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Psychoses in epilepsy: A comparison of postictal and interictal psychoses

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ABSTRACT

We retrospectively analyzed data of patients with epilepsy (n = 1434) evaluated with prolonged EEG monitoring in order to estimate the prevalence of postictal psychosis (PP) and interictal psychosis (IP), to investigate a potential association of psychosis subtype with epilepsy type, and to assess differences between PP and IP. The overall prevalence of psychosis was 5.9% ($N = 85$); prevalence of PP ($N = 53$) and IP ($N = 32$) was 3.7% and 2.2%, respectively. Of patients with psychosis, 97.6% had localization-related epilepsy (LRE). Prevalence of psychosis was highest (9.3%) in patients with temporal lobe epilepsy (TLE). When comparing PP with IP groups on demographic, clinical, and psychopathological variables, patients with IP were younger at occurrence of first psychosis ($P = 0.048$), had a shorter interval between epilepsy onset and first psychosis ($P = 0.002$), and more frequently exhibited schizophreniform traits (conceptual disorganization: $P = 0.008$; negative symptoms: $P = 0.017$) than those with PP. Postictal psychosis was significantly associated with a temporal seizure onset on ictal EEG ($P = 0.000$) and a higher incidence of violent behavior during psychosis ($P = 0.047$). To conclude, our results support the presumption of a preponderance of LRE in patients with psychosis and that of a specific association of TLE with psychosis, in particular with PP. Given the significant differences between groups, PP and IP may represent distinct clinical entities potentially with a different neurobiological background.

1. Introduction

The relationship between epilepsy and psychosis has attracted the attention of researchers for many centuries. Today, there is considerable evidence that individuals with epilepsy are at an almost 8-fold increased risk of psychosis compared with those without epilepsy; overall prevalence of psychoses in epilepsy is estimated to be at about 6% [1].

Following a proposal on the classification of neuropsychiatric disorders in epilepsy developed by the Commission on Neuropsychiatric Aspects of the International League Against Epilepsy [2], psychoses in epilepsy may best be classified according to the temporal relation between psychosis and seizures. While alternative psychosis (i.e., an inverse relationship between seizures and psychosis, with or without paradoxical normalization of the EEG) is considered a rare and controversially viewed phenomenon, postictal psychosis (PP) and interictal psychosis (IP) are frequently encountered in clinical practice. Postictal psychosis, first evaluated by Logsdail and Toone [3], is characterized by antecedent seizures and typically develops after a silent period ("lucid interval") following the last seizure. In contrast, IP, as delineated by Slater et al. [4], occurs in a state of seizure-freedom or between habitual seizures.

Most authors believe that psychoses predominantly occur in patients with localization-related epilepsy (LRE), with a pronounced susceptibility to psychosis in patients with a temporal seizure onset. However, there is still conflicting evidence about the association between psychosis and type of epilepsy. There is also an ongoing discussion whether PP and IP actually represent distinct clinical entities within the spectrum of epilepsy-related psychoses.

The aims of our study were i) to investigate the overall prevalence of psychosis in individuals with epilepsy, ii) to assess the prevalence of IP and PP and its potential association with the type of epilepsy, and iii) to compare patients with IP and PP on sociodemographic, clinical, and psychopathological variables.

2. Material and methods

2.1. Patients

Patients with PP or IP were identified retrospectively by reviewing the charts of all patients who underwent prolonged video-EEG monitoring between January 1995 and February 2012 at the Neurological Department of the Medical University of Vienna. A patient was allocated to the group with PP or IP if psychosis was witnessed during monitoring or if the patient's history (based on a written assessment

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composed by a specialist in psychiatry or on a reliable caregiver's report) provided evidence of a history of PP or IP. Patients with a history of psychopathological features being suggestive or indicative of a delirious state (as defined by the ICD-10 criteria for delirium: F05) [5] were not included.

All patients underwent high-resolution MRI brain scan. Inclusion criteria were age above 18 years and a confirmed diagnosis of epilepsy. Type of epilepsy (based on ictal semiology, EEG, and MRI findings) was classified in accordance with the International Classification of Epilepsies [6] as i) localization-related (LRE), ii) generalized (including idiopathic and symptomatic) (GE), or iii) undetermined whether local or generalized. The intake of antiepileptic drugs (AEDs) that may affect mental state, intellectual impairment, or a progressive mass lesion on MRI was not considered an exclusion criterion. The study protocol was approved by the local ethics committee.

2.2. Definition of psychosis

Postictal psychosis was specified using the criteria set down by Logsdail and Toone [3]: (i) development of psychosis within 1 week of a seizure/seizure cluster (following a 24- to 48-h delay between the last seizure and PP); (ii) duration of at least 15 h but <2 months; (iii) altered mental state characterized by delirium or delusions and/or hallucinations in clear consciousness; and (iv) no evidence of causative factors of psychosis such as AED toxicity, previous IP, EEG evidence for status epilepticus, recent history of head injury, or alcohol/drug intoxication/withdrawal.

Interictal psychosis was diagnosed in accordance with the ICD-10 [5] and the operational criteria for IP consistently used in the relevant literature [7,8]: i) presence of hallucinations, delusions or a limited number of severe behavioral abnormalities (related to the criteria for organic hallucinosis: F06.0, organic catatonic disorder: F06.1 or organic delusional disorder: F06.2); ii) no temporal relation of psychosis to seizure activity; iii) first occurrence of psychosis after the onset of epilepsy; and (iv) duration of at least 24 h in a state of clear consciousness. Interictal psychosis included chronic psychosis (at least one episode lasting ≥1 month) and brief (acute) IP (episodes resolving within 1 month).

2.3. Items of investigation

The following variables were compared between groups with PP and IP: sex, age at evaluation, age at epilepsy onset, family history of epilepsy (≥one first-degree relative with epilepsy), seizure type (in accordance with the latest version of the International Classification of Seizures [6]), monthly seizure frequency (any kind of seizures: simple partial, complex partial, generalized), intellectual function (which was classified as impaired in patients who had attended special school, relating to an IQ < 70 in the Wechsler Abbreviated Scale of Intelligence), presence of any MRI pathology (hippocampal atrophy/sclerosis, mass lesions, developmental and vascular malformations, posttraumatic and postinflammatory lesions), age at occurrence of first psychosis, interval between onset of epilepsy and first psychosis, EEG data (lateralization of ictal/interictal epileptiform discharges; localization of the seizure focus whether temporal or extratemporal), and psychopathology.

To assess common features of psychosis, we used the subscale for positive symptoms of the Positive and Negative Syndrome Scale (PANSS [9]) as a framework. Psychiatric assessment was performed by a psychiatrically trained rater who was blinded to clinical information. The following items were classified as being present or absent: i) delusions, ii) conceptual disorganization, iii) hallucinatory behavior, iv) excitement, v) suspiciousness/persecution, and vi) hostility. Given its strong relation with mood disorders (in particular with mania), the item "grandiosity" was not included. Two supplementary features (reportedly being salient features of PP or IP [10,11]) were assessed: i) violent behavior (self-harm or violence directed against others) and ii) negative symptoms (at least one feature of the PANSS negative subscale such as blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity/flow of conversation, and stereotyped thinking). Evaluation of psychopathology was restricted to patients in whom sufficient information on mental status during psychosis was available.

2.4. Statistical analysis

We used a Chi-squared test to compare categorical variables between patients with PP and those with IP. Group differences between numerical data were assessed using unpaired Student's t-tests. When appropriate (i.e., whenever the expected frequency in any one cell was <5), Fisher's exact test was applied. A P-value of <0.05 was considered significant. Analyses were implemented by the Statistical Package for Social Sciences 14.0 (SPSS, Chicago, IL, USA).

3. Results

3.1. Prevalence of psychosis

A total of 1434 patients were diagnosed with epilepsy as confirmed by the results of long-term video-EEG monitoring. Out of these, we identified 85 patients (5.9%) with a history of PP or IP. In 31 patients (36.5%), psychosis was witnessed during video-EEG monitoring (PP: 25/53, 47.2%; IP: 6/32, 18.8%). In another 31 patients (36.5%), a written evaluation by a psychiatric specialist provided evidence of a history of psychosis (PP: 14/53, 26.4%; IP: 17/32, 53.1%). In the remaining 23 patients (27.0%), psychosis was determined by documentation from an informed caregiver (PP: 14/53, 26.4%; IP: 9/32, 28.1%).

Prevalence of PP ($N = 53$) and IP ($N = 32$) was 3.7% and 2.2%, respectively. Within patients with psychosis, the vast majority ($N = 83$; 97.6%) had LRE. Prevalence of psychosis was highest in patients with TLE ($N = 64/684$; 9.3%). Two patients with psychosis had an epilepsy or syndrome undetermined whether local or generalized (2/62; 2.4%). Within patients with GE ($N = 170$), no patient with psychosis was identified. Temporal lobe epilepsy was particularly frequently associated with PP: Of the 64 patients with TLE and psychosis, 48 patients (75.0%) had PP. Prevalence rates in patients with other types of epilepsy and distribution of psychosis subtypes within epilepsy types are shown in Table 1.

3.2. Comparison between groups with PP and IP

When comparing groups with PP and IP, patients with IP had a significantly lower mean age at their first psychotic episode (IP: 29.0 ± 8.3 years; PP: 33.9 ± 12.3 years; $P = 0.048$) and a shorter mean interval between epilepsy onset and first psychosis (IP: 11.9 ± 10.3 years; PP: 20.1 ± 11.8 years; $P = 0.002$). No significant group differences were

Table 1
Psychosis in patients with epilepsy ($N = 1434$).

	LRE			GE	UNDETERM	Total
	TLE	FLE	Others[a]			
	$N = 684$	$N = 155$	$N = 363$	$N = 170$	$N = 62$	$N = 1434$
Psychosis, *N* (%)	64 (9.3)	4 (4.7)	15 (4.1)[b]	0 (0)	2 (2 .4)	85 (5.9)
PP, *N* (%)	48 (75.0)	2 (50.0)	2 (13.3)	0 (0)	1 (50.0)	53 (3.7)
IP, *N* (%)	16 (25.0)	2 (50.0)	13 (86.7)	0 (0)	1 (50.0)	32 (2.2)

TLE, temporal lobe epilepsy; FLE, frontal lobe epilepsy; LRE, localization-related epilepsy; GE, generalized epilepsy (idiopathic and symptomatic); UNDETERM, epilepsies or syndromes undetermined whether local or generalized.

[a] Includes cases with occipital lobe epilepsy ($N = 36$), parietal lobe epilepsy ($N = 19$), and multifocal epilepsies or focal epilepsies with undetermined seizure onset ($N = 308$).

[b] Occipital lobe epilepsy: 1/36 (2.7%); parietal lobe epilepsy: 1/19 (5.3%); multifocal epilepsies or focal epilepsies with undetermined seizure onset: 13/308 (4.2%).