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Psychiatric Co-Morbidities of Epilepsy in the University Hospitals of Ouagadougou, Burkina Faso

Djingri Labodi LOMPO^{1*}, Julie Adeline KYELEM², Alassane ZOUNGRANA¹, Fabienne KERE¹, Christian NAPON² and Athanase MILLOGO³

¹Tingandogo University Hospital, Health Sciences Training and Research Unit, Joseph Ki-Zerbo University, Ouagadougou, Burkina Faso.

²Yalgado Ouédraogo University Hospital of Ouagadougou, Health Sciences Training and Research Unit, Joseph Ki-Zerbo University, Ouagadougou, Burkina Faso.

³Sourô Sanou University Hospital of Bobo-Dioulasso, Health Sciences Training and Research Unit, Joseph Ki-Zerbo University, Ouagadougou, Burkina Faso.

ABSTRACT

Introduction: Psychiatric co-morbidities in epilepsy are dominated by depression, anxiety disorders and psychotic disorders. They have a negative impact on epilepsy, particularly in terms of increased psychological suffering, impaired quality of life and reduced seizure control. This study was carried out at the Ouagadougou university hospitals, Burkina Faso, with the aim of contributing to better management of patients with epilepsy. Its objectives were to describe the psychiatric co-morbidities of epilepsy and to identify the associated factors.

Patients and Methods: Prospective, descriptive and analytical, multicentre, hospital-based, cross-sectional study, which took place in the Ouagadougou University Hospitals, from 10/07/2021 to 15/12/2021, and involved patients undergoing outpatient treatment for epilepsy. The diagnosis of depressive syndrome was established using the Neurological Disorders Depression Inventory for Epilepsy (NDDIE) scale and that of generalized anxiety disorder using the Generalized Anxiety Disorder -7 (GAD-7) scale. The diagnosis of psychotic disorder was established by psychiatric expertise. The characteristics of patients with epilepsy and the frequency and characteristics of psychiatric comorbidities were analyzed. A bivariate analysis was used to identify factors associated with the risk of depressive syndrome or generalized anxiety disorder, using EPI INFO 7.1.10 software. The value of $p \leq 0.05$ was retained.

Results: One hundred and eleven (111) patients were included in this study, 64 of whom were men (57.7%). The mean age of the patients was 36.9+/-13 years with a mean age of onset of the first seizures of 29+/- 14.8 years. Epilepsy was focal in 56.8%. A high risk of generalized anxiety disorder was detected in 44/111 patients, i.e. 39.6%; an anxiety syndrome was confirmed in 18 patients after psychiatric expertise, i.e. 16.2%; no factors associated with anxiety disorders were identified. A high risk of a major depressive episode was detected in 41/111 patients, i.e. 36.9%; a major depressive syndrome was diagnosed in 25 patients after psychiatric expertise, i.e. 22.5%. Epilepsy with focal neurological signs was significantly associated with a risk of major depressive disorder ($p=0.012$).

Conclusion: Depression, anxiety and chronic psychosis are frequent psychiatric comorbidities of epilepsy in our context, hence the importance of integrated neuropsychiatric management.

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Introduction

Epilepsy co-morbidities are defined as characterized conditions that are not incidentally associated with epilepsy and are observed at any time during the course of the epilepsy and are not a direct consequence of the epilepsy [1]. Data in the literature show an increased frequency of depression (5 to 20 times higher incidence), anxiety disorders and psychotic disorders in patients with epilepsy compared with the general

population. Indeed, it is estimated that around one in three epilepsy patients will develop a psychiatric pathology during their lifetime (compared with one in five in the general population), dominated by mood and anxiety disorders. Patients suffering from focal epilepsy, particularly temporal epilepsy and drug-resistant epilepsy, are more likely to present with psychiatric disorders [2,3]. The relationship between epilepsy and psychiatric co-morbidities could be explained by

Contact: Djingri Labodi Lompo, Tingandogo University Hospital, Health Sciences Training and Research Unit, Joseph Ki-Zerbo University, Ouagadougou, Burkina Faso.

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the existence of common pathogenic mechanisms operating in both epilepsy and psychiatric disorders [4,5].

Co-morbidities have a considerable impact, not only in terms of psychological suffering and altered quality of life, but also on the control of epileptic seizures and the efficacy and tolerance of anti-epileptic treatments. It seems that the existence of a psychiatric disorder associated with epilepsy increases the risk of non-response to anti-epileptic treatments and surgical treatment, increases the risk of death and adds to the socio-economic cost of treatment. Epilepsy and psychiatric disorders are pathologies, which frequently give rise to attitudes of rejection, and the existence of an association further increases the disruption of personal and professional projects and the risk of stigmatization [1-3].

Given the high frequency of epilepsy in our context on the one hand, and on the other hand the massive repercussions of psychiatric comorbidities on the quality of life of epilepsy patients, and their negative impact on the balance of epilepsy, it seemed appropriate to us to carry out the present study in order to contribute to better management of epilepsy patients. This was a prospective cross-sectional hospital study conducted in 2021 in the University Hospitals of Ouagadougou in Burkina Faso, the objectives of which were to describe the psychiatric comorbidities of epilepsy and to identify the associated factors.

Patients and Methods

This was a prospective, descriptive and analytical, multicenter, hospital-based, cross-sectional study, which took place in the Ouagadougou university hospitals (Yalgado Ouedraogo, Tingandogo and Bogodogo university hospitals), from 10/07/2021 to 15/12/2021, i.e. for a period of 05 months. The study-involved patients treated for epilepsy in the neurology departments of the 3 study centers. Patients aged ≥ 18 years, followed for epilepsy diagnosed by a senior neurologist for at least 6 months, in the said services, having given their informed consent to participate in the study, were included in the study.

Patients aged < 18 years, or who had not given their consent to participate in the study, or whose diagnosis was less than 6 months old, or whose diagnosis of epilepsy was uncertain, were not included.

The following psychiatric co-morbidities were sought, whether inter-ictal or post-ictal, on the basis of data in the literature: mood disorders with a depressive tendency (depressive syndrome), anxiety disorders and psychotic disorders [6,7].

The diagnosis of epilepsy has been established by a senior physician specialising in neurology, on the basis of the occurrence in a patient of at least 2 unprovoked or spontaneous epileptic seizures more than 24 hours apart, with or without an electroencephalogram (EEG).

In the context of epilepsy, the diagnosis of depressive syndrome was made using the Neurological Disorders Depression Inventory for Epilepsy (NDDIE) scale and that of generalised anxiety disorder using the Generalized Anxiety Disorder -7 (GAD-7) scale. The diagnosis of psychotic disorders was

made by our senior psychiatrists. The diagnosis of cognitive or behavioral disorders was based on complaints expressed by the patient and/or his family. The sampling technique was non-random, with systematic recruitment of epileptic patients followed as outpatients or hospitalized in the neurology departments of our study centers during the study period.

The following variables were analysed: socio-demographic: age, gender, occupation, level of education, marital status, place of residence; antecedents: risk factors for epilepsy; clinical: type of seizures, age of onset of seizures (year), frequency of seizures, type of epilepsy or epileptic syndrome, etiology of epilepsy, duration of epilepsy, clinical examination data; paraclinical: EEG data, neuroradiological data (CT or brain MRI); treatment: anti-epileptic drugs used, outcome of treatment; psychiatric comorbidities noted: types, frequency. For each patient collected, a pre-established individual data collection form was used, containing information about the patient, his or her illness and treatment, and any psychiatric co-morbidities encountered. The neurological and psychiatric consultation and hospitalization registers of the 3 university hospitals served as databases for the study population. Eligible patients were then contacted by telephone for an interview and clinical examination. During the interview with each patient, after explaining the nature of the study and obtaining the patient's verbal informed consent, we carried out an interview and clinical examination and used the various complementary examinations (EEG and/or brain CT or MRI), possibly supplemented by a documentary review of the patient's medical file and health record. The Neurological Disorders Depression Inventory for Epilepsy (NDDIE) and the Generalized Anxiety Disorder-7 (GAD-7) questionnaires were systematically administered to each patient to screen for the risk of major depressive disorder and the risk of generalized anxiety disorder. Patients with epilepsy who had an NDDIE > 15 score were screened for risk of depressive syndrome and those with a GAD-7 > 7 score were screened for risk of generalized anxiety disorder. These patients were then invited to attend the specialist psychiatric consultation in order to confirm or rule out the suspected psychiatric comorbidity.

The NDDIE questionnaire, designed and validated in English and then translated and validated in French, is a screening tool for the depressive syndrome in the context of epilepsy. It is a rapid screening self-questionnaire consisting of the following six items: everything is a struggle; nothing I do is right; I feel guilty; I'd be better off dead; I feel frustrated; I have difficulty finding pleasure. Each item is rated from 1 to 4 according to its frequency (1: Never; 2: Rarely; 3: Sometimes; 4: Always or often). It takes into account the specific features of depression in patients with epilepsy and, for example, does not assess the dimension of sadness, which is non-specific. A score above 15 (ranging from 6 to 24) indicates a high risk of a current major depressive episode.

The GAD-7 (Generalized Anxiety Disorder -7) questionnaire is a rapid, reliable tool, validated in French (4) and relevant for screening for generalized anxiety disorder. The GAD-7 scale consists of the following seven items: a feeling of nervousness, anxiety or tension; an inability to stop worrying or to control

one's worrying; excessive worrying about different things; difficulty in relaxing; restlessness such that it is difficult to hold still; a tendency to be easily upset or irritable; a feeling of fear as if something terrible might happen. Each item is scored from 0 to 3 (0: Never; 1: Several days; 2: More than half the time; 3: Almost every day, over the past two weeks). The total score is obtained by adding up the score obtained for each item (score ranging from 0 to 21). A total score strictly greater than 7 should raise suspicions of generalized anxiety disorder. The GAD-7 is not a diagnostic scale for generalized anxiety disorder, nor is it a severity scale for the disorder. It is a screening scale. When the score is higher than 7, it is advisable to have the diagnosis confirmed by a clinical psychiatric assessment.

The data were recorded on a microcomputer and analyzed using EPI INFO software version 7.1.10. Microsoft Word and Excel were used to write the document and construct the figures. Quantitative variables were expressed in terms of mean +/- standard deviation, and qualitative variables in terms of numbers and percentages. The chi-square test was used to compare qualitative variables for numbers greater than or equal to 5, and the Fischer exact test for numbers less than 5. Student's t-test was used to compare quantitative variables. A bivariate analysis using the risk of depression (present/absent) as the dependent variable and the characteristics of the epilepsy patients as the independent variables was used to identify the factors associated with the risk of depression. The same procedure was used to identify factors associated with the risk of generalized anxiety. A p-value of less than 0.05 was considered statistically significant.

The data was collected with the authorization of the general management of the various health facilities.

The data collection forms were filled in on site after obtaining the patient's consent, and the data collected remained confidential.

Results

During our study period, 111 patients were enrolled. The mean age of our patients was 36.9 +/- 13 years (18 to 82 years). The majority of patients (64 or 57.7%) were male, with a sex ratio of 1.4:1. The 25-35 age group was the most represented, with 56 cases (50.4%). The majority of patients had at least secondary education (67.6%), were married (59.5%), were civil servants (28.8%) or in the informal sector (24.3%); 36 patients (32.4%) had a history of potentially epileptogenic brain lesions.

The mean age at onset of seizures was 29 +/- 14.8 years (2 to 78 years). The average duration of epilepsy was 8.1 +/- 8.3 years (1 to 54 years). The majority of patients, 57 cases (51.4%), had generalized seizures. Generalized tonic-clonic seizures (GTCS) with 45 cases (40.5%), focal seizures (FS) without altered consciousness with 32 cases (28.8%) and FS with secondary tonic-clonic bilateralisation with 25 cases (22.5%) were the most frequent types of epileptic seizures. The most frequent frequency of seizures was monthly, with 51 cases (46%). Focal neurological deficit in 39 cases (35%), cognitive deterioration in 18 cases (16.2%) and behavioural disorders in 20 cases (18%)

were the main neuropsychological clinical signs observed. On inter-critical EEG, 98 patients (88.3%) had paroxysmal epileptic abnormalities. Epilepsy was focal in 56.8%. Cerebral CT scans were performed in 59 cases (53.2%) and revealed potentially epileptogenic cerebral lesions in 22 cases (37.3%), dominated by cortical atrophy in 11 cases (18.6%). The etiologies of the epilepsies were known in 65 patients (58.6%), dominated by presumed genetic causes in 29 cases (26.1%) and central nervous system infections in 15 cases (13.5%). Carbamazepine (41 cases, 36.9%) and phenobarbital (33 cases, 29.7%) were the most commonly prescribed anti-epileptic drugs. The distribution of patients according to socio-demographic, clinical, paraclinical and therapeutic characteristics is summarised in Table 1.

Table 1: Breakdown of patients by socio-demographic, clinical, paraclinical, etiological and therapeutic characteristics.

Socio-demographic variables	Numbers (n=111)	Percentages (%)
Male gender		
Age groups		
<25 years	17	15.3
25- 35 years old	39	35.1
36 - 45 years old	32	28.8
46 - 55 years old	9	8.1
56 - 65 years old	11	9.9
>65 years old	3	2.7
Level of education		
No	14	12.6
Primary	22	19.8
Secondary	54	48.7
Superior	21	18.9
Marital status		
Married	66	59.5
Single	44	39.6
Divorced	1	0.9
Socio-professional categories		
Civil servant	32	28.8
Pupils/students	24	21.6
Informal sector/farmers	27	24.3
Housekeeper	11	9.9
Unemployed	7	6.3
Craft trade	6	5.4
Retired	4	3.6
Risk factors for epilepsy		
History of potentially epileptogenic brain lesions	36	32.4
Family history of epilepsy	14	12.6
Types of crisis		
Generalised seizures	57	51.3
Generalised motor seizures	53	47.7
Other generalised seizures	8	0.9
Tonic-clonic generalised seizures	45	40.5
Non-motor generalised seizures	4	3.6
Focal seizures	54	48.6
With altered consciousness	22	19.8
Without impairment of consciousness	32	28.8
Focal seizure with secondary bilateral tonic-clonic onset	25	22.5
Average frequency of epileptic seizures		
Daily	7	6.3
Weekly	14	12.6

Monthly	51	46
Quarterly	5	4.5
Annual	34	30.6
Associated neurological and neuropsychological signs		
Focal neurological deficit (BMI, post-stroke neurological deficit, aphasia)	39	35.1
Major cognitive disorders (mental retardation, memory problems, intellectual disability, etc.)	18	16.2
Permanent behavioural problems	28	25.5
EEG aspects		
Normal EEG		
Paroxysmal epileptic seizures	98	88.3
Generalised / diffuse paroxysms	32	32.6
Lateral paroxysms (Hemispheric)	12	12.2
Localised / focused paroxysms		
Fronts	38	38.7
Occipitals	3	3.0
Temporary	8	8.1
Parietal	5	5.1
Results of cerebral CT scan	n= 59	Percentage (%)
Normal brain CT	32	54.2
Cerebral atrophy (cortical and/or cortico-subcortical)	11	18.6
Porencephalic cavity	6	10.2
Stroke after-effects	5	8.5
Other lesions (hippocampal sclerosis =1, meningioma=2, cavernoma=1, glioma =1)	5	8.5
Causes of epilepsy		
Epilepsy of known causes		
Presumed genetic	29	26.1
After-effects of cranioencephalic trauma	10	9
Stroke after-effects	5	4.5
Central nervous system infections	15	13.5
Perinatal encephalopathy	6	5.4
Brain tumour	3	2.7
Other	2	1.8
Epilepsy of unknown cause	41	36.9
Anti-epileptic drugs used		
Carbamazepine	41	36.9
Phenobarbital	33	29.7
Lamotrigine	22	19.8
Sodium valproate	15	13.5
Levetiracetam	4	3.6
Gabapentin	1	0.9

As part of the screening for generalized anxiety disorder, the average GAD-7 score was 7+/-3.4 points (extremes 0 to 15); a high risk of generalized anxiety disorder was detected in 44/111 patients, i.e. 39.6%; an anxiety syndrome was confirmed in 18 patients after psychiatric expertise, i.e. 16.2%.

As part of the screening for the risk of a major depressive episode, a mean NDDI-E score of 11.8+/-3.9 points (extremes 6 to 19 points) was found; a high risk of a major depressive episode was detected in 41/111 patients, i.e. 36.9%; a major depressive syndrome was diagnosed in 25 patients after psychiatric expertise, i.e. 22.5%.

Among our patients with epilepsy, 6 (5.4%) were also under psychiatric care for chronic psychotic disorders with a schizophrenic aspect, occurring during an inter-critical period.

In bivariate analysis, only a duration of epilepsy >15 years tended to be associated with the risk of generalised anxiety disorder (p=0.09) (see Table 2).

Table 2: Results of bivariate analysis looking for factors associated with the risk of generalised anxiety disorder.

Independent variables	Risk of generalised anxiety disorder	No risk of generalised anxiety disorder	P
Male sex	26 (40.6%)	38(59.3%)	0.4
Age ≤ 25 years	6(35.2%)	11(64.7%)	
Age > 25	38(40.4%)	56(59.5%)	0.35
Educated	37(38.1%)	60(61.8%)	
Not instructed	7(50%)	7(50%)	0.20
Rural residence	2 (22.2%)	7 (77.7%)	
Urban residence	42 (41.1%)	60(58.8%)	0.14
Single	15 (34%)	29(65.9%)	
Married	29(43.9%)	37(56%)	0.47
In operation	38 (38%)	62 (62%)	
Retired	3 (75%)	1 (25%)	
Unemployed	3 (42.9%)	4 (57.1%)	0.63
Presence of risk factors for epilepsy	19(38%)	31(62%)	
No risk factors for epilepsy	25(40.9%)	36(59%)	0.37
Focal seizures	19(35.1%)	35(64.8%)	
Generalised seizures	25(43.8%)	32(56.1%)	0.17
Frequent attacks	30 (41.7%)	42 (58.3%)	
Rare crises	14 (35.9%)	25 (64.1%)	0.76
Generalised epilepsy	21(43.7%)	27(56.3%)	
Focal epilepsy	23(36.5%)	40(63.4%)	0.36
Presence of focal neurological signs	16(47%)	18(52.9%)	
Absence of focal neurological signs	28(36.3%)	49(63.6%)	0.14
Duration of epilepsy ≤ 15 years	33 (35.9%)	59 (64.1%)	
Duration of epilepsy > 15 years	11 (57.8%)	8 (42.2%)	0.09
Generalised or diffuse epileptic paroxysms	17 (38.6%)	27 (61.4%)	
Focal epileptic paroxysms	20(37%)	34(62.9%)	0.91
Presence of potentially epileptogenic brain lesions on CT scan	7(31.8%)	15(68.1%)	
Absence of potentially epileptogenic brain lesions on CT scan	14(36.8%)	24(63.1%)	0.35
Monotherapy	40 (40%)	60(60%)	
Pluritherapy	4 (36.3%)	7(63.6%)	0.54

Concerning the risk of major depressive disorder, in bivariate analysis, only epilepsy with focal neurological signs was significantly associated with the risk of major depressive disorder (p=0.012) (see table 3).

Table 3: Results of bivariate analysis looking for factors associated with the risk of major depressive disorder in patients with epilepsy.

Variables	Yes	No	P
Gender			
Female	16(34%)	31(65.9%)	
Male	25(39%)	39(60.9%)	0.29
Age			
<25	5(29.4%)	12(70.5%)	
≥ 25	36(38.3%)	58(61.7%)	0.25

Level of education			
Educated	36(37.1%)	61(62.8%)	0.46
Not instructed	5(35.7%)	9(64.2%)	
Residence			
Rural	2(22.2%)	7(77.7%)	0.28
Urban	39(38.2%)	63(61.7%)	
Marital status			
Single	15(33.3%)	30(66.6%)	0.80
Married	26(39.3%)	40(60.6%)	
Profession			
Assets	38(38%)	62(62%)	0.78
Retired	1(16.6%)	5(83.3%)	
Unemployed	2(50%)	2(50%)	
Risk factors for epilepsy			
Yes	22(44%)	28(56%)	0.08
No	19(31.1%)	42(68.8%)	
Type of epileptic seizures			
Focal seizures	22(40.7%)	32(59.2%)	0.35
Generalised seizures	19(33.3%)	38(66.6%)	
Frequency of attacks			
Rare crises	14 (35.9%)	25 (64.1%)	0.91
Frequent attacks	27(37.5%)	45(62.5%)	
Type of epilepsy			
Focal length	21(32.8%)	43(67.2%)	0.63
General	20(42.5%)	27(57.4%)	
Associated neurological abnormalities			
Yes	18(52.9%)	16(47.1%)	0.012
No	23(28.7%)	54(67.5%)	
Length of time epilepsy lasts			
<5	30(32.6%)	32(67.4%)	0.17
≥15	11(57.8%)	8(42.1%)	
Type of paroxysms			
Generalised or diffuse paroxysms	9 (28.1%)	23 (71.9%)	0.65
Focal paroxysms	28 (35.4%)	51 (64.6%)	
Epileptogenic lesions on CT scan			
Yes	9(40.9%)	13(59%)	0.18
No	11(28.9%)	27(71%)	
Type of treatment			
Monotherapy	38(38%)	62(62%)	0.36
Dual therapy	3(27.2%)	8(72.7%)	

Discussion

The limitations of this study include the relatively small size of our sample and its cross-sectional nature, including adult epilepsy patients from different cultural backgrounds, mainly living in urban areas. In this study we were only interested in anxiety, depression and psychosis, whereas the psychiatric comorbidities of epilepsy are more numerous and complex [8-10]. However, these few limitations do not call into question the validity of our study and allow comparisons with other data in the literature.

Several studies have assessed the prevalence of psychiatric disorders in epilepsy. They are characterised by considerable heterogeneity, due to differences in study populations (population studies versus hospital studies, all types of epilepsy versus selected epilepsies, in particular focal temporal or frontal epilepsy, epilepsy refractory to treatment; adult epilepsy versus child epilepsy, etc.) and study types (psychiatric comorbidities diagnosed by specialist psychiatric examination versus screening by self-report using scales, prospective versus retrospective studies).

Some population-based studies have found several psychiatric comorbidities confirmed by a specialist psychiatric examination, with the following prevalence rates: mood disorders, 24 to 74%; depression, 30%; anxiety disorders, 10 to 25%; psychoses, 2 to 7% and personality disorders, 1 to 2% [6,8,9,11]. In a recent hospital study in Brazil, depression (22.8%), anxiety disorders (17.8%) and psychosis (10%) were the main psychiatric comorbidities clinically diagnosed in epilepsy [12]. Almost similar results were found in our study: depressive syndrome 22.5%, generalised anxiety syndrome 17.2%, psychosis 5.2%.

On the other hand, studies by Strine et al. (2005) and Kobau et al. (2006), which assessed the prevalence of psychiatric comorbidities in a population on the basis of self-reported depressive and/or anxiety symptoms using questionnaires, found higher rates, of around 1/3 of epilepsy patients for the depressive syndrome and 15% for generalised anxiety disorder [13,14]. Our study, like other hospital studies carried out in Morocco, using self-screening questionnaires, also found high prevalences, in the order of 25.8% and 35.1% for major depressive episodes (36.9% for our study) and 28.1% and 48.2% for anxiety disorders (39.6% for our study) [15,16]. This discrepancy is not surprising, since not all psychiatric symptoms necessarily represent psychiatric pathologies.

It has been reported that the prevalence of major depression is higher in patients with frontal or temporal lobar epilepsy or refractory epilepsy, or epilepsy secondary to an epileptogenic structural lesion, or in patients with learning difficulties. The development of depression may be a reaction to life stress, or more generally linked to biological factors, such as frontal or temporal lobar dysfunction, or the adverse effects of MAEs [11,17]. In our series, we found a significant link between the risk of depression and focal neurological signs associated with epilepsy.

The prevalence of psychosis in epilepsy reported in studies varies from 2 to 7% [17-21]. This prevalence is higher in patients with frontal or temporal lobar epilepsy and/or refractory epilepsy, ranging from 10% to 19% in most studies [17]. These disorders may take the form of chronic interictal psychosis with a schizophrenic appearance, as in our study, or an episodic psychotic state usually associated with epileptic activity. Epilepsy and psychosis may result from a brain dysfunction common to both; however, psychosis may be a consequence of epileptic activity through remodelling of amygdalo-hippocampal networks [18-21].

Conclusion

Depression, anxiety and chronic psychosis are frequent psychiatric comorbidities of epilepsy in our context. The depressive syndrome appears to be more frequent in patients with epilepsy caused by lesions. Our study confirms the value of integrated neurological and psychiatric management of epilepsy.

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