Quality of Life Perception in Patients With Intractable Epilepsy or Pseudoseizures

Joshua I. Breier, PhD; Kathleen L. Fuchs, MS; Bonnie L. Brookshire, PhD; James Wheless, MD; Azreena B. Thomas, MD; Jules Constantinou, MD; L. James Willmore, MD

Objectives: To contrast and compare self-reported quality of life in patients with intractable epilepsy and pseudoseizures and to examine the relationship between self-reports and objective measures of cognitive functioning in both of these groups.

Design: Case series using profile analysis and analysis of covariance.

Setting: University epilepsy surgery program.

Participants: Forty-three patients with intractable complex partial seizures of unilateral temporal lobe origin and 25 patients with pseudoseizures.

Measures: Quality of Life in Epilepsy Inventory-89; neuropsychological tests assessing verbal memory, nonverbal memory, naming, and attention; and the Depression Scale (2) of the MMPI-2 (Minnesota Multiphasic Personality Inventory).

Results: Patients with pseudoseizures described themselves as more limited in the physical health domain than patients with complex partial seizures. Self-perceptions of cognitive functioning were similar between groups, despite the superior performance of patients with pseudoseizures on objective measures. Self-perception of cognitive dysfunction was related to mood disorder in the pseudoseizure group only, and there were no relationships between subjective and objective measurements of cognitive status within this group independent of mood disorder. For the complex partial seizures group, relationships between subjective and objective measures of cognitive function were dependent on the side of seizure onset.

Conclusions: Results are consistent with hypotheses that suggest that patients with pseudoseizures focus on physical rather than psychological explanations for stress, and that this focus is related, at least in a subgroup of patients, to mood disorder. Results also provide support for the validity of the Quality of Life in Epilepsy Inventory-89 in populations with intractable seizure disorder, although there is evidence for a possible floor effect on some of the subscales.

Arch Neurol. 1998;55:660-665
PATIENTS, MATERIALS, AND METHODS

PATIENTS AND METHODS

Subjects were 68 patients who had undergone comprehensive evaluation for intractable seizures at the Texas Comprehensive Epilepsy Program at the University of Texas Health Science Center in Houston. This was a consecutive series of patients for whom QOLIE data were available. Forty-three patients had complex partial seizures (CPS) of either right (n = 23) (right temporal lobe epilepsy [RTLE]) or left (n = 20) (left temporal lobe epilepsy [LTLE]) temporal lobe origin. Twenty-five were found to have pseudoseizures. Pseudoseizures were identified by recording at least 3 events identified by the accompanying observer as typical. This was always a person who knew the patient and observed the patient’s seizures. An independent assessment of behaviors, scalp electroencephalographic patterns, and event duration must conform to nonepileptic seizures. If a definite diagnosis cannot be made by the above-mentioned methods the patient is suspected of having seizures and further observation is required along with continued treatment with anticonvulsant medication. Patients in this latter group, as well as patients with suspected frontal lobe seizures, were excluded from this study. All patients in both the CPS and pseudoseizure groups had more than 12 seizures or events in the past year. This has been characterized as a severe seizure disorder by Devinsky et al.3 All patients with pseudoseizures had an intractable disorder as well. Patients with CPS had the side of their seizure onset identified with a combination of procedures including 24-hour scalp and sphenoidal videoelectroencephalographic telemetry monitoring, magnetic resonance imaging, and neuropsychological testing. Magnetoencephalographic studies, interictal and ictal single photon emission computed tomography, and intracranial electrodes were used to provide further localization data in some cases. All patients with CPS underwent intracarotid sodium amobarbitol testing as well, and eventually underwent unilateral temporal lobectomy. Patients with evidence of structural lesions on magnetic resonance imaging scans, other than hippocampal sclerosis or history of closed head injury, were excluded from the study. Demographic and seizure variables for the groups are presented in Table 1. Differences between pseudoseizure and epileptic groups for continuous variables were evaluated using a t-test. Group differences for categorical variables were evaluated using a chi-square test. There were no significant relationships between any of these variables and neuropsychological measures or the Minnesota Multiphasic Personality Inventory Depression Scale 2 (MMPI-2).

MATERIALS AND PROCEDURES

Each subject was given the QOLIE questionnaire to complete while inpatient at the Epilepsy Monitoring Unit, Hermann Hospital, Houston. One representative test was chosen from the neuropsychological test battery as a measure of verbal memory, nonverbal memory, language, and attention, respectively. Verbal memory was measured using the Verbal Selective Reminding Test.16 The Verbal Selective Reminding Test involves the initial presentation of a 12-word list for free recall. On each of up to 11 subsequent trials the subject is reminded only of the words not recalled on the previous trial, and instructed to recall the whole list as first presented, in any order. Total number of words recalled after a 30-minute delay was used as the independent variable. Nonverbal memory was assessed using the Non-Verbal Selective Reminding Test.17 The subject is shown 8 boxes, each containing a different random array of 5 black dots. A specific dot in each box is shown to the subject, who is asked to point to the particular dot in each box after all the boxes have been presented. The remainder of the test is analogous to the verbal selective reminding test in that the subject is only reminded of positions for incorrect responses, but is required to give a response to all the boxes for up to 7 subsequent trials. Because delayed memory data were not available for a number of subjects for the Non-Verbal Selective Reminding Test, the total number of items recalled across the 8 trials was used as the dependent variable. The Non-Verbal Selective Reminding Test has been found to be sensitive to preoperative right temporal lobe dysfunction in a population of adult patients with epilepsy of mixed cause.16 Language was assessed with the Boston Naming Test,19 a test of the ability to name line drawings of common objects. The dependent variable used was total net score. Immediate attention was assessed with the Digit Span subtest of the Wechsler Adult Intelligence Scale—Revised.20 The dependent variable used was the age-corrected scaled score (mean = 10; SD = 3).

self-esteem.3,18 Devinsky et al3 found significant negative correlations between the 4 factor scores derived from the QOLIE scales—seizure-specific effects, cognition, physical health, and mental health—and neurotoxicity, systemic toxicity, and health care utilization by patients. Patients who had been free of seizures reported better scores than did patients who had reported a high frequency of seizures. Perrine et al10 administered the QOLIE, a battery of neuropsychological measures, the Profile of Mood States, and a neurotoxicity rating scale to 304 patients with primarily mild to moderate epilepsy. Factors associated with mood, psychomotor speed, verbal memory, and language correlated significantly with selected scales of the QOLIE. The mood factor showed the highest correlation with quality of life scales; however, even with the effects of mood removed from analyses, cognitive abilities, as assessed by neuropsychological tests, were significantly related to self-report indexes of quality of life. Thus, Perrine et al10 concluded that both objectively assessed cognitive abilities and mood state have a significant impact on perceived quality of daily functioning.

To date, to our knowledge, no published studies have assessed the sensitivity of the QOLIE to the effects of more severe seizure disorders. Devinsky et al5 reported that only 31 of 304 patients in their validation sample had a high seizure frequency, and only 10% of the patients in the study by Perrine et al10 had very frequent seizures (>100 simple partial, absence, or myoclonic seizures, >12 complex partial seizures, and >4 generalized tonic-clonic sei-
Additionally there have been no reports regarding the sensitivity of the QOLIE to the effects of pseudoseizures, even though between 6% and 40% of patients evaluated in epilepsy treatment centers are found to have unambiguous pseudoseizures.8-10 Pseudoseizures are defined as the absence of evidence of epileptiform activity during an event captured through electroencephalography and video monitoring.8,11 Individuals with intractable pseudoseizures are often subjected to the adverse effects of anticonvulsant medications, are unable to drive, and may have experienced discrimination in both vocational and social situations. In addition, memory function may be affected by the presence of a significant mood disorder or other psychopathologic manifestations. Therefore, patients with pseudoseizures may report a negative impact on their quality of life, similar to patients with epilepsy.

In this study we examined the self-perceptions of quality of life, as reported on the QOLIE, in 2 patient groups: individuals with intractable seizures of either right or left temporal lobe origin and those with pseudoseizures. Since depression has been found to be common in both groups12,13 and has been associated with increased complaints of poor memory function,2,6 we examined the relationship between self-perceived cognitive status as reported on the QOLIE and objective neuropsychological measures of cognition, as well as the independence of these relationships from the effects of mood disorder. We predicted that, as Perrine et al6 found, mood state would be related to self-perception of cognitive function, but that cognitive function, as assessed by objective neuropsychological measures, would also have a significant impact on perceived quality of daily living. As memory processes for verbal and nonverbal material may be differentially affected by side of seizure origin,14,15 we also hypothesized that a material-specific relationship between memory performance on neuropsychological tests and self-perceived memory difficulty as reported on the QOLIE would be found in patients with epilepsy but not in patients with pseudoseizures. For the pseudoseizure group the degree of mood disorder was expected to account for most of the variance in self-report of cognitive function.

**Table 1. Demographic and Seizure Variables by Group**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pseudoseizure (n = 25)</th>
<th>Epileptic (n = 43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD age, y (range)</td>
<td>35.1 ± 11.5 (17-52)</td>
<td>35.7 ± 9.2 (20-55)</td>
</tr>
<tr>
<td>Age at onset, y* (mean)</td>
<td>27.7 (13.4)</td>
<td>15.3 (11.5)</td>
</tr>
<tr>
<td>Duration,* (mean)</td>
<td>7.5 (7.6)</td>
<td>21.1 (10.1)</td>
</tr>
<tr>
<td>Seizure frequency per month (mean)</td>
<td>35.8 (68.5)</td>
<td>12.2 (23.7)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education, y</td>
<td>13.3 ± 1.9</td>
<td>13.6 ± 1.8</td>
</tr>
<tr>
<td>WAIS FSIQ†</td>
<td>90.8 ± 13.6</td>
<td>88.4 ± 11.7</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>22</td>
<td>11</td>
</tr>
<tr>
<td>Males</td>
<td>6</td>
<td>9</td>
</tr>
</tbody>
</table>

*Significant difference groups at P < .01.
†WAIS indicates Wechsler Adult Intelligence Scale; FSIQ, Full-Scale Intelligence Quotient.

**Table 2. Group Performances on Neuropsychological Tests**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pseudoseizure</th>
<th>Epileptic</th>
<th>Tukey Comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal Memory (VSR, delay)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD of total items recalled</td>
<td>10.0 ± 2.4</td>
<td>6.8 ± 3.9</td>
<td>8.0 ± 3.0</td>
</tr>
<tr>
<td>z Score</td>
<td>−0.6</td>
<td>−2.3</td>
<td>−1.0</td>
</tr>
<tr>
<td>Nonverbal Memory (NVS Ry total)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD of total items recalled</td>
<td>42.9 ± 13.1</td>
<td>37.1 ± 10.4</td>
<td>31.2 ± 11.2</td>
</tr>
<tr>
<td>z Score</td>
<td>0.2</td>
<td>−0.3</td>
<td>−0.7</td>
</tr>
<tr>
<td>Language (Boston Naming Test)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD of total score</td>
<td>53.0 ± 5.6</td>
<td>46.8 ± 7.7</td>
<td>48.1 ± 9.7</td>
</tr>
<tr>
<td>z Score</td>
<td>−0.9</td>
<td>−2.6</td>
<td>−2.1</td>
</tr>
<tr>
<td>Attention (WAIS-R Digit Span)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD of standard score</td>
<td>8.4 ± 3</td>
<td>9.7 ± 2.6</td>
<td>8.4 ± 2.6</td>
</tr>
<tr>
<td>z Score</td>
<td>−0.5</td>
<td>−0.1</td>
<td>−0.5</td>
</tr>
</tbody>
</table>

*VSR indicates Verbal Selective Reminding Test; NVSR, Non-Verbal Selective Reminding Test; P, pseudoseizure group; RTLE, right temporal lobe epilepsy; LTLE, left temporal lobe epilepsy; and WAIS-R, Wechsler Adult Intelligence Scale–Revised.
LTLE, or RTLE) as the independent variable. Follow-up pairwise comparisons were made using Tukey HSD. Results are presented in Table 2 and suggest generally reduced verbal memory and language abilities for the patients with LTLE, and reduced nonverbal memory for the patients with RTLE compared with the patients with pseudoseizure.

RESPONSE PROFILES ON THE QOLIE

The 17 scales from the QOLIE were grouped into 4 domains as suggested by the factor analyses performed by Devinsky et al. These domains included (1) seizure-specific effects (seizure worry [SW], medication effects [ME], health discouragement [HD], work or driving or social function [W/D/S]); (2) cognitive (language, attention/concentration [A/C] and memory); (3) physical health (health, physical functioning [PF], role limitations/physical [RL/P], and pain); and (4) mental health (overall quality of life [QOL], emotional well-being [EW], role limitations/emotional [RL/E], social isolation [SI], social support [SS], and energy or fatigue [EF]) domains. See the “Results” section of the text for analyses of group differences between profiles.

The Quality of Life in Epilepsy Inventory-89 T scores for pseudoseizure (triangles) and complex partial seizure (CPS) (squares) groups on A, seizure-specific effects (seizure worry [SW], medication effects [ME], health discouragement [HD], work or driving or social function [W/D/S]); B, cognitive (language, attention/concentration [A/C] and memory); C, physical health (health, physical functioning [PF], role limitations/physical [RL/P], and pain); and D, mental health (overall quality of life [QOL], emotional well-being [EW], role limitations/emotional [RL/E], social isolation [SI], social support [SS], and energy or fatigue [EF]) domains. See the “Results” section of the text for analyses of group differences between profiles.

LTLE, or RTLE) as the independent variable. Follow-up pairwise comparisons were made using Tukey HSD. Results are presented in Table 2 and suggest generally reduced verbal memory and language abilities for the patients with LTLE, and reduced nonverbal memory for the patients with RTLE compared with the patients with pseudoseizure.

RESPONSE PROFILES ON THE QOLIE

The 17 scales from the QOLIE were grouped into 4 domains as suggested by the factor analyses performed by Devinsky et al. These domains included (1) seizure-specific effects (seizure worry, health discouragement, medicine effects, and work or driving or social function); (2) cognition (language, memory, and attention); (3) physical health (role limitations/physical, pain, health perceptions, or physical function); and (4) mental health (overall quality of life, emotional well-being, role limitations/emotional, social isolation, social support, and energy or fatigue). Group differences within each of these domains were examined using a multivariate approach to profile analysis, with seizure group (CPS or pseudoseizure) as the between-subjects variable and scores on the domain subscales as the within-subjects variables. Profile analysis examines 3 hypotheses: (1) flatness, or whether scale elevations on the QOLIE, collapsed across between-subjects groupings, differ; (2) shape, or the effect of group membership on the pattern of response on QOLIE subscales; and (3) elevation, or the effect of group membership on an average or composite of the QOLIE domain subscales. In the current analyses, the interest focused on group effects, which would include the effect of shape, or whether CPS and pseudoseizure groups differ in their patterns of self-perception within a domain, and elevation, or whether there is an overall group difference in degree of response collapsed across within-domain scales. In the presence of an effect of shape (group by measure interaction) the effects of elevation are ignored and the effects of group membership on differences between individual scales within the domains are examined. A preliminary profile analysis comparing the 2 CPS groups indicated no differences, and the QOLIE data for the LTLE and RTLE groups were collapsed.

Response profiles on the QOLIE domains for the CPS and pseudoseizure groups are presented in the Figure. Coding of responses is such that the lower the T score the lower the self-perception of functioning on that scale and domain. Profile analyses comparing CPS and pseudoseizure groups indicated no significant group effects for the seizure-specific effects and cognitive domains. As can be seen in the Figure, A and B, the pseudoseizure and CPS groups tended to perceive themselves as functioning similarly in the seizure-specific and cognitive domains. Consistent with the relative severity of illness in patients with CPS, T scores for some subscales of the seizure-specific effects domain for this group were almost 1 SD (1 SD = 10 T) below the normative group (T score = 50). For the physical health domain there was a sig-

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nificant group effect ($F[1,66] = 29.81; P=.001$), indicating that the average score on the subscales in this domain was different between the 2 groups. As can be seen in the Figure, C, the pseudoseizure group reported significantly decreased physical health compared with the CPS group across domain scales. For the mental health domain there was a significant group by domain scale interaction ($F[5,62] = 4.24; P<.002$) indicating that the profile of subscale scores was different for the 2 groups. Follow-up analyses, using $P<.008$ as a critical value to maintain a familywise experimental error rate less than .05, indicated that the only significant group difference was on the energy or fatigue scale. As can be seen in the Figure, D, the pseudoseizure group rated itself as experiencing more fatigue and lower energy levels than did the CPS group.

These findings suggest that patients with pseudoseizures perceive themselves as experiencing a similar impact of their seizure disorder as do patients with CPS on many aspects of cognitive function and mental health. This is despite the findings that patients with pseudoseizures perform at significantly higher levels than patients with CPS on objective language and memory tests. Interestingly, patients with pseudoseizures also reported a lower degree of physical health than those with CPS.

### RELATIONSHIP BETWEEN THE DEPRESSION SCALE OF THE MMPI-2 AND SUBJECTIVELY EXPERIENCED COGNITIVE FUNCTION AS MEASURED BY THE QOLIE

We examined the relationship between the Memory, Language, and Attention/Concentration Scales of the QOLIE and the Depression Scale (clinical scale 2) MMPI-2 for individuals with pseudoseizures and CPS using separate correlation analyses. For both the pseudoseizure and epileptic groups the Depression Scale of the MMPI-2 correlated significantly with the Memory, Language, and Attention/Concentration Scales (range of Pearson correlation coefficients, −0.35 to −0.61; $P<.05$).

### RELATIONSHIP BETWEEN SUBJECTIVELY AND OBJECTIVELY MEASURED COGNITIVE STATUS INDEPENDENT OF MOOD STATE

We examined the relationship between objective and subjective measures of cognitive performance using the MMPI-2 Depression Scale as a covariate to control for the effects of depression. There was no significant difference between the CPS (mean ± SD, 58.1 ± 11.9) and pseudoseizure (mean ± SD, 62.5 ± 9.5) groups on the Depression Scale of the MMPI-2. For the pseudoseizure group there were no relationships between Memory, Language, and Attention/Concentration Scales on the QOLIE and neuropsychological tests independent of depression ($P>.30$). For the RTLE group there was a significant relationship between nonverbal memory and self-perception of memory function ($F[1,14] = 7.4; P<.02$) independent of the effects of level of depression. For the LTLE group there were significant relationships between the memory scale of the QOLIE and delayed verbal memory on the Verbal Selective Reminding Test ($F[1,13] = 5.8; P<.03$) and between the language scale of the QOLIE and the Boston Naming Test ($F[1,13]=11.02; P<.006$). These effects were independent of the presence of depression.

In contrast to previous studies using the QOLIE, our study compared responses of patients with severe epilepsy with a group of patients with pseudoseizures. Whereas patients in other studies6,8,12 presented with a broad range of causes, type, and severity of seizures, all the patients with epilepsy in this study had temporal lobe seizures that met the criteria of Devinsky et al5 for being classified as severe in frequency (>12 seizures per year). Consistent with the severity of their seizure disorder, this patient group reported a quality of life generally below (T score <50) that reported for patients in the QOLIE normative group. The lowest scores reported by this group were for scales measuring seizure-specific effects, such as seizure worry, health discouragement, and work or driving or social function. However, the mean overall T score of 44 was only two thirds of 1 SD below the normative mean. Devinsky et al5 also reported similar findings, noting a trend for patients with less severe epilepsy to have higher scores than those with more severe seizures. The lack of more significant differences was attributed to factors such as the use of medication and family support that may influence patient responses. Also, the system used for classification of epilepsy severity that was developed and used by Devinsky et al5, and also used in this study, may not reflect all the differences that have a significant impact on quality of life. Another possibility is that the QOLIE may not differentiate quality of life between patients with moderate and severe seizure frequency adequately because of a floor effect.

The patients with pseudoseizures reported a similar overall quality of life as those with CPS. The QOLIE includes items regarding medication effects, discouragement secondary to health difficulties, and worry regarding seizures and their effect on work, driving, and social function. Intractable seizures of either origin are likely to result in loss of driving privileges and negatively impact social and vocational functioning. All patients in our study were receiving anticonvulsant medications at the time of evaluation, and patients with both CPS13 and pseudoseizures8,12 may experience significant emotional difficulties. The finding that patients with pseudoseizures perceive themselves as having relatively greater physical limitations than those with CPS is consistent with various models of the cause of pseudoseizures, including psychodynamic models that emphasize the role of conversion disorder,26 learning theory models that emphasize the secondary gain available from adoption of a sick role,27 and suggestions of possible predisposing neurologic dysfunction in at least a subgroup of this population.28 Therefore, it is not unexpected that both groups reported similar levels of dysfunction regarding seizure-specific and emotionally related variables, and that patients with pseudoseizures emphasized their cognitive and physical dysfunction.
Like Perrine et al., we found that mood state was a strong predictor of the overall quality of life scale in patients with epilepsy. However, unlike Perrine et al., we found that mood state did not explain a significant portion of the variance in self-perception of cognitive function in this group. This may be due to the use of the Profile of Mood States by Perrine et al., which provides a broader measure of mood than the MMPI-2. In addition, our study sample had more severe seizure disorder than that reported by Perrine et al. Therefore, the effects of seizure disorder on cognition are likely more significant in our group, and potentially have a greater impact, relative to mood, on perceptions.

In our analyses there was no relationship between objective and subjective measurements of cognitive function for the patients with pseudoseizures independent of level of depression. This is consistent with a psychological explanation for self-perception of reduced cognitive function in patients with pseudoseizures. Perrine et al. found that neuropsychological test performance in patients with epilepsy was related to self-report indexes of quality of life even with the effects of mood removed from the analysis. For the patients with CPS in our study the relationship between neuropsychological test performance and perceived cognitive function was independent of mood disorder, but dependent on side of seizure onset. Specifically, naming and verbal memory were related to self-perceptions of language and memory dysfunction, respectively, in the LTLE group only, while deficits in memory for nonverbal material were related to reports of memory disorder in the group with RTLE only. This is consistent with reports of material-specific memory deficits based on laterality of seizure disorder, with deficits in nonverbal memory associated with RTLE and deficits in verbal memory associated with LTLE. Our finding of a material-specific relationship between objective and subjective measures of memory and language provides evidence for the validity of the cognitive domain scale on the QOLIE as a measure of self-perception of cognitive dysfunction, rather than mood disorder, in patients with intractable CPS.

Although our CPS group tended to score below the QOLIE normative group, the differences were often not as large as might have been expected. As discussed earlier, this may have been related to increased degree of social support, inadequate operational definition of severity, or a floor effect of the instrument. While our results generally support the validity of the QOLIE as a self-report measure of quality of life in patient groups with intractable CPS as well as pseudoseizures, further research regarding the validity of the QOLIE in well-defined seizure groups is necessary. This will be of particular importance if the instrument is to be used to quantify change in self-perception after seizure surgery in groups with intractable seizures, or after appropriate pharmacological or psychotherapeutic intervention in groups with pseudoseizures.

Accepted for publication July 9, 1997.

We thank Janelle L. Queng, BA, and Major Bradshaw, BA, who organized and coded the data for analysis.

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REFERENCES