

Epilepsy in Neurodegenerative Disease: Narrative Review

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ABSTRACT

An overview of geographical accuracy of worldwide (DBS) system of epilepsy as been taken in the consideration. We concluded that the some of the risk factors, etiology and pathophysiology that causes epilepsy. The major of the Epilepsy caused by aberrant electrical activity in the brain, epilepsy is a persistent neurological disorder. Excitatory and inhibitory neurotransmitter imbalance is frequently seen in epilepsy, which raises the risk of uncontrolled neuronal firing and increases neuronal excitability. Our conclusion in this review is a very complicated medical condition. Many effective to management of epilepsy in neurodegenerative disorder, and know deep brain stimulating therapy came into existence to treat the frequency and intensity of seizures in epileptic patients.

Keywords: *Brain Stimulating Therapy, Epilepsy, Neurodegenerative Disorder, Risk Factor, Etiology, Pathophysiology*

Overview of Epilepsy caused by aberrant electrical activity in the brain, epilepsy is a persistent neurological disorder. One safe and useful neurointerventional method for treating movement disorders is deep brain stimulation. Subcortical structure electrical stimulation may have an inhibitory effect on seizure generators that start epileptic episodes. A neurosurgeon implants the DBS device during a surgery. Electrical impulses from the neurostimulator device are sent straight to the brain via through the thin wires known as electrodes, which block the brain signals that trigger seizures (1). From brief periods of unconsciousness to full-blown seizures that may include convulsions, altered sensations, or loss of consciousness, this aberrant activity can cause a wide range of symptoms. Recurrent seizures, which are brief episodes of involuntary movement that can affect the whole body or just a portion of it are its defining feature (2) [stat pearls] They can also occasionally be followed by loss of consciousness and control over bladder or bowel movements. Although 10% of people worldwide experience one seizure in their lifetime, one seizure does not necessarily indicate epilepsy. Having two or more unprovoked seizures is considered epilepsy. (3) [Health Information]

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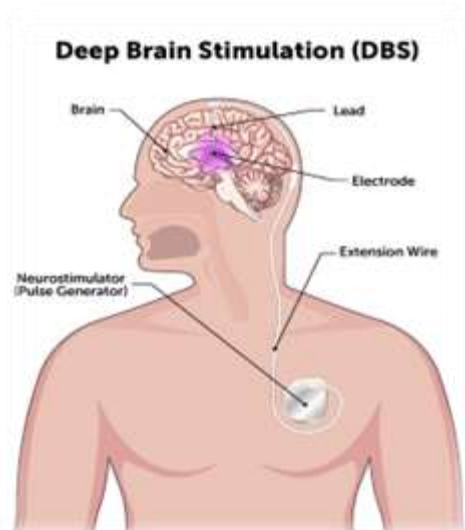


Figure.01: Deep brain stimulation involves surgically placing electrodes deep into the brains of people with Parkinson's to relieve the stiffness, tremors, and rigidity the disease causes.

Types of Epilepsy: There are several linked disorders with unique characteristics that collectively make up epilepsy, rather than a singular disorder.

Numerous forms of epilepsy have been clarified by recent studies:

- I. **Partial seizures (focal onset seizures):** start in a particular area in the brain and that cause limited symptoms like odd feelings, movements, or altered consciousness. More accurate localization of these seizures has been made possible by advancements in neuroimaging, which has improved surgical therapy choices.
- II. **Generalized Onset Seizures:** These seizures can cause convulsions and a loss of consciousness because they involve aberrant electrical activity throughout the entire brain. Personalized treatment options are made easier by the recent genetic research that has revealed some of the underlying causes of generalized epilepsy.

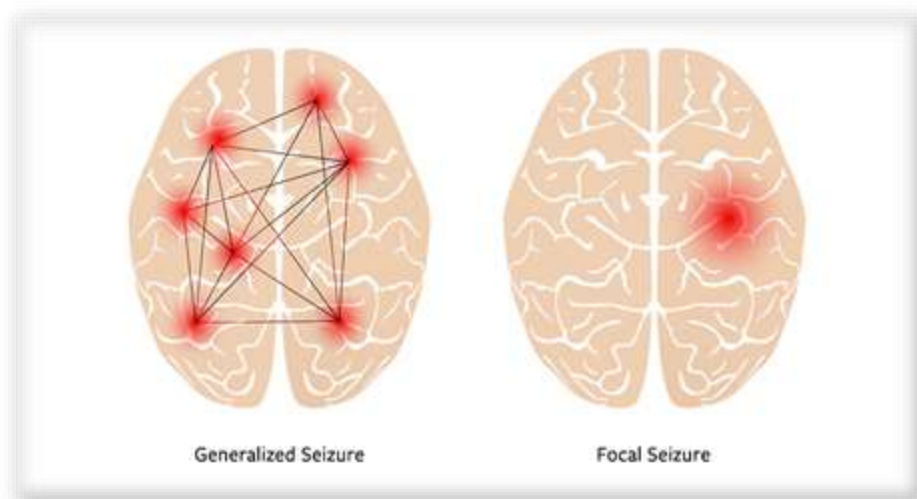


Figure.02: Generalized seizures affect both sides of the brain whereas focal seizures happen in one area of the brain.

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III. Muscles in the body stiffen during tonic seizures:

These are usually found in the arms, legs, and back.

- a. Muscle jerking occurs repeatedly on both sides of the body during clonic seizures.
- b. Upper body, arm, or leg jerks or twitches are a result of myoclonic seizures.

A person experiencing atonic seizures may experience a loss of normal muscle tone, which may result in unintentional falls or head drops. (3) [Health Information]. (4).

IV. **Temporal Lobe Epilepsy:** Epilepsy is frequently linked to seizures that start in the brain's temporal lobes. More knowledge and treatment possibilities for temporal lobe epilepsy have resulted from recent research on the connection between the illness and memory and cognition. (7)

V. **Frontal Lobe Epilepsy:** Movements and behaviors that are intricate and frequently. The particular difficulties in identifying and treating frontal lobe epilepsy have been the subject of recent research (5)

Geographical assurances of worldwide epilepsy

About 1% of people worldwide suffering from epilepsy and about one-third those cases are unresponsive to treatment ,however large number of people lack a single securely detachable seizure onset zone (SOZ).Neurostimulation also know as neuromodulation has emerged as significant therapeutic modality for these .In the US (VNS),responsive neurostimulation (RNS),and (DBS)the anterior thalamus are the three forms of neuromodulation for epilepsy are approved DBS has been used to treat clinical epilepsy at a number of locations, such as the thalamus, hippocampus , cerebellum , hypothalamus , nucleus acumens. (6) Temporal Lobe Epilepsy (TLE) is the most frequent focal epilepsy and the most common cause of drug-resistant seizures in adults. Volumetric Magnetic resonance imaging (MRI) studies have demonstrated the association of TLE with hippocampal sclerosis (HS), identified in approximately 65% of patients amygdala-hippocampal atrophy, and volumetric changes in thalamic nuclei.1–8 These anatomic changes have been previously correlated with various clinical features of epileptic seizure, including the age of onset of intractable seizures, duration of epilepsy, presence of secondary generalized seizure, and postoperative seizure outcome. Additional research demonstrates that there are direct or reciprocal connections between neural structures the mesial temporal lobe, accounting for the temporal lobe and thalamic structural alterations. (7), (9)

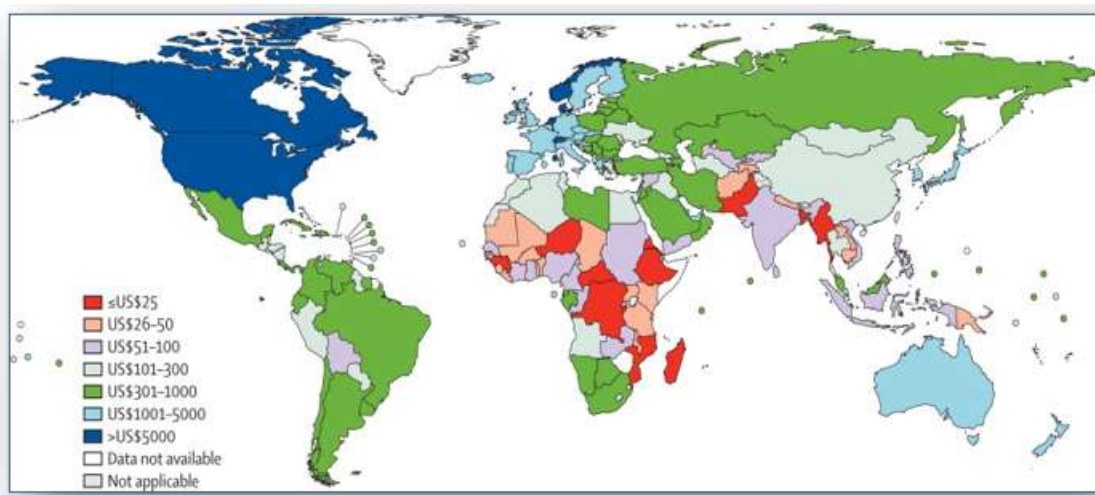


Figure.03 *Geographical assurances of worldwide epilepsy*

MATERIALS AND METHODS

This study is offered as an informal overview of epilepsy treatment using thalamic stimulation.

Selected and summarized reviewed literature were obtained from PubMed. In light of the author's own engagement in studies in this field over several decades, a critical interpretation of the data is offered. (8)

RISK FACTORS

There are multiple risk factors for epilepsy, and the disorder can develop for a variety of causes. It's crucial to remember that many people with risk factors never have seizures, and having one or more risk factors does not ensure that someone will acquire epilepsy. The following are some typical epilepsy risk factors:

- A. Family History: There may be a higher chance if they have a history of epilepsy or other neurological disorders in the family. People who have family members who have the condition are more vulnerable to certain forms of epilepsy because they have a genetic component.
- B. Brain Trauma and Injuries: Trauma to the head, particularly if it results in brain damage, can raise the chance of developing epilepsy. This includes injuries sustained in sports, falls, and accidents that result in traumatic brain injuries (TBIs).. (10)
 - I. Brain Infections: Meningitis or encephalitis are examples of brain infections that can lead to epilepsy, particularly if the infections result in brain damage.
 - II. Brain Tumors: The existence of brain tumors can cause seizures and interfere with regular brain function. The type and location of the tumor determine the risk for DBS system.
 - III. Neurological Conditions: There may be a correlation between an increased risk of epilepsy and certain neurological conditions, such as autism, multiple sclerosis, or Alzheimer's disease. (11)
 - IV. Prenatal Exposure: Drug, alcohol, or medication use by the mother during her pregnancy may expose the unborn child to certain substances or infections, which may raise the child's risk of developing epilepsy.
 - V. abnormalities in the developing brain
 - VI. bleeding within the skull
 - VII. Brain blood vessel abnormalities
 - VIII. severe brain damage or brain oxygen deprivation
 - IX. brain growths
 - X. brain infections like encephalitis or meningitis
 - XI. A stroke brought on by an artery blockage (12,f13)

Therapies for epilepsy / treatment

- a) Among the therapies are medications known as anti-epileptic drugs (AEDs).
- b) surgery to remove the seizure-inducing small brain region.
- c) a process that involves inserting a tiny electrical device inside the body to help regulate seizures.
- d) a unique diet that can help manage seizures, known as the ketogenic diet.

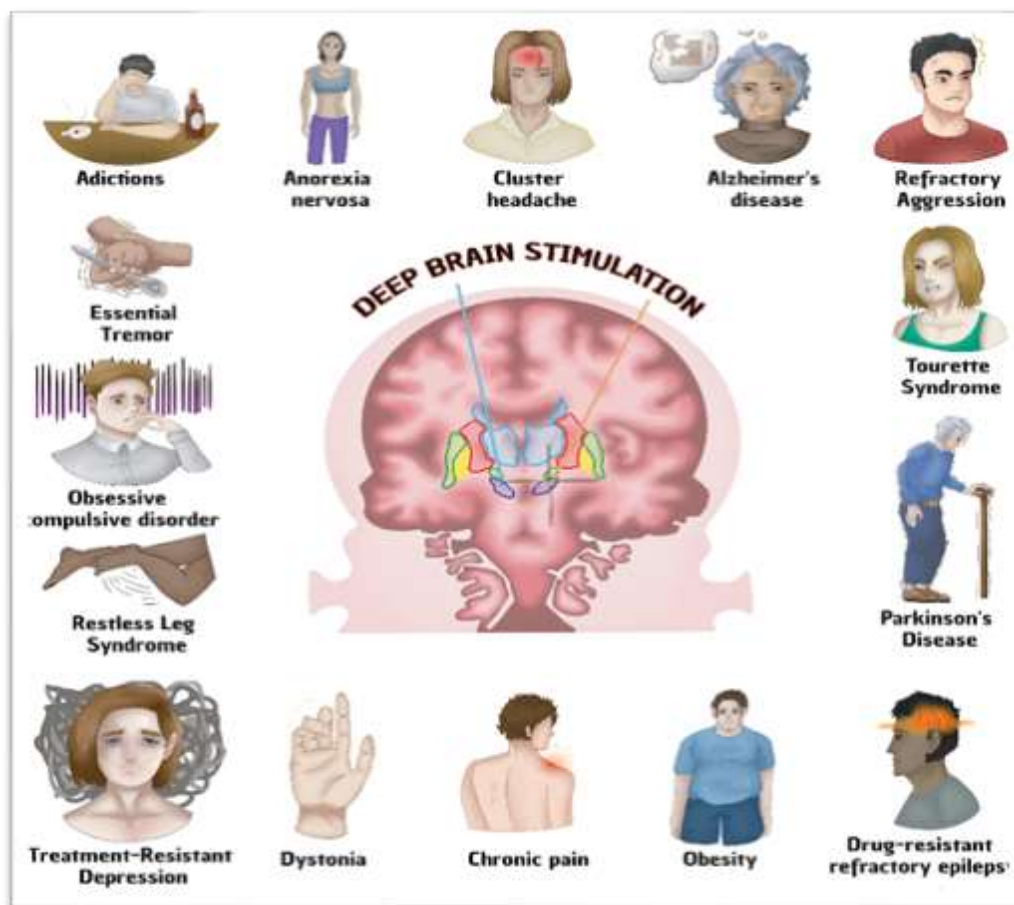


Figure.04: DEEP BRAIN STUMALATING

ETIOLOGY OF EPILEPSY

The precise cause of epilepsy, a neurological condition marked by recurrent seizures, can be complicated and variable. They have many numbers of recognized etiological factors and possible triggers for epilepsy, even though the underlying causes are not always evident:

- I. Genetic Factors: A genetic component is present in many epilepsy cases. A family history of epilepsy and specific genetic mutations can raise the risk of improving the condition.
- II. Brain Abnormalities: Epilepsy can result from structural abnormalities in the brain, including brain tumors, abnormalities in brain development, and scars from head trauma. The brain's regular electrical activity may be interfered with by these anomalies.
- III. Head Injuries. Even long-since-past injuries can occasionally lead to

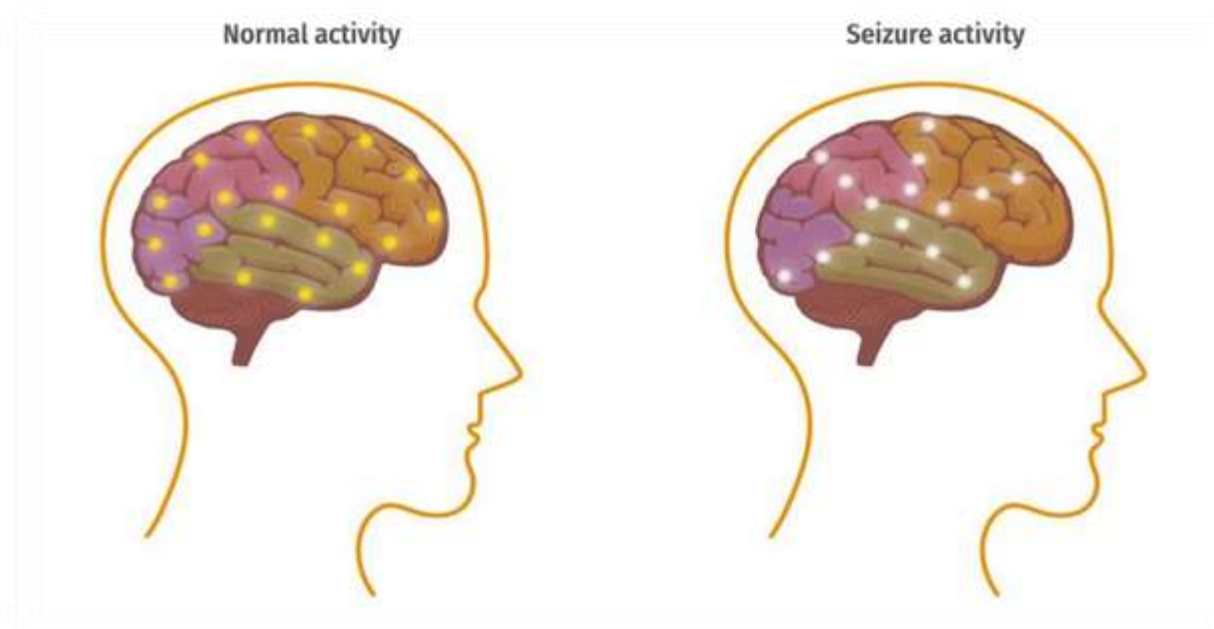


Figure.05: An illustration of normal and seizure activity in the brain

TREATMENT FOR DBS EPILEPSY IN GENERAL

- I. Medications (Antiepileptic Drugs, or AEDs): Medications are frequently the first line of treatment for epilepsy. Antiepileptic medications come in a wide variety; the selection of a medication is contingent upon the specific type of seizure as well as individual factors. Finding each person's most effective and well-tolerated medication may take some time. (14)
- II. Ketogenic Diet: Research has demonstrated that this high-fat, low-carb diet can effectively reduce seizures, especially in children with epilepsy. Usually, it is taken into consideration when medicine isn't giving enough control. (15)
- III. Vagus Nerve Stimulation (VNS): The main therapy can lessen seizures by stimulating the vague nerve through the implantation of a device. According to the international League Against Epilepsy (ILAE) report drug resistant epilepsy is defined the inability to suppress seizures activity for more than a year even when two or more carefully chosen antiepileptic medication are used effectively as monotherapy. one of the main treatment drug resistant in individuals, those who are not capable for surgery (16) (19)
- IV. (RNS) A more recent treatment called responsive neurostimulation (RNS) entails implanting a gadget in the brain that tracks brain activity and stimulates the patient electrically if abnormal activity is seen. (17)
- V. Target Areas: Certain brain regions linked to seizures are often where the electrodes are implanted in The thalamus and the anterior nucleus of the thalamus are cautious targets.

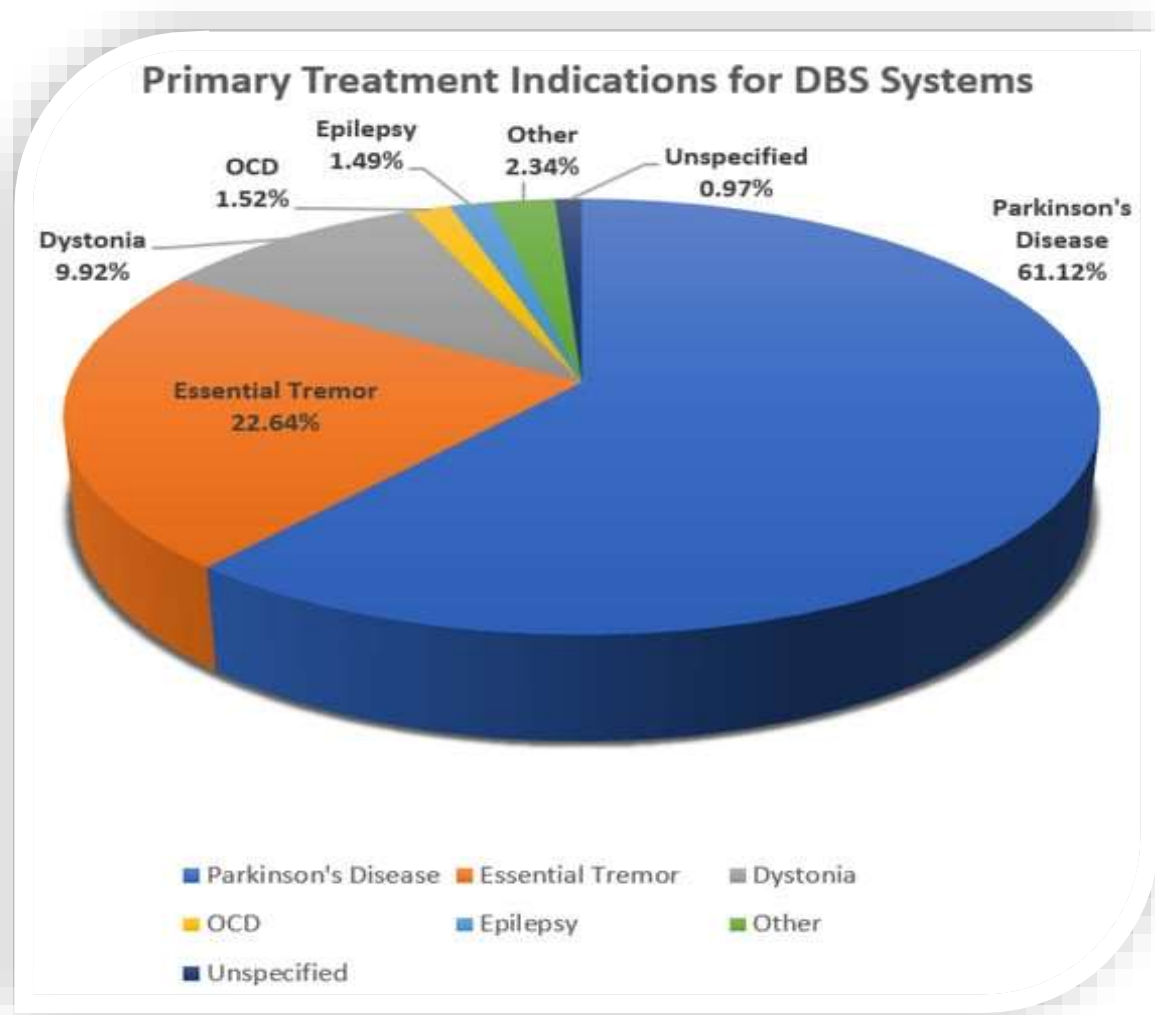


Figure.06: This picture shows the indication for (DBS) epilepsy that includes

- a) Dystonia
- b) OCD
- c) Epilepsy
- d) Parkinson's disease
- e) Unspecified
- f) Others

This indication should under taken for the primary treatment for (DBS) system (23)

PATHOPHYSIOLOGY OF EPILEPSY

- i. An imbalance between neuronal excitability and inhibition**
- ii. The balance between excitatory and inhibitory signals controls how quickly neurons fire in a healthy brain.**
 - a. Excitatory and inhibitory neurotransmitter imbalance is frequently seen in epilepsy, which raises the risk of uncontrolled neuronal firing and increases neuronal excitability. (17)
- iii. Ion Channel Function Abnormalities**
 - a. Electrical signals that involve the passage of ions—charged particles—across cell membranes are used by neurons to communicate.

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- b. Ion channel mutations or abnormalities can interfere with the normal flow of ions, which can cause neurons to become hyperexcited and develop the risk of seizures.
- iv. **Unbalanced Neurotransmitters**
 - a. Chemical messengers called neurotransmitters are responsible for sending signals between neurons. For the brain to function normally, neurotransmitter balance is essential.
 - b. Neurotransmitter imbalances, especially those involving excitatory effects (e.g., glutamate), may be a factor in elevated neuronal excitability and seizures.
- v. **The abnormalities in structure**
 - a. Unusual neuronal activity in certain regions of the brain can lead to seizures due to structural anomalies in the brain, known as tumors, malformations, or scar tissue from trauma.(18)(20)
- vi. **Genetic Elements**

Certain genetic mutations can make a person more prone to seizures, and there is evidence that certain forms of epilepsy have a genetic basis.

The development and operation of neurotransmitter systems, ion channels, and other brain circuitry components may be influenced by genetic factors.
- vii. **Brain Network Failure**
- viii. **More and more research is pointing to epilepsy as a network disorder involving aberrant interactions between several brain regions.**

Diagnosis for deep brain stimulating epilepsy

i. **Medical Background:**

The medical professional will start by obtaining a thorough medical history, which will include details about the patient's history of seizures, their frequency and length, any potential triggers, and any accompanying symptoms.

A comprehensive medical history will also contain details regarding the patient's general health, previous illnesses, prescribed drugs, (20)

- ii. **EEG (Electroencephalogram):** An essential test for epilepsy diagnosis is the EEG. Electrodes affixed to the scalp are used to measure the electrical activity of the brain. Unusual patterns, like abrupt waves or spikes, may be a sign of epilepsy. The patient may have an EEG while they are at rest or while engaging in particular activities that may cause seizures.(22)

Tests on Blood

- iii. To rule out metabolic or systemic conditions that may be causing seizures, blood tests may be performed.

Additionally, genetic testing might be taken into consideration, particularly in situations where epilepsy can have a hereditary component. (21)
- iv. **Testing Neuropsychologically:** Tests of neuropsychology can be used to analyze memory, cognitive function, and other areas of brain activity.
- v. **Surgery for Implants**
 - a. The patient has the permanent electrodes and pulse generator surgically implanted if the interdisciplinary team decides (DBS) is the best course of action (it is placed in the chest area). (22,23)
- vi. **Before Surgery Assessment**
 - a. Preoperative testing, which includes video EEG monitoring, neuropsychological testing, and other specialized tests, is usually performed on patients who are being considered for DBS. This evaluates the effect of seizures on cognitive function and assists in identifying the precise region of the brain causing seizures. (22,24)

CONCLUSION

The conclusion of this review, we have numerous forms of epilepsy like, partial seizures, generalized seizures, temporal and frontal lobe epilepsy. The diagnosis approach is a component of the epilepsy evaluation, we have antiepileptic medication, ketogenic diet, vagus nerve stimulation (VNS), responsive neurostimulation (RNS). This are all medication came into treatment of epilepsy in deep brain stimulating system. It is an complex disorder where it epilepsy can effect more of patients, where all therapy are fail, and know deep brain stimulating system came into existence to treat the frequency and intensity of seizures in epileptic patients. Epilepsy caused by an aberrant electrical activity in the brain, it can prevent by the when a neurosurgeon implants the DBS device during surgery, the recent review concluded that the some the risk factory, Etiology, pathophysiology, we have some diagnosis patterns like; Electro cardio gram (ECG), test on blood, Testing Neuropsychologically, surgery for implants The US FDA recently approved deep brain stimulating therapy for epilepsy based on their trail of review articles.

REFERENCES

1. Zanzibari N (2019) et al. Deep Brain Stimulation and Drug-Resistant Epilepsy: A Review of the Literature. *Front Neurol.* 6; 10:601. doi: 10.3389/fneur.2019.00601.
2. Sarmast ST (2020) et al. Current Classification of Seizures and Epilepsies: Scope, Limitations and Recommendations for Future Action. *Cureus.* 20;12(9). doi: 10.7759/cureus.10549.
3. Ziaei M(2023) et al. Social Cognition in Temporal and Frontal Lobe Epilepsy: Systematic Review, Meta-analysis, and Clinical Recommendations. *J Int Neuropsychol Soc.* (2):205-229. doi: 10.1017/S1355617722000066.
4. Hu Y (2016) et al. Impaired social cognition in patients with interictal epileptiform discharges in the frontal lobe. *Epilepsy Behav.* 46-54. doi: 10.1016/j.yebeh.2016.01.027.
5. Angélica Marta Lopes (2023) et al. Serum levels of oxidative stress biomarkers is changed in pharma coresistant mesial temporal lobe epilepsy patients with or without disorders, *Brain Disorders, Volume11*, doi.org/10.1016/j.dscb.2023.
6. Robert S. Fisher, (2023). Deep brain stimulation of thalamus for epilepsy, *Neurobiology of Disease, Volume179*, doi.org/10.1016/j.nbd.
7. Blume WT (2003). Diagnosis and management of epilepsy. *CMAJ.*18;168(4):441-8.
8. Yang L, (2021) et al. Risk Factors for Epilepsy: A National Cross-Sectional Study from National Health and Nutrition Examination Survey 2013 to 2018. *Int J Gen Med.* doi: 10.2147/IJGM.S323209.
9. Nguyen R, Téllez Zenteno JF (2009). Injuries in epilepsy: a review of its prevalence, risk factors, type of injuries and prevention. *Neurol Int.*16;1(1). doi: 10.4081/ni.2009.e20.
10. Xue-Ping (2019) et al. Risk factors for drug-resistant epilepsy: A systematic review and meta-analysis. *Medicine* 98(30). DOI: 10.1097/MD.00000000000016402.
11. Walsh S (2016) et al. A systematic review of the risks factors associated with the onset and natural progression of epilepsy, *Neurotoxicology.*;61:64-77.doi:10.1016/j.neuro.2016.03.011.
12. A systematic review (2017) of the risks factors associated with the onset and natural progression of epilepsy, *Neuro Toxicology, Volume61*,64-77, doi.org/10.1016/j.
13. Ułamek-Kozioł M (2019) et al. Ketogenic Diet and Epilepsy. *Nutrients*;11(10):doi: 10.3390/nu11102510.
14. Enry C. (2023). Neuro-stimulation in focal epilepsy: A systematic review and meta-analysis, *Epilepsy & Behavior, Volume 142*,

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15. Foutz TJ, Wong M (2022). Brain stimulation treatments in epilepsy: Basic mechanisms and clinical advances. *Biomed J.* 45(1):27-37. doi: 10.1016/j.bj.2021.08.010.
16. Anwar H (2023) et al. Epileptic seizures. *Discoveries (Craiova)*. 12;8(2): e110. doi: 10.15190/d.2020.7.
17. Lam J (2021) et al. Cognitive outcomes following vagus nerve stimulation, responsive neurostimulation and deep brain stimulation for epilepsy: A systematic review. *Epilepsy Res.* 172:106591. doi: 10.1016/j.eplepsyres.2021.106591.
18. Vetkas A, (2022). Deep brain stimulation targets in epilepsy: Systematic review and meta-analysis of anterior and centromedian thalamic nuclei and hippocampus. *Epilepsia.* 63(3):513-524. doi: 10.1111/epi.17157.
19. Touma L, (2022) et al. Neurostimulation in people with drug-resistant epilepsy: Systematic review and meta-analysis from the ILAE Surgical Therapies Commission. *Epilepsia.* 63(6):1314-1329. doi: 10.1111/epi.17243.
20. Sprengers M, (2021) et al. Deep brain and cortical stimulation for epilepsy. *Cochrane Database Syst Rev.* 18;7(7). doi: 10.1002/14651858.CD008497.
21. Loh A (2022) et al. Probing responses to deep brain stimulation with functional magnetic resonance imaging. *Brain Stimul.* 15(3):683-694. doi: 10.1016/j.brs.2022.03.009.
22. Bucur M, Papagno C (2023). Deep Brain Stimulation in Parkinson Disease: A Meta-analysis of the Long-term Neuropsychological Outcomes. *Neuropsychol Rev.* 33(2):307-346. doi: 10.1007/s11065-022-09540-9.
23. Kokkonen A (2022) et al. Neurobiological effects of deep brain stimulation: A systematic review of molecular brain imaging studies. *Neuroimage.* doi: 10.1016/j.neuroimage.2022.119473.
24. Wang S (2023) et al. Comorbidity of epilepsy and attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. *J Neurol.* 270(9):4201-4213. doi: 10.1007/s00415-023-11794-z.
25. Lehner J, (2022) et al. Sleep quality and architecture in Idiopathic generalized epilepsy: A systematic review and meta-analysis. *Sleep Med Rev.* doi: 10.1016/j.smrv.2022.101689.
26. Chan HY (2023) et al. Economic evaluations of nonpharmacological treatments for drug-resistant epilepsy: A systematic review. *Epilepsia.* 64(11):2861-2877. doi: 10.1111/epi.17742.
27. Salanova V. (2018) Deep brain stimulation for epilepsy. *Epilepsy Behav.* 88S:21-24. doi: 10.1016/j.yebeh.2018.06.041. Epub 2018 Jul 17. PMID: 30030085.

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Conflict of Interest

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