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Review Article

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The Mind's Maze: Epilepsy's Path to Psychosis

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Abstract

The nature of relationship between psychosis and epilepsy is an intricate and multifaceted subject matter that has intrigued researchers and clinicians for centuries. While not all individuals with epilepsy experience psychosis, there is a recognized correlation among the two conditions, particularly in cases of temporal lobe epilepsy (TLE). In this article, we will delve into various aspects of the relationship between psychosis and epilepsy, including associated stigma, clinical features, and timely treatment implications. Additionally, we will explore the risks and dangerousness associated with peri-ictal phase of epilepsy and would look into the associated risks to self and others including changes in mental state in patients suffering from epileptic attack, and subsequent consequences. We also conducted a qualitative survey in the region of Mersey Care National Health Service (NHS) Foundation Trust in UK on "Epilepsy and Psychosis", which could well reflect a wider public opinion.

Keywords: Epilepsy, Seizures, Temporal Lobe Epilepsy, Peri-Ictal Psychoses, Post-Ictal Psychosis, Vincent Van Gogh, Schizophrenia

1. Background

The association between epilepsy and psychosis has garnered significant attention from neurologists and psychiatrists since the nineteenth century. Both conditions have suffered from stigma due to historical superstitions, ignorance, and misbeliefs. Even though the efforts to combat stigma have been ongoing, there is limited expertise on the prodigy of double stigma of having both conditions simultaneously [1]. Stigma not only leads to discrimination and violations of civil and human rights but also reduces access to healthcare and adherence to treatment, resulting in increased morbidity and mortality [2].

In earlier periods such as Classical Antiquity and the Middle Ages, people did not view "madness" (a term they used broadly for mental health issues) as a mental disorder but rather as divine malady or demonic possession [3]. This period was remarkably challenging for those with psychotic illness and epilepsy due to limited understanding of the human brain and mind. Epilepsy was considered a sacred illness imposed by the gods, with treatments involving sacrifices and religious rituals led by priests. For centuries, it was also believed that epilepsy was instigated by evil spirits or divine punishment [4].

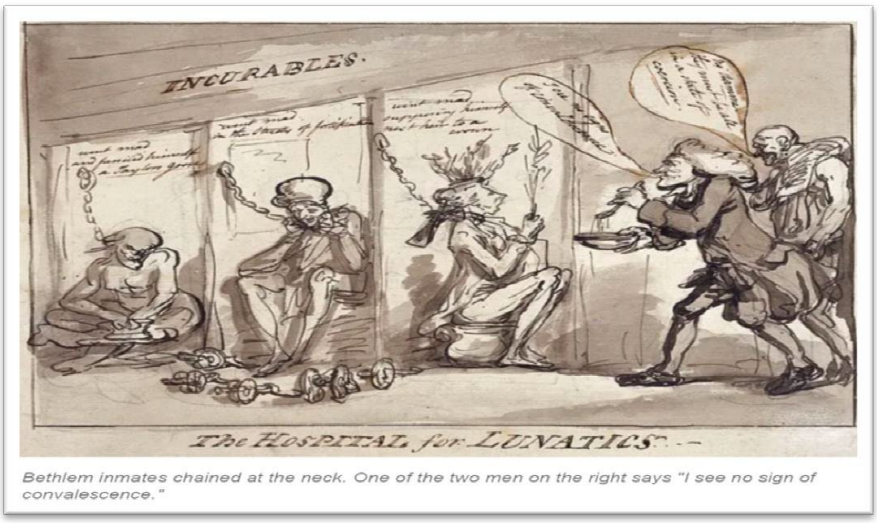

Figure 1: Bethlem Royal Hospital, London: England's first asylum for treatment of mental illness. For many years, it was a place of inhumane conditions. Members of the general public were charged admission to visit the mad house, as though the patients were exhibits in a zoo [5].

Similarly, during the Middle Ages, individuals with psychosis were often imprisoned alongside criminals or confined in lunatic asylums, leading to fear, isolation, and harsh treatment (Figure 1). Treatments mainly involved physical punishments, torture, sacrifices, and religious rituals which involved shoving, i.e. pulling the patient through a natural opening, such as a stone crevice or a hollow tree, could also help prevent seizures, bloodletting, drinking the blood of animals or fallen gladiators and eating the flesh of corpses, with these ceremonies influencing later "exorcisms" (driving out of demons) (Figures 2 and 3). For centuries, it was also believed that these two illnesses were linked with witchcraft [6,7]

Figure 2: Shoving: A child is pulled through a hole in a tree, photo from 1922 (8)

Figure 3: Bloodletting in Värmland, Sweden, 1918 - used as a cure for epilepsy. Drinking human or animal blood was also frequently used as a treatment method [8].

As Western society progressed, attitudes towards mental illness improved. Philippe Pinel, during the French Revolution, advocated for humane treatment, freeing patients from chains and manacles [6]. Scientific interest replaced religious beliefs, leading to a better understanding of mental health. Over time, a consensus has emerged regarding the relationship between epilepsy and associated psychosis.

2. Prevalence of Psychosis in Epilepsy

It is generally accepted that individuals with epilepsy are at a higher risk of psychosis compared to the general population, with prevalence rates varying depending on the population studied and definitions used. Gaitatziz et al. narrated that six percent of people with epilepsy in the general population appear to suffer from a psychiatric disorder, while this rises to 10–20% in populations with temporal lobe epilepsy (TLE) [9]. TLE, characterized by seizures originating in the temporal lobes, is closely associated with psychiatric comorbidities, including psychosis. Gaitatziz et al. studied psychiatric morbidities in epilepsy and gave that the ballpark prevalence of psychosis in population-based studies between 2-7%, which is significantly higher than the prevalence in the general population 1.5-3.5% [9,10]. In TLE specifically, the prevalence of psychosis is estimated to be around 7% [11]. Vinti et al. studied the link among the two in paediatric population and reported that the prevalence of psychiatric disorders in patients with TLE is higher (79%) than in generalized epilepsy (47%) particularly in the paediatric population [12].

3. Onset of Psychosis in Relation to Epilepsy

Psychosis in epilepsy can manifest at different stages, classified based on its temporal relation to seizures. Terms like "peri-ictal," "inter-ictal," and "para-ictal" describe phases around, between, and during seizures, respectively. While not everyone with epilepsy experiences psychosis, its occurrence varies among individuals. Peri-ictal psychiatric symptoms are often overlooked despite their significant contribution to disability and distress in epilepsy. Increased awareness and clinical attention to peri-ictal psychosis is crucial for improving outcomes and well-being [13]. This article focuses on the link between epilepsy and psychosis, particularly highlighting the post-ictal phase of peri-ictal psychosis and emphasizing the dangers of untreated or undiagnosed cases.

4. Decoding Peri-ictal Psychoses

It is crucial to emphasise that the classification and understanding of peri-ictal psychoses is complex, and individual experiences can differ. Peri-ictal psychosis is a complex and less well-understood aspect of epilepsy. Recognition of this phenomenon is growing, and researchers are working to understand its underlying mechanisms better and to develop effective treatment approaches.

It has been reported that psychiatric comorbidities, including peri-ictal psychosis, can substantially contribute to the suffering among individuals with epilepsy [14]. Despite this, it still remains least acknowledged by clinicians and often gets missed. This may be due, in part, to the fact that seizures themselves can be dramatic events, and psychiatric symptoms may be overshadowed or attributed solely to the seizure activity.

Pre-ictal psychosis, a type of peri-ictal psychosis, is less recognized and less common [15]. Symptoms vary widely among individuals and typically occur in the hours or days leading up to a seizure. The duration and nature of these symptoms depend on various factors such as seizure type, frequency, and overall health. Predicting seizure onset precisely is challenging due to variability. Optimized seizure management is key in controlling the pre-ictal phase, with psychotropic medications generally not recommended.

Ictal psychosis commonly arises from non-convulsive status epilepticus, primarily originating in the temporal lobe, occasionally in the frontal lobe. Episodes are usually brief (<1-3 minutes), with abrupt onset and resolution [16,17]. Symptoms vary widely, encompassing behavioural, affective, cognitive, and perceptual manifestations often associated with typical temporal lobe automatisms. Treatment typically focuses on managing epilepsy efficiently, with antipsychotic medications generally not recommended as ictal psychosis [15].

5. Post-Ictal Phase and Psychosis

The postictal phase indicates a period of time instantly after a seizure. The presentation is diverse and symptoms differ greatly among individuals. Some patients show evidence of fluctuating consciousness, disorientation, and confusion (postictal confusion) throughout the episode, whereas for others, post-ictal aggression is often a response to a bystander or first responder. In 1881, WR Gowers in his book Epilepsy and Other Chronic Convulsive Diseases states that "*Occasionally, after a fit, or, more frequently, after a series of fits, an attack of mental disturbance may come on which lasts for several days. It may be simply a demented state, or there may be hallucinations, with irritability and even violence*' [18].

The postictal phase following a seizure can last from seconds to days, during which the brain typically recovers [19]. The symptoms of post-ictal psychosis usually manifest several hours to a week after a seizure cluster. Confusion, post-ictal fear, and frustration are relatively common symptoms in the immediate post-ictal phase and can lead to aggressive and violent outbursts in someone with epilepsy. This antagonistic behaviour is not considered as post-ictal psychosis. People are still recuperating in the immediate post-ictal state, and they can be shaken up, incredibly confused, have difficulty verbalising their emotions, and unable to appreciate what is going on. This feeling could be analogous to as if someone has pressed the 'reset' button on their brains. It is crucial to note that this is not post-ictal psychosis, although it can be very easily misidentified as one. Such fear and confusion can effortlessly morph into hostility and aggression if a surrounding witness or first responder makes efforts to prevent the affected individual from wandering or fumbling about, without recognising or understanding how to interact with someone who just has had a seizure [20, 21].

After the immediate postictal state and before the onset of psychiatric symptoms, there's a silent period known as the lucid interval, indicating a return to normal mental state. This period helps to differentiate between postictal confusion and postictal psychosis [22,23]. Though not extensively studied, the lucid interval typically lasts between 1 to 6 days, with some cases as short as 2 hours, as discussed by O Devinsky in 2008 [24-26].

Postictal psychosis is regarded as the most commonly encountered form of peri-ictal psychosis, accounting for nearly 25% of all psychoses of epilepsy [12,15]. It is seldom reported in subjects with a generalized epilepsy type and is generally triggered by a cluster of focal to bilateral tonic–clonic seizures. Patients with a late age of onset of the epilepsy and with temporal-lobe epilepsy with temporal and extratemporal structural lesions appear to be mostly affected by postictal psychosis [15,27].

Postictal psychosis presents with distinct clinical features, including "herald symptoms" that serve as a warning of an impending episode, such as restlessness, irritability, and insomnia [28]. Symptoms often vary and encompass a range of psychotic experiences like hallucinations and thought disorder. Individuals experiencing postictal psychosis may lack insight into their behaviour and may not recall the episode afterward due to the disruption of memory formation during seizures. They may be talking to others and having a plausible conversation, but afterward have no recollection. This is because the seizures can affect the normal functioning of the brain, including areas responsible for memory formation and consolidation. The abnormal electrical activity during a seizure may disrupt the encoding and storage of new memories [19]. Moreover, seizures can also befall during sleep, and could be linked with amnesia (diurnal seizures), which can further complicate diagnosis and understanding of postictal psychosis. This lack of awareness or memory poses a challenge in identification and treatment, often leading to serious consequences.

Healthcare professionals stress the importance of recognizing signs of post-ictal psychosis in individuals with a history of seizure clusters. Specific questioning from both the individual and their caregivers is crucial for gathering information about the symptoms such as changes in behaviour, thoughts, and emotions following seizures. Involving caregivers provides valuable insight as the information aids in understanding the condition severity and tailoring treatment strategies to support individuals with epilepsy linked to post-ictal psychosis.

Post-ictal psychosis is treatable and prompt recognition of the condition is critical in minimizing morbidity. As they say, prevention is better than a cure. In 1988, Logsdail and Toone studied postictal psychosis and set down a diagnostic criterion for recognizing postictal psychosis [29]. The criteria is widely accepted and is as follows:

1. Onset of confusion or psychosis within 1 week of the return of apparently normal mental function
2. Duration of 1 day to 3 months
3. Mental state characterized by:
    a. Clouding of consciousness, disorientation, or delirium
    b. Delusions or hallucinations, in clear consciousness
    c. A mixture of (a) and (b)
4. No evidence of factors, which may have contributed to the abnormal mental state:
    a. Anticonvulsant toxicity
    b. A previous history of interictal psychosis
    c. EEG evidence of status epilepticus
    d. Recent history of head injury or alcohol/drug intoxication

Table: Logsdail and Toone's Criteria for Postictal Psychosis [29].

6. The Perilous Nexus between Epilepsy and Psychosis

The interplay of epilepsy and psychosis creates a landscape of uncertainty where navigating the boundaries of reality becomes precarious. Understanding the nuances of epilepsy and psychosis is crucial for managing associated dangers effectively and providing appropriate support to those affected.

We conducted a qualitative survey capturing the thought process of 35 mental health professionals regarding "epilepsy" and "psychosis". The survey was done in one of the workshops that was held in Mersey Care NHS (National Health Service) Foundation Trust, United Kingdom, and was attended by 35 consultant psychiatrists across the trust. Online survey link was shared during the workshop to assist us in recording their instinctive responses. Attendees were asked to list three words that come to their minds when they hear the terms 'psychosis and epilepsy'. The results of the survey are displayed using word cloud format below (Figure 4). The larger the font, the more popular the word response was. This word cloud is demonstrative, and attendees showed widespread opinions. One of the worrying things that can be noticed from the display is that although people are aware that postictal psychosis is a complicated presentation and is difficult to manage, what is barely mentioned is the 'risks' associated with epilepsy and psychosis. The 'dangerousness' linked with these two condition is not mentioned at all. This is certainly appalling, and it shows a dire need to educate and remind people of how crucial it is to recognise and manage postictal psychosis instantly to improve prognosis and to reduce the risks. It is important to understand that post-ictal psychosis is a medical emergency, and it must be treated as an emergency. People could display episodes of violence and suicide, and if correctly recognised, we could aid in prevention by intervening early.

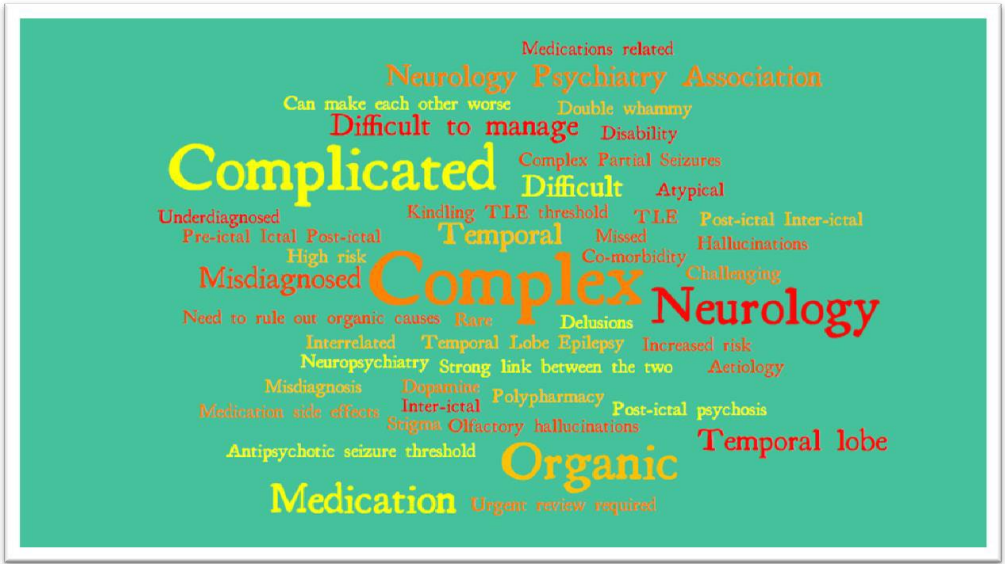

Figure 4: Word Cloud displaying results of survey conducted at Mersey Care NHS Foundation Trust, United Kingdom [30].

Post-ictal psychotic behaviour can manifest severe symptoms like hallucinations, delusional thinking, impaired judgment, and extreme agitation. Compared to interictal psychosis, those experiencing postictal psychosis are more likely to have visual hallucinations, religious and grandiose delusions, pressured speech, and illusions of familiarity, according to Devinsky, 2008 [26]. Reports indicate that sudden religious conversion and violent behaviour is more prevalent during the postictal period [31,32]. Conversely, patients with interictal psychosis typically present with referential and persecutory delusions alongside auditory hallucinations [26,33].

Individuals experiencing post-ictal psychosis are in an extreme vulnerable state. The altered mental state during this period may pose serious risks to the affected individual and those around them secondary to verbal and physical violence, which could have life-threatening consequences. The potential for impulsive actions based on delusional thinking or acting on the distorted perceptions can be significant. Cases are reported where people with post-ictal psychosis have been incarcerated for committing acts of violence, including homicide or attempted homicide in response to the auditory hallucinations or the delusional thinking.

There are reports and media highlights of people committing crimes including murder in post-ictal psychosis state linked with epilepsy. Kanemoto et al (2005) in his study informed that 23% episodes of postictal psychosis were linked with violence and aggression towards others, and 7% involved suicide attempts. On the contrary, only 1% of the cases studied of post-ictal confusion resulted in violence towards others. There was no suicidal behaviour reported (0%) that was associated with post-ictal confusion. The study concluded that *well-directed violent and self-destructive behaviour was not a feature of epileptic psychosis in general but a specific hallmark of postictal psychosis* [34].

In another study by Fukuchi et al, researchers scrutinised the records of 43 deceased patients with well-classified epilepsy providing special attention to suicide cases. It was noted that temporal lobe epilepsy (TLE) was closely associated with the death among the patients suffering from epilepsy [35]. All six suicides that occurred were encountered in patients with TLE: three jumped in front of a moving train while in the midst of an episode of postictal psychosis. Other recognised demises connected to postictal psychosis involve a suicide completed by jumping into the centre of a stairwell from the 12th floor of an epilepsy centre, and another patient stabbing his wife [26]. One of the case studies of homicide during the event of postictal psychosis reported that a man in late twenties took his mother's life in response to postictal paranoia, agitation, and delusions and subsequently called the police, but could not recall the specific conversation. Later in psychological assessment after the homicide, he did not remember his 911 call either [36].

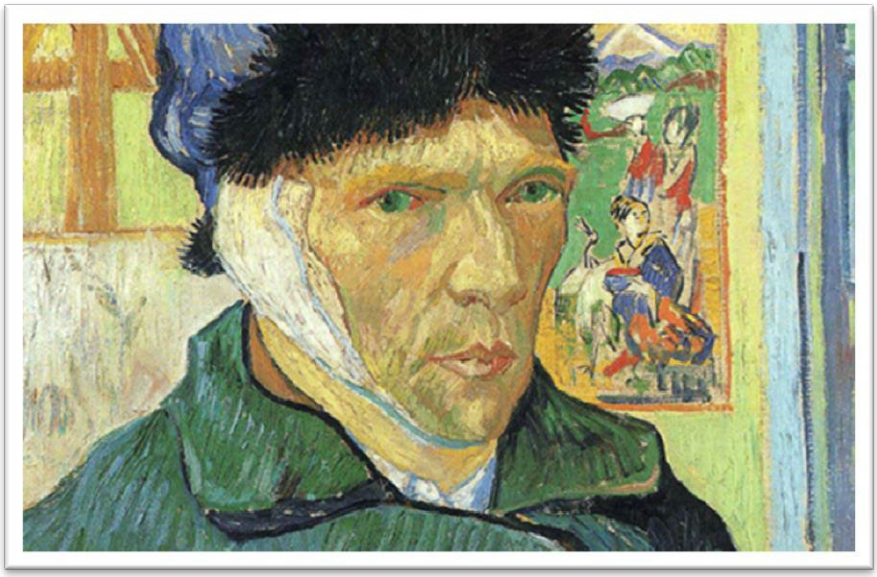

Figure 5: Vincent Van Gogh Self-Portrait with Bandaged Ear, 1889 (37)

Vincent van Gogh, born in 1853 in Zundert, Netherlands, a renowned Dutch artist who has left an indelible mark on the art world as a post-impressionist painter. He was believed to be suffering from enduing mental health challenges. In 1888, whilst he was residing in the sun-drenched region of Provence in the South of France, Vincent van Gogh suffered a catastrophic breakdown concluding in an act of self mutilation. The artist sliced off almost his entire ear with a razor (37, 38).

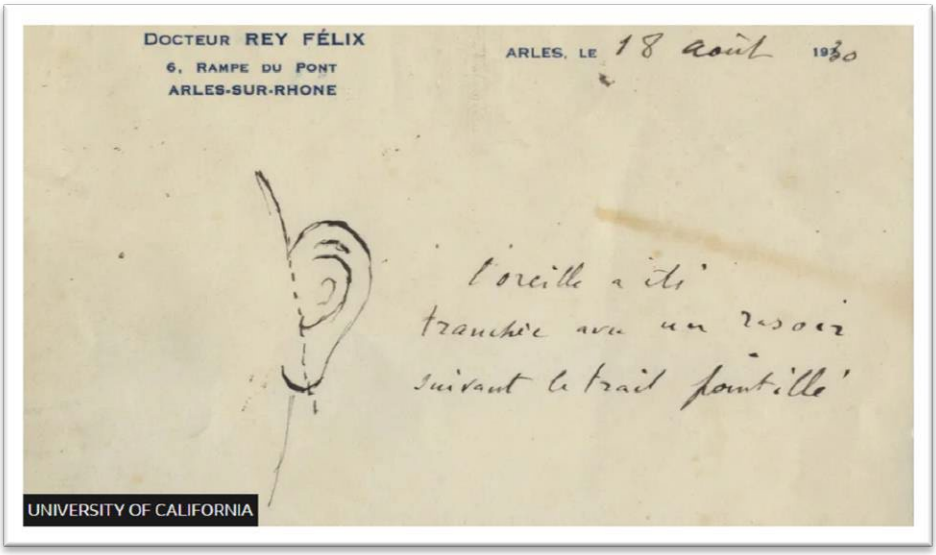

Figure 6: Letter from Dr Felix Rey with drawing of Vincent van Gogh's mutilated ear, 18 August 1930, The Bancroft Library, University of California, Berkeley (38)

Why did he commit a torturous act? What was going on in his mind at the time? What was Vincent suffering from? No one knows for sure what his accurate motive was. The lack of detailed medical records and the limited understanding of mental health in the late 19th century makes it challenging to provide a conclusive evidence or diagnosis, although many theories are made on this subject, some of which are more plausible than others. Despite limited evidence, Blumer reviewed and discussed the highlights of van Gogh's life and letters in view of better understanding of the intricacy of his illness. Vincent van Gogh was believed to have an eccentric personality, unstable moods, and suffered from recurrent psychotic episodes during the last two years of his life. Blumer also shared that in a study of the artist's life and medical history published in 1956, Henri Gastaut identified van Gogh's major illness during the final two years of his life as temporal lobe epilepsy (TLE) precipitated by the use of absinthe [39]. Additionally, it is widely believed that he took his own life in 1890 at the age of 37, although the specific circumstances surrounding his death have been a subject of debate. It is however important to note that historical accounts, especially those from 19th century, may not provide a complete and accurate understanding of individual's mental health, and diagnoses should be approached with caution, recognising the limitations in available information.

7. Treatment Implications for Better Outcomes

Postictal psychosis, while self-limiting in many cases, requires careful observation or supervision from caregivers. Neuroleptic medications or psychotherapy has not shown significant benefit, as most patients tend to revert to their premorbid state within a week irrespective of the intervention utilised [40]. Nevertheless, intervention is essential where mental state is deteriorated, or patient is floridly psychotic. Healthcare professionals, caregivers, and individuals with epilepsy should be aware of associated risks and take appropriate safety measures, including ensuring medication compliance, close monitoring of mental state, removing potential harm sources, and seeking immediate medical attention for severe symptoms.

The complexity of post-ictal psychosis underscores the importance of a multidisciplinary approach to its management. This involves collaborative work between neurologists, psychiatrists, and other professionals to develop comprehensive care plans addressing both seizure disorder and psychiatric symptoms. Medications can be used to manage symptoms, and hospitalization may be necessary in extreme cases to ensure a safe and controlled environment. Increased awareness, ongoing research, and clinical attention to post-ictal psychosis is essential for improving outcomes and overall well-being of the affected individuals.

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