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Psychiatric comorbidity, health, and function in epilepsy☆

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Abstract

Epilepsy is a chronic condition that has complex effects on social, vocational, and psychological function. Several psychiatric disorders have been shown to have increased prevalence in persons with epilepsy compared to the general population. Depression appears to be the most common psychiatric comorbidity, but anxiety and other diagnoses have not been extensively investigated. Several studies have found that depression or psychological distress may be the strongest predictors of health-related quality of life, even including seizure frequency and severity, employment, or driving status. Despite the high prevalence and adverse effects of comorbid psychiatric disorders in epilepsy, very little is known about optimal treatment strategies, or even the efficacy of standard treatments. Further research is needed to increase understanding of the mechanisms of psychiatric illness in epilepsy, the effects of depression and anxiety on long-term clinical outcomes, and the most effective treatments.

Keywords: Epilepsy; Seizures; Function; Quality of life; Psychiatric; Comorbid

1. Introduction

As reviewed in multiple publications [1–5], depression and anxiety are prevalent in epilepsy [6–11], and many people with recurrent seizures may have one or both psychiatric disorders. Bipolar disorder and cognitive disorders also occur at an increased rate in epilepsy compared with the general population. Despite the high prevalence of psychiatric comorbidity in epilepsy, very few studies have evaluated the relationship of overall health, function, and well-being to mood disorders in epilepsy. As Hermann et al. recently noted:

> There is presently only a preliminary understanding of the additional burdens posed by comorbid psychiatric disorders in chronic epilepsy, even though these burdens seem to be significant. Within the epilepsy literature there is little understanding of the temporal course and synchrony between depression and associated psychosocial disability, no information regarding medical utilization, or health-care costs associated with depression in epilepsy, and only the most rudimentary understanding of the more general consequences of comorbid depression [4].

This article examines the studies that have attempted to define the association of specific psychiatric disorders with aspects of health, function, and quality of life in persons with recurrent seizures. Increased knowledge and awareness of the adverse effects of comorbid psychiatric conditions should improve mechanistic and patient-oriented research as well as the clinical care in epilepsy.

2. Studies of psychiatric comorbidity and quality of life in epilepsy

Although the impact of psychiatric comorbidity on quality of life and function has been a relatively poorly studied area of epilepsy management, several investigators have studied the relationships between mood, depression, and psychological distress and quality of life in

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patients with epilepsy using validated and reliable instruments.

Perrine et al. evaluated 257 patients from 25 epilepsy centers in the United States with the Quality of Life in Epilepsy Inventory (QOLIE)-89 [12], as well as objective tests of memory, verbal abilities, spatial functions, psychomotor, and cognitive processing speed, cognitive flexibility, and mood [13]. Factors that assessed mood, psychomotor speed, verbal memory, and language correlated significantly with selected scales of the QOLIE-89 inventory ($P < 0.0001$) and were predictive of overall quality of life ($P < 0.002$ to $P < 0.0001$). However, the mood factor had the strongest correlations with QOLIE-89 scales ($r = -0.20$ to $r = -0.73$) and was the strongest predictor of quality of life in regression analyses (46.7% explained variance, $P < 0.0001$). Although the inclusion of mood-related items in the QOLIE-89 nearly ensures significant association of mood, the robustness of the association suggested that mood might have a unique and potent role in poor quality of life in many patients with epilepsy. This was one of the first studies that used reliable and valid instruments to measure both quality of life and mood in persons with epilepsy. The study did not, however, evaluate specific aspects or mood, such as depression, anxiety, or thought disorder.

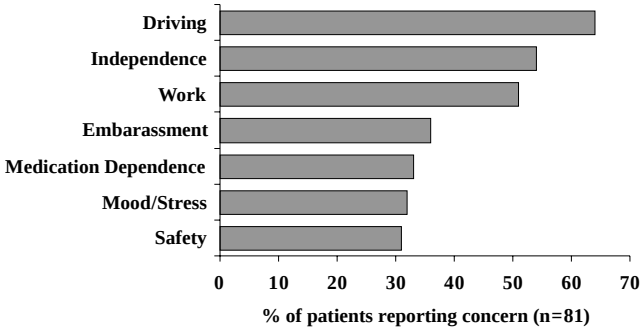

Fig. 1. Concerns listed by more than one third of patients who have had one or more seizures in the past 6 months [15].

Lehrner et al. investigated 56 consecutive patients with temporal lobe epilepsy confirmed by video EEG monitoring [14]. Reliable and valid instruments developed for native German speakers assessed health-related quality of life and depression [14]. They found that depression was the single strongest predictor for each domain of health-related quality of life (HRQOL). The significant association of depression with HRQOL persisted after controlling for seizure frequency, seizure severity, and other psychosocial variables. This study offers cross-cultural validation of the importance of mood for health outcomes in epilepsy.

Gilliam et al. used a method of direct assessment of patients' concerns to identify the importance of mood problems from the patients' perspective [15]. Eighty-one consecutive adult patients in the epilepsy clinic were asked to list in order of importance to them the concerns of living with epilepsy. Enrollment criteria included having a seizure within the past 6 months and currently taking an antiepileptic drug (AED). One third of the participants spontaneously listed mood as an important concern, as shown in Fig. 1.

Another study of 125 adults who were more than 1 year from temporal lobe resection for refractory epilepsy used the Epilepsy Surgery Inventory (ESI)-55 [16] to evaluate predictors of quality of life. Because most patients were seizure-free and legally driving, and 30% had discontinued AEDs, this sample allowed comparison of various aspects of epilepsy to specific components of subjective health [17]. As shown in Table 1, the Profile of Mood States summary score had the highest correlation of all three composite scales of the ESI-55, including Physical Health and Role Function.

Linear regression analysis confirmed that mood had the strongest association with subjective health, independent of seizures, driving status, medication requirement, or employment. Intelligence had no significant correlation with quality of life. These data are

Table 1
Univariate Pearson correlation coefficients for ESI-55 Composite Scale Scores with clinical variables within the postoperative group ($n = 125$) [17]

	Mental health	Physical health	Role function
Profile of Mood States summary score[a]	−0.762**	−0.528**	−0.532**
Employment	0.273**	0.373**	0.410**
Driving	0.290**	0.381**	0.349**
AED-free	0.214*	0.277**	0.300**
Seizure-free	0.188	0.193*	0.262**
Age[a]	0.079	0.022	−0.002
Gender	0.018	−0.024	−0.066
Postoperative performance IQ[a]	0.105	0.181	0.137
Postoperative verbal IQ[a]	0.097	0.148	0.147

* Correlation is significant at $P < 0.05$ level (two-tailed).
** Correlation is significant at $P < 0.01$ level (two-tailed).
[a] Indicates continuous variables evaluated with the Pearson r correlation; all other clinical variables are dichotomous and were evaluated with the Pearson point-biserial correlation.

Table 2
Final stepwise regression models for the association of Epilepsy Surgery Inventory (ESI)-55 composite scales with conventional clinical variables ($n = 125$) [17][a]

ESI-55 composite scale (dependent variable)	Independent variable	r^2
Role function	1.Mood status	0.276
	2.Employment	0.370
	3.Medication use	0.400
Mental health	1.Mood status	0.569
	2.Driving	0.588
Physical health	1.Mood status	0.269
	2.Employment	0.340
	3.Driving	0.372

Additional independent variables in the analysis included seizure-free status, age, gender, and verbal and performance IQ, but were not significantly associated ESI-55 composite scale scores.

[a] All r^2 values in each model are cumulative and significant at a level of $P < 0.0001$.

summarized in Table 2. Lack of analysis of specific aspects of mood was also a limitation of this study.

An important study by Suurmeijer et al. analyzed typical clinical variables such as seizure frequency, age of onset, number of AEDs, as well as aspects of social functioning and psychological distress [18]. As in the previously discussed studies, reliable and valid instruments were employed for psychosocial and quality of life assessments. Consistent with the findings of other investigators, none of the clinical variables independently correlated with quality of life, but psychological distress accounted for the largest amount of variance in self-perceived quality of life, as presented in Table 3.

Hermann et al. recently published an investigation of comorbid psychiatric symptoms and quality of life in temporal lobe epilepsy [19]. Several aspects of this study offer important data for further understanding of the nature of psychiatric symptoms in epilepsy and their impact on self-perceived function and well-being. Healthy subjects ($n = 38$) were included, and all mood and quality-of-life instruments were previously determined to be reliable and valid. The Symptom Checklist-90-R (SCL-90-R), a brief, multidimensional, self-report inventory, was used to evaluate a broad range of psychological problems and symptoms of psychopathology. Compared with healthy controls, patients with epilepsy exhibited significantly higher (worse) scores across all but one of the 12 SCL-90-R scales. Among patients with epilepsy, increasing chronicity was associated with significantly higher (worse) scores across all SCL-90-R scales and increased emotional–behavioral distress was associated with lower (worse) scores across all 17 QOLIE-89 scales, as shown in Table 4. Although depression and phobic anxiety had the largest differential scores compared with healthy controls, no specific psychiatric condition emerged as more prevalent or predictive of poor quality of life. Also, certain factors associated with limbic dysfunction such as underlying pathology (e.g., mesial temporal sclerosis) could confound the association of chronicity with more severe psychiatric symptoms, but MRI or PET findings were not controlled for in the study.

Table 3
Correlation of quality of life assessment with demographic, clinical, and psychological variables [Adapted from reference [18]]

Independent variable	Dependent variable quality of life (VAS-DT) r
Sex	0.01
Age	0.07
Onset	−0.06
Seizure frequency	−0.14*
Side effects of AEDs	−0.21**
Perception of epilepsy seizures	−0.36***
Health perceptions	0.41***
Perception of stigma of epilepsy	−0.17**
Life fulfillment	0.36***
Loneliness	0.43**
General adjustment to epilepsy	0.46***
Self-esteem	0.46**
Mastery	0.46***
Mental health	0.52***
Psychological distress	−0.52***

AED = antiepileptic drugs

Source. Adapted, with permission, from Suurmeijer et al. [18].

* $P = 0.02$ (all one-sided).

** $0.01 < P < 0.001$ (all one-sided).

*** $P < 0.001$ (all one-sided).

A study of a consecutive sample of epilepsy clinic adult outpatients evaluated the association of severity of depression symptoms with self-reported health status [20]. All patients received the QOLIE-89 and the Beck Depression Inventory. The mean age of the group was 39 years (SD 12.9) and there were 94 (48%) women. The mean combined complex partial and generalized tonic–clonic seizure frequency was 4.3/month for the previous 6 months, and 28% had been seizure-free for more than 6 months. Fifty-one percent were on one antiepileptic drug, 28% were on two, 18% were on three, and 3% were on four. After controlling for age, sex, complex partial and generalized tonic–clonic seizure frequency, and depressive symptoms, we found that severity of depression correlated with HRQOL (correlation $r = 0.49$, $P < 0.001$), but not seizure frequency (correlation $r = 0.01$, $P = 0.93$) as shown in Fig. 2.

3. Discussion and conclusions

In this article we reviewed those studies that have used validated instruments to examine the effects of psychiatric comorbidity in epilepsy on health-related quality of life and functional outcomes. Given the nature and prevalence of a variety of psychiatric comorbidities in epilepsy, which are discussed in more detail in other publications within this supplement [21–23], the impact of these on health-related quality of life and

Table 4
Correlations between emotional–behavioral distress and health-related quality of life

	Global Severity Index	Symptom Distress Index	Depression
Health perceptions	−0.54**	−0.57**	−0.50**
Overall quality of life	−0.60**	−0.52**	−0.63**
Physical function	−0.44**	−0.41**	−0.42**
Role limitation: physical	−0.54**	−0.43**	−0.51**
Role limitation: emotional	−0.63**	−0.55**	−0.63**
Pain	−0.45**	−0.40**	−0.42**
Work/driving/social	−0.61**	−0.54**	−0.52**
Energy/fatigue	−0.57**	−0.62**	−0.62**
Emotional well-being	−0.70**	−0.67**	−0.67**
Attention/concentration	−0.70**	−0.70**	−0.63**
Health discouragement	−0.64**	−0.57**	−0.59**
Seizure worry	−0.41**	−042**	−0.38**
Memory	−0.48**	−0.48**	−0.36**
Language	−0.58**	−0.51**	−0.50**
Medication effects	−0.48**	−0.40**	−0.46**
Social support	−0.29**	−0.17	−0.19
Social isolation	−0.64**	−0.56**	−0.63**
Total	−0.84**	−0.77**	−0.79**

Source. Adapted, with permission, from Hermann et al. [19].
*$P < 0.05$.
**$P < 0.05$.

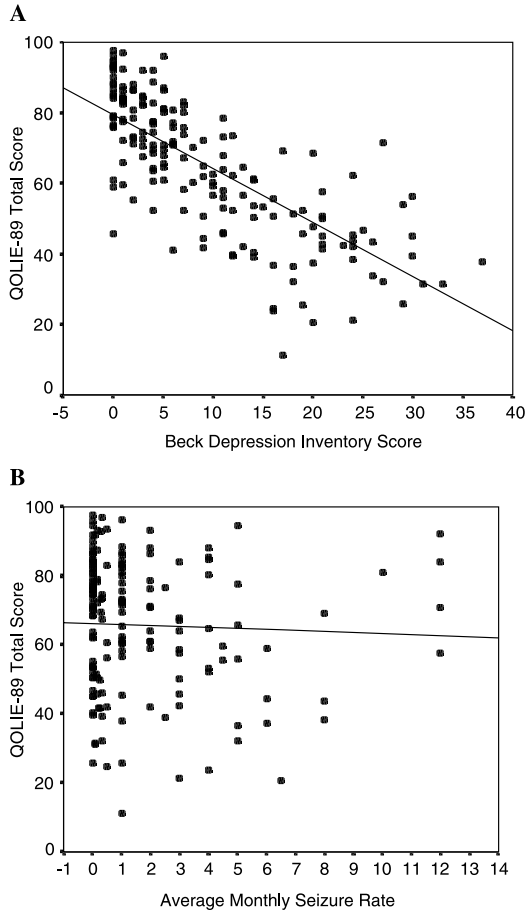

Fig. 2. Scatterplot of health-related quality of life (QOLIE-89 Global Score) with (A) depression symptoms ($r = -0.49$, $P = 0.001$), and (B) average monthly seizure rates ($r = 0.01$, $P = 0.93$) ($n = 195$) [20].

functional outcomes is not adequately studied. The literature published to date has identified general mood disturbance, depression, and psychological distress, which are independent of seizure frequency and seizure control, as significant predictors of quality of life impairment among people with epilepsy.

In evaluating what is known to date about the impact of psychiatric comorbidities on quality of life and functional outcome in epilepsy it is important to consider that the ability to do so is limited by the instruments we choose to use and the psychiatric symptoms and syndromes we examine. Anxiety disorders are prevalent comorbidities among people with epilepsy [22] but their impact on health-related quality of life and functional outcome has not been well studied. We know from studies in the general population of people with anxiety disorders reported in the psychiatric literature, that both syndromal levels of psychopathology and subthreshold levels of symptoms are associated with marked impairment in quality of life and psychosocial function [24]. The extent to which these findings are generalizable to people with epilepsy and comorbid anxiety disorders is unknown, but intuition and empirical clinical experience suggest that such disorders do have an important impact on the lives of the epilepsy patients in our care. Similarly, we know little of the impact of other psychiatric comorbidities and conditions such as psychosis, nonepileptic seizures, attention-deficit/hyperactivity disorder, and aggression in the epilepsy population.

Every treating clinician knows that many of the epilepsy patients in their care have impaired quality of life and function and that stringent seizure control is

essential if outcome is to be optimized. This is well supported in the literature [25]. We also believe that clinicians are aware that comorbid symptoms also impact quality of life. However, clinical experience and intuition alone are not sufficient to help us move forward in quantifying and understanding the impact of comorbid psychiatric disorders and symptoms on outcome and function and additional prospective studies using the appropriate instruments and variables are needed. In the meantime, sufficient evidence does exist to mandate that the impact of psychiatric comorbidities in epilepsy is important and we should be cognizant of this in our day-to-day management of patients and in the selection of pharmacotherapy.

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