

The effect of seizure severity on quality of life in epilepsy

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Abstract

Seizure severity is an important aspect of epilepsy. The relationship between seizure severity and quality of life in epilepsy, however, has been incompletely explored. With a data set of 118 women from the baseline phase of a clinical treatment trial, the relationship between seizure severity and aspects of quality of life was evaluated. Two domains of the Quality of Life in Epilepsy-31 (QOLIE-31) correlated highly significantly with seizure severity: Seizure Worry ($r = -0.265$, $P = .004$) and Social Functioning ($r = -0.280$, $P = 0.002$). Two additional domains were significantly correlated: Overall Quality of Life ($r = -0.210$, $P = 0.023$) and Cognitive ($r = -0.209$, $P = 0.024$). When the potentially confounding effect of depression, measured by the Beck Depression Inventory, was controlled for, the regression of seizure severity with QOLIE-31 Seizure Worry remained significant ($P = 0.006$, $R^2 = 0.153$), as did the regression with QOLIE-31 Social Functioning ($P = 0.002$, $R^2 = 0.184$) and the regression with QOLIE-31 Cognitive ($P = 0.037$, $R^2 = 0.30$). These findings indicate that severe and potentially injurious seizure behaviors contribute to anxiety and socially avoidant behavior for persons with intractable epilepsy.

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1. Introduction

Seizure severity is an important aspect of epilepsy. The relationship between quality of life in epilepsy and seizure severity, however, has been incompletely explored. Further, because various seizure severity scales have been used in clinical research, this association is limited by the scope of the seizure severity scale. A review of the extant methods of seizure severity assessment [1] revealed a commonality among scales, with most assessing seizure frequency, type, duration, postictal events, postictal duration, the occurrence of injuries, automatisms, seizure clusters, warnings, tongue biting, incontinence, and overall functional impair-

ment. In the development of a new seizure severity scale, seizure “bothersomeness” and “the most bothersome aspect” of a seizure also emerged as important components of seizure severity [2].

Depression has a profound influence on patients’ reporting of seizure severity, as noted by Cramer et al. in 2003 [3]. These investigators found that clinically depressed people with epilepsy reported higher levels of all aspects of seizure severity, as well as increased difficulties with overall seizure recovery, when compared with a nondepressed epilepsy control group. However, this cross-sectional study cannot be interpreted as indicating that depression worsens seizure severity; the direction of a possible causal relationship between depression and seizure severity is not demonstrated.

Quality of life is of major import when assessing the impact of illness and treatment of illness, and comprises

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several components. Aspects of quality of life can be measured somewhat objectively, using scales to assess physical areas of the patient's life such as fatigue, appetite loss, and dyspnea, for example, in the evaluation of quality of life in patients with lung cancer [4]. A second component of quality of life is more subjective, usually psychological in nature [5]. Therefore, quality-of-life domains run the gamut from external (e.g., physical restrictions within an environment) to internal (e.g., psychological variables), and encompass cognitive, as well as interpersonal, constituents [5]. Schachter underscores that the goal of treating patients with epilepsy should be to proffer a life without medical and/or psychosocial complications of seizures and, thereby, minimize the adverse effect of epilepsy on overall quality of life [6].

Depression is the most powerful predictor of quality of life in epilepsy [7,8], having even more effect than other clinical variables such as seizure frequency and localization. Because depression impacts the reporting of seizure severity as well as quality of life in epilepsy, it is a potential confounder when evaluating the relationship between seizure severity and quality of life.

One small study has previously evaluated the association between quality of life and seizure severity. Morrow et al., in 2000, followed 10 patients who received vagal nerve stimulators to control their seizures for an average of 18 months postimplantation [9]. The overall percentage reduction in seizure frequency over time for the group was approximately 30%. Seizure severity scores measured using the Liverpool Seizure Severity Scale revealed that there was a significant reduction in the ictal phase of seizures. Results at 12 months indicated that their health-related quality of life was identical to that at baseline, suggesting that this reduction in seizure severity was not associated with improvement in overall quality of life.

We were interested in further exploration and refinement of any possible relationship between seizure severity and quality of life by determining whether seizure severity was inversely associated with specific aspects of quality of life measured by the QOLIE-31. The rationale behind this investigation is the tacit relationship one would expect to find between the severity of epilepsy and quality of life. In other words, as the severity of seizures increases, we expect to see a concomitant decrease in the quality of life in patients with epilepsy, while controlling for an important confounder in this relationship, depression.

2. Methods

2.1. Participants

One hundred eighteen subjects were evaluated, all of whom were women between the ages of 18 and 45. All women had at least two seizures of any type per month. Data obtained at the initial visit of the baseline phase of subjects enrolled in the double-blind, placebo-controlled, randomized trial entitled Progesterone Therapy for Women with Epilepsy were used. This population was used because it was a sample of patients with refractory epilepsy with available relevant data.

2.2. Materials

2.2.1. Quality of Life in Epilepsy-31

The Quality of Life in Epilepsy-31 (QOLIE-31) instrument is a self-administered questionnaire [10]. It includes seven subscales: Overall Quality of Life, Seizure Worry, Emotional Well-Being, Energy/Fatigue, Cognitive, Medication Effects, and Social Function. These responses can yield seven individual scores (per subtest) and a total (composite) score.

2.2.2. National Hospital Seizure Severity Scale

The National Hospital Seizure Severity Scale (NHS3) is a refined version of the Chalfont Seizure Severity Scale [11]. The principal advantages of the new version are that it is easily administered, the limits of reliability have been delineated, and construct validity for the scale is available. The scale is administered by a health professional during an interview with a patient and a witness to the seizures. It contains seven seizure-related factors and generates a score from 1 to 27. A seizure severity score is generated for each seizure type the patient experiences. For the purposes of this study, the highest seizure severity score (most severe) was used for the visit analyzed.

2.2.3. Beck Depression Inventory

The Beck Depression Inventory (BDI) is a 21-item self-report measure that assesses the severity of depressive symptoms [12]. Each item is scored from 0 to 3, with higher scores indicating more severe symptoms.

2.3. Statistical methods

Statistical analyses were Spearman's correlations for univariate analyses and multivariate linear regression for assessing the independent effect of seizure severity on quality-of-life domains after controlling for mood scores. All *P* values were two-sided with statistical significance evaluated at the $\alpha = 0.05$ level. Ninety-five percent confidence intervals (95% CI) were also calculated to assess the precision of the β values obtained.

3. Results

One hundred eighteen subjects were evaluated, all of whom were women between the ages of 18 and 45. Two domains of the QOLIE-31 correlated significantly with seizure severity: Seizure Worry ($r = -0.265$, $P = 0.004$) and Social Function ($r = -0.280$, $p = 0.002$). Two additional domains correlated significantly: Overall Quality of Life ($r = -0.210$, $P = 0.023$) and Cognitive ($r = -0.209$, $P = 0.024$, respectively). Although depression, as measured by the BDI, can account for 18% of the variance of the Seizure Worry subscale [7], controlling for depression still indicated that the regression of seizure severity with QOLIE-31 Seizure Worry remained significant ($P = 0.006$, $R^2 = 0.153$, $\beta = -1.175$; 95% CI = 0.366 to -1.984), as did the regression with QOLIE-31 Social Function ($P = 0.002$, $R^2 = 0.184$, $\beta = -1.172$; 95% CI = 0.449 to -1.895) and the regression with QOLIE-31 Cognitive ($P = 0.037$, $R^2 = 0.30$, $\beta = -0.733$, 95% CI = 0.051 to -1.415). The robust R^2 value with the *P* value just reaching statistical significance for an effect of the Cognitive domain on seizure severity in this analysis indicates that BDI scores had a marked effect on producing the R^2 value compared with the seizure severity for the Cognitive domain of the QOLIE-31.

Because associations with seven primary outcomes were analyzed using linear regression, the issue of multiplicity of

outcomes (i.e., similar to the concept of multiple comparisons) may be a concern. Although an evaluation of the preceding outcomes was defined a priori, readers may wish to evaluate statistical significance at a modified α level of $0.05/7$ associations = 0.007. At this α level, statistical significance is achieved when the P value for a given association is less than 0.008. Even at this modified α level, the regressions for QOLIE-31 Seizure Worry ($P = 0.006$) and QOLIE-31 Social Function ($P = 0.002$) still remained significant. However, the effect of QOLIE-31 Cognitive is not significant by this standard. See Table 1 for the results of associations between seizure severity and all QOLIE-31 domains.

4. Discussion

This study provides evidence that there is an association between seizure severity and quality of life, even when controlling for depression. Specifically, these results suggest that seizure severity may promote the development or exacerbation of worry and anxiety and/or socially avoidant behaviors.

The Social Function subscale of the QOLIE-31 measures such tasks as social activities (e.g., visiting with friends or relatives), leisure time (e.g., hobbies, going out), driving, and vocational limitations. These components of the scale appear to reflect one very important motif, independence. As such, the physical aspects of sei-

zure severity alone can have an impact on day-to-day activities. This can have a mounting effect on an individual's interpersonal relationships, financial situation, and self-efficacy. If seizure severity does indeed have an effect on autonomy, then improving seizure severity could result in a concomitant increase in these particular domains.

Seizure Worry, as measured by the QOLIE-31, consists of such items as worry about future seizures, apprehension over future injury resulting from seizures, trepidation over adverse side effects of medication regimens, and social embarrassment over having seizures. The explanation for seizure severity influencing worry seems cogent. Severe seizures can place individuals in physically threatening (sometimes life-threatening, e.g., while driving) circumstances.

The Cognitive domain of the QOLIE-31 consists of questions concerning memory, concentration, and reasoning. Although progressive cognitive impairment is associated with epilepsy [13], the association between perceived cognitive abilities and seizure severity in this cross-sectional study is not intuitive. There was no systematic attempt to obtain the scale scores within a defined postictal period, during which an association between seizure severity and cognitive perception might be expected.

Being able to untwine quality of life and seizure severity seems difficult, and they may be tapping into similar underlying constructs or go hand in hand. In other words, lack of independence can exacerbate worry and anxiety, and anxiety can have an influence on social functioning as well. Quality of life and seizure severity appear to have overlapping qualities, and this may cloud the differentiation between predictor and outcome variables.

Devellis et al. [14] applied the theoretical framework of learned helplessness to individuals with epilepsy, and incorporated seizure severity into the factors contributing to helplessness. They predicated their research on the assumption that exposure to naturally occurring aversive, uncontrollable stimuli, such as a seizure, can produce learned helplessness in a naturalistic setting, outside the laboratory. They found that seizure severity, frequency, and perceived controllability or predictability of seizures contribute significantly to learned helplessness scale scores. These results supplement the findings of our present study, which suggest that the quality of a seizure experience can result in anxiety and socially avoidant behavior, measured as seizure worry and social functioning.

The association of seizure severity with seizure worry implies an effect of seizure severity on anxiety. Anxiety itself has an important effect on quality of life in epilepsy. In a study evaluating the differential effect of anxiety and depression on quality of life in persons with partial epilepsy, depression was again found to be the most influential predictor of quality of life, accounting for about 50% of the variance in quality-of-life scores. However, anxiety was also a strong predictor of quality of life, contributing to one-third of the variance in scores [15].

The results herein can be compared with those of Goldstein and Harden, who demonstrated that the relationship

Table 1
Correlation and multivariate linear regression (controlling for mood scores) between seizure severity and QOLIE-31 domains ($N = 118$)

QOLIE-31 domain	Spearman's correlation coefficient and P value	P value R^2 value ^a / β value ^a /95% CI ^a
Overall QOL	$r = -0.210$ $P = 0.023$	$P = 0.107$
Seizure Worry	$r = -0.265$ $P = 0.004$	$P = 0.006$ $R^2 = 0.153$ $\beta = -1.175$ 95% CI = 0.366 to -1.984
Social Function	$r = -0.280$ $P = 0.002$	$P = 0.002$ $R^2 = 0.184$ $\beta = -1.172$ 95% CI = 0.449 to -1.895
Cognitive	$r = -0.209$ $P = 0.024$	$P = 0.037$ $R^2 = 0.30$ $\beta = -0.733$ 95% CI = 0.051 to -1.415
Emotional Well-Being	$r = -0.089$ $P = 0.342$	$P = 0.770$
Medication Effects	$r = -0.023$ $P = 0.802$	$P = 0.994$
Energy/Fatigue	$r = -0.155$ $P = 0.096$	$P = 0.316$

between seizure frequency and anxiety is counterintuitive [16]. They found that among persons with refractory epilepsy, anxiety levels measured with the Hamilton Anxiety Scale inversely correlated with seizure frequency; this phenomenon itself may be a manifestation of learned helplessness. However, this finding is in contradistinction to the results of the current study, in which there was a positive correlation between seizure severity and anxiety as measured by the Seizure Worry subscale of the QOLIE-31. These findings suggest that seizure severity and seizure frequency may affect anxiety in persons with epilepsy quite differently.

One limitation of this study entails the differentiation between clinical and statistical significance. Although the correlations among quality-of-life domains and seizure severity when controlling for depression were significant, the percentage of variance accounted for by regression of seizure severity with quality of life was fairly small. It is clear that multiple factors, most importantly depression, anxiety, and antiseizure medication side effects [8,17], affect quality of life in epilepsy. Medication side effects, as measured by the Adverse Event Profile, have been shown to significantly correlate with quality of life in epilepsy [8,17] and are strong predictors of quality-of-life scores. This effect was not accounted for in this study; however, no significant associations between the Medication Effects domain of the QOLIE-31 and seizure severity were found in this study, suggesting that medication adverse effects are not a confounder for the association between seizure severity and quality of life.

Although a clear directional relationship of the association between depression and seizure severity has not been demonstrated, patients with epilepsy frequently report emotional stress as a seizure precipitant [18]. It is therefore possible that the direction of the relationship is a worsening of seizure frequency and severity caused by emotional stress and depressive symptoms. These observations should provide an impetus for further exploration into the complexity of explaining the relationship of seizure severity to both psychiatric comorbidity and quality of life in epilepsy.

Second, the population that was selected to be a part of this study, a clinical treatment trial using women of child-bearing potential with frequent partial seizures, may be quite homogeneous. As such, the external validity of this study should be further evaluated using a larger population more representative of persons with epilepsy.

Overall, even taking into account these limitations, the findings herein suggest that reducing seizure severity may significantly improve the quality of life of persons with epilepsy.

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