

# Health-related quality of life (HRQOL), activity of daily living (ADL) and depressive mood disorder in temporal lobe epilepsy patients

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We determined the interrelations of chronological age, age at seizure onset, duration of seizure disorder, cognitive functioning (IQ), scales of activities of daily living, depressive mood disorder and measures of health-related quality of life (HRQOL). Furthermore, we investigated the association of the laterality of seizure onset zone and absence/presence of hippocampal atrophy and/or sclerosis (HA/HS) with measures of HRQOL, activities of daily living (ADL) and depressive mood disorder. In the setting of pre-surgical epilepsy evaluation, a sample of 56 patients with temporal lobe epilepsy (TLE) was studied using the Bonner Skalen für Epilepsie (BPSE) and the depression inventory D-S of von Zerssen. Patients reported high levels of dependency on others and poor coping capabilities. Our data also showed specific ADL-behaviour suggesting social withdrawal and isolation. Our results indicate emotional impairment as a major problem in TLE, because 45% of our patients scored in the depressive range of the D-S depression scale. Depression score was found to be a powerful predictor of self-reported quality of life after adjusting for seizure-related variables, demographic variables and cognitive functioning (IQ). The only scale showing a significant laterality effect was ADL-home. No relationship between the dependent measures of HRQOL, ADL-social, ADL-cultural, depressive mood disorder and laterality of the epileptogenic zone or absence/presence of HA/HS was found. HRQOL and depressive mood disorder are strongly interrelated indicating that patients with depressive symptoms report lower quality of life and specific patterns of ADL. HRQOL, ADL and depressive mood disorder are largely independent of biological markers such as laterality of seizure onset zone and absence/presence of HA/HS in TLE.

*Key words:* TLE; health-related quality of life; depressive mood disorder; pre-surgical evaluation.

## INTRODUCTION

Quality of life refers to an individual's overall well-being and daily functioning. Health-related quality of life (HRQOL) can be divided into three principal components: physical health, e.g. general health, daily functioning, symptoms such as pain, physical disability; mental health, e.g. mood, self-esteem, perception of well-being, perceived stigma; and social health, e.g. social activities and relationships<sup>1</sup>.

Most epileptic seizures are associated with repeated disabling and distressing episodes of loss of consciousness which often result in personal embarrassment and loss of dignity. Stigma, discrimination, vocational difficulties, social exclusion, transportation problems, and a wide variety of other psychosocial difficulties are similarly associated with epilepsy<sup>2</sup>. Such problems may ultimately lead to changes in lifestyle, in particular in the area of ADL and this may eventually influence self-reported quality of life in patients with TLE. We an-

tipated that patients with TLE would report specific ADL-behaviours such as less participation in social and cultural activities. Additionally, we predicted that such ADL-behaviours have a negative impact on perceived quality of life in TLE patients.

Another factor that may influence the perceived quality of life in TLE patients is depression. Several review articles suggest that depression may be one of the most frequent psychological complications of epilepsy<sup>3–5</sup>. Most reports have consistently failed to detect a relationship between a wide variety of seizure-related variables such as seizure type, age at onset, seizure duration, seizure frequency and presence or absence of a structural lesion in general populations of epilepsy patients<sup>6–8</sup>. Considerable interest has focused on the question of whether the side of seizure onset zone has significant influence on the incidence of depression. While some investigations reported an increased incidence of depression among patients with left-sided TLE<sup>9–11</sup> others failed to confirm these findings<sup>12–15</sup>.

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The relationship between HRQOL and depression in TLE is unclear, as no study has directly related HRQOL and clinical depression in TLE to our knowledge so far. We hypothesized that depression will have a major influence on HRQOL in TLE because similar influences have been shown in other chronic diseases<sup>16</sup>.

In the present study we chose to study patients with intractable TLE to obtain a better understanding of the relation between psychosocial functioning, ADL and mood in order to improve intervention strategies. Thus, we examined interrelations between measures of HRQOL, ADL and depressive mood disorder. We also investigated the influence of seizure-related measures such as laterality of seizure onset zone, absence/presence of hippocampal atrophy and/or sclerosis (HA/HS), seizure frequency, age at seizure onset and duration of seizure disorder on HRQOL and depressive mood disorder in patients with TLE.

## MATERIALS AND METHODS

### Setting and patients

All patients suffered from medically refractory TLE and were evaluated for possible epilepsy surgery. Pre-surgical workup included prolonged video-EEG monitoring using scalp/sphenoidal electrodes, high resolution magnetic resonance imaging (MRI), interictal single photon emission tomography (SPECT), and in selected cases a complete neuropsychological assessment including Wada-testing for lateralization of speech and memory.

Temporal lobe epilepsy was defined by typical clinical seizure semiology observed during prolonged video-EEG monitoring, temporal spikes on interictal EEG and ictal EEG patterns localized to the temporal lobes. We included only patients with HA/HS on high resolution MRI and patients with normal MRI in our study. Patients with other structural lesions were excluded from further analysis. Patients were categorized as either having hippocampal atrophy and/or hippocampal sclerosis (presence of HA/HS) or having a normal MRI scan (absence of HA/HS).

On the basis of the interictal spike distribution patients with >90% spikes over one temporal lobe were defined as unitemporal following the criteria of Chung *et al.*<sup>17</sup>. We included only patients with unitemporal spikes in this study. Patients with bitemporal interictal epileptogenic discharges were excluded. The side of the interictal spike focus corresponded to the side of HA/HS on MRI in all patients.

Patients received questionnaires for assessment of self-reported HRQOL, ADL, and depression on the day of admittance to the Epilepsy Monitoring Unit while still on full dose of their antiepileptic medications.

Table 1 illustrates the demographic characteristics of the patients and details of their seizure disorder. We included 56 patients in this study. Of the 34 patients with left-sided TLE, 22 patients showed HA/HS and 12 patients had normal MRI scans. Of the 22 patients with right-sided TLE, 17 patients showed HA/HS and five patients had normal MRI scans. There were no significant statistical differences between patient groups concerning chronological age, age at onset and duration of seizure disorder, IQ-testing, education, male/female ratio (chi-squared = 2.41;  $P > 0.12$ ) and radiological findings (chi-squared = 0.99;  $P > 0.32$ ). IQ-testing was performed with the MWT-B<sup>18</sup> which is a standardized vocabulary test with good correlation to general intelligence as well as to education.

### Measures assessing HRQOL

The Bonner Psychosoziale Skalen für Epilepsie (BPSE) developed by Helmstaedter *et al.*<sup>19</sup> was administered to all patients. We used part I for assessment of HRQOL which addresses the impact of epilepsy/seizures on various areas of the patient's life and considers self-reported, epilepsy-related impairment in multiple domains. Questions were mostly adapted from the West Haven–Yale Multidimensional Pain Inventory (WHYMPI). Patients had to answer questions in the style of 'To what degree do seizures/epilepsy affect your health/work performance/family life/emotional well-being etc.' on a 7-point Likert scale. In the original study Helmstaedter *et al.* derived six impairment scales from factor analysis with satisfactory scale reliability (Cronbach  $\alpha$ ) for most scales ranging from 0.56–0.88. For the scales 'physical well-being'; 'activity/capability'; 'relations and family'; 'emotions/moods' high scores indicate high self-perceived impairment; for the scales 'independence' and 'coping/control' low scores indicate high self-perceived impairment.

### Measures assessing ADL

We used the daily activities subscales of the BPSE for measurement of ADL. Patients reported their daily activities ranging from activities at home and within the family (ADL-home), social activities, mostly outdoor and involving contact with other persons (ADL-social) and cultural/political/hobby activities (ADL-cultural). ADL scales were also derived from factor analyses in the original study by Helmstaedter *et al.* with satisfactory scale reliability (Cronbach  $\alpha$ ) ranging from 0.71–0.83. High scale scores indicate frequent activities concerning the specific ADL areas.

Table 1: Patient characteristics.

	LTLE ( <i>N</i> = 34) mean (SD)	RTLE ( <i>N</i> = 22) mean (SD)
Chronological age	33.1 (9.4)	36.6 (10.3)
Age at seizure onset	12.5 (12.4)	12.7 (8.5)
Duration of seizure disorder	20.3 (9.5)	24.0 (12.1)
Seizure frequency per month	9.8 (14.7)	14.1 (20.7)
MWTB-IQ	100.4 (9.4)	102.2 (14.9)
Education (years)	10.4 (2.4)	9.0 (1.0)
Male/female <sup>a</sup>	18/16	7/15
Absence of HA-HS/presence of HA-HS <sup>a, b</sup>	12/22	5/17

<sup>a</sup>Chi-squared test; NS. <sup>b</sup> HA/HS.

Table 2: Percentage of high-scoring TLE patients on measures of HRQOL, ADL and depression.

Scales	Number of high-scoring patients
BPSE-HRQOL	
Physical	7 (13%)
Activity/capability	15 (27%)
Relations and family	7 (13%)
Emotions/moods	22 (39%)
Independence	35 (63%)
Coping/control	30 (54%)
BPSE-ADL	
Home	20 (36%)
Social	7 (12%)
Cultural	4 (7%)
Depression	
D-S	25 (45%)

## Measures assessing depressive mood disorder

The German Depression Scale D-S of von Zerssen, a self-report measure with demonstrated reliability and validity<sup>20</sup>, was used to measure levels of depressive mood disorder. Subjects were asked for ratings on a 4-point scale concerning symptoms of depression. High scores refer to a more severe depressive mood disorder and those patients with scores >10 were assigned as prone to depressive mood disorder.

## Data analysis

First, we calculated the percentage of patients with elevated scores on different subscales of the HRQOL and ADL scales according to the BPSE manual. The total score of a subscale was defined to be high if the mean rating per item was higher than midpoint. In order to classify patients with depressive mood disorder we used a cut-off score of >10 on the D-S raw data for the diagnosis of depressive mood disorder. Subsequently, a chi-squared test was used for the depression score to assess effects of laterality (left-sided TLE, right-sided TLE).

Second, we performed six separate stepwise multiple-regression analyses with each HRQOL subscale of the BPSE as a dependent variable and chronological age, age at seizure onset, duration of seizure

disorder, laterality groups (left-sided TLE, right-sided TLE), MRI results (absence/presence of HA/HS), gender, MWTB-IQ, depression score, ADL-home, ADL-social, ADL-cultural as independent variables in order to determine the influence of clinical, demographic and behavioural/cognitive variables on self-reported HRQOL measures.

Third, we calculated product-moment correlations between seizure frequency and depression, ADL-home, ADL-social, ADL-cultural for the whole patient sample.

Fourth, we performed 2 × 2 analyses of variance (ANOVA) with laterality of TLE (left, right) and MRI (normal, HA/HS) as independent variables and the six HRQOL subscales, ADL-home, ADL-social, ADL-cultural and the depression score as dependent variables.

## RESULTS

### Percentage of patients with elevated scores on the BPSE and D-S

We found that 39% of patients scored high on emotional impairment, 63% of patients on independence and 53% of patients on coping/control. Analysis of the ADL scales revealed that 36% of patients performed activities at home with their family, whereas only 13% reported social activities and only 7% cultural activities.

Of the patients 44.6% were classified as suffering from depressive mood disorder (D-S scores >10; 13 (38.2%) of left-sided TLE patients, 12 (54.5%) of right-sided TLE). No significant influence of laterality of the seizure onset zone on depressive mood disorder could be detected (chi-squared = 1.43; *P* > 0.23).

Table 2 displays the results of the patient's self-reported impairments.

### Relationship of HRQOL to clinical, demographic and behavioural/cognitive variables

The results of stepwise multiple regression analysis controlling for confounding variables such as lateral-

Table 3: Results of separate stepwise multiple regression analyses.

Scale	$R^2$	$P$	Significant predictors (Beta)
Physical well-being	0.27	<0.001	Depression (0.52)
Activity/capability	0.21	<0.001	Depression (0.46)
Relations and family	0.11	<0.001	Depression (0.32)
Emotional/mood	0.38	<0.001	Depression (0.67) ADL-cultural (0.26)
Independence	0.33	<0.001	Depression (-0.57)
Coping/control	0.38	<0.001	Depression (-0.63) seizure frequency (0.27)

ity of TLE, presence/absence of HA/HS, sex, age at onset, chronological age, duration of disease, seizure frequency showed a significant ( $P < 0.001$ ) effect of depression score on all HRQOL scales. The positive correlation between depression score and 'physical well-being'; 'activity/capability'; 'relations and family'; 'emotions/moods' indicates that patients with increased depression scores show poorer quality of life. In addition, the depression score was negatively correlated with 'independence' showing that patients who feel more independent are less depressed and also negatively correlated with 'coping/control' indicating that those patients who have a better coping style again feel less depressed. Seizure frequency was a co-predictor for 'coping/control' and ADL-social was a co-predictor for 'emotional impairment' (Table 3).

#### Relationship of seizure frequency to depressive mood disorder and ADL

The correlational analyses indicated a moderate relationship between seizure frequency and depression score ( $r = 0.24$ ;  $P = 0.07$ ). Seizure frequency correlated negatively with both ADL-cultural ( $r = -0.37$ ;  $P < 0.01$ ) and ADL-social ( $r = -0.29$ ;  $P < 0.05$ ). The correlation between seizure frequency and ADL-home was small and nonsignificant ( $r = 0.10$ ;  $P > 0.44$ ).

#### Relationship of laterality of the seizure onset zone and presence/absence of HA/HS to HRQOL, ADL and depression

ANOVA revealed a significant effect of laterality ( $F(2, 54)$ ;  $P < 0.034$ ) on ADL-home, but no effect of presence/absence of HA/HS ( $P > 0.05$ ) and also no significant interaction ( $P > 0.05$ ). For all other dependent variables of the HRQOL scales, ADL scales and depression score separate ANOVAs showed that neither laterality of TLE ( $F(2, 54)$  all  $P \geq 0.10$ ); presence/absence of HA/HS ( $F(2, 54)$  all  $P \geq 0.10$ ) nor interaction were significant ( $F(2, 54)$  all  $P \geq 0.10$ ).

## DISCUSSION

Our results can be summarized as follows. First, patients with TLE reported emotional impairment, feeling of dependence and less developed coping capabilities to be their major areas of self-concern. They further seem to have a specific pattern of ADL. They are highly active at home interacting with their family and they report almost no cultural and social activities. Second, depression score was the major predictor in all six HRQOL scales. Third, only ADL-home was significantly related to the laterality of the seizure onset zone indicating that right-sided TLE patients are more active at home than left-sided TLE patients. We did not find any other relationship between the laterality of the seizure onset zone and absence/presence of HA/HS with HRQOL, ADL-social, ADL-cultural and depressive mood disorder, respectively.

Our results indicate that 'emotional impairment', 'independence' and 'coping and control' were the predominant areas of impairment in TLE patients while patients felt less impaired in the domains of 'physical well-being', 'relations/family' and 'activity/capability'. These results are similar to the study by Helmstaedter *et al.* in 58 TLE patients<sup>19</sup>. Their patients indicated emotional impairment as their main problem as well, while they did not report impairments in 'independence' and 'coping/control' measures.

Frequent activities at home and in the family context predominated in our patients, whereas few patients participated in social and cultural activities. Our results concerning the specific patterns of ADL-behaviour corroborate previous reports<sup>19,24</sup>. One reason for such a restricted lifestyle may be fear of injury and of social embarrassment. Nelen<sup>25</sup> reported that accidents at home and during leisure activities are less common in people with epilepsy than in the general population probably due to a restricted lifestyle. Such a lifestyle may eventually lead to withdrawal and social isolation.

We found that depression score was a powerful predictor of HRQOL and ADL measures. The more depressive the symptoms patients had indicated, the poorer were their quality of life, and social and cultural activities. Interestingly, seizure frequency was not a significant predictor for depressive mood and HRQOL measures except for the coping/control scale indicating that poor self-reported mood and quality of life are independent of the number of seizures experienced per month. However, seizure frequency was negatively correlated to social and cultural activities demonstrating that patients with more seizures tend to withdraw from social and cultural events.

Depressive symptoms are a recognized interictal psychiatric problem in TLE<sup>21</sup>. We also found that 45% of our patients met the clinical criteria of self-reported depressive mood disorder. No effect of laterality and ab-

sence/presence of HA/HS on self-reported depressive mood disorder was evident in our study corroborating several previous reports<sup>9, 14–17, 22</sup>. Other studies, however, suggested an association between left-sided TLE and depression<sup>9–11</sup>. Victoroff *et al.*<sup>23</sup> described a complex association between laterality of the seizure onset zone, interictal hypometabolism and depression. In patients with left-sided epileptic foci they found a higher incidence of lifetime episodes of depression, whereas they found no association between current depression measured by means of a self-reported rating scale. To summarize, whether there is an effect of laterality of the side of seizure origin on depression remains unclear and further studies are warranted.

The finding that laterality of seizure origin and absence/presence of HA/HS had no effect on HRQOL indicates that self-assessment of psychosocial well-being is independent of these biological markers in TLE.

In conclusion, our data support and extend previous studies concerning the relationship of HRQOL, ADL and depressive mood disorder in TLE patients, indicating some suggestions for intervention. In the treatment of TLE patients, besides seizure control, it is also important to pay special attention to the presence of depressive mood disorder. Thus, improving a patient's mood by means of pharmacological and/or psychological intervention should also improve the self-reported psychosocial situation and lifestyle<sup>26</sup>. Programs aiming to increase a patient's psychological resources and social interests may in turn result in both improvements in mood and HRQOL scores. However, the effectiveness of such interventions in TLE patients should be the goals for future investigations.

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