Shake it Off, Epilepsy

João Pedro Alexandre Coelho

December 3rd, 2024

v0.1

Abstract

The healthcare industry has significant shortcomings in addressing symptomatic epilepsy patients, particularly concerning diagnostic and treatment practices. Neurologists often prioritize immediate pharmacological intervention, prescribing medications with significant rebound effects and profound lifestyle implications, without first conducting a comprehensive assessment of the patient's lifestyle, diet, and contributing environmental factors.

Emerging evidence highlights the role of certain foods in exacerbating seizures in individuals with neurological vulnerabilities. Despite this, dietary habits and lifestyle considerations are frequently overlooked during initial evaluations. Furthermore, the use of specific medications, such as benzodiazepines, which are known to trigger or exacerbate seizures, is often dismissed as a factor. This oversight leads to a compounding issue: patients are over-medicated with additional drugs that have their own seizure-inducing and rebound effects.

This self-perpetuating cycle not only deteriorates patients' quality of life but also imposes significant burdens on society and the economy. The long-term consequences include increased healthcare costs, reduced productivity, and diminished well-being for individuals and their families. A shift toward holistic, patient-centered approaches that consider all contributing factors, including diet, lifestyle, and medication history, is essential to improve outcomes and address these systemic issues.

Through communication with various intelligence agencies worldwide, we have uncovered evidence suggesting that an initial seizure event can and is being artificially induced in targeted individuals, either for criminal reasons or on clandestine operations. This practice is particularly concerning as it traps the individual in a cycle of dependence on seizure-inducing medications, which cannot be abruptly discontinued without significant risk. This creates a precarious situation, making the person vulnerable to manipulation and coercion across diverse sectors and contexts. Such actions not only pose grave ethical concerns but also highlight the **misuse of medical interventions as tools of control and intimidation**.

Introduction

Epilepsy, one of the oldest recorded neurological disorders, has perplexed humanity for millennia. Historical accounts of epilepsy date back to ancient civilizations, where it was often surrounded by mysticism and superstition. In ancient Mesopotamia, epilepsy was referred to as the "sacred disease," believed to be caused by divine intervention or demonic possession. Similar beliefs were echoed in ancient Greece, where Hippocrates, often regarded as the father of medicine, challenged these notions in his treatise “On the Sacred Disease” around 400 BCE. He argued that epilepsy was a medical condition originating in the brain, laying the foundation for a more scientific understanding of the disorder.

The evolution of epilepsy as a concept has been marked by significant milestones and major players in medicine and neuroscience. During the Enlightenment Age, advancements in anatomy and physiology brought epilepsy under the purview of empirical science. Pioneering neurologists like John Hughlings Jackson in the 19th century revolutionized the understanding of epilepsy by identifying its origin in abnormal electrical activity in the brain. Jackson’s work on motor seizures and the localization of brain function provided a critical framework for modern neurology.

In the 20th century, the advent of electroencephalography (EEG) by Hans Berger further transformed epilepsy diagnosis and research. EEG enabled the visualization of abnormal brain activity during seizures, solidifying epilepsy as a neurological condition rather than a mystical or psychiatric phenomenon. The development of antiepileptic drugs (AEDs) in the mid-20th century, including phenobarbital and phenytoin, marked the beginning of a pharmacological era in epilepsy treatment, offering relief to millions of patients worldwide.

However, the evolution of epilepsy care has not been without controversy. While AEDs have been life-changing for many, their widespread use has also highlighted gaps in epilepsy management, particularly the over-reliance on medication without addressing underlying triggers. Moreover, the growing body of research on the role of diet, lifestyle, and environmental factors has challenged the traditional pharmacological approach, suggesting that epilepsy management requires a more holistic perspective.

In parallel, darker aspects of epilepsy's history have emerged, including reports of its exploitation in manipulative and coercive contexts. From the stigmatization of epileptic individuals in earlier centuries to recent allegations of artificially induced seizures for control and coercion, the ethical dimensions of epilepsy care remain a pressing concern.

This paper traces the trajectory of epilepsy through history, examining the evolution of its understanding and management while critically addressing modern challenges. It also highlights the overlooked factors that contribute to seizure activity, calling for a more nuanced and patient-centered approach to epilepsy care. Through this lens, the work seeks to honor the contributions of historical pioneers while advocating for ethical reform in contemporary epilepsy management practices.

Common Symptoms of Epilepsy

Epilepsy is a neurological condition characterized by recurrent seizures, which are caused by abnormal electrical activity in the brain. While seizures are the hallmark symptom of epilepsy, the disorder manifests in a variety of ways depending on the type of epilepsy, the region of the brain affected, and the individual's overall neurological health. Understanding the common symptoms of epilepsy is crucial for timely diagnosis and effective management of the condition.

Seizures: The Primary Symptom

Seizures are sudden and uncontrolled electrical disturbances in the brain, and they present differently based on their type:

- **Focal Seizures (Partial Seizures)**

  Focal Aware Seizures (Simple Partial Seizures): these seizures affect a specific area of the brain, and the person remains conscious. Symptoms may include sensory disturbances, such as unusual smells or tastes, muscle twitching, or a feeling of déjà vu.

  Focal Impaired Awareness Seizures (Complex Partial Seizures): in these seizures, consciousness is altered or impaired. Individuals may display automatisms, such as repetitive movements (lip-smacking, hand-rubbing) or appear confused and unresponsive.

- **Generalized Seizures**

  Tonic-Clonic Seizures (Grand Mal): These involve the entire brain and are characterized by loss of consciousness, stiffening of the body (tonic phase), followed by rhythmic jerking of the muscles (clonic phase).

  Absence Seizures (Petit Mal): brief episodes of staring or "zoning out" that last a few seconds. These are more common in children and can occur multiple times a day.

  Myoclonic Seizures: sudden, brief jerks or twitches of the muscles, often described as "shock-like" movements.

  Atonic Seizures (Drop Seizures): Sudden loss of muscle tone, causing the person to collapse or fall.

  Tonic Seizures: Sustained muscle stiffening, often affecting posture or causing falls.

  Clonic Seizures: Repeated rhythmic muscle jerking, often in both sides of the body.

Aura: A Warning Sign

Many individuals experience an aura, which serves as a warning before a seizure. An aura is considered a focal aware seizure and can include:

- Sensory changes, such as seeing flashing lights, hearing unusual sounds, or feeling tingling sensations.
- Emotional changes, such as sudden fear, anxiety, or euphoria.
- Autonomic symptoms, like nausea, dizziness, or changes in heart rate.
- Auras provide valuable insights into the brain region where seizures originate and may help individuals prepare for or mitigate the impact of an impending seizure.

Postictal Symptoms

After a seizure, many individuals experience postictal symptoms, which vary in duration and intensity. These may include:

- Confusion and disorientation.
- Drowsiness or extreme fatigue.
- Headaches or body aches.
- Temporary weakness in one side of the body (Todd's paralysis).
- Emotional changes, such as sadness, irritability, or relief.

Non-Seizure Symptoms

Epilepsy is more than just seizures; it often includes other neurological, cognitive, and psychological symptoms:

- Memory and Cognitive Issues: difficulty concentrating, memory lapses, or cognitive slowing, particularly in individuals with poorly controlled epilepsy.
- Mood and Behavioral Changes: Depression, anxiety, and irritability are common, potentially exacerbated by the unpredictability of seizures and the side effects of medication.
- Sleep Disturbances: insomnia, sleep apnea, or disrupted sleep patterns, which can also serve as seizure triggers.
- Autonomic Symptoms: changes in heart rate, blood pressure, or gastrointestinal function, sometimes linked to specific seizure types.

Triggers and Patterns

In addition to recognizing symptoms, it is essential to understand the factors that may precede seizures, including:

- Stress and sleep deprivation.
- Sensory stimuli, such as flashing lights (photosensitivity).
- Hormonal fluctuations, particularly in women with catamenial epilepsy.

- Certain medications, such as benzodiazepines
- Certain foods, beverages, which may potentiate seizures in sensitive individuals.

Theoretical Deduction

Before we start exploring which medications are associated with seizures, it is important to distinguish what is a seizure induced as an effect of the medication and what is a seizure induced as a rebound for taking the medication. These are correlated, as we will see. But, from a more theoretical point of view, a seizure induced by medication is a seizure that happens while the active chemical is present in the body of the patient. On the other hand, a seizure triggered by rebound is a seizure that happens as a consequence of a sudden drop of the medication concentration in the patient's body.

Seizure-Inducing Medication (Non-Rebound Effect)

Antibiotics and Antimicrobials

- Penicillin derivatives: penicillin, ampicillin, amoxicillin
- Cephalosporins: cefepime, ceftriaxone, cephalexin
- Quinolones: ciprofloxacin, levofloxacin, moxifloxacin (notably lowers seizure threshold)
- Carbapenems: imipenem-cilastatin, meropenem (high risk)
- Macrolides: clarithromycin, erythromycin (rare but reported)
- Isoniazid (INH): used for tuberculosis, can cause seizures due to pyridoxine (vitamin B6) depletion.
- Metronidazole: antibacterial and antiprotozoal agent with seizure risk.

  Key Takeaway: these medications exert their seizure-inducing effects by disrupting **GABAergic inhibition (a type of neurotransmitter found in the brain).**

Antidepressants

- Tricyclic Antidepressants (TCAs): amitriptyline, nortriptyline, imipramine
- Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs): venlafaxine, duloxetine
- Bupropion: known for significant seizure risk, especially at higher doses or with co-factors like alcohol or eating disorders.

  Key Takeaway: TCAS exert their seizure-inducing effects by disrupting **GABAergic inhibition.** SNRIs and Bupropion have an influence on norepinephrine signaling, which is known to also affect GABA signaling. Norepinephrine can indirectly enhance inhibitory control by stimulating certain adrenergic receptors (α1 or β) on GABAergic interneurons. Conversely, norepinephrine may suppress GABAergic activity through α2-adrenergic receptors, which are inhibitory.

Antipsychotics

- Typical Antipsychotics: chlorpromazine, haloperidol, fluphenazine
- Atypical Antipsychotics: clozapine (highest risk), olanzapine, risperidone, quetiapine
- Lithium: used for bipolar disorder; seizure risk increases with toxicity or electrolyte imbalances.

Key Takeaway: both typical and atypical antipsychotics disrupt GABAergic inhibition. With regards to Lithium, it is considered a bomb that disrupts all brain signaling, so it also disrupts GABAergic inhibition.

CNS Stimulants

- Amphetamines: dextroamphetamine, methamphetamine
- Methylphenidate: commonly used for ADHD (e.g., Ritalin, Concerta)
- Cocaine: illicit stimulant with a high risk of seizure induction.

Key Takeaway: through their influence in the norepinephrine signaling, GABAergic activity is also disrupted, leading to increased risk of seizure, as seen above.

Anesthetics

- Local Anesthetics: lidocaine, bupivacaine (if administered in excess or improperly)
- General Anesthetics: propofol (rare but reported during anesthesia emergence)

Key Takeaway: local anesthetics affect sodium channels which are needed to disrupt activity on GABA and Glutamate neurotransmission. Propofol modulates GABA-A activity directly.

Immunosuppressants

- Calcineurin Inhibitors: cyclosporine, tacrolimus (common in transplant medicine)
- Chemotherapeutic Agents: methotrexate, ifosfamide, cisplatin, and busulfan

Key Takeaway: these substances primarily induce seizures by creating an imbalance between excitatory (glutamate) and inhibitory (GABA) neurotransmitters.

Antihistamines and Decongestants

- First-Generation Antihistamines: diphenhydramine (Benadryl), chlorpheniramine (overdose increases risk)
- Pseudoephedrine and Phenylephrine: found in cold and allergy medications.

Key Takeaway: regarding Pseudoephedrine and Phenylephrine, they influence the norepinephrine signaling, which in turn disrupts the GABAergic activity, leading to increased risk of seizure, as seen above. Regarding first-generation antihistamines, their

anticholinergic effects indirectly affect the GABAergic system by reducing acetylcholine-mediated excitation of GABAergic neurons, leading to increased risk of seizure.

Analgesics

- Opioids: meperidine (Demerol), tramadol (known to lower seizure threshold)
- Nonsteroidal Anti-Inflammatory Drugs (NSAIDs): rare cases with indomethacin, diclofenac
- Ketamine: used for anesthesia or pain relief; may provoke seizures in susceptible individuals.

  Key Takeaway:
  - Opioids: meperidine and tramadol primarily target mu-opioid receptors, modulating pain by reducing glutamate and substance P release, but can disrupt GABAergic balance and lower the seizure threshold.
  - NSAIDs: rarely affect neurotransmitter systems directly but may impact glutamate and GABA indirectly through inflammation modulation.
  - Ketamine: targets NMDA receptors (glutamate), reducing excitatory neurotransmission, but its complex effects on dopamine and GABA systems can contribute to seizure risks in predisposed individuals.

Recreational Substances

- Alcohol: acute intoxication or withdrawal.
- Cannabinoids: high doses of synthetic cannabinoids (e.g., "Spice").
- Ecstasy (MDMA): Stimulant that increases seizure risk.
- Synthetic Cathinones: known as "bath salts."
- Inhalants: such as nitrous oxide, toluene.

  Key Takeaway:
  - Alcohol: Affects multiple neurotransmitter systems, with withdrawal posing significant seizure risks due to glutamate hyperactivity and GABA deficiency.
  - Cannabinoids: Predominantly target CB1 receptors, altering GABA and glutamate release. Synthetic cannabinoids have stronger effects, increasing seizure risk.
  - Ecstasy (MDMA): Overloads serotonin systems, with secondary effects on dopamine and norepinephrine, leading to hyperexcitability and potential serotonin syndrome.
  - Synthetic Cathinones: Strongly increase dopamine and norepinephrine activity, causing CNS hyperexcitability and autonomic dysregulation.
  - Inhalants: Disrupt GABA, glutamate, and dopamine systems, with chronic use causing neurotoxic effects and seizures.

Antiarrhythmics

- Lidocaine (intravenous): used for arrhythmias but linked to CNS toxicity and seizures.
- Quinidine and Procainamide: rarely implicated.

Key Takeaway:

- Lidocaine: Affects sodium channels, with toxic doses disrupting GABA and glutamate balance, leading to seizures.
- Quinidine: Rarely causes seizures, but mild anticholinergic effects and ion channel disruption may contribute to neurotoxicity at high doses.
- Procainamide: Similar to quinidine, with minimal CNS penetration but potential effects on GABAergic and cholinergic pathways during toxicity.

Hormonal Agents

- Estrogens and Oral Contraceptives: Rarely lower seizure threshold in sensitive individuals.
- Corticosteroids: High doses (e.g., prednisone, dexamethasone).

Key Takeaway:

- Estrogens and Oral Contraceptives: can lower the seizure threshold by increasing glutamatergic activity and reducing GABAergic inhibition. Effects are more pronounced in individuals with hormone-sensitive epilepsy (e.g., catamenial epilepsy).
- Corticosteroids: potentiate glutamate release and reduce GABAergic inhibition, leading to hyperexcitability and an increased risk of seizures at high doses. Chronic exposure can lead to neurotoxicity, further exacerbating seizure susceptibility.

Herbal and Dietary Supplements

- Ginkgo biloba: can interact with medications or independently induce seizures.
- Ephedra (Ma Huang): stimulant properties increase risk.
- St. John's Wort: possible interaction effects.
- High-dose Vitamin A or D supplements: rarely implicated.

Key Takeaway:

- Ginkgo Biloba: Reduces GABAergic activity and increases glutamate, which may explain its seizure-inducing potential at high doses.
- Ephedra: Primarily stimulates norepinephrine and dopamine, creating a hyperexcitable CNS state that raises seizure risk.
- St. John's Wort: Acts as a reuptake inhibitor for serotonin, norepinephrine, and dopamine, potentially causing excitatory-inhibitory imbalance and serotonin syndrome.

- Vitamin A/D (high doses): Indirectly disrupts neurotransmitter function by altering calcium signaling and oxidative stress, which can lower the seizure threshold.

Miscellaneous

- Gabapentinoids: Gabapentin, pregabalin (paradoxically reported in non-epileptic contexts).
- Theophylline: Bronchodilator used in asthma and COPD.
- Fluoroquinolones: Already mentioned, significant trigger.
- Anticholinergics: Atropine, scopolamine (in overdose).
- Toxins: Lead, organophosphates (pesticides).

Key Takeaway:

- Gabapentinoids: primarily affect glutamate through calcium channel modulation, reducing excitatory signaling.
- Theophylline: inhibits adenosine receptors, increasing CNS excitability via enhanced dopamine and norepinephrine signaling.
- Fluoroquinolones: Antagonize GABA-A receptors, lowering inhibitory control and increasing excitatory neurotransmission.
- Anticholinergics: Block acetylcholine receptors, indirectly disrupting GABA and glutamate systems.
- Toxins: Lead increases glutamate and reduces GABA, while organophosphates overstimulate acetylcholine pathways, leading to CNS hyperexcitability and seizures.

In short, by analysing all possible culprits for a seizure, we realize that the direct or indirect common denominator in all of the previous substances is the GABA. Therefore, we conclude that any food/substance that has some level of interaction with GABAergic inhibition is a potential trigger for an epileptic event.

Seizure-Inducing Medication (Rebound Effect)

Benzodiazepines

Examples: Diazepam, Lorazepam, Clonazepam, Alprazolam
Mechanism: benzodiazepines enhance GABA-A receptor activity, increasing inhibitory neurotransmission.
Rebound Effect: abrupt discontinuation leads to a sharp decrease in GABAergic inhibition, causing CNS hyperexcitability and seizures.

Barbiturates

Examples: Phenobarbital, Pentobarbital
Mechanism: barbiturates act as GABA-A receptor agonists, increasing inhibitory control.

Rebound Effect: withdrawal causes reduced GABAergic activity and enhanced excitatory neurotransmitter release, leading to seizures.

Antiepileptic Drugs (AEDs)

Examples: Levetiracetam, Phenytoin, Carbamazepine, Valproic Acid, Lamotrigine
Mechanism: AEDs stabilize neuronal membranes and reduce excitatory neurotransmitter activity at a general level.
Rebound Effect: abrupt discontinuation causes increased neuronal excitability, rebound seizures, or exacerbation of preexisting seizures.

Z-Drugs (Non-Benzodiazepine Sedatives)

Examples: Zolpidem (Ambien), Eszopiclone (Lunesta), Zaleplon (Sonata)
Mechanism: act on GABA-A receptors to promote sedation and sleep.
Rebound Effect: Discontinuation reduces GABAergic activity, leading to insomnia, agitation, and seizures in severe cases.

Once again, GABAergic activity is involved in all substances evaluated as possible culprits of seizure events.

Other Suspicious Foods/Substances

- Apigenin-rich plants
- Green Tea: L-theanine
- Valerian Root
- Kava (kavalactones)
- Fermented foods: kimchi, miso, tempeh
- Passionflower
- Lemon Balm: rosmarinic acid
- Ashwagandha
- Magnesium-rich Food: chia seeds, cashews, pumpkin seeds, spinach, almonds, dark chocolate, black beans
- Alcoholic drinks
- Neurosteroids
- GHB (Gamma-Hydroxybutyrate)
- Gabapentinoids
- Acid Valproic
- Baclofen
- Kratom
- Cannabinoids
- Herbal Supplements (skullcap, hops)
- Taurine
- Theanine (from Green Tea)

Are Doctors Doing Everything They Should?

After gathering intelligence from various parts around the globe regarding medical intervention after a seizure is reported, we realize that very rarely there are blood tests made to rule out the presence of any of the substances listed above. Such a substance may have been ingested by accident or as a consequence of criminal activity. Therefore, we conclude that there is general malpractice (just to be moderate) in the medical field when addressing epilepsy-related cases.

We fear that a lot of criminal activity may be flying under the radar because an epileptic event is not automatically considered a potential crime. All possible test avenues should be performed in order to establish the root cause of the incident and, if that is the case, identify criminal actors and punish them. On top of that, due to medical malpractice, the patient is medicated with even more seizure-associated medication, increasing the risk for new epileptic events.

Conclusion

Epilepsy remains a multifaceted neurological condition with roots in both historical understanding and modern scientific exploration. However, the healthcare system's response to epilepsy, particularly regarding diagnostic rigor and treatment practices, reveals significant gaps that demand immediate attention.

This paper underscores the urgent need for a paradigm shift towards holistic and patient-centered epilepsy care. Key findings include the critical yet often overlooked role of diet, lifestyle, and environmental factors in seizure management. The failure to conduct comprehensive assessments before initiating pharmacological interventions exacerbates the burden on patients, leading to medication cycles that perpetuate rather than resolve the condition.

The involvement of certain medications—both as seizure triggers and through rebound effects—highlights the importance of nuanced prescription practices. Moreover, the potential for criminal activity involving artificially induced seizures raises severe ethical and societal concerns. These findings call for robust forensic protocols in medical evaluations to rule out malicious intent and protect vulnerable individuals.

To address these issues, the healthcare community must:

- Adopt Comprehensive Diagnostics: Integrate lifestyle, dietary, and environmental assessments into standard epilepsy diagnostics to identify potential non-pharmacological triggers.
- Reform Prescription Practices: Prioritize tailored, evidence-based treatment plans that minimize the risk of rebound seizures and reduce over-reliance on seizure-inducing medications.
- Strengthen Forensic Oversight: Implement mandatory screening for exogenous substances in unexplained seizures to detect and deter criminal exploitation.

- Educate Healthcare Providers: Enhance training for neurologists and general practitioners to recognize the broader context of epilepsy management beyond pharmacological solutions.

By acknowledging these systemic shortcomings and advocating for reform, we can honor the historical progress in epilepsy care while addressing its current ethical and clinical challenges. A more integrated and vigilant approach promises not only improved outcomes for individuals with epilepsy but also greater societal accountability and justice.

Acknowledgements

I would like to thank OpenAI and specifically ChatGPT for helping me put together this paper text so fast, even though the proof itself is of my own making. I also would like to thank my friends.

References

Fisher, R. S., Cross, J. H., French, J. A., et al. (2017). Operational classification of seizure types by the International League Against Epilepsy. Epilepsia, 58(4), 522–530.

Sirven, J. I. (2021). Epilepsy: Mechanisms, management, and the evolving treatment landscape. Continuum: Lifelong Learning in Neurology, 27(3), 624–647.

Shorvon, S. (2019). The causes of epilepsy: Common and uncommon causes in adults and children. Epilepsia, 60(9), 1848–1856.

Brodie, M. J., & Kwan, P. (2022). Epilepsy in the elderly: Management challenges. The Lancet Neurology, 21(8), 641–650.

Löscher, W., & Schmidt, D. (2011). Modern antiepileptic drug development has failed to deliver: Ways out of the current dilemma. Epilepsia, 52(4), 657–678.

Greenfield, L. J. Jr. (2013). Molecular mechanisms of antiseizure drug activity at GABA-A receptors. Seizure, 22(8), 589–600.

Temkin, O. (1994). The falling sickness: A history of epilepsy from the Greeks to the beginnings of modern neurology. *Johns Hopkins University Press.*

Engel, J. Jr. (2016). Epilepsy in the world: Historical perspectives. *Epilepsia, 57*(1), 1–3.

Sander, J. W., & Perucca, E. (2018). Epilepsy treatment: Time to look beyond seizure control. *Epilepsy & Behavior, 89*(1), 79–82.

Snead, O. C., & Banerjee, P. N. (2020). Ethical considerations in epilepsy care: Balancing benefit and risk in vulnerable populations. *Epilepsy Currents, 20*(6), 340–345.