To what extent does depression influence quality of life of people with pharmacoresistant epilepsy in Argentina?

Laura Scévola [a,c], Mercedes Sarudiansky [a], Alejandra Lanzillotti [a], Silvia Oddo [a,b], Silvia Kochen [a,b], Luciana D'Alessio [a,b]

[a] *Epilepsy Center, Ramos Mejía y El Cruce Hospital, EnyS-CONICET, Buenos Aires, Argentina*

[b] *Universidad de Buenos Aires, IBCN-CONICET, Buenos Aires, Argentina*

[c] *Mental Health Center, Ramos Mejía Hospital, Buenos Aires, Argentina*

Abstract

Introduction: Depression is the most frequent psychiatric co-morbidity in patients with epilepsy. Lifetime preva- lence of depression is reported more frequently in temporal lobe epilepsy and is estimated at 35%. This co- morbidity appears to be related with various mechanisms. The aim of this study was to determine the quality of life (QoL) of patients with pharmacoresistant epilepsy with and without co-morbid depression in an Argentin- ean population.

Methods: Patients admitted to the video-EEG monitoring unit during the period 2010–2013 went through a stan- dardized psychiatric assessment using SCID-I (Structured Clinical Interview for Axis I diagnoses of DSM-IV), BDI II (Beck Depression Inventory) GAF (Global assessment of functioning), and Q LES Q-SF (for quality of life). Patients were divided in two groups: with and without depression (according to DSM-IV). Sociodemographic data, BDI II scores, GAF, and quality of life (QoL) were compared between the two groups. Comparisons were made using Student's *t*-test and Mann—Whitney *U* test. Frequency distributions were compared by Chi-square test. Spearman correlation coefficients were determined.

Results: Seventy-seven patients with pharmacoresistant epilepsy were eligible for this study, 41 patients were included in the group with depression (mean BDI II 15.93), and 36 in the group without depression (mean BDI II 3.36) ($p = 0.001$). The overall QoL was significantly lower in the group with depression compared to the group without depression (p b 0.01). The most affected areas were: physical health ($p = 0.013$), mood ($p = 0.006$), course activities (referring to school as well as to hobbies or classes outside of school) ($p = 0.003$), leisure time activities ($p = 0.011$), social activities ($p = 0.047$), general activities ($p = 0.042$), and medication ($p = 0.022$). Severity of depression according to BDI II had a negative correlation with overall QoL (r - 0.339, p b 0.01). No correlations were found between seizure frequency, QoL and BDI II.

Conclusion: Patients with pharmacoresistant epilepsy and co-morbid depression reported worst QoL. Depression disrupts daily functioning (leisure, social functioning) and is a negative influence for subjective perception of health and medication. Interdisciplinary treatment should be considered (neurology— psychiatry— psychotherapy).

1. Introduction

Depressive disorders are the most frequent psychiatric co-morbidity in patients with epilepsy. Thirty percent of people with pharmacore- sistant epilepsy suffer from psychiatric disorders and the lifetime prev- alence of depression is estimated at 35% [1—4].

In recent years, the existence of common pathogenic pathways between depression and epilepsy has been suggested. Different neurotrans- mitters and neurobiological alterations involving psychic functioning and emotional processing have been found in both conditions. Furthermore, some antiepileptic drugs (AEDs) may cause depression or intensify symptoms, while others may improve mood [1,5,6]. On the other hand, there are psychosocial factors that contribute to depression, like social stig- ma, family overprotection, low socio-economic level, low self-esteem, un- employment, and the chronicity of the disease [1,7—9].

There is a clear association between depression and poor quality of life (QoL) in people with epilepsy [1—10]. Increased levels of depressive symptoms were associated with lower quality of life [11]. Many studies found that QoL in people with epilepsy is lowered by epilepsy severity and poor seizure control, AED side effects, cognitive impairment, underlying neurological disease, perceived stigma, and incomplete sei- zure control after epilepsy surgery [12—19]. Nevertheless, co-morbid psychiatric illnesses, especially depression, represent a significant factor that negatively influences QoL, even more than seizure frequency [11, 20—23].

• Corresponding author at: Padilla 1270 d. 1414, Buenos Aires, Argentina.

E-mail address: laurascevola@gmail.com (L. Scévola).

The aim of this study was to determine the association between co-morbid depression and QoL in patients with pharmacoresistant epilepsy in an Argentinean population. Few data are available on this subject in South America, so we consider that this work is essential to cover a gap of knowledge in the region [24].

2. Methods

Patient selection

Patients consecutively admitted to the Epilepsy Center of Hospital Ramos Mejía (ECRMH) during 2010-2013 were included. Patients were admitted to confirm the diagnosis of epilepsy and to determine the possibility of surgical treatment. The ECRMH is the major public referral center of epilepsy in Buenos Aires City, Argentina. As a tertiary referral center, it serves a population drawn from other parts of the country, with high rates (70-80%) of pharmacoresistant epilepsy. All patients received AEDs according to international protocols. The Public Epilepsy Program facilitates access to major AEDs which are freely available [25,26]. Sociodemographical data (age, educational level, occupational status, marital status) were obtained from electronic medical records.

Inclusion criteria

Patients aged between 18 and 65 years with pharmacoresistant epilepsy with and without positive MRI findings were included. Pharmacoresistant epilepsy was defined as a failure to achieve sustained seizure control (no seizures for a period of 12 months or prolongation of three times the preintervention interseizure interval, whichever is longer), with at least two trials of well-tolerated, appropriately chosen, and adequately scheduled AEDs (irrespective of being administered as monotherapy or in combination) [27].

Patients with depression were considered when depressive disorder was the principal psychiatric diagnosis (according to SCID-I) and fulfilled criteria for at least one current and/or past episode of Axis I affective (depressive) disorder according to DSM-IV [28] including: Major Depressive Disorder, Dysthymic disorder and Adjustment disorder with Depressed Mood. Only patients with primary depressive disorder were included.

Exclusion criteria

Patients with generalized epilepsy and/or non pharmacoresistant epilepsy were excluded.

Patients who met criteria for other main psychiatric disorder codified in AXIS I of DSM-IV (according to SCID-I) were also excluded. In these cases, depressive symptoms may be secondary to other main psychiatric disorders, such as psychotic disorders, bipolar disorders, anxiety disorders, substance abuse disorders, etc. Patients with co-morbid psychogenic non-epileptic seizures (PNES) and mental retardation (attending a special school and/or having an IQ b 70 according to the Wechsler Adult Intelligence Scale, third edition) (WAIS-III) [29] were also excluded.

Complementary studies

Video EEG evaluation

All patients included in this study had a diagnosis of pharmacoresistant epilepsy and underwent video-EEG evaluation in order to determine the epilepsy subtype, the epileptogenic zone, and the possibility of epilepsy surgery. For video-EEG monitoring, a Stellate-Bioscience EEG machine at a 200-Hz sample rate was used. All ictal recordings were obtained using the international 10-20 system, with the addition of temporal electrodes of the 10-10 system. Referential montages as well as longitudinal–bipolar and transverse bipolar montages were used for the analysis.

2.2.2. Magnetic resonance imaging

All patients had magnetic resonance imaging (MRI) with a temporal lobe epilepsy protocol. The sequences used were the following: Sagittal plane T1-weighted image for the purpose of detecting the hippocampus in the parasagittal slices; inversion-recovery (IR) pulse sequence, fluid-attenuated IR (FLAIR), and three-dimensional gradient echo sequence (volumetric), perpendicular to the long axis of the hippocampus, and T2-weighted axial sequence parallel to the long axis of the hippocampus.

Psychiatric assessment

Psychiatric diagnoses

All patients were evaluated using a standardized psychiatric assessment – the Structured Clinical Interview for Axis I diagnoses of DSM-IV (SCID-I)– [30]. Global assessment of functionality (GAF) was determined in all patients. The GAF is a numeric scale (0 through 100) comprised in Axis V of DSM-IV [28]. This scale rates the social, occupational,

Table 1
Demographic and clinical variables in patients with pharmacoresistant epilepsy with and without co-morbid depression (n = 77).

		With depression (n = 41)	Without depression (n = 36)	p-value
		n (%)		
Sex	Women	22 (53.66)	17 (47.22)	0.573
	Men	19 (46.34)	19 (52.78)	
Employment	Unemployed	11 (27)	8 (22)	0.662
	Underemployed	9 (22)	12 (33)	
	Working	11 (27)	11 (31)	
	Student	7 (17)	4 (11)	
	Disability	3 (7)	1 (3)	
Education	Less than 12 years	20 (49)	26 (72)	0.036
	More than 12 years	21 (51)	10 (28)	
Marital status	Single	21 (51)	21 (58)	0.587
	Married	17 (42)	13 (36)	
	Divorced	3 (7)	1 (3)	
Epilepsy type	Temporal	38 (93)	32 (89)	0.494
	Parietal	0 (0)	1 (3)	
	Frontal	3 (7)	2 (5)	
	Occipital	0 (0)	1 (3)	
Age				
Mean (SD)		32.10 (9.63)	32.81 (13.33)	
Median (range)		32.00 (19-54)	27.50 (18-63)	0.686
Mean rank		39.96	37.90	
Sum of ranks		1638.50	1364.50	
Age at onset of epilepsy				
Mean (SD)		12.77 (9.27)	10.12 (8.63)	0.204
Duration of epilepsy				
Mean (SD)		20.30 (10.89)	22.36 (13.59)	0.465
Seizure frequency				
Mean (SD)		7.73 (9.94)	10.50 (10.98)	
Median (range)		4 (0-30)	4.50 (1-30)	0.071
Mean rank		34.74	43.85	
Sum of ranks		1424.50	1578.50	
GAF total score				
Mean (SD)		69.73 (11.68)	72.11 (7.27)	
Median (range)		70.00 (19-88)	71.50 (55-90)	0.298
Mean rank		36.96	41.32	
Sum of ranks		1515.50	1487.50	
QlesQ total score				
Mean (SD)		64.99 (15.29)	77.56 (11.70)	0.001
BDI–II total score				
Mean (SD)		15.93 (7.89)	3.36 (2.92)	
Median (range)		14.00 (1-36)	3.00 (0-10)	0.001
Mean rank		55.56	20.14	
Sum of ranks		2278.00	725.00	

Bold signifies statistical significance.

and psychological functioning of adults according to the psychiatrist's perspective.

Beck Depression Inventory was administered (BDI II) [31] to quantify the severity of depressive symptoms. The BDI II is a widely used self-administered scale consisting of 21 items. The final score ranges between 0 and 63. A score of 10 points or over indicates presence of depressive symptoms.

The psychiatric assessment was performed by trained psychiatrists, during the video-EEG monitoring (which usually lasts five days). Psychiatric evaluation was carried out when patients were lucid, able to answer all the questions. If the patient had a seizure, the interview was interrupted until the postictal period ended.

2.3.2. Quality-of-life assessment

In this study, a QoL generic scale designed to study any health condition was chosen.

Quality of life was measured with the Quality of Life Enjoyment and Satisfaction Questionnaire Short Form (Q-LES-Q SF) [32]. It is a self-report test designed to enable investigators to easily obtain sensitive data of the degree of enjoyment and satisfaction experienced by subjects in various areas of daily functioning. It has been shown to offer high internal consistency, validity, and reproducibility in non-psychiatric populations and in patients within a range of psychiatric illnesses.

Statistical analyses

Two groups of patients with and without co-morbid depression, according to inclusion and exclusion criteria, were compared. For continuous variables, Student's *t*-test and/or Mann-Whitney *U*-test were determined. Proportions were evaluated using Chi-square test for independence (χ^2). Correlations between continuous variables were examined using a Spearman's rank correlation coefficient. The statistical significance was fixed at p b 0.05.

Ethical committee and informed consent

Approval of the Ethics Committee of Ramos Mejía Hospital was obtained to conduct the study in accordance with the ethical standards established in the 1964 Declaration of Helsinki, and all the subjects submitted informed consent.

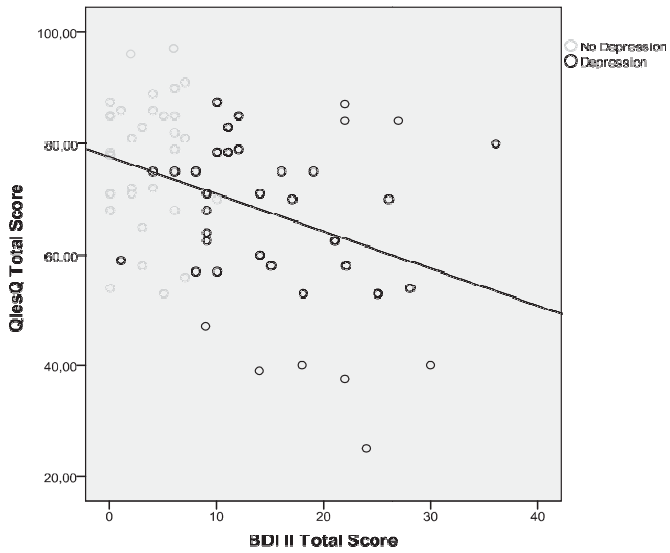

Fig. 2. Correlation between QoL and depression severity. ($Rho = -0.339, p = 0.003$).

3. Results

During 2010–2013, 150 patients were consecutively admitted, 104 completed all the protocols, and 77 were eligible for inclusion. Fifteen patients were excluded because of significant cognitive dysfunction and 12 because of other main co-morbid psychiatric disorders codified in Axis I (nine psychotic disorders, one post traumatic stress disorder, one anxiety disorder, and one substance abuse). Forty-one patients who met criteria for depression and 36 patients without depression were included. No significant differences in age, sex, and seizure frequency were found between the groups. Sociodemographic data are shown in Table 1.

Mean BDI II score was significantly higher in the group with co-morbid depression (p = 0.001). GAF score did not show significant differences (Mann–Whitney *U*-test) (Table 1).

Mean QoL was significantly lower in the group with co-morbid depression (p = 0 .001). Significant differences with lower scores were observed in the areas: physical health (p = 0.013), mood (p = 0.006), course activities (referring to school as well as to hobbies or classes outside of school) (p = 0.003), leisure time activities (p = 0.011),

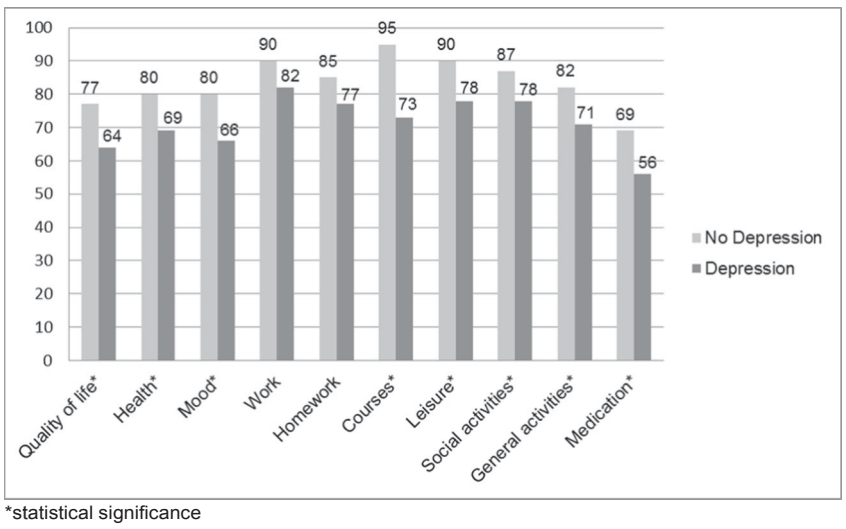

Fig. 1. Differences in QlesQ ítems between patients with pharmacoresistant epilepsy with or without co-morbid depression. Asterisk signifies statistical significance.

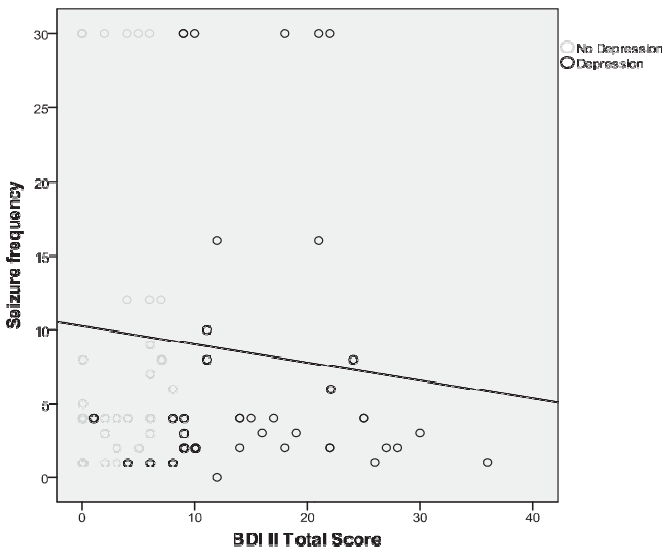

Fig. 3. Correlation between seizure frequency and depression severity. (*Rho* = −0.078, *p* = 0.499).

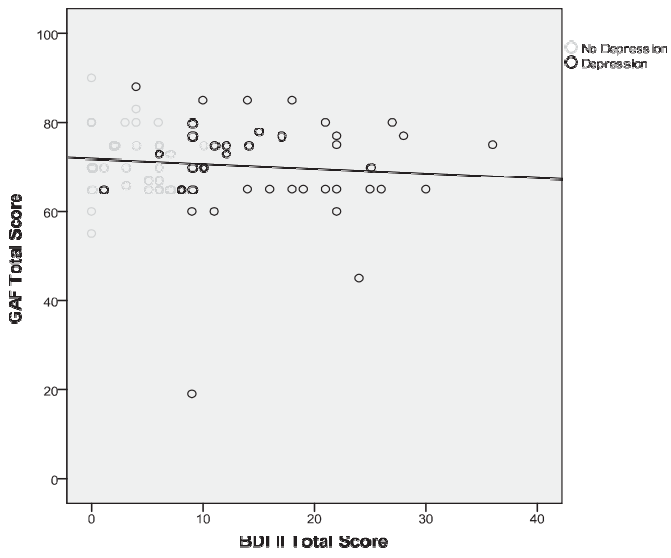

Fig. 5. Correlation between general functioning and depression. (*Rho* = −0.125, *p* = 0.280).

social activities (p = 0.047), general activities (p = 0.042), and medication (p = 0.022) (Mann–Whitney *U*-test) (Fig. 1).

There was a significant negative correlation between BDI II score (severity of depression) and QoL (Spearman's rho = − 0.339; p = 0.003) (Fig. 2). No significant differences were found between seizure frequency/BDI II score (Fig. 3), seizure frequency/QoL (Fig. 4), and GAF/BDI II score (Fig. 5).

The subtypes of depression, classified according DSM-IV are shown in Fig. 6.

4. Discussion

The link between epilepsy and depression is complex. Depression could be a risk factor for developing epilepsy [2,4,5,33,34] and people with epilepsy suffer depression more frequently than the general population, particularly patients with pharmacoresistant epilepsy compared to patients with well-controlled seizures [1]. In this study, we analyzed the QoL of patients with focal pharmacoresistant epilepsy with confirmed diagnosis by video-EEG monitoring in a tertiary care center in Argentina and determined the presence of co-morbid depression using DSM-IV nosography. Many studies determined the QoL in patients with epilepsy [11-19] and in patients with epilepsy and depression [20–23,35], nevertheless these studies did not use psychiatric structured interviews based on current nosography, such as DSM-IV [28] and/or ICD-10 [36]. These interviews are important to diagnose and exclude other psychiatric disorders (anxiety, posttraumatic stress disorder, psychosis), which can also result in high scores on depression scales (for example, BDI II).

Despite different sociocultural and environmental factors, in this study we found that the negative correlation of depression and quality of life was similar to that reported in other regions [2,7–10,15,20,24]. However, a lack of BDI II correlation with GAF was found. This finding

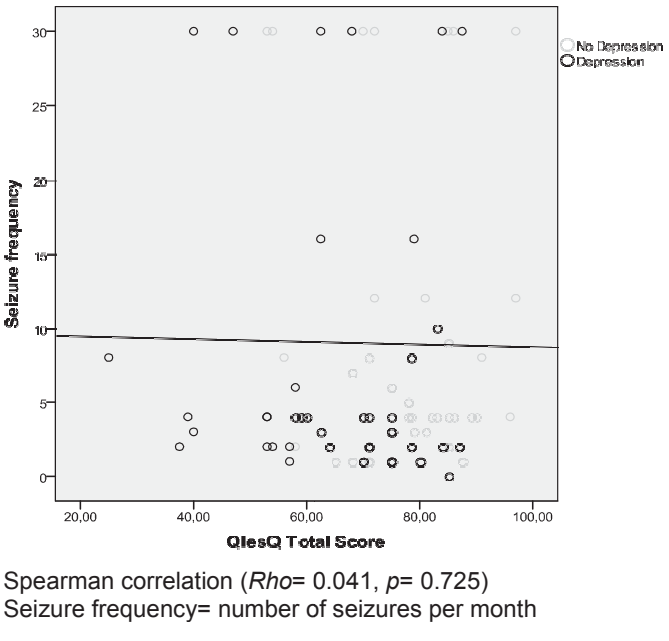

Fig. 4. Correlation between seizure frequency and QoL (*Rho* = 0.041, *p* = 0.725) Seizure frequency = number of seizures per month.

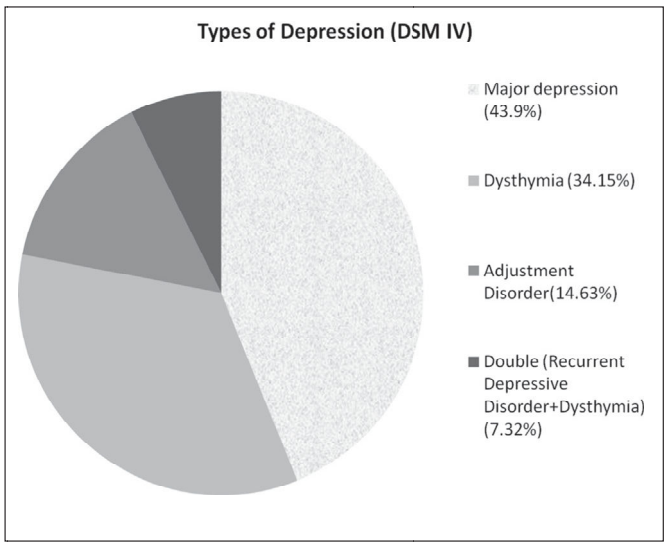

Fig. 6. Subtypes of depression according to DSM-IV.

may be explained because quality of life emphasizes the patient's perception and experience of the disease, while GAF reflects the physician's assessment of general functioning.

In this study we found the absence of significant correlations between seizure frequency and QoL. Similar to these results, other studies from tertiary epilepsy referral centers found that depression was associated with low health-related QoL that persisted after controlling for seizure frequency, seizure severity, and other psychosocial variables [15,20–23]. Nevertheless our study was determined in patients admitted for video-EEG monitoring, and we cannot extrapolate these results to all epilepsy patients. Indeed, there are still controversies in the literature, and data available based on community samples demonstrated depression was associated with frequent seizures [35,37].

In this study, patients with depression had a poor health perception and reported lower QoL score in the area referred to as physical health. This finding may indicate that being depressed makes patients feel less healthy. Also, a negative illness perception, which is especially high in people with epilepsy (due to the stigma, chronicity, and complexity of epilepsy) was found as an important link between depression and QoL [38].

Another interesting result is that in this sample, patients with comorbid depression had a higher educational level than non-depressed patients. Meanwhile, no significant differences were found in the employment variables. This fact contradicts local research which reports that lower educational levels and unemployment are related to probable depression [39]. Nevertheless, cross-sectional studies indicate that these variables can present different patterns depending on the context (i.e. in Japan, less-educated people had lower risk of Major Depressive Disorder, while in other Asian countries the pattern was inverted) [40]. This leads us to speculate that other aspects, such as cultural variables, life impact of a chronic condition or illness perception, might be affecting the rates of depression in our sample.

In the present study, patients with depression reported worse QoL regarding AEDs. Luoni et al. found that adverse effects of medication predicted negative QoL and that patients with co-morbid depression reported more adverse effects than those without depression [15]. Furthermore, depressive symptoms have been found to have a negative effect on the severity of adverse events related to AEDs in people with epilepsy [15,41,42].

A proper diagnosis of depression may inform the choice of AED, considering the positive or negative effects that they may have on mood [21,41,42]. In this regard, reducing the adverse effects of AEDs and treating depression will likely improve the QoL [43].

Psychiatric disorders, like depression, often occur in patients with epilepsy, but the diagnosis is frequently missed and therapeutic opportunities are often lost. It is important to diagnose the subtype of depression and rule out other psychiatric illnesses. Comprehensive treatment of patients with epilepsy requires an accurate diagnosis of co-morbidities, including depression [44,45].

Some limitations of this study must be mentioned. A scale of QoL applicable to any disease and not specific for epilepsy was used. Nevertheless, this scale (Q LES Q SF) describes the principal areas of functioning and is also applicable in patients with other psychiatric disorders that may present during video-EEG monitoring (i.e. psychogenic non epileptic seizures). Furthermore, these results may be applicable only to a limited population; specifically, patients with pharmacoresistant epilepsy who underwent video-EEG monitoring.

Additionally, the epilepsy center is a referral center specialized on epilepsy surgery and a younger population is overrepresented among patients who enter into the epilepsy surgical program. Few studies discuss video-EEG monitoring in the elderly and these patients represent a small percentage of admissions to epilepsy monitoring units [46]. Finally, in some patients, AEDs are partially reduced during video-EEG monitoring and some acute behavioral changes may appear, especially after seizures. Nevertheless, this modification should not affect the results of SCID-I, since the interview analyzes the patient's entire history (transversal and longitudinal assessment).

5. Conclusion

Depression is a frequent co-morbidity found in patients with pharmacoresistant epilepsy. This study shows cross-cultural aspects, the importance of depression in epilepsy, and the influence of depression on QoL. Severity of depression is linked to quality of life more than seizure frequency. A proper diagnosis and treatment of depression may be an important contribution to wellness of people with pharmacoresistant epilepsy.

Conflicts of interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

AcknowledgThents

Part of this research was carried out with the Carrillo Oñativia Grant from the Ministry of Health of Argentina.

We thank Nicolas Lombardi for revising the language.

References

[1] Gaitatzis A, Trimble MR, Sander JW. The psychiatric comorbidity of epilepsy. Acta Neurol Scand 2004;110:207–20.
[2] Kanner AM, Schachter SC, Barry JJ, Hersdorffer DC, Mula M, Trimble M, et al. Depression and epilepsy: epidemiologic and neurobiologic perspectives that may explain their high co-morbid occurrence. Epilepsy Behav 2012;24:156–68.
[3] Shamim S, Hasler G, Liew C, Sato S, Theodore WH. Temporal lobe epilepsy, depression, and hippocampal volume. Epilepsia 2009;50:1067-71.
[4] Lambert MV, Robertson MM. Depression in epilepsy: etiology, phenomenology, and treatment. Epilepsia 1999;40(Suppl. 10):S21–47.
[5] Jobe P. Common pathogenic mechanisms between depression and epilepsy: an experimental perspective. Epilepsy Behav 2003;4:S14–24.
[6] Harden CL. The comorbidity of depression and epilepsy. Epidemiology, etiology and treatment. Neurology 2002;59:549–55.
[7] Suurmeijer TP, Reuvekamp MF, Aldenkamp BP. Social functioning, psychological functioning, and quality of life in epilepsy. Epilepsia 2001;42:1160-8.
[8] Djibuti M, Shakarishvili R. Influence of clinical, demographic, and socioeconomic variables on quality of life in patients with epilepsy: findings from Georgian study. J Neurol Neurosurg Psychiatry 2003;74:570-3.
[9] Gilliam F, Hecimovic H, Sheline Y. Psychiatric comorbidity, health and function in epilepsy. Epilepsy Behav 2003;4:S26–30.
[10] Perrine K, Hermann BP, Meador KJ, Vickrey BG, Cramer JA, Hays RD, et al. The relationship of neuropsychological functioning to quality of life in epilepsy. Arch Neurol 1995;52:997–1003.
[11] Tracy JI, Dechant V, Sperling MR, Cho R, Glosser D. The association of mood with quality of life ratings in epilepsy. Neurology 2007;68:1101-7.
[12] Laxer KD, Trinka E, Hirsch LJ, Cendes F, Langfitt J, Delanty N, et al. The consequences of refractory epilepsy and its treatment. Epilepsy Behav 2014;37:59–70.
[13] Hermann BP. Quality of life in epilepsy. J Epilepsy 1992;5(3):153–65.
[14] Jacoby A, Snape D, Baker GA. Determinants of quality of life in people with epilepsy. Neurol Clin 2009;27:843–63.
[15] Luoni C, Bisulli F, Canevini MP, De Sarro G, Fattore C, Galimberti CA, et al, SOPHIE Study Group. Determinants of health-related quality of life in pharmaco resistant epilepsy: results from a large multicenter study of consecutively enrolled patients using validated quantitative assessments. Epilepsia 2011;52:2181–91.
[16] Bishop M, Allen CA. The impact of epilepsy on quality of life: a qualitative analysis. Epilepsy Behav 2003;4(3):226–33.
[17] Szaflarski M, Meckler JM, Privitera MD, Szaflarski JP. Quality of life in medication-resistant epilepsy: the effects of patient's age, age at seizure onset, and disease duration. Epilepsy Behav 2006;8(3):547–51.
[18] Jacoby A. Stigma, epilepsy, and quality of life. Epilepsy Behav 2002;3(6):10–20.
[19] Hamid H, Blackmon K, Cong X, Dziura J, Atlas LY, Vickrey BG, et al. Mood, anxiety, and incomplete seizure control affect quality of life after epilepsy surgery. Neurology 2014;82(10):887–94.
[20] Garcia M, Garcia Morales I, Gil-Nagel A. Prevalence of depressive symptoms and their impact on quality of life in patients with drug-resistant focal epilepsy (IMDYVA study). Epilepsy Res 2015;110:157–65.
[21] Lehrner J, Kalchmayr R, Serles W, Olbrich A, Pataraia E, Aull S, et al. Health related quality of life (HRQOL), activity of daily living (ADL) and depressive mood disorder in temporal lobe epilepsy patients. Seizure 1999;8:88–92.
[22] Borges Gonçalves E, Cendes F. Depression in patients with refractory temporal lobe epilepsy. Arq Neuropsiquiatr 2011;69(5):775-7.

[23] Boylan LS, Flint LA, Labovitz DL, Jackson SC, Starner K, Devinsky O. Depression but not seizure frequency predicts quality of life in treatment-resistant epilepsy. Neurology 2004;62:258–61.
[24] Jovel CAE, Salazar SR, Rodríguez CR, Mejía FE. Factors associated with quality of life in a low-income population with epilepsy. Epilepsy Res 2016;127:168–74.
[25] Kochen S, Melcon M. Prognosis of epilepsy in a community-based study: eight years of follow-up in an Argentine community. Acta Neurol Scand 2005;112:370-4.
[26] D'Alessio L, Scévola L, Fernandez Lima M, Oddo S, Solís P, Seoane E, et al. Psychiatric outcome of epilepsy surgery in patients with psychosis and temporal lobe drug-resistant epilepsy: a prospective case series. Epilepsy Behav 2014;37:165–70.
[27] Kwan P, Arzimanoglou A, Berg AT, Brodie MJ, Hauser WA, Mathern G, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia 2010;51(6): 1069–77.
[28] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders Text Revision (DSM-IV-TR). Washington: American Psychiatric Press; 2000.
[29] Wechsler D. Test de Inteligencia para adultos (WAIS) Manual. Buenos Aires: Editorial Paidós; 1995.
[30] First M, Gibbon M, Spitzer R, Williams J, Smith L. Entrevista Clínica Estructurada para los trastornos del Eje I del DSM-IV, SCID-I. Barcelona: Masson; 1999.
[31] Beck AT, Steer RA, Brown GK. Beck depression inventory: second edition manual. San Antonio, TX: The Psychological Corporation; 1996.
[32] Endicott J, Nee J, Harrison W, Blumenthal R. Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. Psychopharmacol Bull 1993;29:321-6.
[33] Hermann BP, Seidenberg M, Bell B. Psychiatric co-morbidity in chronic epilepsy: identification, consequences, and treatment of major depression. Epilepsia 2000; 41(2):S31–41.
[34] Tellez-Zenteno JF, Patten SB, Jette N, Williams J, Wiebe S. Psychiatric comorbidity in epilepsy: a population-based analysis. Epilepsia 2007;48:2336–44.
[35] Cramer J, Blum D, Reed M, Fanning K. The influence of comorbid depression on quality of life for people with epilepsy. Epilepsy Behav 2003;4:515–21.
[36] World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva, Switzerland: WHO; 1992.
[37] Blum D, Reed M, Metz A. Prevalence of major affective disorders and manic/hypomanic symptoms in persons with epilepsy: a community survey. Neurology 2002;58(Suppl. 2):A174.
[38] Shallcross A, Becker D, Singh A, Friedman D, Montesdeoca J, French J, et al. Illness perceptions mediate the relationship between depression and quality of life in patients with epilepsy. Epilepsia 2015;56(11):186–90.
[39] Leiderman EA, Lolich M, Vázquez GH, Baldessarini RJ. Depression: point-prevalence and sociodemographic correlates in a Buenos Aires community sample. J Affect Disord 2012;136(3):1154-8.
[40] Kessler RC, Bromet EJ. The epidemiology of depression across cultures. Annu Rev Public Health 2013;34:119.
[41] Mula M, Schmitz B. Depression in epilepsy: mechanisms and therapeutic approach. Adv Neurol Disord 2009;2(5):337–44.
[42] Perucca P, Jacoby A, Marson AG, Baker GA, Lane S, Benn EK, et al. Adverse antiepileptic drug effects in new-onset seizures: a case-control study. Neurology 2011;76:273-9.
[43] Kanner AM, Barry JJ, Gilliam F, Hermann B, Meador KJ. Depressive and anxiety disorders in epilepsy: do they differ in their potential to worsen common antiepileptic drug–related adverse events? Epilepsia 2012;53(6):1104–8.
[44] García-Morales I, de la Peña Mayor P, Kanner A. Psychiatric co morbidities in epilepsy: identification and treatment. Neurologist 2008;14(6):15–25.
[45] Devinsky O. Psychiatric co morbidity in patients with epilepsy: implications for diagnosis and treatment. Epilepsy Behav 2003;4(S4):2–10.
[46] McBride AE, Shih TT, Hirsch LJ. Video-EEG monitoring in the elderly: a review of 94 patients. Epilepsia 2002;43(2):165-9.