Evaluating quality of life in epilepsy: The role of screening for adverse drug effects, depression, and anxiety

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ABSTRACT

Objective: The objective of this study was to evaluate the contribution of validated screening tools for antiepileptic drug (AED) adverse effects, depression, and anxiety to measure the quality of life (QoL) in people with epilepsy (PWE).

Methods: Patients in a tertiary epilepsy service were screened for quality of life (using QOLIE-31), major depressive disorder (MDD) (NDDI-E), generalized anxiety disorder (GAD) (GAD-7), and AED effects (AEP). Mini International Neuropsychiatric Interview (MINI) generalized anxiety disorder module was also performed. For AEP validation in French, the internal structural validity was analyzed. Dimensional (NDDI-E and GAD-7 scores) and categorical (MDD and GAD) analyses were performed to investigate interactions between QoL and AEP.

Results: A total of 132 (87 females) subjects were included. The French version of the AEP demonstrated satisfactory psychometric properties (Cronbach's α 0.87). Correlations between NDDI-E, GAD-7, AEP, and QOLIE-31 scores were high, and significant for all subscales of QOLIE-31; no effect of seizure-related variables was seen. Some sex differences in QOLIE-31 subscales were found, and mean AEP score was higher in females. Age, sex, NDDI-E, GAD-7, and AEP scores accounted for 61% of variance of QOLIE-31 scores. Differential effects were seen on QOLIE-31 subscales: AEP strongly correlated with all subscales; GAD-7 scores more strongly correlated with "Seizure Worry"; NDDI-E with "Energy-Fatigue"; and both NDDI-E and GAD-7 scores strongly correlated with "Emotional Well-Being". Categorical analysis of groups with MDD alone, GAD alone, MDD + GAD, and neither MDD nor GAD showed significant differences in AEP and QOLIE-31 scores, with MDD + GAD showing the most AED effects and the poorest QoL.

Significance: The combination of screening tools for depression (NDDI-E), anxiety (GAD-7), and AED effects (AEP) has a strong power for evaluating QoL in PWE. Coexisting MMD and GAD were associated with the poorest quality of life and the highest AEP scores.

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1. Introduction

It is increasingly recognized that optimal epilepsy care is based on managing "more than seizures", by taking into account consequences and comorbidities of epilepsy at the individual level [1]. Health-related quality of life (QoL) in people with epilepsy (PWE) is known to be influenced by many variables including seizure freedom, comorbid psychiatric problems, and burden of antiepileptic drug (AED) adverse effects, as well as cognitive function, psychosocial factors, and perceived stigma [1–3]. A recent large study of pharmacoresistant epilepsy showed AED adverse effects and depression symptoms to account for most of the variance of the QOLIE-31 score, whereas epilepsy-related variables such as seizure frequency and epilepsy type had no effect [4]. These results accorded with Gilliam's landmark study that launched the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) [5], a reliable and accurate short self-reported questionnaire that has since been promoted as a multilingual screening tool for major depressive disorder (MDD) in PWE [6].

Given the high prevalence of AED adverse effects and their known impact on QoL, assessment of perceived AED side effects is important [7], but routine screening appears to be rare in practice [1]. Specific screening instruments allow more effective assessment of symptoms than an unstructured interview, and provide a means of quantifying these [8]. The Adverse Events Profile (AEP) is a reliable and accurate self-reported questionnaire that was developed over 20 years ago to evaluate the most common negative AED adverse effects reported by

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patients taking AED [9], whose routine use in the epilepsy clinical setting has been advocated [8], and which has now been validated in Spanish [10], Chinese [11], Portuguese [12], Korean [13], and Bulgarian [14] language versions.

Apart from AED effects, depression has emerged as the other main determinant of QoL in epilepsy [4,5]. However, anxiety is increasingly recognized to be highly prevalent and disabling, with a significant, independent effect on QoL that appears to be at least as great as that of depression [15–18]. Indeed, anxiety disorders have recently been highlighted as an important and relatively "neglected" comorbidity in epilepsy [19]. In order to promote screening for generalized anxiety disorder (GAD), the most frequent anxiety disorder in PWE, the Neuropsychiatry Commission of the International League Against Epilepsy (ILAE) has encouraged multilanguage validation of the GAD-7 questionnaire, a reliable and accurate short self-reported questionnaire to diagnose GAD in epilepsy [20]. While MDD and GAD are often related, and may have some overlapping symptoms as well as overlap with AED effects [19], the GAD-7 and NDDI-E questionnaires have been shown to provide different information and are thus, well-suited as complementary instruments for rapid screening in the clinical setting [20]. The coexistence of anxiety and depressive disorders in epilepsy appears particularly detrimental [16], being associated with higher rates of suicidal ideation [21] and poorer QoL [16], although information on prevalence of this group is still quite scarce [19]. Individually, anxiety and depressive disorders are each associated with increased reported adverse effects of AED [22]. The interactions between AED effects, anxiety, and depression and their effect on the QoL in PWE are recognized to be complex [22,23] with, in addition, some evidence of sex differences in clinical expression [24]. However,

very few previous studies have simultaneously examined all of these variables. In addition, existing studies show quite heterogeneous methodology, with most using screening instruments that evaluate depressive ± anxiety *symptoms* (using validated scales such as the Beck Depression Inventory (BDI) or the Hospital Anxiety and Depression Scale), and a smaller number identifying the presence or absence of a specific *diagnostic condition* (MDD or GAD as comorbid psychiatric disorder associated with epilepsy) using criterion-based structured interview such as the MINI (see Table 1). It should be borne in mind that screening instruments, while often providing valuable data, should not be used and interpreted as psychiatric diagnoses [32].

In order to evaluate interactions between QoL, depression, anxiety, and AED adverse effects in a population of people with epilepsy (PWE), we used validated standard screening tools (NDDI-E, GAD-7, AEP, and QOLIE-31). Dimensional (depressive and anxiety symptoms) and categorical (MDD and GAD) analyses were performed to investigate interactions between QoL and AEP. No French version of the AEP was available, so we also assessed the validity and reliability of a translated version.

2. Methods

2.1. Participants

People with epilepsy (PWE) were recruited from the Clinical Neurophysiology Department of the Timone University Hospital, Marseille and the Hôpital Henri Gastaut, Marseille (these 2 centers forming part

Table 1
Summary of literature: articles 2000–2017 measuring QoL in adult PWE using a validated tool (QOLIE-89 or QOLIE-31), associated with at least one validated measure of depression and/or anxiety, as well the AEP.

Author	Year	Journal	Population	Instruments	Results
Chen et al. [25]	2016	Epilepsy & Behav	N = 260, single medical center Taiwan	QOLIE-31, HADS, AEP	Anxiety symptoms, depression symptoms and AED effects predicted QoL
Park et al. [13]	2012	J Korean Epilepsy Soc	N = 312 patients from S Korea	QOLIE-31, BDI, BAI, AEP	Korean validation study of AEP. AEP scores correlated with QOLIE-3, BDI, and BAI; anxiety scores strongest predictor of AEP.
Hecimovic et al. [26]	2012	Epilepsy & Behav	N = 193, tertiary center outpatients	QOLIE-89, BDI, AEP	This study focused on suicidal ideation. QOLIE-89, AEP, and BDI scores worse in group with suicidality features
Martins et al. [12]	2011	Epilepsy & Behav	N = 100, Brazilian tertiary center	QOLIE-31, HADS, AEP	Brazilian–Portuguese validation study of AEP. AEP highly correlated with QOLIE-31 and HADS. No difference symptomatic/generalized epilepsies
Luoni et al. [4]	2011	Epilepsia	N = 809 (multicenter Italian), all pharmacoresistant	QOLIE-31, BDI, AEP	BDI (depression symptoms) and AEP similar and main effect on QoL; no effect seizure frequency
Yue et al. [24]	2011	Epilepsy & Behav	N = 247 from single Chinese neurology department	QOLIE-31, Hamilton Depression Rating Scale, Self-Rating Anxiety Scale, AEP	AEP strongest predictor of QOLIE in women; in men, AEP and anxiety symptoms
Kwon and Park [27]	2011	Epilepsy & Behav	N = 150 PWE seizure-free at least 1 year and on monotherapy, Korea	QOLIE-31, BDI, AEP	BDI score was a stronger predictor of QOLIE (all subscales) than AEP score.
Carreño et al. [10]	2009	Epilepsy & Behav	N = 266 multicenter Spanish outpatient study	QOLIE-31, HADS, AEP	Validation study of Spanish AEP. AEP score correlated independently with QOLIE-31, anxiety score, and depression score
da Silva et al. [28]	2007	Epilepsy & Behav	N = 250 outpatients in Brazil	QOLIE-31, BDI, AEP	Validation study of Brazilian–Portuguese QOLIE-31; correlated with AEP and BDI
Gilliam et al. [5]	2006	Neurology	N = 205, mixed seizure types and severity (multicenter US)	QOLIE-89, MINI (depression), SCID (depression), BDI, CES-D; AEP	"NDDI-E score, independent of AEP, predicted subjective health status (QoL)". AEP also predicted QoL. >70% variance of QOLIE-89 explained by these 2 factors. Variance QOLIE was 0.57 for NDDI and 0.68 for AEP.
Szaflarski et al. [29]	2006	Epilepsy & Behav	N = 99, medication resistant patients from monitoring unit single center US	QOLIE-89, Profile of Mood States (POMS) (depression profile) and AEP	Strong association QoL/depression and QoL/AEP
Ettinger et al. [30]	2004	Neurology	N = 775, community postal survey	QOLIE-89, AEP, CES-D	CES-D scores associated with poorer QoL and AED effects
Gilliam et al. [8]	2004	Neurology	N = 62 adult outpatients with epilepsy	QOLIE-89, AEP	Linear relation AEP and QOLIE-89
Gilliam [31]	2002	Neurology	N = 195, consecutive outpatients with epilepsy	QOLIE-89, AEP, BDI	AEP stronger effect than BDI in predicting QOLIE

AEP = Adverse Events Profile; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; CES-D = Center for Epidemiological Studies Depression Scale; HADS = Hospital Anxiety and Depression Scale; MINI = Mini International Neuropsychiatric Interview; NDDI-E = Neurological Disorders Depression Inventory for Epilepsy (NDDI-E); QOLIE = Quality of Life in Epilepsy; SCID = Structured Clinical Interview for DSM.