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Review

The classification of neuropsychiatric disorders in epilepsy: A proposal by the ILAE Commission on Psychobiology of Epilepsy

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Abstract

The classification of psychiatric disorders in epilepsy has evolved considerably from the first attempts in the 19th century. A dedicated subcommission of the ILAE Commission on Psychobiology of Epilepsy (now the Commission on Neuropsychiatric Aspects) has developed this classification proposal. The aim of this proposal is to separate disorders comorbid with epilepsy and those that reflect ongoing epileptiform activity from epilepsy-specific disorders, and to attempt to subclassify the epilepsy-specific disorders alone. Further, the classification of epilepsy-specific psychiatric disorders has largely followed their relationship to the ictus, with factors such as relationship to antiepileptic drug (AED) change being coded as additional information. Finally, this proposal presents a clinical and descriptive system of classification rather than an etiological classification on the grounds that there is currently inadequate information for the latter approach to be employed globally.

Keywords: Epilepsy; Classification; Psychoses; Depression; Anxiety; Personality

1. Introduction

The European psychiatrists of the 19th and early 20th centuries were the first to look at the classification of psychiatric disorders in epilepsy [see 1 for review]. Samt [2,3], proceeding from a bewildering classification given earlier by Falret [4], clearly defined ictal and interictal differences. Essentially, since that time, classifications have been concerned with this major division.

Psychotic states have been the main focus of study, and little attention has been paid to the classification of other psychiatric problems, including the elusive but important concept of personality change. Further, it is only since the 1950s that classification has been influenced by the use of the electroencephalogram, which not only markedly changed our view of epilepsy, but also, within the field of epilepsy per se, dramatically influenced classification [5,6].

The problem of classification is compounded by the fact that the International League Against Epilepsy [7] and World Health Organization [8] classifications of seizures and epilepsy do not take psychopathology into account.

To develop a useful but nonetheless realistic classification of the psychopathology of epilepsy, it is important to embrace not only the spectrum of psychiatric diagnoses as given by current psychiatric terminology, as in ICD-10 [9] and DSM-IV [10], but also those diagnoses related to the classification of seizures and epilepsy. This should be combined with considerable clinical experience in understanding these associations.

While there are different ways of classifying mental states, the clinical approach of observing patients over a prolonged period is by far the most important.

Although there is good clinical evidence suggesting that the psychiatric disorders of epilepsy are clinically distinct, they do not find a place in the current classification systems

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in psychiatry, such as ICD-10 and DSM-IV. In addition, operational rules that exist ensure that they are subsumed within categories (e.g., organic mental disorder), in a way that may be neither appropriate nor accurate.

As these disorders are phenomenologically distinct, and may respond to specific therapeutic measures e.g. [11], this is clearly unsatisfactory. The present effort has evolved through the 'International League Against Epilepsy' Commission on Psychobiology of Epilepsy. A sub-commission on classification of Neuropsychiatric disorders was established with the three authors as core members. The discussion involved not only the members of the ILAE commission, but also experts in Neuropsychiatry of Epilepsy who attended presentations of the draft versions of this classification and those who were invited to comment on these proposals. The proposal of the commission being presented here has evolved through this process of expert consensus directed at developing a more comprehensive and acceptable system of classification for psychiatric disorders in epilepsy.

2. The problem of comorbidity

Patients with epilepsy, similar to patients with other chronic medical illnesses, have an increased incidence of common mental disorders [12]. These comorbid disorders do not usually have specific distinguishing features that separate them from those seen in other medical illnesses or those seen in the community. Included here are anxiety and phobic disorders, minor and major depression, and obsessive–compulsive disorder. In addition, patients with epilepsy also have comorbid major psychiatric disorders such as bipolar-affective disorder and undifferentiated forms of schizophrenia. Comorbid mental disorders, therefore, should be classified using conventional criteria.

Suggestion: Ignore the presence of epilepsy in making the diagnosis to prevent the imposition of the "organic" category on these conventional psychiatric classifications.

3. Psychopathology as a presenting feature of epileptic seizures

Psychiatric symptoms are often a feature of the seizure itself. Auras of simple partial seizures include psychiatric symptoms like anxiety and panic, hallucinations in various modalities, and even transient abnormal beliefs. Abnormal (sometimes bizarre) behavior can also characterize partial seizures arising from the frontal and temporal lobes that often do not generalize. Subclinical seizure activity (often nonconvulsive status) can also present with catatonic features and other neuropsychiatric manifestations like apathy and aggression [see 13 for review].

Well-defined ictal states are included here:

- Complex partial seizure status: presents with impaired awareness
- Simple partial seizure status (aura continua): presents with intact awareness
- Absence status (spike–wave stupor): presents with a stuporous state and, at times, with minor myoclonic manifestations

Specify: Relationship to EEG as described later in this article.

4. Interictal psychiatric disorders that are specific to epilepsy

There are disorders that are seen specifically in patients with epilepsy. These have distinct clinical descriptions and may respond to specific forms of treatment. These disorders can be broadly divided into the following categories.

4.1. Cognitive dysfunction

Patients with epilepsy refractory to treatment suffer from cognitive dysfunction due either to the epilepsy itself, to the complications of epilepsy, or to antiepileptic drugs. Impairments include difficulties with memory, language, executive functions, visuospatial ability, and sensorimotor and perceptual functions. These impairments may be general or specific [14].

Some specific neurocognitive deficits, such as the Landau–Kleffner syndrome, can be associated with specific EEG changes such as electrical status epilepticus of slow wave sleep (ESES) and continuous spike and wave in slow wave sleep (CSWS), to be included here [15].

4.2. Psychoses of epilepsy

4.2.1. Interictal psychosis of epilepsy

This paranoid psychosis is characterized by strong affective components but not affective flattening usually. Features may include command hallucinations, third-person auditory hallucinations, and other first-rank symptoms. There is a preoccupation with religious themes. Personality and affect tend to be well preserved unlike in other forms of schizophrenic psychosis. Psychotic features are usually independent of seizures, although they may manifest as seizure freedom lessens [13].

Include schizophrenia-like psychosis of epilepsy.

Exclude cases fulfilling criteria for undifferentiated or hebephrenic schizophrenia.

4.2.2. Alternative psychosis

The patient alternates between periods of clinically manifest seizures and normal behavior, and other periods of seizure freedom accompanied by a behavioral disturbance. The behavioral disturbance is often accompanied by paradoxical normalization of the EEG (forced normalization) [5,6]. The behavioral disturbance is polymorphic with paranoid and affective features. The diagnosis of alternative psychosis [16] should be made in the absence of the EEG. If EEG confirmation is available, the diagnosis should be qualified further as "with forced normalization of the EEG."

Include forced normalization/paradoxical normalization [17]. Include also cases with relative normalization as defined by Krishnamoorthy and Trimble [18].

Exclude continuing interictal psychosis or postictal psychosis (recent cluster of seizures) and nonconvulsive status with psychiatric manifestations.

4.2.3. Postictal psychosis

Postictal psychosis follows clusters of seizures (rarely single seizures) usually after a 24- to 48-hour period of relative calm (the lucid interval). These episodes can last from a few days to several weeks, but usually subside in 1 or 2 weeks. Confusion and amnesia may be present. The content of thought is paranoid, and visual and auditory hallucinations may be present. Manifestations are often polymorphic, with affective features and a strong religious theme [13].

Include cases with a clear history of a cluster of seizures or an isolated single seizure (in a patient who has been seizure free). The first manifestation of abnormal behavior should occur within a 7-day period from the last seizure [19].

Exclude postictal confusion and nonconvulsive status with psychiatric manifestations.

4.3. Affective-somatoform (dysphoric) disorders of epilepsy

Intermittent affective-somatoform symptoms are frequently present in chronic epilepsy; they manifest in a pleomorphic pattern and include eight symptoms: irritability, depressive moods, anergia, insomnia, atypical pains, anxiety, phobic fears and euphoric moods. **[[AU: Only seven symptoms are listed.]]** These symptoms occur at various intervals and tend to last from hours to 2 or 3 days, although they might, on occasion, last longer. Some of the symptoms may be present continually at a baseline from which intermittent fluctuations occur. The presence of at least three symptoms generally coincides with significant disability [11]. The same affective-somatoform symptoms occur during the prodromal and postictal phases and need to be coded as such if they are of clinical significance.

4.3.1. Interictal dysphoric disorder

Intermittent dysphoric symptoms (at least three of the above) are present, each to a troublesome degree. In women, the disorder is manifest (or accentuated) in the premenstrual phase.

4.3.2. Prodromal dysphoric disorder

Irritability or other dysphoric symptoms may precede a seizure by hours or days and cause significant impairment.

4.3.3. Postictal dysphoric disorder

Symptoms of anergia or headaches, as well as depressed mood, irritability, and anxiety, may develop after a seizure and be prolonged or exceptionally severe.

4.3.4. Alternative affective-somatoform syndromes

Depression, anxiety, depersonalization, derealization, and even nonepileptic seizures have been reported as presenting manifestations of forced normalization [17]. These may be diagnosed in the absence of an EEG, as described previously, and in the face of EEG evidence coded as "with forced normalization of EEG."

Include brief but disabling changes in affect.

Exclude patients fulfilling ICD-10 and DSM-IV criteria for major depression, dysthymia, and cyclothymia.

5. Personality disorders

Patients with chronic epilepsy may show distinct personality changes that tend to be subtle. Three types are recognized:

1. A deepening of emotionality with serious, highly ethical, and spiritual demeanor [20].
2. A tendency to be particularly detailed, orderly, and persistent in speech and action, that is, viscosity [21].
3. A labile affect with suggestibility and immaturity (referred to as eternal adolescence) [22].

These personality changes may be coded as personality disorders only if present to a degree that interferes significantly with social adjustment.

4.1. Hyperethical or hyperreligious group
4.2. Viscous group
4.3. Labile group
4.4. Mixed (two or more of the above)
4.5. Other

Diagnoses should be coded in this category as follows.

- No personality trait accentuation or disorder
- Personality trait accentuation but not disorder
- Personality disorder specific to epilepsy

Exclude patients fulfilling criteria for well-defined DSM-IV or ICD-10 personality disorders.

5.1. Anxiety/phobia

Specific phobias such as fear of seizures [23], agoraphobia, and social phobia may occur as a result of recurrent seizures. This may occur either as part of the interictal dysphoric disorder, in which case that diagnosis is preferred, or alone, in which case they should be coded here. Unlike comorbid psychiatric disorder, the phobias revolve around epilepsy, and the fear of the situation and subsequent avoidance are linked to the fear of having a seizure in that situation and the possible consequences.

6. Other relevant information (to be recorded for all patients if possible)

6.1. Relationship to EEG change

Characteristic changes in EEG could accompany disorders with psychiatric presentations, such as generalized absence status, simple and complex partial seizures, and encephalopathy (organic brain syndrome); or there may be an absence or reduction of EEG abnormalities, compared with previous and subsequent EEGs as in forced normalization. The EEG is thus an important investigative tool, and the findings at the time of psychiatric disturbance need to be coded separately as follows.

- EEG not available/not done
- EEG remains unchanged
- Nonspecific EEG change
- Specific EEG change (please specify)

6.2. Anticonvulsant-induced psychiatric disorders

As drugs used in the treatment of epilepsy may contribute to the development of psychiatric disorders, it is important that this is specified as an additional category. As both anticonvulsant induction [24] and withdrawal [25] are known to precipitate behavioral change, this needs to be specified, as does the specific anticonvulsant probably responsible, if possible. This also has prognostic and therapeutic implications, as often the only course of action available to the treating professional is withdrawal of the offending agent.

- Details of AED therapy not known/not documented
- No change in AED treatment
- AED institution (in a 30-day period prior to psychiatric disorder)
- AED withdrawal (in a 7-day period prior to psychiatric disorder)
- Both AED institution and withdrawal during 30-day period

Note: Specify AEDs.

7. Discussion

In this proposal we have focused on psychiatric disorders specific to epilepsy, rather than comorbid psychiatric disorders in general. We have been persuaded to take this approach because comorbid psychiatric disorders are well described in current classification systems, and there is no need to replicate this here, and clinical evidence seems to suggest that psychiatric disorders specific to epilepsy do exist, are poorly described, often go unrecognized, and are not covered by current systems of classification of psychiatric disorders or of epilepsy.

We have also adopted a descriptive approach to classification, akin to the ICD-10 and DSM-IV classification systems, rather than an etiological approach as taken by others e.g., [26]. This decision to take a descriptive approach was made because the etiological approach in this case would involve making an assumption (potentially flawed) linking the presumed cause and psychopathology. Further, etiological classifications require some degree of investigative support and clinical expertise, both of which may be limited in smaller centers around the world and in developing nations. The descriptive approach, on the other hand, relies on good

Table 1
ILAE classification: Key categories, clinical features and conclusions

Category	Clinical features	Key conclusions in draft classification proposal
The problem of co morbidity	• Anxiety and phobic disorders • Minor and major depression • Obsessive compulsive disorder • Other somatoform, dissociative and neurotic disorders	No different from the range of common mental disorders prevalent in the community and in clinic/hospital populations. Classification should be as per ICD-10 and DSM-IV
Psychopathology as presenting symptom of epileptic seizures	Altered awareness, confusion, disorientation, memory disturbances, anxiety, dysphoria, hallucinations and paranoid syndromes	Complex partial, simple partial and absence status and other epilepsy syndromes can be diagnosed; clinically supported by EEG
Interictal psychiatric disorders that are specific to epilepsy	• Cognitive dysfunction including memory complaints	• Maybe general or specific; diagnosed with standard neuropsychological tests
	• Psychoses of epilepsy	• To be classified based on the relationship to seizure-prodromal, inter-ictal, post-ictal and alternating
	• Affective somatoform disorders • Personality disorders	• Hyperethical, viscous, labile, mixed and other • Both trait accentuation and disorder to be coded
	• Anxiety and phobias specific to epilepsy	• Fear of seizures recognised as a distinct and disabling entity
Other information of relevance	• Relationship to AED therapy	Coded as not documented; associated with institution and/or withdrawal with specified time periods for both
	• Relationship to EEG change	Presence or absence of associated EEG change documented

history taking and observation, both cornerstones of good clinical medicine, the world over [27].

We have chosen to describe disorders specific to epilepsy as a separate category, rather than integrate them into subsections of the existing classifications, such as ICD-10 and DSM-IV. This decision to propose an independent classification of neuropsychiatric disorders specific to epilepsy has been made because an attempt to integrate these within the aforementioned systems would, in our opinion, cause considerable confusion to the user, and dilute attention away from psychiatric disorders specific to epilepsy.

Having chosen to focus on psychiatric disorders specific to epilepsy, while encouraging the use of existing systems for nonspecific comorbid psychiatric disorders, we propose to direct our efforts toward refining this system of classification, developing consensus among experts, and making the refined system of classification operational.

The ultimate aim of this commission would be to advocate for the inclusion of this classification system within existing systems of classification in psychiatry, such as ICD-11 and DSM-V, and within the forthcoming ILAE system of classification of epilepsy and its syndromes.

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