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# Prevalence of psychiatric comorbidities in temporal lobe epilepsy: the value of structured psychiatric interviews

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**ABSTRACT –** *Background*. Although many studies have demonstrated a high prevalence of psychiatric disorders in epileptic patients, most have used unstructured psychiatric interviews for diagnosis, which may lead to significant differences in results. Here we present a study evaluating the prevalence of major psychiatric comorbidities in a cohort of South Brazilian patients with temporal lobe epilepsy using a structured clinical interview. *Methods*. Neuropsychiatric symptoms were analyzed in 98 patients (39 men and 59 women) with temporal lobe epilepsy. Patient mean age was 43 years old, and mean duration of epilepsy was 25 years. Patients were diagnosed according to the ILAE Classification of Epileptic Syndromes using clinical, EEG, and neuroimaging criteria. All patients participated in the Structured Clinical Interview for DSM-IV (SCID). *Results*. Fifty-three patients (54.1%) presented major psychiatric comorbidities. Mood disorders were observed in 42 patients (42.9%), the most common being neuropsychiatric disorders. Anxiety disorders were the second most frequent disorders, observed in 18 patients (18.4%). Psychotic disorders and substance abuse were each observed in six patients (6.1%). There were no clinical variables regarding epilepsy characteristics (age of onset, duration, response to antiepileptic drugs) and no MRI features associated with psychiatric disorders. A seven-fold increased risk of mood disorders was identified in patients with inter-ictal EEG abnormalities associated with the left hemisphere. *Conclusion*. Relative to previous reports, we identify a high prevalence of psychiatric disorders in TLE patients, although our data is similar to that observed in other studies which have used similar structured interviews in populations of epileptic patients attending tertiary centres. The wide variation in percentages is probably attributable to the different patient groups investigated and to the even greater variety of diagnostic methods. Structured psychiatric interviews may contribute to a better evaluation of the true prevalence of psychiatric comorbidities in temporal lobe epilepsy.

**Key words:** epilepsy, psychiatry, mental disorders, SCID, prevalence, comorbidities, mood disorders, anxiety disorders

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Epilepsy is a common neurological disorder. The world prevalence of epilepsy is estimated to range from 0.5 to 1.5% (Sander, 2003). The term "epilepsy" encompasses different neurological disorders characterized by a tendency towards recurrent epileptic seizures. Epileptic seizures are the clinical correlates of paroxysmal events generated by an enduring condition of hyperexcitability and hypersynchrony of brain electrical activity. The clinical spectrum of epilepsy encompasses many different neurobehavioural comorbidities (Elger and Schmidt, 2008). Epilepsy and neurobehavioural conditions may share some physiopathological, genetic, and environmental mechanisms (Gaitatzis *et al.*, 2004; Hermann *et al.*, 2008).

The association between epilepsy and psychiatric disorders has been known since ancient times, but has been marked by an explosion of studies during the last two decades (Devinsky, 2003). Prevalence of psychiatric comorbidities ranges from 20 to 40% in patients with epilepsy, and in selected populations may be two-fold higher (Pond and Bidwell, 1960; Silberman *et al.*, 1994; Perini *et al.*, 1996; Blumer *et al.*, 1998; Davies *et al.*, 2003; Swinkels *et al.*, 2005; Tellez-Zenteno *et al.*, 2005). Different definitions of psychiatric comorbidities, different study populations, and most importantly, different forms of psychiatric evaluation are factors that may explain the observed variability. Studies with structured psychiatric interviews are still lacking.

The objective of the present study was to determine the prevalence of major psychiatric disorders in a cohort of patients with TLE living in South Brazil using a structured psychiatric evaluation, and compare the findings with studies conducted around the world. Our study may therefore contribute to a better understanding of the worldwide prevalence of psychiatric comorbidities in epilepsy.

## Methods

We studied a cohort of 98 consecutive Caucasian patients (59 women and 39 men) with TLE, from March 2007 to December 2008. Patients were selected from the epilepsy outpatient clinic at the Hospital de Clinicas de Porto Alegre, a tertiary hospital located in the Southern region of Brazil. Porto Alegre is the capital of Rio Grande do Sul state. The city has a population of 1,416,735, mostly composed of European immigrants (Portuguese, German, and Italian), distributed in an area of 496.8 $km^2$. The annual per capita income is U$ 4840.91 (IBGE Cidades@ 2009). Economy is based on industry, commerce and services. In Brazil, health is the responsibility of the state and access is universal. For the rest of the country, health, education and safety are provided by both public and private services. It is estimated that about two thirds of the population uses governmental services.

The inclusion criterion for the study was the presence of electroclinical and neuroimaging features of TLE, according to the ILAE classification for epileptic seizures and syndromes (Commission on Classification and Terminology of the International League Against Epilepsy, 1989; Maillard *et al.*, 2004; Pascual, 2007). Patients less than 18 years old or with generalised epilepsies, extratemporal epilepsies, mental retardation (IQ scores below 70), brain tumour, systemic disease (*e.g.* systemic erythematous lupus, AIDS), or penetrating head trauma were excluded.

After giving written informed consent, all patients participated in the Structured Clinical Interview for DSM-IV (SCID) (First *et al.*, 2001) which was divided into six modules for the detection of one or more lifetime diagnoses using the Axis I Diagnostic and Statistical Manual, fourth edition (DSM-IV) (American Psychiatric Association, 2000). Inter-ictal spikes were independently reviewed by two board-certified electroencephalographers (JAB and CMT) who were blind to the psychiatric evaluation. Whenever the results were discordant, EEGs were reviewed by the two examiners together to reach a consensus. When available, all MRI examinations were reviewed to determine aetiology. Seizure control was assessed by an events calendar completed by the patient. Seizures occurring more than once a month were considered uncontrolled. Data regarding prior and current antiepileptic treatments, as well as the use of any psychotropic or sedative drug (*e.g.* antidepressants, antipsychotics), were registered in a database for statistical analyses.

Results were displayed in a percentage form. We analyzed the association of psychiatric diagnosis with the main aspects of TLE (control of seizures, inter-ictal EEG, MRI abnormalities, presence of aura). We compared results of patients with and without a positive SCID for these aspects using Pearson's chi-square test. All results were expressed using OR (95% CI). A significant level was considered when $p < 0.05$. The study was approved by the Ethics Committee of the Hospital de Clínicas de Porto Alegre.

## Results

Mean age of the study population was 43.3 (± 12.3) years (range: 20-75 years), with a mean age at first seizure of 18.1 (± 14.3) years (range: 3-67 years) and a mean duration of epilepsy of 25.3 (± 12.9) years (range: 2-51 years). The main clinical characteristics of the study population are shown in *table 1*. Fifty-three patients (54.1%) were diagnosed with at least one lifetime psychiatric disorder. Forty-two of the SCID-positive patients (42.9%) had a mood disorder, 18 (18.4%) had an anxiety disorder, six (6.1%) had a psychotic disorder and six patients had alcohol or drug abuse (*table 2*). An association between mood

**Table 1.** Clinical features of the patients studied.

| | | Number of patients (%) |
|---|---|---|
| Gender | Men | 39 (39.8%) |
| | Women | 59 (60.2%) |
| Controlled seizures | Yes | 40 (40.8%) |
| | No | 58 (59.2%) |
| Aura | Yes | 64 (65.3%) |
| | No | 34 (34.7%) |
| Family history of epilepsy | Yes | 45 (45.9%) |
| | No | 53 (54.1%) |
| Family history of psychiatric disorders | Yes | 38 (38.8%) |
| | No | 60 (61.2%) |
| Initial precipitant insult | Yes | 24 (24.5%) |
| | No | 74 (75.5%) |
| EEG temporal focus lateralization | Right | 32 (32.7%) |
| | Left | 58 (59.2%) |
| | Not lateralized | 8 (8.2%) |
| MRI | Normal | 20 (20.4%) |
| | Abnormal | 23 (23.5%) |
| | Not available | 45 (45.9%) |
| Antiepileptic drugs | Monotherapy | 47 (48.0%) |
| | Polytherapy | 51 (52.0%) |
| Psychotropic drugs | No drugs | 78 (79.6%) |
| | One drug | 16 (16.3%) |
| | Combined therapy | 4 (4.1%) |

**Table 2.** DSM-IV Axis I psychiatric diagnoses.

| Diagnosis | Number of patients (%) |
|---|---|
| Mood disorders | 42 (42.9%) |
| Major depression | 24 (24.5%) |
| Dysthymic disorder | 8 (8.1%) |
| Past depressive episode | 6 (6.1%) |
| Past manic episode | 2 (2.0%) |
| Bipolar disorder | 1 (1.0%) |
| Anxiety disorders | 18 (18.4%) |
| Generalised anxiety disorder | 5 (5.1%) |
| Panic disorder | 4 (4.1%) |
| Post-traumatic stress disorder | 3 (3.1%) |
| Panic with agoraphobia | 2 (2.1%) |
| Specific phobia | 2 (2.1%) |
| Obsessive compulsive disorder | 2 (2.1%) |
| Psychotic disorders | 6 (61.%) |
| Substance abuse | 6 (61.%) |

and anxiety disorders was the most common psychiatric comorbidity observed, present in 22 patients (41.5%).

Major depression was the most frequent mood disorder observed in our series, present in 57% of the patients with mood disorders and in 25% of all patients. Dysthymic disorder was observed in 19% of patients with mood disorders (8% of all patients). A past depressive episode was reported in 14% of patients with mood disorders and in 6% of the total patient series. Generalised anxiety disorder was present in five patients (28% of patients with anxiety disorders and 5% of all patients), and panic disorder in six (two with agoraphobia). Post-traumatic stress disorder was observed in three patients *(table 2)*.

Our findings were compared with other reports with different methodological characteristics and are presented in *table 3*. The overall prevalence of psychiatric disorders in our patients was 54%, with mood disorders twice as common as anxiety disorders *(table 2)*. Relative to previous reports, these values are high, but similar to those observed in other European or South American studies which used similar structured interviews in populations of epileptic patients attending tertiary centres (Edeh and Toone, 1987; Araújo Filho *et al.*, 2008). Moreover, we found a greater prevalence of psychiatric disorders in our patients when compared with the general population of Porto Alegre; data published in a previous study (Almeida-Filho *et al.*, 1997) *(table 4)*.

Although there was a tendency of patients with uncontrolled epilepsy to present some lifetime psychiatric disorder, we did not find any statistical difference between patients with and without lifetime psychiatric disorders, based on the presence of MRI abnormalities, inter-ictal EEG features, control of seizures, or presence of aura *(table 5)*.

EEG and MRI features were analyzed separately in order to search for risk factors of psychiatric disorders in TLE patients. We categorized EEG data in only right, only left, and bilateral inter-ictal temporal discharges. Involvement of the left side (dominant hemisphere) was significant for lifetime mood disorders in TLE patients, with a risk of 7.1 ($p = 0.007$). Less than half of our patients had MRI scans ($n = 43$). There was no association between presence (uni- or bilateral) or absence of hippocampal sclerosis with lifetime psychiatric disorders, or specifically depression, in our patients.

## Discussion

We observed a high prevalence of lifetime psychiatric disorders in our TLE patients, of whom 54.1% presented with psychiatric comorbidities. The main psychiatric diagnoses found in our series were mood disorders (42 patients, 42.9% of the total), followed by anxiety disorders (18 patients, 18.4% of the total). Psychotic disorders and substance abuse were each observed in six patients (6.1%) *(table 2)*.

Our results are consistent with the literature. Most reports show that mood disorders are the most frequent psychiatric comorbidity in TLE patients (Kanner, 2005; Schmitz, 2005). According to previous reports, a higher prevalence of psychiatric comorbidities was observed in epileptic patients studied at tertiary centres (40-60%) (Victoroff *et al.*, 1994; Ring *et al.*, 1998; Grabowska-Grzyb *et al.*,

**Table 3.** Geographical distribution of psychiatric comorbidities in epilepsy.

| Continent | Country | Authors | N | Instrument | Population | Psychiatric disorders | Mood disorders | Anxiety disorders | Psychosis | Substance abuse |
|---|---|---|---|---|---|---|---|---|---|---|
| North America | USA | Victoroff *et al.*, 1994 | 60 | SCID–DSM-III-R | TLE; candidates for surgery | 70% | 58.3% | 31.7% | 13.3% | - |
| | | Ettinger *et al.*, 2004 | 775 | CES-D | Epilepsy; community-based | - | 36.5% | - | - | - |
| | | Strine *et al.*, 2005 | 427 | Kessler 6 scale | Epilepsy; community-based | - | 32.6% | 14.4% | - | - |
| | | Kobau *et al.*, 2006 | 131 | Health Style Survey (self-reported depression and anxiety) | Epilepsy; community-based | - | 39% | 39% | - | - |
| | Canada | Tellez-Zenteno *et al.*, 2007 | 253 | CIDI | Epilepsy; community-based | 23.5% | 17.4% | 12.8% | - | - |
| Europe | UK | Pond and Bidwell, 1960 | 245 | Unstructured psychiatric interview | Children with epilepsy; community-based | 29% | - | - | - | - |
| | | Graham and Rutter, 1970 | 63 | Unstructured psychiatric interview | Children with epilepsy; community-based | 28.6% | - | - | - | - |
| | | Edeh and Toone, 1987 | 88 | CIS | Epilepsy; selected by general practitioners (GP) | 48% | 22% | 15% | 3.4% | - |
| | | Davies *et al.*, 2003 | 67 | SCID | Epilepsy; community-based | 37% | - | - | - | - |
| | | Gaitatzis *et al.*, 2004 | 5834 | ICD-9 | Epilepsy; selected from a database generated by GP | 41% | 18.2% | 11.1% | 9% | 2.4% |
| | | Mensah *et al.*, 2006 | 499 | HADS | Epilepsy; from GP | - | 11.2% | - | - | - |
| | Italia | Perini *et al.*, 1996 | 38 | SADS, BDI, STAIX1, STAIX2 | JME and TLE (selected) patients | 80% (TLE), 22% (JME) | 55% (TLE), 17% (JME) | 15% (TLE), 11% (JME) | - | - |
| | Netherlands | Swinkels *et al.*, 2001 | 209 | CIDI | Epilepsy; tertiary epilepsy centre | - | 24.9% | 29.7% | 0.5% | 20.1% |
| | Czech Republic | Havlová, 1990 | 225 | Chart review (unstructured) | Cohort of epileptic children | 6.7% | - | - | - | - |
| | Iceland | Gudmundsson, 1966 | 654 | Clinical interview (unstructured) | Epilepsy (community-based) | 54.5% | - | - | 9% | - |
| | | Stefansson *et al.*, 1998 | 241 | ICD-9 | Epileptic patients receiving benefits | 35.3% | - | - | 6.2% | 5% |

| Continent | Country | Authors | N | Instrument | Population | Psychiatric disorders | Mood disorders | Anxiety disorders | Psychosis | Substance abuse |
|---|---|---|---|---|---|---|---|---|---|---|
| | Sweden | Forsgren, 1992 | 713 | Chart review (unstructured) | Epilepsy; community-based | 5.9% | - | - | 0.7% | - |
| | Finland | Jalava and Sillanpaa, 1996 | 94 | Chart review and ICD-9 | Epilepsy; selected from different sources | 24% | - | - | 3.1% | - |
| | Denmark | Bredkjaer *et al.*, 1998 | 67 | ICD-8 | Epilepsy; community-based | 16.8% | - | - | - | - |
| Asia | India | Hackett *et al.*, 1998 | 26 | ICD-10 | Epilepsy; community-based | 23.1% | - | - | - | - |
| Africa | Nigeria | Gureje, 1991 | 204 | CIS | Epilepsy; tertiary centre | 37% | - | - | 30% | - |
| South America | Brazil | Araújo Filho *et al.*, 2008 | 270 | SCID | Refractory TLE and JME from a tertiary epilepsy centre | 50% (TLE), 49% (JME) | 25.8% (TLE), 19% (JME) | 14.1% (TLE), 23% (JME) | 15.8% (TLE), 3% (JME) | 2% (JME) |
| | | Our study | 98 | SCID | TLE; selected from a tertiary epilepsy centre | 54.1% | 42.9% | 18.4% | 6.1% | 6.1% |

2006; Briellmann *et al.*, 2007), while population-based studies showed an intermediate prevalence of about 20% (Edeh and Toone, 1987; Jacoby *et al.*, 1996; Ettinger *et al.*, 2004; Mensah *et al.*, 2006). Nevertheless, in all studies the frequencies of psychiatric disorders among epileptic patients were higher than in the general population (12.2-16.2%) (Kessler *et al.*, 2003; Hasin *et al.*, 2005; Patten *et al.*, 2006).

Several authors have reported a wide variability of psychiatric comorbidities in epileptic patients. The prevalence of these comorbidities varies according to the type of patient and psychiatric disorder studied, the duration of the study (last 12 months or lifetime), and the type of diagnostic procedure used (structured interview or self-applicable questionnaire) (Silberman *et al.*, 1994; Perini *et al.*, 1996; Blumer *et al.*, 1998). For example, community-based studies of epileptic patients with structured interviews have identified prevalence of psychiatric comorbidities ranging from 23.5% to 37.5%, always higher than in the general population (10-20%). In contrast, studies using ICD diagnoses and data from administrative registries have shown more varied results (ranging from 16.8 to 60%) (Pond and Bidwell, 1960; Shukla *et al.*, 1979; Jalava and Sillanpaa, 1996; Bredkjaer *et al.*, 1998; Hackett *et al.*, 1998; Stefansson *et al.*, 1998). The highest prevalence was found in populations extracted from lists of individuals with some other associated disease, and therefore probably with a selection bias (Pond and Bidwell, 1960; Shukla *et al.*, 1979).

The increase in prevalence of psychiatric disorders seems to be directly proportional to the increase in the severity of neurological disorders; from patients with chronic non-neurological diseases, non-epileptic neurological diseases, generalised epilepsies, extratemporal focal epilepsies, non-surgically treatable TLE through to patients eligible for surgery (Manchanda *et al.*, 1996; Glosser *et al.*, 2000; Wrench *et al.*, 2004). The prevalence of psychiatric disorders in TLE patients is, in general, two-fold greater than in the general population (Tellez-Zenteno and Wiebe, 2008). Our data closely resemble data observed from other selected populations of epileptic patients (Davies *et al.*, 2003; Araújo Filho *et al.*, 2008). The high prevalence of psychiatric disorders in our study is therefore consistent with the finding that most of our patients (60%) did not have proper seizure control *(table 1)*, as previously described (Almeida-Filho *et al.*, 1997).

Another interesting aspect is the observation that studies conduced with structured interviews tend to point to higher frequencies of neuropsychiatric disorders in epilepsy *(table 3)*. Because the use of structured psychiatric interviews is relatively more recent and limited to smaller populations, it is possible that larger epidemiological studies might underestimate the true prevalence of psychiatric disorders in epilepsy. Thus, further observations are necessary to clarify these matters.

**Table 4.** Prevalence of psychiatric comorbidities in our patients and in Porto Alegre (Almeida-Filho *et al.*, 1997).

| Psychiatric diagnosis | TLE patients (n = 98) | General population (n = 6,471) |
|---|---|---|
| Overall | 54.1% | 42.5% |
| Mood disorders | 42.9% | 11.3% |
| Anxiety disorders | 18.4% | 9.6% |
| Psychotic disorders | 6.1% | 2.4% |
| Substance abuse | 6.1% | 9.2% |

**Table 5.** Analysis of associations between psychiatric disorders and main clinical aspects of TLE.

| | SCID + | SCID - | Risk ($_{95\%}$CI) | p |
|---|---|---|---|---|
| Controlled epilepsy | 20 | 18 | | |
| Uncontrolled epilepsy | 42 | 18 | 2.1 (0.9-4.9) | 0.09 |
| Unilateral temporal EEG spikes | 32 | 19 | | |
| Bilateral temporal EEG spikes | 30 | 17 | 1.1 (0.5-2.4) | 1.0 |
| Abnormal MRI | 12 | 11 | | |
| Normal MRI | 12 | 8 | 0.6 (0.2-1.6) | 0.4 |
| Presence of aura | 43 | 22 | | |
| Absence of aura | 19 | 14 | 1.4 (0.6-3.4) | 0.5 |

For about 40% of our patients, we observed more than one type of lifelong psychiatric disorder; most frequently mood and anxiety disorders. Although this association has been recognized since ancient times, the pathophysiological mechanisms are still poorly understood (Temkin, 1971). Studies with adults and children suffering from epilepsy have shown a high prevalence of this comorbidity in association with epilepsy, sometimes up to 70% (Jones *et al.*, 2005; Kobau *et al.*, 2006). Depression, anxiety and epilepsy seem to share some biological and structural mechanisms related to limbic system dysfunction; an area of research intensely investigated over the last few years.

Fear is a frequent type of aura, observed in about 15% of TLE patients (Devinsky *et al.*, 1995) which sometimes mimics panic attacks (Kanner *et al.*, 2004). A previous study (Strine *et al.*, 2005) found a high prevalence of post-ictal anxiety symptoms in epileptic patients. However, we could not observe this association because there were too few patients with anxiety symptoms in our sample. Goldstein *et al.* (1999) observed an inverse correlation between seizure frequency and post-ictal anxiety symptoms. The authors suggested that this inverse association might be caused by "habituation" of the anxiety generator circuits (mostly amygdala) due to high seizure frequency, causing seizures to be processed as ordinary events. Another possibility is that this inverse correlation could be due to the "learned helplessness" phenomenon (Hermann *et al.*, 1996). Further research is needed to clarify these aspects.

There is much evidence suggesting that TLE and depression may share common pathogenic mechanisms (Kondziella *et al.*, 2007). For example, in both TLE and depression small volumes of frontal lobes have been found (Lavretsky *et al.*, 2007; Mueller *et al.*, 2007). High-resolution MRI studies have shown that hippocampal volumes in depression are decreased bilaterally (Sheline, 2003) or in the left hippocampus only (Bremner *et al.*, 2000). In TLE, volumes may be reduced at the site of seizure origin (Baxendale *et al.*, 2005; Mueller *et al.*, 2007) or, when combined with depression, reduced bilaterally (Baxendale *et al.*, 2005). Nevertheless, $^{1}$H magnetic resonance spectroscopy (MRS) studies revealed reduced glutamate concentrations in the anterior cingulate cortex in depressed adults (Auer *et al.*, 2000) and children (Mirza *et al.*, 2004). In a study by Hasler *et al.* (2007), levels of glutamate/glutamine and GABA were also decreased in prefrontal dorsomedial and ventromedial regions. In TLE, most studies using inter-ictal fluorodeoxyglucose-positron emission tomography (FDG-PET) have confirmed hypometabolism of epileptogenic temporal regions (Manno *et al.*, 1994) such as the hippocampus (Semah *et al.*, 1995), often bilaterally (Joo *et al.*, 2004; Kim *et al.*, 2006). Indeed, orbitofrontal hypometabolism of glucose has been suggested to be a predisposing risk factor for the development of depression in patients with TLE (Salzberg *et al.*, 2006). The relevant mechanisms may include extension of sclerosis and cell loss from the temporal lobe to extratemporal structures (Semah, 2002) or compensatory neuronal inhibition (Salzberg *et al.*, 2006). Alternatively, orbitofrontal hypometabolism may occur secondary to depression or be merely a marker for general cerebral dysfunction associated with TLE (Salzberg *et al.*, 2006).

A strong hypothesis derived from these data, which requires further research, is that neuronal hyperexcitability may be expressed either as impairment of emotions or seizure activity.

One limitation of our study was the inability to identify mood disorders not yet classified by DSM-IV (Krishnamoorthy *et al.*, 2007). Another limitation was the cross-sectional design which did not permit us to identify psychiatric disorders temporally related to seizures (peri-ictal and inter-ictal symptoms). In these situations, mood disorders are different in epileptic patients when compared to subjects from the general population. There is increasing recognition of an association between epilepsy and an affective-somatoform disorder called "inter-ictal dysphoric disorder". The main symptoms of this provisional psychiatric diagnosis are short temper and euphoria. Other less specific symptoms such as depression, pain, insomnia, fear and anxiety, also compose this newly recognised entity (Blumer *et al.*, 2004). As is the case for mood disorders, there is also a common diagnosis of psychotic symptoms in epileptic patients not listed in DSM-IV. This disorder has been named "alternate psychosis", a concept proposed by Tellenbach (1965) based on observations by

Landolt (1953), and typifies a genuine psychosis of epilepsy (POE) due to its close relationship with epileptic activity. At times, ictal psychotic symptoms may be due to a focal non-convulsive status epilepticus, with continuous subclinical epileptiform activity involving one frontal or temporal lobe (Schmitz and Trimble, 2008). Post-ictal psychosis has a prevalence of about 7% in refractory epileptic patients (Tellez-Zenteno *et al.*, 2007), especially when a double independent epileptic focus is present (Graham and Rutter, 1970). Landolt (1953) observed a paradoxical EEG normalisation in epileptic patients during the manifestation of psychotic symptoms, and called this phenomenon "Forced Normalization". Finally, mood changes preceding (Blanchet and Frommer, 1986) or following the epileptic event (Kanner and Balabanov, 2002) are relatively frequent. As ictal phenomena, however, depression (Taylor and Lochery, 1987; Robertson, 1992) and mania (Barczak *et al.*, 1988, Humphries and Dickinson, 1988) are much less frequent.

Although structured interviews are necessary for accurate determination of psychiatric diagnoses in epilepsy, their application in a busy clinical setting is not always feasible. Most rating scales and self-report questionnaires have been developed to screen for psychopathology in non-epileptic patients. Nevertheless, validated screening instruments (such as the Mood Disorder Questionnaire and NDDI-E) were specifically developed to screen for the presence of psychiatric disorders (especially mood disorders) in patients with epilepsy. These instruments are self-rating, can be completed in a few minutes, and can be used with confidence since the risk of overlap with adverse AED effects or pre-existing cognitive problems is minimised (Hirschfeld *et al.*, 2000; Jones *et al.*, 2005; Gilliam *et al.*, 2006).

## Conclusion

In our series of TLE patients, we have found a high prevalence of psychiatric disorders. The most frequent diagnoses were mood and anxiety disorders, which occurred simultaneously in 40% of patients. Our data are consistent with the literature and, in particular, similar to data from European studies *(table 3)*. This is of particular interest since our studied population was composed of European descendents. Thus, the prevalence of psychiatric comorbidities in epileptics in a given population may remain similar to an ancestral population, independent of location in the world. This observation suggests that genetic predisposing factors may be more relevant than eventual environmental factors, an interesting aspect which merits further research. Moreover, with regards to the high prevalence of psychiatric comorbidities in TLE patients, our study is consistent with growing evidence in the literature indicating that TLE and psychiatric disorders share similar physiopathological mechanisms. □

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## References

Almeida-Filho N, Mari JJ, Coutinho E, *et al.* Brazilian multicentric study of psychiatric morbidity: methodological features and prevalence estimates. *Br J Psychiatry* 1997; 171: 524-9.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders IV (Text revision)*. Washington: American Psychiatric Press, 2000.

Araújo Filho GM, Rosa VP, Lin K, Caboclo LOSF, Sakamoto AC, Yacubian EMT. Psychiatric comorbidity in epilepsy: a study comparing patients with mesial temporal sclerosis and juvenile myoclonic epilepsy. *Epilepsy Behav* 2008; 13: 196-201.

Auer DP, Putz B, Kraft E, Lipinski B, Schill J, Holsboer F. Reduced glutamate in the anterior cingulate cortex in depression: an *in vivo* proton magnetic resonance spectroscopy study. *Biol Psychiatry* 2000; 47: 305-13.

Barczak P, Edmunds E, Betts T. Hypomania following complex partial seizures: a report of three cases. *Br J Psychiatry* 1988; 152: 137-9.

Baxendale S, Thompson PJ, Duncan JS. Epilepsy and depression: the effects of comorbidity on hippocampal volume – a pilot study. *Seizure* 2005; 14: 435-8.

Blanchet P, Frommer GP. Mood change preceding epileptic seizures. *J Nerv Ment Dis* 1986; 174: 471-6.

Blumer D, Montouris G, Davies K. The interictal dysphoric disorder: recognition, pathogenesis, and treatment of the major psychiatric disorder of epilepsy. *Epilepsy Behav* 2004; 5: 826-40.

Blumer D, Wakhlu S, Davies K, Hermann B. Psychiatric outcome of temporal lobectomy for epilepsy: incidence and treatment of psychiatric complications. *Epilepsia* 1998; 39: 478-86.

Bredkjaer SR, Mortensen PB, Parnas J. Epilepsy and non-organic non-affective psychosis. National epidemiologic study. *Br J Psychiatry* 1998; 172: 235-8.

Bremner JD, Narayan M, Anderson ER, Staib LH, Miller HL, Charney DS. Hippocampal volume reduction in major depression. *Am J Psychiatry* 2000; 152: 973-81.

Briellmann RS, Hopwood MJ, Jackson GD. Major depression in temporal lobe epilepsy with hippocampal sclerosis: clinical and imaging correlates. *J Neurol Neurosurg Psychiatry* 2007; 78: 1226-30.

Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989; 30: 389-99.

Davies S, Heyman L, Goodman R. A population survey of mental health problems in children with epilepsy. *Dev Med Child Neurol* 2003; 45: 292-5.

Devinsky O. Psychiatric comorbidity in patients with epilepsy: implications for diagnosis and treatment. *Epilepsy Behav* 2003; 4 (Suppl. 4): 2-10.

Devinsky O, Abramson H, Alper K, *et al.* Postictal psychosis: a case control series of 20 patients and 150 controls. *Epilepsy Res* 1995; 20: 247-53.

Edeh J, Toone B. Relationship between interictal psychopathology and the type of epilepsy: results of a survey in general practice. *Br J Psychiatry* 1987; 151: 95-101.

Elger CE, Schmidt D. Modern management of epilepsy: a practical approach. *Epilepsy Behav* 2008; 12: 501-39.

Ettinger A, Reed M, Cramer J. Depression and comorbidity in community-based patients with epilepsy or asthma. *Neurology* 2004; 63: 1008-14.

First MB, Spitzer RL, Gibbon M, Williams J. *Structured Clinical Interview for DSM-IV–TR Axis I disorders–non patient ed.* (SCI I/NP – 2/2001 Revision). Biometric Research Department: New York, 2001.

Forsgren L. Prevalence of epilepsy in adults in northern Sweden. *Epilepsia* 1992; 33: 450-8.

Gaitatzis A, Trimble MR, Sander JW. The psychiatric comorbidity of epilepsy. *Acta Neurol Scand* 2004; 110: 207-20.

Gilliam FG, Barry JJ, Hermann BP, Meador KJ, Vahle V, Kanner AM. Rapid detection of major depression in epilepsy: a multicentre study. *Lancet Neurol* 2006; 5: 399-405.

Glosser G, Zwil AS, Glosser DS, O'Connor MJ, Sperling MR. Psychiatric aspects of temporal lobe epilepsy before and after anterior temporal lobectomy. *J Neurol Neurosurg Psychiatry* 2000; 68: 53-8.

Goldstein MA, Harden CL, Ravdin RD, Labar DR. Does anxiety in epilepsy patients decrease with increasing seizure frequency? *Epilepsia* 1999; 40 (Suppl. 7): 60-1.

Grabowska-Grzyb A, Jedrzejczak J, Naganska E, Fiszer U. Risk factors for depression in patients with epilepsy. *Epilepsy Behav* 2006; 8: 411-7.

Graham P, Rutter M. Organic brain dysfunction and child psychiatric disorder. *Br Med J* 1970; 3: 695-700.

Gudmundsson G. Epilepsy in Iceland: a clinical and epidemiological investigation. *Acta Neurol Scand* 1966; (Suppl. 25): 1-124.

Gureje O. Interictal psychopathology in epilepsy: prevalence and pattern in a Nigerian clinic. *Br J Psychiatry* 1991; 158: 700-5.

Hackett R, Hackett L, Bhakta P. Psychiatric disorder and cognitive function in children with epilepsy in Kherala, South India. *Seizure* 1998; 7: 321-4.

Hasin DS, Goodwin RD, Stinson FS, Grant BF. Epidemiology of major depressive disorder: results from the National Epidemiologic Survey on Alcoholism and Related Conditions. *Arch Gen Psychiatry* 2005; 62: 1097-106.

Hasler G, van der Veen JW, Tumonis T, Meyers N, Shen J, Drevets WC. Reduced prefrontal glutamate/glutamine and gamma-aminobutyric acid levels in major depression determined using proton magnetic resonance spectroscopy. *Arch Gen Psychiatry* 2007; 64: 193-200.

Havlová M. Prognosis in childhood epilepsy. *Acta Univ Carol Med Monogr* 1990; 135: 1-105.

Hermann B, Seidenberg M, Jones J. The neurobehavioural comorbidities of epilepsy: can a natural history be developed? *Lancet Neurol* 2008; 7: 151-60.

Hermann BP, Trenerry MR, Colligan RC. Learned helplessness, attributional style, and depression in epilepsy. Bozeman Epilepsy Surgery Consortium. *Epilepsia* 1996; 37: 680-6.

Hirschfeld RM, Williams JB, Spitzer RL, *et al.* Development and validation of a screening instrument for bipolar spectrum disorder: the Mood Disorder Questionnaire. *Am J Psychiatry* 2000; 157: 1873-5.

Humphries SR, Dickinson PS. Hypomania following complex partial seizures. *Br J Psychiatry* 1988; 152: 571-2.

Jacoby A, Baker GA, Steen N, Potts P, Chadwick DW. The clinical course of epilepsy and its psychosocial correlates: findings from a UK community study. *Epilepsia* 1996; 37: 148-61.

Jalava M, Sillanpaa M. Concurrent illnesses in adults with childhood-onset epilepsy: a population-based 35-year follow-up study. *Epilepsia* 1996; 37: 1155-63.

Jones JE, Hermann BP, Barry JJ, Gilliam F, Kanner AM, Meador KJ. Clinical assessment of Axis I psychiatric morbidity in chronic epilepsy: a multicenter investigation. *J Neuropsychiatry Clin Neurosci* 2005; 17: 172-9.

Joo EY, Lee EK, Tae WS, Hong SB. Unitemporal VS bitemporal hypometabolism in mesial temporal lobe epilepsy. *Arch Neurol* 2004; 61: 1074-8.

Kanner AM. Depression in epilepsy: a neurobiologic perspective. *Epilepsy Curr* 2005; 5: 21-7.

Kanner AM, Soto A, Gross-Kanner H. Prevalence and clinical characteristics of postictal psychiatric symptoms in partial epilepsy. *Neurology* 2004; 62: 708-13.

Kanner AM, Balabanov A. Depression and epilepsy: how closely related are they? *Neurology* 2002; 58 (Suppl. 5): 27-39.

Kessler RC, Berglund P, Demler O, *et al.* The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA* 2003; 289: 3095-105.

Kim MA, Heo K, Choo MK, *et al.* Relationship between bilateral temporal hypometabolism and EEG findings for mesial temporal lobe epilepsy: analysis of 18F-FDG PET using SPM. *Seizure* 2006; 15: 56-63.

Kobau R, Gilliam F, Thurman DJ. Prevalence of self-reported epilepsy or seizure disorder and its associations with self-reported depression and anxiety: results from the 2004 HealthStyles Survey. *Epilepsia* 2006; 47: 1915-21.

Kondziella D, Alvestad S, Vaaler A, Sonnewald U. Which clinical and experimental data link temporal lobe epilepsy with depression? *J Neurochem* 2007; 103: 2136-52.

Krishnamoorthy ES, Trimble MR, Blumer D. The classification of neuropsychiatric disorders in epilepsy: a proposal by the ILAE commission on psychobiology of epilepsy. *Epilepsy Behav* 2007; 10: 349-53.

Landolt H. Some clinical EEG correlations in epileptic psychoses (twilight states). *Electroencephalogr Clin Neurophysiol* 1953; 5: 121.

Lavretsky H, Ballmaier M, Pham D, Toga A, Kumar A. Neuroanatomical characteristics of geriatric apathy and depression: a magnetic resonance imaging study. *Am J Geriatr Psychiatry* 2007; 15: 386-94.

Maillard L, Vignal JP, Gavanet M, *et al.* Semiologic and electrophysiologic correlations in temporal lobe seizures subtypes. *Epilepsia* 2004; 45: 1590-9.

Manchanda R, Schaefer B, McLachlan RS, *et al*. Psychiatric disorders in candidates for surgery for epilepsy. *J Neurol Neurosurg Psychiatry* 1996; 61: 82-9.

Manno EM, Sperling MR, Ding X, *et al*. Predictors of outcome after anterior temporal lobectomy: positron emission tomography. *Neurology* 1994; 44: 2331-6.

Mensah SA, Beavis JM, Thapar AK, Kerr M. The presence and clinical implications of depression in a community population of adults with epilepsy. *Epilepsy Behav* 2006; 8: 213-9.

Mirza Y, Tang J, Russell A, *et al*. Reduced anterior cingulate cortex glutamatergic concentrations in childhood major depression. *Am Acad Child Adolesc Psychiatry* 2004; 43: 341-8.

Mueller SG, Laxer KD, Schuff N, Weiner MW. Voxel-based T2 relaxation rate measurements in temporal lobe epilepsy (TLE) with and without mesial temporal sclerosis. *Epilepsia* 2007; 48: 220-8.

Pascual MRQ. Temporal lobe epilepsy: clinical semiology and neurophysiological studies. *Semin Ultrasound CT MRI* 2007; 28: 416-23.

Patten SB, Wang JL, Williams JV, *et al*. Descriptive epidemiology of major depression in Canada. *Can J Psychiatry* 2006; 51: 84-90.

Perini GI, Tosin C, Carraro C, *et al*. Interictal mood and personality disorders in temporal lobe epilepsy and juvenile myoclonic epilepsy. *J Neurol Neurosurg Psychiatry* 1996; 61: 601-5.

Pond DA, Bidwell BH. A survey of epilepsy in fourteen general practices: II. Social and psychological aspects. *Epilepsia* 1960; 1: 285-99.

Ring HA, Moriarty J, Trimble MR. A prospective study of the early postsurgical psychiatric associations of epilepsy surgery. *J Neurol Neurosurg Psychiatry* 1998; 64: 601-4.

Robertson MM. Affect and mood in epilepsy: an overview with a focus in depression. *Acta Neurol Scand Suppl* 1992; 140: 127-32.

Salzberg M, Taher T, Davie M, *et al*. Depression in temporal lobe epilepsy surgery patients: an FDG-PET study. *Epilepsia* 2006; 47: 2125-30.

Sander JW. The epidemiology of epilepsy revisited. *Curr Opin Neurol* 2003; 16: 165-70.

Schmitz B. Depression and mania in patients with epilepsy. *Epilepsia* 2005; 46 (Suppl. 4): 45-9.

Schmitz B, Trimble M. Psychoses and forced normalization. In: Schachter SC, Holmes GL. *Behavioral Aspects of Epilepsy*. Kasteleijn-Nolst Trenité DGA. New York: Demos Medical Publishing, 2008: 235-43.

Semah F. Temporopolar metabolic abnormalities in temporal lobe epilepsies. *Epileptic Disord* 2002; 4: S41-9.

Semah F, Baulac M, Hasboun D, *et al*. Is interictal temporal hypometabolism related to mesial temporal sclerosis? A positron mission tomography/magnetic resonance imaging confrontation. *Epilepsia* 1995; 36: 447-56.

Sheline YI. Neuroimaging studies of mood disorder effects on the brain. *Biol Psychiatry* 2003; 54: 338-52.

Shukla GD, Srivastava ON, Katiyar BC, Joshi V, Mohan P. Psychiatric manifestations in temporal lobe epilepsy: a controlled study. *Br J Psychiatry* 1979; 135: 411-7.

Silberman EK, Sussamn N, Skillings G, Callanan M. Aura phenomena and psychopathology: a pilot investigation. *Epilepsia* 1994; 35: 778-84.

Stefansson SB, Olafsson E, Hauser WA. Psychiatric morbidity in epilepsy: a case controlled study of adults receiving disability benefits. *J Neurol Neurosurg Neurology* 1998; 64: 238-41.

Strine TW, Kobau R, Chapman DP, Thurman DJ, Price P, Balluz LS. Psychological distress, comorbidities, and health behaviors among U.S. adults with seizures: results from the 2002 National Health Interview Survey. *Epilepsia* 2005; 46: 1133-9.

Swinkels WAM, Kuyk J, van Dyck R, Spinhoven P. Psychiatric comorbidity in epilepsy. *Epilepsy Behav* 2005; 7: 37-50.

Swinkels WAM, Kuyk J, De Graaf EH, Van Dyck R, Spinhoven PH. Prevalence of psychopathology in Dutch epilepsy patients: a comparative study. *Epilepsy Behav* 2001; 2: 441-7.

Taylor DC, Lochery M. Temporal lobe epilepsy: origin and significance of simple and complex auras. *J Neurol Neurosurg Psychiatry* 1987; 50: 673-81.

Tellenbach H. Epilepsie als anfallsleiden und als psychose: üeber alternative psychosen paranoider prägung bei "forcierter normalisierung" (Landolt) des elektroencephalogramme epileptischer. *Nervenarzt* 1965; 36: 190-202.

Tellez-Zenteno JF, Wiebe S. Prevalence of psychiatric disorders in patients with epilepsy: what we think we know and what we know. In: Kanner AM, Schachter S, eds. *Psychiatric Controversies in Epilepsies*. Amsterdam: Elsevier Inc, 2008: 1-18.

Tellez-Zenteno JF, Patten SB, Jetté N, Williams J, Wiebe S. Psychiatric comorbidity in epilepsy: a population-based analysis. *Epilepsia* 2007; 48: 2336-44.

Tellez-Zenteno JF, Wiebe S, Patten SB. Psychiatric comorbidity in epilepsy: a population based analysis. *Epilepsia* 2005; 46: 264-5.

Temkin O. *The falling sickness*. Baltimore: The John Hopkins Press, 1971.

Victoroff JI, Benson F, Grafton ST, Engel Jr J, Mazziotta JC. Depression in complex partial seizures. Electroencephalography and metabolic correlates. *Arch Neurol* 1994; 51: 155-63.

Wrench J, Wilson SJ, Bladin PF. Mood disturbance before and after seizure surgery: a comparision of temporal and extratemporal resections. *Epilepsia* 2004; 45: 534-43.