epilepsy: A review of the literature. *Frontiers in Neurology*, 10. https://doi.org/10.3389/fneur.2019.00601.

Bouwens van der Vlis, T. A., Schijns, O. E., Schaper, F. L., Hoogland, G., Kubben, P., Wagner, L., Rouhl, R., Temel, Y., & Ackermans, L. (2018). Deep brain stimulation of the anterior nucleus of the thalamus for drug-resistant epilepsy. *Neurosurgical Review*, 42(2), 287–296. https://doi.org/10.1007/s10143-017-0941-x

Salanova, V., Witt, T., Worth, R., Henry, T. R., Gross, R. E., Nazzaro, J. M., Labar, D., Sperling, M. R., Sharan, A., Sandok, E., Handforth, A., Stern, J. M., Chung, S., Henderson, J. M., French, J., Baltuch, G., Rosenfeld, W. E., Garcia, P., Barbaro, N. M.,

… Bergen, D. (2015). Long-term efficacy and safety of thalamic stimulation for drug-resistant partial epilepsy. *Neurology*, 84(10), 1017–1025. https://doi.org/10.1212/wnl.0000000000001334

Tellez-Zenteno, J. F., McLachlan, R. S., Parrent, A., Kubu, C. S., & Wiebe, S. (2006). Hippocampal electrical stimulation in Mesial Temporal Lobe epilepsy. *Neurology*, 66(10), 1490–1494. https://doi.org/10.1212/01.wnl.0000209300.49308.8f

Fisher, R. S., Uematsu, S., Krauss, G. L., Cysyk, B. J., McPherson, R., Lesser, R. P., Gordon, B., Schwerdt, P., & Rise, M. (1992). Placebo-controlled pilot study of Centromedian thalamic stimulation in treatment of intractable seizures. *Epilepsia*, 33(5), 841–851. https://doi.org/10.1111/j.1528-1157.1992.tb02192.x

Velasco, F., Velasco, M., Jiménez, F., Velasco, A. L., Brito, F., Rise, M., & Carrillo-Ruiz, J. D. (2000). Predictors in the treatment of difficult-to-control seizures by electrical stimulation of the centromedian thalamic nucleus. *Neurosurgery*, 47(2), 295–305. https://doi.org/10.1097/00006123-200008000-00007

Upton, A. R. M., Amin, I., Garnett, S., Springman, M., Nahmias, C., & Cooper, I. S. (1987). Evoked metabolic responses in the Limbicstriate system produced by stimulation of anterior thalamic nucleus in man. *Pacing and Clinical Electrophysiology*, 10(1), 217–225. https://doi.org/10.1111/j.1540-8159.1987.tb05952.x

Hodaie, M., Wennberg, R. A., Dostrovsky, J. O., & Lozano, A. M. (2002). Chronic anterior thalamus stimulation for intractable epilepsy. *Epilepsia*, 43(6), 603–608. https://doi.org/10.1046/j.1528-1157.2002.26001.x

Kerrigan, J. F., Litt, B., Fisher, R. S., Cranstoun, S., French, J. A., Blum, D. E., Dichter, M., Shetter, A., Baltuch, G., Jaggi, J., Krone, S., Brodie, M., Rise, M., & Graves, N. (2004). Electrical stimulation of the anterior nucleus of the thalamus for the treatment of intractable epilepsy. *Epilepsia*, 45(4), 346–354. https://doi.org/10.1111/j.0013-9580.2004.01304.x

Lee, K. J., Jang, K. S., & Shon, Y. M. (2006). Chronic deep brain stimulation of subthalamic and anterior thalamic nuclei for controlling refractory partial epilepsy. *Advances in Functional and Reparative Neurosurgery*, 87–91. https://doi.org/10.1007/978-3-211-35205-2_17

Andrade, D. M., Zumsteg, D., Hamani, C., Hodaie, M., Sarkissian, S., Lozano, A. M., & Wennberg, R. A. (2006). Long-term follow-up of patients with thalamic deep brain stimulation for epilepsy. *Neurology*, 66(10), 1571–1573. https://doi.org/10.1212/01.wnl.0000206364.19772.39

Lim, S., Lee, S., Tsai, Y., Chen, I., Tu, P., Chen, J., Chang, H., Su, Y., & Wu, T. (2007). Electrical stimulation of the anterior nucleus of the thalamus for intractable epilepsy: A long-term follow-up study. *Epilepsia*, 48(2), 342–347. https://doi.org/10.1111/j.1528-1167.2006.00898.x

Osorio, I., Overman, J., Giftakis, J., & Wilkinson, S. B. (2007). High frequency thalamic stimulation for inoperable mesial temporal epilepsy. *Epilepsia*, 48(8), 1561–1571. https://doi.org/10.1111/j.1528-1167.2007.01044.x

Fisher, R., Salanova, V., Witt, T., Worth, R., Henry, T., Gross, R., Oommen, K., Osorio, I., Nazzaro, J., Labar, D., Kaplitt, M., Sperling, M., Sandok, E., Neal, J., Handforth, A., Stern, J., DeSalles, A., Chung, S., Shetter, A., … Graves, N. (2010). Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy. *Epilepsia*, 51(5), 899–908. https://doi.org/10.1111/j.1528-1167.2010.02536.x

Lee, Kyung Jin, Shon, Y. M., & Cho, C. B. (2012). Long-term outcome of anterior thalamic nucleus stimulation for intractable epilepsy. *Stereotactic and Functional Neurosurgery*, 90(6), 379–385. https://doi.org/10.1159/000339991

Piacentino, M., Durisotti, C., Garofalo, P. G., Bonanni, P., Volzone, A., Ranzato, F., & Beggio, G. (2015). Anterior thalamic nucleus deep brain stimulation (DBS) for drug-resistant complex partial seizures (CPS) with or without generalization: Long-term evaluation and predictive outcome. *Acta Neurochirurgica*, 157(9), 1525–1532. https://doi.org/10.1007/s00701-015-2498-1

Fenoy, A. J., & Simpson, R. K. (2014). Risks of common complications in deep brain stimulation surgery: Management and avoidance. *Journal of Neurosurgery*, 120(1), 132–139. https://doi.org/10.3171/2013.10.jns131225

Mar-Barrutia, L., Real, E., Segalás, C., Bertolín, S., Menchón, J. M., & Alonso, P. (2021). Deep brain stimulation for obsessive-compulsive disorder: A systematic review of worldwide experience after 20 years. *World Journal of Psychiatry*, 11(9), 659–680. https://doi.org/10.5498/wjp.v11.i9.659

Hariz, M., & Blomstedt, P. (2022). Deep brain stimulation for parkinson's disease. *Journal of Internal Medicine*, 292(5), 764–778. https://doi.org/10.1111/joim.13541

Krishna, V., King, N. K., Sammartino, F., Strauss, I., Andrade, D. M., Wennberg, R. A., & Lozano, A. M. (2016a). Anterior nucleus deep brain stimulation for refractory epilepsy. *Neurosurgery*, 78(6), 802–811. https://doi.org/10.1227/neu.0000000000001197

Doležalová, I., Kunst, J., Kojan, M., Chrastina, J., Baláž, M., & Brázdil, M. (2019). Anterior thalamic deep brain stimulation in epilepsy and persistent psychiatric side effects following discontinuation. *Epilepsy Behavior Reports*, 12, 100344. https://doi.org/10.1016/j.ebr.2019.100344