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Review Article

Epilepsy, Mental Health Disorder, or Both?

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Temporal lobe epilepsy (TLE), a subset of the seizure disorder family, represents a complex neuropsychiatric illness, where the neurological presentation may be complemented by varying severity of affective, behavioral, psychotic, or personality abnormalities, which, in turn, may not only lead to misdiagnosis, but also affect the management. This paper outlines a spectrum of mental health presentations, including psychosis, mood, anxiety, panic, and dissociative states, associated with epilepsy that make the correct diagnosis a challenge.

"Dostoyevsky called himself an epileptic... it is highly probable that this so-called epilepsy was only a symptom of his neurosis and must accordingly be classified as hystero-epilepsy—that is, as severe hysteria"
Z. Freud. Dostoyevsky and Parricide, 1928

1. Introduction

Seizures are common in the general population. The incidence of a first, unprovoked seizure in Rochester, Minn, was measured at 61/100,000 person-years [1]. According to the Global Campaign Against Epilepsy (GCAE) [2], epilepsy, defined as recurrent, unpredictable, and typically unprovoked seizure activity, is estimated to affect 50 million people worldwide with the incidence of 40–70/10,000 per year [3], affecting mostly children, since approximately two thirds of the seizures start in the early years of life. By the Epilepsy Foundation statistics, the incidence rises again in the elderly, with the prevalence of 3% by the time a person reaches 75 years of age [4]. This suggests that in patients who are in their 30s to 40s, the onset of the recurrent generalized tonic-clonic seizures may be secondary, arising from a continuation of simple partial seizures, frequently signifying the underlying focal CNS pathology, or general medical condition, such as an altered endocrine or metabolic states.

Decades ago epilepsy was considered a nosological entity within the realm of psychiatric illness, but now the diagnosis and treatment assignment is left up to neurologists by default, necessitating expertise or at least familiarity with similar clinical presentations related to other medical and mental health conditions. Extensive collaboration or shared care with internists and psychiatrists therefore makes clinical sense, but unfortunately not always possible.

The diagnosis of epilepsy is a clinical one, with the electroencephalography (EEG) findings supporting the diagnosis if positive, but not excluding it if negative [5, 6]. Up to 20% of patients with the clinical diagnosis of epilepsy would have a normal EEG, whether as 2% of the general population could have characteristic spike-and-wave EEG abnormalities. Routine EEG, still the first choice in ambulatory setting, is augmented with continuous EEG (cEEG) monitoring and video-EEG telemetry, which is crucial for confirming the diagnosis of a seizure disorder where there are diagnostic uncertainties or where treatment decision is based on such confirmation [7]. The role of these diagnostic modalities varies from supportive to irreplaceable, for example, in differentiating psychogenic nonepileptic seizures (PNESs) when compared

to other available diagnostic procedures [8]. Patients, presenting with features of a psychiatric illness, often require much more complex approach. Mirsattari et al. recently showed [9] that, even in absence of routine EEG abnormalities and normal head computed tomography (CT) scan, the comprehensive assessment including brain magnetic resonance imaging (MRI) and video-EEG telemetry could be of a paramount importance. Telemetry input is difficult to underestimate when deciding to discontinue antiepileptic drugs (AEDs)—in one study the telemetry monitoring resulted in changing the management in 74% of cases [10].

Indeed, clinical presentations could be easily mistaken for the variety of medical and surgical conditions, including head injury, febrile seizures, meningoencephalitis, and tumors. Other conditions that could be commonly misdiagnosed for epilepsy include but are not limited to hypoglycemia, sleep disorders, migraines, transient ischemic attacks (TIAs), paroxysmal movement disorders, and transient global amnesia (TGA), just to name a few [11, 12]. CT of the brain appears of a limited value, but MRI could be of a diagnostic assistance in identifying mesial temporal sclerosis (MTS). MTS is the most common cause of TLE. It is characterized by atrophic hippocampus with histological picture of neuronal loss and gliosis, which manifests with an increased signal on T2/fluid attenuated inversion recovery (FLAIR) MRI sequences and decreased signal on inversion recovery sequences [13, 14]. early single-photon emission tomography (SPECT) studies were found not to be helpful, specifically in diagnosing TLE, at times leading to false lateralization [15], but ictal SPECT and SISCOM (subtraction ictal spect coregistred to MRI) have been found to provide complementary diagnostic information in the presurgical investigation of medically intractable TLE patients in epilepsy monitoring units (EMUs). The recent advances in diffusion tensor imaging (DTI) appear promising in delineating the disease substrate [16]. Magnetoencephalography (MEG) reflecting the state of electrical activity within the neurons offers better accuracy in localizing the focus of epileptogenic activity compared to EEG due to the elimination of artifacts from the surrounding tissues and high temporal resolution. It is used in some centres for presurgical evaluation and was found to be an important diagnostic modality in "inconclusive" cases [17]. Positron emission tomography (PET) [18] scanning has been transformed from a confirmatory tool of assessing aberrations in glucose metabolism to a rather precise instrument of specific ligands tracing/uptake, assisting in localizing and understanding the neurochemical basis of CNS pathology. Finally, with the help of the combination of functional MRI (fMRI) and EEG, it has become possible to construct a specific brain "mapping," invaluable in making surgical decisions in patients with epilepsy. The combination of imaging techniques with EEG, targeted at different physiological levels of brain architecture, appears most promising [19].

Despite all the above mentioned advances in imaging, clinical decision-making and EEG continue to be the cornerstone of the diagnostic approach. When the plausible "organic" cause is apparent, the onset of partial or generalized seizures, while considered secondary to general medical condition, may still suggest epilepsy, or at least make it part of the differential diagnosis. The diagnostic path then could swing to the epilepsy as a "diagnosis of exclusion," but on the other hand, acute onset of panic attack, especially without any overt triggers, could be misleading. Furthermore, if one adds PNES (which could be viewed as part of the conversion disorder) to the clinical presentation of anxiety, the diagnosis of "true" epilepsy may not be even considered. In the busy emergency departments (EDs), this scenario could easily lead to referral to psychiatrists, if the noncontrast head CT and lab results appear within normal limits.

There have been years of debate whether or not mental health problems experienced by patients with TLE are separate comorbidities or integral parts of the same pathophysiological process. If some disorders, particularly affective, could be attributed to global emotional response to chronic and debilitating illness (i.e., apprehension of seizures, stigma, social isolation, etc.), the symptoms of psychosis on the other hand would be more difficult to explain. It does therefore appear that both typical and atypical clinical presentations with, at times, layers of psychiatric symptoms evolving gradually or sporadically over the course of a seizure disorder might have the common pathophysiological mechanisms, that have not precisely been identified yet.

2. Temporal Lobe Epilepsy (TLE)

Seizure-like activity, at some point experienced by many, may not necessarily represent a seizure disorder per se, unless the clinical manifestation continues to unfold further in time with repeated pattern of the neurological manifestation, including abnormal sensation, motor abnormalities, level of consciousness, dysregulation of an autonomic nervous system, affective, behavioral changes, or a combination of all.

Temporal lobe seizures, the single most common adult seizure type [20], are also called "complex partial seizures" or "psychomotor epilepsy," which could be defined as a chronic neurological condition with recurrent seizures as main characteristic feature. In fact, it should probably be viewed as a spectrum of seizure disorders, rather than an isolated nosological unit, with at least two subtypes, namely, mesial temporal lobe epilepsy (MTLE) and lateral temporal lobe epilepsy (LTLE) with the epileptogenic focus on the outer temporal lobe surface. The condition nevertheless often appears "fluid," with both types coexisting and/or generating each other. This type of a synchronized neuronal activity appears somewhat unique because of a presence of aura and so-called "twilight" state of consciousness with poor recollection of preceding events.

Classically, the presentation of TLE would include some form of aura, occurring in up to 80% of patients with epilepsy, manifesting by somatosensory psychiatric autonomic symptoms or their combination. This is followed by ictal, postictal, and then interictal states. Screening for automatisms (or semipurposeful seemingly automated movements), frequently observed in ictal state, should become norm in every clinical patient encounter—this is

commonly missed only because a witness might not necessarily consider it relevant to report. Examples include lip-smacking, chewing or swallowing, picking at buttons, or other repetitive hand movements. Patients would often appear semireactive to their environment, picking up nearby objects such as telephones or pencils but in a trance-like state with likely no recollection of the events. Speech output may also be automatic or semiresponsive, perseverative at times. Usually, a postictal period of either confusion or dysphasia occurs, the duration of which varies from minutes to hours, but rarely days, and sometimes inversely proportional to baseline cognitive abilities. Other features that suggest a diagnosis of temporal lobe originating seizures include short duration (1-2 minutes), early onset, and a history of childhood febrile convulsions [21]. Sleep-onset panic attacks [22] and the lack of response to typical panic disorder treatments should also raise questions.

It is believed that up to 30% of patients with epilepsy have some form of a psychiatric condition [23]. Psychiatric manifestations of epileptic seizures have been known for years, both for idiopathic cases and those describing patients with seizures with mental health abnormalities following traumatic brain injuries [24]. One recent survey on comorbidities in epilepsy [25] found that neuropsychiatric conditions such as anxiety, depression, bipolar disorder, ADHD, sleep, and movement disorders were more likely to be self-reported by patients with epilepsy than those without it.

Misdiagnoses, namely, labeling secondary psychiatric syndromes with primary psychiatric diagnoses, usually derive from limited understanding of the diverse manifestations of epileptic seizures and could probably be grouped into

(i) psychosis/schizophrenia,

(ii) unipolar depression or bipolar disorder,

(iii) anxiety and/or panic disorder,

(iv) cognitive decline and behavioral aberrations.

3. Psychosis

Psychosis can be defined as an altered mental state with the presence of either or the combination of hallucinations, delusions, and thought disorganization to the extent of altering one's capacity to function. Pathological substrate in psychosis involves the same limbic structures in TLE with or without involvement of the frontal and parietal lobes, the combination of which results in discrete psychotic phenomena [26]. The inner relationship between psychosis and epilepsy appears rather complex, but, from the practical standpoint, it may be important to distinguish these symptoms to a particular TLE phase, that is, during aura, ictal (during the event), postictal (after the event), interictal (in-between seizures), and iatrogenic, representing anticonvulsants sideeffects [27].

The prevalence of psychoses in patients with epilepsy is about 2 to 7% in the general population but measured at approximately 20–60% of those seen in psychiatric departments [28]. Psychosis, the exact prevalence of which is difficult to estimate, can be related to each seizure event or present in a persistent fashion, fully simulating schizophrenia or schizoaffective disorder if coupled with affective dysregulation. The clinical presentation strongly suggestive of schizophrenia may be so convincing, especially if patients present only with psychotic features [29], that in one study when formally applying criteria for schizophrenia, half of the patients with epilepsy and psychosis could have been easily diagnosed with schizophrenia alone [30]. To make matters worse from the diagnostic standpoint, there also appears to be a cohort of patients with both epilepsy and schizophrenia concurrently existing [31]. Under the circumstances, it would be prudent to pay specific attention to the onset of the first symptom or sign and the response (if any) to anticonvulsant or antipsychotic medication. Even then it may not provide enough evidence to differentiate reliably.

Indeed, not only these two conditions share seemingly the same neuropsychiatric features, but the order of onset of each of these raises the famous "chicken and egg" question. In an attempt to answer the question which of these two separate entities comes first, Adachi et al. [32] came to the conclusion that because of common features and linear distribution of time intervals, so-called "psychosis-epilepsy" and "epilepsy-psychosis" represent the same condition. If true, it seems plausible that since psychosis is a purely clinical entity, the pathophysiologic mechanism responsible for generating these symptoms may be disease independent, that is, appear secondary to electric or chemical disruptions, whether idiopathic, caused by metabolic abnormalities or the host of other offenders. Not all patients with TLE, however, show these abnormalities. There is some evidence that the age of epilepsy onset (earlier age) predispose patients to develop psychotic symptoms, mostly interictally [33, 34]. Other predisposing factors include the presence of borderline intellectual functioning [35] and a family history of epilepsy or psychosis [36]. As for the psychiatric premorbid factors, high prevalence of mood disorders in first- and second-degree relatives, rather than potentially predisposing personality traits, schizotypal, and paranoid in particular, was reported [37].

Half a century ago in a classic text, Slater et al. [38] stated that there were no definite shifts in personality and affective dysregulation in TLE patients, exhibiting hallucinations and delusions, accounted for 3/4 of the studied population. Interestingly, there was also no uniform psychotic presentation in both patients with TLE and schizophrenics without epilepsy. Same could be attributed to the course of illness, whether relapsing-remitting or progressing. The negative symptoms, however, were thought to appear more predominantly in patients with TLE, which were deemed independent of past affective disorders and resulting in greater neuropsychological deficits [39]. Other authors [40] suggest that TLE psychosis lacks the negative symptoms of schizophrenia with more benign and variable course. From the clinical standpoint therefore, it would be safe to assume that just the presence of mostly negative or positive symptoms is neither specific nor sensitive. Since psychosis is a manifestation of the brain dysfunction (symptom) and not a separate disease category, duration of it offers no significant assistance in deciding the secondary process

versus psychiatric illness—in both cases the duration could be highly variable as well as a severity.

Irrespective of the clinical caveats, psychosis in TLE may have either relapsing-remitting course (concurrent with seizures), chronic (involving interictal phase), or combinatory with various complexity and expressiveness of thought disorder or perceptual abnormalities. Preictal states, as well as ictal phase in TLE, may present as an "umbrella" of altered sensorium, including

(i) illusions (apart from pure illusion phenomenon experiences by many disease-free individuals, distortions of vision aka micro-, macro-, or palinopsia),

(ii) visual (lines, abstract images, geometric shapes, or colors that appear similar to migrainous aura, localizing to the occipital lobe [41]),

(iii) auditory (music, often repetitive; voices, at times distorted of muffled [42]),

(iv) olfactory or gustatory hallucinations,

which may not necessarily lead to loss of consciousness, but may represent either an isolated seizure or a part of it, with or without further progression to motor abnormalities or dissociative states. More complex hallucinations with experiential phenomena can follow [43], comprising dream sequences, flashbacks, and brief or prolonged profound affective symptoms such as sadness, happiness, fear, or anxiety. Patients, usually unresponsive, may demonstrate complex behavior, including seemingly purposeful activity (walking, dressing, chewing, or even repeating phrases). Patients may retain partial responsiveness [44], another strong potential for misdiagnosis. Finally, Kraft et al. [45] described complex ictal psychotic phenomena such as forced thinking, thought withdrawal and insertion.

The specifics of symptoms and their timing seem dependent on the spread of the seizure focus in each individual, but it is worth noting that the particular features of complex partial seizures must be absent before an ictal cause for psychosis is ruled out. The wide variability in presentation and relative low frequency make systematic evaluation of these phenomena problematic, but identification of seizure activity leading to anticonvulsant treatment tends to result in psychiatric improvements [45] although, to the best of our knowledge, there are no randomized, controlled studies outlining this issue. Because of the frequently observed motor abnormalities, ictal psychosis may not necessarily present a diagnostic dilemma.

Postictal psychosis is also common, accounting for 25% of epileptic psychoses [46], and would usually follow the prolonged seizure activity with generalized tonic-clonic seizures in particular. Because this seizure type is easily recognized by physicians and lay-people alike, there is usually no difficulty in identifying the cause. The uncertainty arises when these events do not seem related, even though rarely there is a lucid interval of one to six days prior to the onset of psychosis. Kanner et al. [47] reported 10% of patients with history of depression as predictive factor, experiencing postictal psychosis with the median duration of 18 hours, which corresponds to the findings of others. As to the specifics of the presentation, it varies from grandiose and religious delusions with elevated moods [48] to mixed manic-depressive like psychosis or bizarre behavior [49]. From the practical perspective, confusion in emergency rooms in respect to the differential diagnosis stems from convulsions not being witnessed, or with appearance of the mental health problems in patients following a nonconvulsive seizure. Thus, in an attempt to delineate the differential path, applying DSM IV criteria per se might not be sufficient—one needs to take into account the past medical and mental health history, pace of the development of psychotic symptoms, fluctuations on the level of consciousness, and, finally, the responsiveness or lack of thereof to antipsychotic medications.

Interictal psychoses seem most troublesome to differentiate from a pure psychiatric illness. Many authors would again argue that the distinction between the neurologic and psychiatric boundaries in these individuals is arbitrary or artificial [45], since the judgment is based solely on clinical observation. Schizophrenia-like psychosis in epilepsy is not that common but well documented [38]. These individuals present quite similarly to paranoid schizophrenia with perceptional abnormalities, with a mean latency of about 14.1 years after onset of epilepsy although with a wide range. Clinically, factors that distinguish these patients from having pure schizophrenic illness were reported to include a typically better premorbid function, a preservation of affect, religious, moral, or ethical interests [50, 51], absence of negative symptoms, formal thought disorder, and catatonia [29, 52]. A study of 282 epilepsy patients with psychosis compared to 658 epileptic controls concluded that earlier age at onset of epilepsy (mean 12.8 versus 14.6 yrs), a family history of psychosis (5.5% versus 0.3% in controls), complex partial seizures or generalized tonic-clonic seizures, and borderline intellectual functioning were predictors for developing interictal psychosis [53]. The clinical utility of the data is debatable as the absolute differences between groups appear small. Case reports of patients with this overlap of symptoms highlight the difficulties in both diagnosis and management, even though anticonvulsants tend to improve clinical outcomes [54, 55]. The global outcome in epileptic schizophrenic patients tends to be worse, perhaps reflecting organicity in their illness [31].

Another caveat deserving consideration is so-called "forced normalization" or "alternative psychosis" phenomenon, associated with normalized EEG secondary to anticonvulsants (phenytoin, carbamazepine, ethosuximide) but with exacerbation of psychotic symptoms [56], manifesting mainly in paranoid delusions or other symptoms, including depression, mania, anxiety, and lasting for days or weeks. Lastly, in patients with medically intractable TLE, surgical approach may precipitate the onset of the psychotic features [57]. This process could be qualitatively different from the previously seen signs of psychosis (if any), and, in other cases, psychiatric condition would just remain unchanged with postoperative seizure improvement [58].

Summarizing, symptoms and signs of psychosis may appear at any phase of the epileptic disorder and require meticulous history taking and trials of medication to speculate on exact diagnostic modality.

4. Psychogenic Nonepileptic Seizures (PNESs)

PNESs represent the whole cluster of a seizure-like disorder, either occurring separately and independently from epilepsy or complementing it. It could be defined as manifestation of similar if not identical signs of seizures in absence of paroxysmal neuronal discharge. Symptoms that are consciously produced for conscious reasons (i.e., malingering), those consciously produced for unconscious reasons (forms of factitious disorder), and physiologic seizure-like activity secondary to medical conditions belong to separate categories. Unconsciously produced symptoms for unconscious reasons, as in conversion disorder, which include a great variety of neurological presentations, appear more appropriate description of this pathological state. Ironically, even though this phenomenon probably represents one of those cornerstone diagnostic modalities that act as s pivotal point in swinging patient care between specialties, neither neurologists nor psychiatrists have any reliable tools for diagnosis and management.

Emergency department physicians are facing these challenges on a regular basis, especially when psychogenic seizures (frequently labeled as "pseudoseizures") are the only visible clinical manifestation. Frequently, giving the benefit of the doubt and acting out of the worst possible scenario for the sake of safety, these presentations could be diagnosed and treated as epilepsy if no apparent physiological explanation exists. Unfortunately, years could pass before the diagnosis is made—according to one study [59], the time between the onset of symptoms and diagnosis could exceed several years—the laboratory, electrophysiological, and imaging studies searching for the cause usually take extensive amount of time and resources.

In an attempt to clinically differentiate psychogenic from nonpsychogenic seizure activity, one needs to bear in mind that classic grand mal tonic-clonic presentation with tongue biting, urinary incontinence, and complete unresponsiveness during the ictal phase is rare in PNES. Clonic muscle jerks in PNES are often symmetrical with the eyes closed, falls rarely involve serious body injuries, benign automatisms are rare, and postictal confusion, if present, does not reach the level commonly seen postictally in patients with TLE. Length of psychogenic seizures frequently exceeds 5 minutes [60]; these patients would more likely have a history of chronic pain or fibromyalgia [61], depression and dissociative states [62]. Other factors include history of childhood sexual, emotional or physical abuse [63], history of unipolar depression or anxiety disorders [64], along with somatoform and conversion disorders [65].

One could easily see psychogenic seizures as part of conversion disorder, which includes a whole array of neurological presentations involving motor, sensory, and coordination abnormalities, difficult to diagnose in emergency settings and even more difficult to treat. Stigma of having a mental health condition, shame, and denial may make the therapeutic alliance with these patients problematic [60], and with an absence of evidence-based therapeutic approach showing significant benefit [66, 67], patients may fall in-between family physicians, psychiatrists, and neurologist with minimal, if any, relief. In terms of management, a recent review [68] suggests different types of cognitive behavioral therapy (CBT) as a preferred treatment modality. This was echoed by a pilot study by Goldstein et al. suggesting CBT as more effective in reducing the frequency of seizures than standard medical care alone [69].

5. Dissociative Symptoms

Strictly speaking, by the DSM IV criteria, dissociative disorders embrace several subtypes: depersonalization disorder, dissociative amnesia, dissociative fugue, dissociative identity disorder, and "not otherwise specified" or NOS disorder. DSM V working group (http://www.dsm5.org/) suggests to include derealization disorder in the first category and add substance-induced dissociative disorder as a clearly defined subgroup. Dissociative symptoms, if not viewed in the context of epilepsy, are usually associated with the mind compartmentalizing unpleasant or severely traumatic memories from consciousness, thus associated with posttraumatic stress disorders (PTSD), acute stress or conversion disorder. In simple terms, all dissociative states to some extent embrace the disconnection of self from the surroundings as a protection mechanism.

This phenomena may occur as an aura, during preictal or immediate postictal states, with or without affective component or anxiety. In patients with TLE, there is some evidence [54], echoed by others [70], that the presence of dissociative states, defined by the Dissociative Experience Scale (DES), is predictive of psychogenic or pseudoepileptic rather than epileptic seizure occurrence. Other authors [71] suggest the sole presence of dissociative symptoms indicative as responsible for nonepileptic seizures, but under condition of a presence of memory impairment, psychological traumas/PTSD, personality, or affective disorder. The literature reflecting psychiatric overtones in TLE outlines dissociative symptoms primarily in context of psychogenic seizures, with evidence that the presence of dissociative states may have a negative impact on psychogenic seizure outcome [72].

6. Anxiety and Panic

Anxiety in humans is a natural response required for adaptation and as such is not pathological by itself. However, when the sense of worry or apprehension becomes excessive (compared to what would be experienced by most under the circumstances) or uncontrollable, it starts to affect the quality of life and from that point requires professional attention. In fact, in combination with unipolar depression, it is anxiety with or without panic that frequently motivate patients to seek help not the mood. There is a clear distinction between a fear and anxiety with the latter reflecting rather apprehensive response to unknown, internal, or conflictual situation. Pathophysiology of anxiety includes dysregulation of inhibitory neurotransmitters (GABA specifically) [73], as well as dopamine, epinephrine, and serotonin, coupled with impaired secretion of corticotropin-releasing hormone and cortisol. Literature suggests that severely affected patients,

with refractory epilepsy, high seizure frequency, would more likely to have multiple comorbidities, including anxiety [74]. At least half of patients with chronic epilepsy would have either affective or anxiety disorder [75] with TLE patients affected more often.

DSM-IV-TR criteria for anxiety disorders appear somewhat soft, perhaps reflecting the clinical reality of the anxiety disorders crossing over with each other, with common features of pathological apprehension in all of them. Generalized anxiety disorder (GAD), panic disorder (PD), obsessive-compulsive disorder (OCD), and different phobias are part of the anxiety spectrum. A classic presentation of simple partial seizures of the mesial temporal lobe easily meets DSM-IV criteria [76] for panic attack: abrupt discrete episode of intense fear or discomfort, reaching maximum intensity within minutes and associated with autonomic arousal, somatic, and mental state symptoms. Muscle tension, "stomach butterflies," hypervigilance, fear of losing control, feelings of getting "crazy," and so forth and as well as psychotic symptoms could be experienced in any phase of epileptic disorder. The seizure typically begins with an aura, commonly accompanied by a visceral sensation (epigastric rising sensation, uneasiness in a chest, stopped or racing heart) and by an overwhelming sense of fear, which in fact, does appear most frequently ictally [77]. Other common auras include derealization, such as *déja vu* (sense that current events had already happened in the past with an ability to predict immediate future); *jamais vu* (sense of unfamiliarity despite familiar surroundings), and, less commonly, depersonalization (sensation of being positioned outside of the body). Palpitations, cold sweats, tremulousness, lightheadedness, and nausea may follow. Fear of having a panic attack, called "reactive," may not be readily distinguishable from other egodystonic feeling of generalized elevated apprehension, not associated with panic attacks. In addition, extreme isolated fear of having a seizure adds to the clinical complexity because, if severe, may qualify for a separate clinical category. Phobias in TLE could be subdivided in two major categories: fear of seizures or consequences of such (possibly resulting in agoraphobia) and unrelated phobias [78].

To qualify for DSM-IV criteria of a panic disorder, attacks must be recurrent, unexpected, and followed by 1-month duration of either persistent concerns, worries about the implications, or a change in behavior, all of which are un-derstandable and predictable responses in this setting. If the diagnosis of epilepsy is not considered at all, likely in the setting of scarce history of seizures, the exclusion for "caused by a general medical condition" may not be applicable, resulting in psychiatric rather than antiepileptic management. Often, however, the same medication could be used for both patients cohorts, but for the different reasons (e.g., mood stabilizers) and secondary improvement of psychiatric symptoms may drive the diagnosis further from neurological. To differentiate panic disorder from epilepsy, one must attempt to elicit a detailed seizure history. It does appear of a paramount importance because the key differentiating clinical features may not necessarily be volunteered neither by patients nor by witnesses. Another reason for poor history is a simple lack of awareness due to the retrograde or anterograde amnesia. If awareness was retained, the patient may give some or all of the history, thus classifying an event as a simple partial temporal lobe seizure. It is, however, more common for awareness or memory function to be disrupted, diagnosed then, if witnessed, as a complex partial seizure.

7. Mood

Affective disorders in TLE are important comorbidities primarily because of suicide potential in all forms of it, including gesture, ideation, or successful attempt, which accounts from 10% to 15% in patients versus 1–1.5% in general population [79, 80]. According to Harden and Goldstein [81], the prevalence of depression appears 5 times more frequently in patients with controlled seizures and 10 times in those with uncontrolled. It is not known whether the depression in these patients could be viewed primarily as part of the primary CNS pathology or as an understandable response to the epileptic disorder with all the hardship of every day coping. Even though some skepticism exists as to the "functional" nature of the affective disorder, there is evidence [82] that controlling the frequency of seizures dramatically improves quality of life, possibly via secondary alleviation of a depressed mood. On the contrary, apparently manic episodes are seen much less often [83].

Affective disorders in patients with TLE have the prevalence of up to 80% based on data gained from a structured interviews along with self-ranking scales [84]. The cause of it is more likely multifactorial, from purely psychological factors [85] to biological [86]. Latter is believed to include hypometabolism in extratemporal regions, hippocampal dysfunction or atrophy, and 5-HT1A-receptor-binding abnormality among other factors [87–90]. Pharmaceutical management, specifically anticonvulsants, may alter affective states as well [91], but it is not known whether or not they may potentiate the depression or just act as cofactors. Based the population-based study [92], there is some evidence that depressive symptoms preceding the onset of epilepsy may be seen up to seven times more frequently among the patients versus the control group, which on one hand suggests involvement of the same anatomical structures in both processes (at least on the functional level), and on another, makes the possibility of interdependency of severity plausible. As Kanner pointed out [93], the presence of a psychiatric illness, depression in particular, may be associated with additional difficulties in seizure control, thus making this form of TLE more treatment-resistant.

Clinical presentation of a mood disorder can appear at any time (preictal, ictal, postictal, interictal), taking many forms from simple irritability and anger to flat affect, guilt, anhedonia, chronic suicidal ideation, and suicide attempts. Interictal dysphoric disorder, known as baseline mood flattening in epilepsy, encompasses many features characteristic for DSM IV criteria for depression, but paradoxically with an addendum of euphoria. kula et al. found [94] that the established interictal dysphoric disorder in 54.8% of cases showed a "clear-cut" relationship with epileptic seizures. The importance of this mild (in comparison with major

depressive disorder) condition lies in its prevalence and, correspondingly, extended drain on quality of life.

8. Cognitive or Behavioral Decline

Not surprisingly, patients with severe intractable epilepsy have worse clinical outcome, with cognitive decline as part of it. A retrospective analysis of 136 patients apart from cognitive deficit itself showed a direct dependency between the frequently of tonic-clonic seizures and level of cognitive impairment [95].

Typical absence seizures, or petit mals, usually first seen in school-age children, while representing a generalized disorder, rarely lead to any convulsions. They are characterized by sudden impairment in awareness, often with a motionless blank stare and cessation of ongoing activities. Duration is typically seconds with a rapid return to baseline and, importantly, there without aura or postictal state [96]. Specifically because of that, observers would not necessarily suspect any seizure activity in these patients—the signs of momentary disorientation, confusion, "not listening," and any form of the compensatory behavior could be easily attributed to one of the mental health conditions.

Absence status epilepticus is another form of paroxysmal abnormality with continuous or nearly continuous absence seizure activity, but with a slightly different presentation, characterized by variable slowness in behavior and mentation, either fluctuating or constant. Despite seemingly complex and unusual presentation, only the US, its incidence was estimated at 65,000–150,000 cases per year [97]. Clinical presentation varies from mild forms to stupor or coma and can easily be mistaken for catatonia. Patients seem apathetic and lethargic as they can still eat, drink, dress themselves, and follow simple commands [98]. Quite often there are some physical clues such as oromotor or manual automatisms that may be present—examples include semipurposeful repeated chewing motions, picking at buttons, or rubbing the nose. During these episodes, intermittent and subtle myoclonic jerks of the eyelids can be seen, quite commonly in children, with the cheek and jaw being additionally involved in adults. Myoclonic jerks as a response to various stimuli (such as sudden noises or lights) are less common. Absence status can last from half an hour to days and rarely leads to generalized tonic-clonic seizures. Unlike convulsive seizures, the act of continued absence status is not thought to cause direct permanent sequelae.

Diagnostic difficulties in this realm are experienced not only by neurologists or psychiatrists, but by physicians of different specialties; it may be seen in a variety of medical conditions, for example, as a complication of general anesthesia [99], reaction to antibiotics [100], or being associated with MELAS, where apart from paroxysmal activities, confusion, paranoid delusions, and behavioral shifts can be observed [101]. Psychiatric manifestations, apart from behavioral, cognitive aberrations, and psychosis, may include memory deficits [102]. In mentally delayed, typical or atypical absence seizures are common, but their recognition can easily be overlooked. An unexplained and significant cognitive or behavioral decline in this population demands further investigations, EEG, or telemetry in particular.

Patients with apparent dementia or other various forms of cognitive decline may turn out having electrical paroxysms. In one study, three patients with gradual memory deterioration over years were referred to a dementia clinic with a tentative diagnosis of Alzheimer's disease (AD). Their workup included an EEG, which identified epileptiform activity in two and waveform abnormalities in the third patient. Neuropsychological scales revealed a reversal of their initial decline above their baseline scores once treatment with anticonvulsants was initiated. However, they did not reach scores for their age equivalents [103].

Neurodegenerative diseases are the recognized epilepsy risks, accounting for 20% of known etiology [1]. The varied EEG abnormalities seen in these clinical conditions cloud clinical interpretation unless clear epileptiform activity is noted. Although anticonvulsants may cause cognitive impairment as a sideeffect (as in most recent report on topiramate) [104], treatment anecdotally improved cognitive status. There may not be a clear-cut algorithm to follow, but clinicians must be aware of epilepsy presenting as AD, or of epilepsy complicating AD, and that in both scenarios anticonvulsants may have an impact on the quality of life.

9. Personality and Life Style

Apart from the presence of the disease, the duration of illness could have further impact on patients' life. Hermann et al. [105] reported that in comparison with the healthy controls, patients with long standing TLE experience chronic emotional and behavioral distress, resulting in significantly poorer quality of life.

To reiterate, apart from biological substrate responsible for personality traits yet to be identified, people with TLE frequently has an altered life style, adjusted for best performance under the circumstances. The latter include psychological burden of social stigma, having seizures, ongoing expectations of such, interictal declines in functioning, and a necessity to take medication for seizure control, often, for life. This starts in the childhood but does affect different age group differently. In one study [106] of 118 children with epilepsy, deterioration in energy levels, attention, and language were less pronounced in older children, who on the other hand were found more affected by decreased self-esteem and anxiety. Families with these children are understandably stressed with the peak emotional response at the onset of the disease [107], with ongoing struggle made worse by unpredictable nature of illness and, with time, behavioral abnormalities [108]. Academically, children with epilepsy appear to do worse, which could also be psychologically detrimental [109]. It was found that higher parent education acts as a self-esteem protective factor in children with processing speed decline [110]; however, little is known about any interventions that may assist early in life to help these young patients function overall better in both social and environmental dominions. Recent study by Rodenburg et al. [111] clearly shows the necessity of early

screening for the psychological problems, paying specific attention to the family issues, social functioning in the transition into adolescent years, and unmet needs.

Adolescents, particularly with childhood onset of epilepsy, continue to be at higher risk of comorbid psychiatric conditions, including affective disorders with increased suicide risks [112]. As time goes by and adolescents turn into young adults, they frequently discover self ineligible for certain jobs, for example, those associated with operating a heavy machinery, public transportation, and so forth. In addition, many, depending on the severity of illness, found themselves crippled by inability to drive, which makes them more dependent than the same age others. The impact of epilepsy on social functioning was found profound and greater than, for example, migraine [113], even though both are chronic neurological conditions and both observe elements of episodic but complete disability.

Many patients with TLE remain unemployed, facing social or personal isolation [114, 115]. Having said that not all carrying the diagnosis of epilepsy are equally affected, severity of a disease, including the presence of comorbidities and/or psychiatric symptoms and signs [116], predictably affects the prognosis. Recently, authors from Spain [117], based on cross-sectional multicenter epidemiological study, revealed 58% employment and 10.9% unemployment rate, with occupational incapacity (12.5%) higher in patients with partial seizures, twofold affecting those with refractory epilepsy. Indeed, the number of medications to keep seizures under control and quantity of seizures add to unemployment risk [115].

Personality in general terms could be defined as a combination of emotional, attitudinal, and behavioral pattern of responses to the environment, not necessarily immediately obvious to an individual. Personality traits, seen in patients with epilepsy (if one assume they do exist) may affect social and occupational interactions further [118]. Manchanda [119], citing current consensus rejecting the term, gave a brief description of "epileptic personality," which does not seem to follow any particular pattern, but at the same time suggesting that the serious social maladjustment could be precipitated or potentiated by such. Interictal behavioral traits were described decades ago [120] and included circumstantiality, dramatization, excessive mental "chewing" (viscosity, hyperreligiosity), and altered sexual behavior. Controversial views, however, persist up to this point [121, 122].

Swinkels et al. [123] showed higher dimensional scores for the epilepsy patients in cluster C personality traits (dependent and avoidant in particular) along with development of maladaptive personality traits, dependent on the duration of the disease. Again, this could be attributed to consequences of having chronic medical condition, but patients with, for example, asthma, did not observe the same tendencies [124]. In TLE patients with left or bilateral seizure foci, a clinically notable elevation of the "viscosity" or, in other words, tendency to be over inclusive, circumstantial, repetitive, and clingy was observed [125]. Other authors [126] suggest that the structure of seizures matters; experience of auras were attributed to the development to both cluster B and C personality traits; avoidant traits were reported in patients with PNES [127]. Attempting to further delineate various discrepancies in opinions, Locke et al. [128] undertook a study of 79 patients subjecting them to the battery of neurophysiological testing, concluding that there is no evidence to suggest any specific personality changes despite the burden of chronic and unpredictable illness, naturally affecting both mood and behavior.

10. Treatment

Management of epilepsy is generally effective, by either medical or surgical means, with the rate of success related to the type and cause of seizure. Since treatable, recognition of an underlying seizure disorder obviously has significant implications. Occasionally, initial misdiagnosis possesses only mild repercussions, as in the case with benign occipital lobe epilepsies being mistaken for migrainous auras [41, 129–131]; however, completely omitting a possible diagnosis of epilepsy in differential may have devastating effects on the lives of afflicted individuals, as the alternate diagnosis is often schizophrenia [38, 45, 51, 132–135], affective disorders [21, 136–139], or (recently becoming more apparent) Alzheimer's disease [103]. Apart from that, there is data that SSRIs or antipsychotic medications may increase seizure risk by affecting the metabolic rate of neurotransmitters [140].

As to the pharmaceutical management of the associated with TLE psychosis, it usually depends on its severity. For example, postictal brief psychosis may not require any intervention, unless delusional believes or perceptual abnormalities threaten to alter the behavior. In interictal psychosis, if not affected by anticonvulsants, atypical antipsychotics may be given, preferably not those changing seizure threshold. Affective disorders are suggested to address starting with SSRI and/or CBT with electroconvulsive treatments (ECT) as last resort [141].

11. Summary

A great variety of epileptic presentations can meet DSM-IV criteria for schizophrenia, brief psychotic disorder, panic attack, generalized anxiety, major depressive disorder, dissociative disorders, dementia, and other conditions under the umbrella of "mental health disorders." According to set criteria, the symptoms cannot be caused by a general medical condition, but the mimicry of epilepsy syndromes can be so convincing, that seizure may not be even considered.

The increasing frequency of case reports suggests that the number of misdiagnoses are not necessarily declining and there are many yet to be discovered. Additionally, epilepsy and psychiatric disorders are not mutually exclusive diagnoses and could easily coexist. Overlooking either diagnosis in a patient afflicted with both may lead to treatment failures.

The outpatient EEG is not a sensitive test since seizure activity is typically episodic, subtle abnormalities can be easily missed, and imaging is commonly unremarkable. Clinicians must rely on their knowledge of varied presentations to consider epilepsy and whether investigations and consultation with the professionals in other subspecialties

are warranted. In difficult cases, referral to an epilepsy monitoring unit for cEEG and video recordings are essential to increase the sensitivity and specificity of the diagnosis. DSM V, to be released in the near future, should identify typical seizure characteristics as exclusion criteria.

Finally, greater collaborations between the disciplines of neurology and psychiatry are required to improve the care for patients that share some characteristic features of the both illnesses but they do not exclusively fall in one or the other camp.

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