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Analysis of psychotic disorders in patients with refractory partial epilepsy, psychiatric diagnoses and clinical aspects

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Introduction. The association between psychotic disorders and epilepsy has been controversial. Different subtypes of psychotic disorders in epilepsy patients have been described according to temporal relationship with seizures-postictal (PIP), interictal (IIP) and bimodal (BP) psychoses are described in literature.

Objectives. Determine clinical characteristics of patients with refractory partial epilepsy and psychoses and compare the results with a control group of patients with refractory partial epilepsy without psychoses.

Methods. A total of 57 patients with refractory partial epilepsy and psychotic disorders (psychotic group [PG]) and 56 patients with refractory partial epilepsy and without psychoses (control group, CG) were evaluated according to DSM-IV criteria and SCID-I. All patients underwent complete neurological, neuroimaging, neuropsychological, and psychiatric assessment. Clinical, demographic and neuroimaging data were compared between patients in CG and PG.

Results. In PG 15 patients (26%) had criteria for PIP, 29 patients (51%) for IIP and 13 patients (23%) for BP. Epilepsy time duration and bilateral hippocampal sclerosis were significantly more frequent in patients with psichosis. PG patients had a longer evolution time of epilepsy and greater frequency of bilateral hippocampal sclerosis ($p < 0.05$). No differences were found between psychoses subtypes.

Conclusions. Longer evolution of seizures and the presence of bilateral hippocampal sclerosis may increase propensity to develop psychoses in patients with refractory partial epilepsy.

Key words:
Refractory partial epilepsy. Postictal psychoses. Interictal psychoses. Bimodal psychoses. Bilateral hippocampal sclerosis.

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Análisis de los trastornos psicóticos en pacientes con epilepsia parcial refractaria, diagnóstico psiquiátrico y características clínicas

Introducción. La asociación entre trastornos psicóticos y epilepsia ha sido motivo de controversias. Actualmente se describen en la literatura diferentes subtipos de trastornos psicóticos en los pacientes con epilepsia de acuerdo con la relación temporal con las crisis: las psicosis postictales (PPI), interictales (PII) y bimodales (PB).

Objetivos. Determinar las características clínicas de pacientes con epilepsia parcial refractaria y psicosis y comparar los hallazgos con un grupo control de pacientes con epilepsia parcial refractaria sin psicosis.

Métodos. Se estudiaron 57 pacientes con epilepsia parcial refractaria y trastornos psicóticos (GP) y 56 pacientes con epilepsia parcial refractaria sin psicosis (GnP) de acuerdo con los criterios del DSM-IV. En todos los pacientes se realizó una evaluación neurológica completa, estudios neurofisiológicos, neuroimágenes y evaluaciones psiquiátricas DSM-IV y SCID-I. Las variables clínicas, demográficas y psiquiátricas fueron comparadas entre los pacientes GP y GnP.

Resultados. En el GP 15 pacientes (26%) cumplían criterios para PPI, 29 pacientes (51%) para PII y 13 pacientes (23%) para PB. Encontramos una duración más prolongada de la epilepsia y una mayor incidencia de esclerosis hipocámpica bilateral en los pacientes GP. Los pacientes de GP presentaron un mayor tiempo de evolución de la epilepsia y una mayor incidencia de esclerosis hipocámpica bilateral ($p < 0,05$). No se observaron diferencias entre los distintos subtipos de psicosis.

Conclusiones. El mayor tiempo de evolución de las crisis epilépticas y la presencia de una esclerosis hipocámpica bilateral podrían incrementar el riesgo de desarrollar psicosis en pacientes con epilepsia parcial refractaria.

Palabras clave:
Epilepsia parcial refrataria. Psicosis postictal. Psicosis interictal. Psicosis bimodal. Esclerosis hipocámpica bilateral.

INTRODUCTION

Controversy is found in the literature regarding the statement that epilepsy patients have a greater risk of developing psychiatric disorders in general and psychosis in particular[1-4]. Epidemiological studies show that individual risk of developing psychosis would be related to the type of epileptic syndrome and response to treatment[2-6]. A higher percentage of psychosis (19 % to 27 %) between epileptic patients belonging to centers specialized in epilepsy, where patients with bad response to treatment predominate, has been observed than in patients with epilepsy who attend non-specialized centers where a lower incidence of psychosis which is closer to that found in the general population (0.7 % to 7 %) is reported[5].

Different subtypes of psychotic disorders in epilepsy have been considered, taking the relationship between the appearance of psychotic symptoms and ictal event into account (ictal classification)[7,8-12]. Post-ictal psychosis (PIP) is characterized because the psychotic symptoms appear within 24 to 48 hours following the occurrence of an epileptic seizure or of several repeated one (cluster seizures or several daily ones). The duration of the psychotic symptoms is short, lasting days or weeks, with total remission of the acute psychotic symptoms. In interictal psychoses (IIP), the psychotic symptoms have no temporal relationship with the seizures and a recurrent and chronic course may occur. Interictal psychoses have been observed on some occasions in seizure-free periods. Thus, they have been related with the phenomenon called «forced normalization of the EEG» (normalization of a previously altered EEG)[7-10]. These forms of psychoses have been called «schizophrenia-like» due to their similarities with schizophrenia[9,10,13].

Both types of psychoses, PIP and IIP, may coexist independently in the same patient and have recently been referred to as bimodal psychoses[14-16]. It is discussed whether postictal, interictal and bimodal psychoses are included in the same unit or not with different clinical forms[15-17].

In this work, we have investigated the clinical characteristics of patients with refractory partial epilepsy and psychoses (PIP, IIP and PB) and have compared the findings with a control group of patients with refractory partial epilepsy without psychosis.

METHODS

A total of 57 patients with refractory partial epilepsy who fulfilled criteria for past and/or current psychotic disorders according to the Axis I of DSM IV (PG) were studied. A second group of 56 patients with refractory partial epilepsy who did not fulfill diagnostic criteria for psychotic disorders were included as control group (nPG).

The 113 patients belonged to a center specialized in epilepsy, Epilepsy Reference Center of the Hospital Ramos Mejía and were studied consecutively between the years 1999 to 2005. All the patients included in this study completed the psychiatric evaluation protocol[18].

The psychiatric evaluation included: conduction of psychiatric interviews with the patients and family, making of a psychiatric clinical history and administration of structured interviews of the DSM IV (SCDI I and II)[19-21].

Epilepsy was diagnosed on the basis of a complete neurological and clinical evaluation, pharmacological history, interictal EEG studies and video-EEG and neuroimages (magnetic resonance imaging, MRI) that made it possible to confirm the diagnosis of epilepsy and locate the epileptogenic zone[22]. Only those patients who had seizures or partial syndrome were included in this study. Patients with generalized epilepsies, background of mental retardation (attendance at a special school) and incomplete evaluations were excluded from this study.

The following endpoints were specifically analyzed: background of febrile seizures, background of epileptic status, background of secondarily generalized seizures and aura characteristics. In regards to the aura, we have only considered the auras that were repeated in a stereotypal way and were followed by a simple or complex partial seizure in order to avoid confusion between the auras and some psychotic symptoms. On the one hand, we analyzed the experiential auras, characterized by complex psychiatric experiences such as *deja vú*, *jamais vú*, emotional changes and other experiences such as depersonalization and derealization. We included the other types of auras, epigastric, autonomic, somatic and sensorial as «non-experiential»[22]. In relationship to the MRI results, type of lesion, topography, presence of unilateral, bilateral hippocampal sclerosis, hippocampal sclerosis plus and malformations of neurodevelopment were defined. In relationship to the neurophysiological results (EEG, video-EEG), epileptogenic zone laterality was established. Patients with controversial results in the images and video were not considered when the epileptogenic zone laterality was considered.

The psychiatric diagnosis of the psychotic disorders was made in accordance with the DSM IV[19,21] and these patients were grouped into PIP, IIP and BP according to the Ictal classification[7,9-12]. The diagnostic criteria used for the PIP were: presence of psychotic episode followed, in less than 24 hours by one or several ictal episodes. For IIP: presence of a psychotic disorder of more than one month's course, in absence of a clear temporal relationship between the onset of the psychotic symptoms and epileptic seizures. Patients with criteria for both types of psychoses in different episodes were considered as a third subgroup, bimodal psychosis (BP).

The control group was made up of patients with partial epilepsy with no background nor psychotic disorders at the time of the psychiatric evaluation.

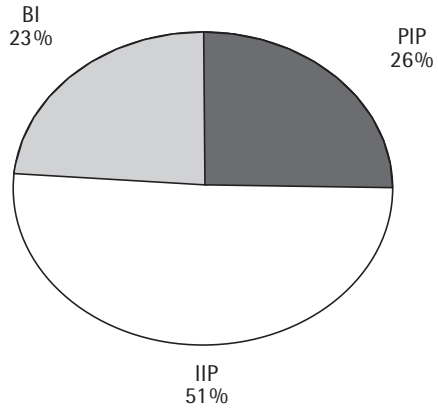

Figure 1

Statistical analysis: the clinical, demographical and neuropsychiatric endpoints were compared between the patients with PG and CG and on the other hand between the group of PIP and CG, the IIP and CG and BP and CG. The data were analyzed using SPSS for Windows. Chi squared and Fisher Test for the qualitative endpoints and the Student' *t* test for quantitative endpoints were calculated.

RESULTS

When the type of partial epilepsy was analyzed in the 113 patients studied, 92 patients (81%), had temporal lobe epilepsy, 9 patients frontal epilepsy and 12 patients parieto-occipital epilepsy (11%). In the PG, the 57 patients fulfilled criteria for at least one type of psychotic disorder according to the DSM IV. According to the ictal classification used, 15 patients (26%) fulfilled criteria for PIP, 29 patients (51%) for PIP and 13 patients (23%) for BP (fig. 1). A total of 56 patients had no type of psychosis or psychotic symptoms (CG).

The following variables analyzed were significant:

- Evolution time of epilepsy was greater in patients with PG and especially in patients with PIP (table 1).
- The presence of experiential aura was less frequent in PG. Furthermore, within this group, it was significantly less in the patients with IIP (table 2).
- The finding of bilateral hippocampal sclerosis in the MRI was significantly more frequent in patients ($p \leq 0.05$) than that observed in the control population (table 3).

DISCUSSION

The relationship between epilepsy and psychotic disorders is complex and controversial and the results found in the literature show significant differences according to the population studied. Partial epilepsies, especially temporal lobe ones, make up the epileptic syndromes that have been most associated to psychotic disorders in epilepsy. However, the mechanisms involved are unknown and constitute a controversial subject[4,8,10,13,17,24-26].

The patients included in this study belong to an epilepsy center specialized in refractory epilepsy and epilepsy surgery. All the patients studied had partial epilepsy refractory to drug treatment and most of them localized epilepsy in the temporal lobe. Many of the patients with psychotic symptoms included were referred previously to the psychiatric consultation by the epileptologist.

According to the results of this study, the evolution time of epilepsy was greater in the total group of patients with psychosis. This observation was previously described by other authors. The initial studies of Slater et al.[13] reported that the appearance of schizophrenia-like psychosis in epileptic patients occurred after10 years of the onset of epilepsy. After that, it was reported that a lower age of onset and greater time of exposure to the seizure were risk factors for the development of both types of psychoses[8,9,10,27,28].

Table 1 Age, age of onset and years of evolution of the epilepsy

Years	Control group (n = 56)	Total psychosis group (n = 57)	p	PIP group (n = 15)	p	IIP group (n = 29)	p	BP group (n = 13)	p
Age at time of evaluation	35.27 ± 10.8	38.72 ± 11.52	0.1	41.6 ± 9.7	0.04	37 ± 10.6	0.45	39.0 ± 15	0.3
Age of onset	13.6 ± 10.6	10.18 ± 10.19	0.12	10.6 ± 9.8	0.38	9.62 ± 8.7	0.11	10.9 ± 13.8	0.5
Evolution time	22.09 ± 11.95	28.54 ± 13.5	0.008	31.0 ± 9.4	0.01	27.4 ± 13.4	0.06	28.0 ± 17.7	0.1

PIP: postictal psychosis; IIP: interictal psychosis; BP: bimodal psychosis.

Table 2 Qualitative endpoints. Control group/total psychosis group

Qualitative endpoints	Control group (n=56)	Psychosis group (n=57)	p
Gender			
Female	25 p. (45%)	19 p. (33%)	ns
Male	31 p. (55%)	38 p. (68%)	ns
Febrile seizures	9 p. (16%)	12 p. (21%)	ns
Status epilepticus	3 p. (5%)	4 p. (7%)	ns
Secondary generalized seizures	20 p. (36%)	19 p. (33%)	ns
Aura	47 p. (84%)	43 p. (75%)	ns
Experiential aura	17 p. (30%)	8 p. (14%)	0,037
Laterality			
Right	29 p. (52%)	22 p. (39%)	ns
Left	24 p. (43%)	19 p. (33%)	ns
Hippocampal sclerosis	20 p. (36%)	21 p. (37%)	ns
Bilateral hippocampal sclerosis	1 p. (2%)	9 p. (16%)	0.008
Malformation of cortical development (MCD)	7 p. (13%)	8 p. (16%)	ns

ns: non-significant; PIP: postictal psychosis; IIP: interictal psychosis; BP: bimodal psychosis.

Within the qualitative endpoints analyzed, the presence of «experiential» aura was observed less frequently in the group of patients with psychosis. These results contradict the previous studies that found a positive association between psychic aura and psychosis. However, other authors have not reported any association when analyzing the experiential aura in patients with psychosis. Thus, the positive association between «psychic or experiential» aura and psychosis is still controversial. Epileptic aura is the part of the seizure that occurs before a loss of consciousness and that can be remembered[22,23]. The use of different methodologies in the recording of the type of psychic or experiential aura may be related with the differences found.

We have observed a significantly greater incidence of bilateral hippocampal sclerosis in all the subtypes of psychoses (PIP, IIP and BP). Unilateral hippocampal sclerosis is the most frequent structural alteration between patients with temporal lobe epilepsy and the finding of a bilateral sclerosis implies a worse prognosis of the epilepsy. Previously, other authors described that these structural alterations and bilateral electrical alterations constitute a risk factor for the development of psychosis[9,10,27,28]. A possible explanation for these findings could be that there would be compensatory mechanisms in the patients with unilateral structural involvement that would occur in the healthy hemisphere which could act as protectors against the development of psychosis while this would not occur in patients with bilateral structural involvement. Greater cerebral structural involvement and greater incidence of lesions caused by neurodevelopment alterations such as gangliogliomas, hemartomas and dysplasia have also been reported in patients with partial epilepsy and «schizophrenic-like psychosis»[29,30,31].

In this work, we have not found any differences between the group of patients with psychosis and the control group

Table 3 Qualitative endpoints. Subtypes of psychosis/control population (n = 113)

Qualitative endpoints	Control group (n = 56)	PIP group (n = 15)	p	IIP group (n = 29)	p	Bimodal psychosis group (n = 13)	p
Febrile seizures	9 p. (16%)	5 p. (33%)	ns	3 p. (10%)	ns	4 p. (14%)	ns
Status epilepticus	3 p. (5%)	2 p. (13%)	ns	1 p. (3%)	ns	1 p. (3%)	ns
Secondary generalized seizures	20 p. (36%)	4 p. (26%)	ns	9 p. (31%)	ns	6 p. (21%)	ns
Aura	47 p. (84%)	11 p. (73%)	ns	24 p. (83%)	ns	8 p. (28%)	ns
Experiential aura	17 p. (30%)	3 p. (20%)	ns	3 p. (10%)	0.056	2 p. (7%)	ns
Laterality							
Right	29 p. (52%)	4 p. (27%)	ns	16 p. (55%)	ns	2 p. (7%)	ns
Left	24 p. (43%)	5 p. (33%)	ns	7 p. (24%)	ns	7 p. (24%)	ns
Bilateral hippocampal sclerosis	1 p. (2%)	2 p. (13%)	ns	4 p. (14%)	0.038	3 p. (10%)	0.021
Malformation of cortical development (MCD)	7 p. (13%)	2 p. (13%)	ns	5 p. (17%)	ns	1 p. (3%)	ns

ns: non-significant; PIP: postictal psychosis; IIP: interictal psychosis; BP: bimodal psychosis.

in relationship to epileptogenic zone laterality. Since the series reported by Flor Henry[32-34], left laterality has been mentioned as a risk factor for the development of psychosis in temporal lobe epilepsy. However, more recent studies have not found any differences in the association between the left focus and psychosis[9,10,26].

CONCLUSIONS

Considering the specific situation of the epilepsy center where the study was conducted and the characteristics of the patients included, the results found are valid for the population of patients diagnosed of refractory partial epilepsy and especially for the temporal lobe location. Greater evolution time of the disease and bilateral hippocampal sclerosis could increase the risk of developing psychosis. We have not observed any differences between the subtypes of psychoses studied.

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