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Predictors of health-related quality of life in patients with epilepsy and psychogenic nonepileptic seizures

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ABSTRACT

Epilepsy and psychogenic nonepileptic seizures (PNES) are associated with reduced health-related quality of life (HRQoL). The present study investigated the profile, relationship, and predictive power of illness perceptions, psychological distress (depression and anxiety), seizure activity, and demographic factors on HRQoL in these patient groups. Patients with epilepsy ($n = 62$) and PNES ($n = 45$) were recruited from a United Kingdom hospital and from membership-led organizations for individuals living with seizures. Patients completed a series of self-report questionnaires assessing: anxiety (GAD-7), depression (NDDI-E), illness perceptions (B-IPQ), HRQoL (NEWQOL-6D), and seizure frequency and severity (LSSS-3). Correlational and hierarchical multiple regression analyses were conducted. Patients with epilepsy reported higher HRQoL and scored lower on measures of depression and anxiety. Patients with PNES perceived their condition as more threatening overall. In both conditions, HRQoL was negatively correlated with more severe illness perceptions and psychological distress. In epilepsy and PNES, psychological distress (epilepsy: 27%; PNES: 24.8%) and illness perceptions (epilepsy: 23.1%; PNES: 23.3%) accounted for the largest amount of variance in HRQoL. Clinical factors were found not to be significant predictors, while demographic factors predicted HRQoL in epilepsy (12.6%), but not in PNES. Our findings support the notion that psychological factors are a stronger predictor of HRQoL in epilepsy and PNES than condition-related and demographic variables. Prior research suggests that anxiety and depression are key predictors of HRQoL; this study demonstrates that the relationship between illness perceptions and HRQoL is similarly close. These findings highlight the importance of addressing patients' beliefs about their condition.

1. Introduction

Epilepsy is a common neurological condition affecting between 5 and 10 per 1000 people in the United Kingdom (UK) [1]. It is a disorder of the brain characterized by recurrent seizures [2]. Psychogenic nonepileptic seizures (PNES) are one of the most important differential diagnoses of epilepsy. PNES superficially resemble epileptic seizures, but are not associated with epileptiform activity. Instead, most PNES are understood as a dissociative response to threatening internal or external stimuli [3]. PNES account for nearly 20% of presentations to seizure clinics [4].

Health-related quality of life (HRQoL) is reduced in epilepsy and PNES [5]. Both patient groups have to adjust to living with seizures and are at an increased risk of experiencing stigma [6,7] and developing psychiatric conditions, such as, mood, personality, and anxiety disorders [8,9]. Despite these commonalities, quantitative and qualitative research has indicated differences between patients' subjective accounts of living with epilepsy and PNES, perhaps reflecting the different etiologies of these disorders [10–12]. What is more, although findings in different studies are not completely consistent, patient groups with PNES tend to score higher than those with epilepsy on measures of anxiety, dissociation, and somatization and lower on measures of HRQoL [5,9]. There also tend to be clear demographic differences between cohorts with PNES or epilepsy which need to be taken into account in comparative studies; whereas epilepsy affects similar numbers of men and women, three quarters of patients with PNES are female, and the age at seizure onset is typically lower in epilepsy [13].

Systematic reviews have explored the most important factors contributing to the reduction in HRQoL in epilepsy and PNES. In epilepsy, Taylor et al. [14] reviewed 93 studies demonstrating that psychological variables (e.g. depression and anxiety) contributed 30–35% of the variance in HRQoL. Condition variables (e.g. seizure frequency and severity) accounted for up to 20% and demographics variables (e.g. age, gender) were "generally" found to have no significant relationship, while the association of educational level was inconsistent across studies. An

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equivalent systematic review of HRQoL in PNES by Jones et al. [15] based on 14 studies found that interpersonal and psychological factors (in particular, depression and anxiety) were negatively correlated with HRQoL, while condition and demographic variables were not significantly associated.

Neither of these systematic reviews considered the effect of illness perceptions on HRQoL although this psychological variable has been demonstrated to have an important influence on HRQoL in other medical conditions [16]. Illness perceptions are subjective emotional and cognitive representations about illness. Research into illness perceptions has predominately been based on the self-regulation model of health. This suggests that individuals are active problem solvers, and in response to a health threat, will generate a mental representation that can then be used as a framework to motivate coping behaviour and illness appraisal [17–19].

There are five components of illness perceptions that can be reliably investigated using the Illness Perception Questionnaire (IPQ) [20] or the Brief IPQ [21]. These are the perceived symptoms, consequences, probable cause, likely duration, and the extent to which the patient perceives that the condition can be cured or kept under control. Using the Brief IPQ, the components can be computed to create an overall perception reflecting how threatening or benign the illness is perceived to be. Illness perceptions have previously been explored in neurological symptom disorders including epilepsy and PNES, using the aforementioned questionnaires [22–28].

In Greek children with epilepsy (10–18 years), Rizou et al. [29] demonstrated that, when age and seizure severity were controlled for, the different components of illness perceptions accounted for 36.6% ($p < 0.001$) of the variance in HRQoL. Shallcross et al. [29] found in patients with epilepsy that the perception of how threatening the illness is overall mediated the relationship between depression and HRQoL, even if demographic and condition variables were controlled for. Similarly, in a study of 50 patients with PNES, Novakova et al. [30] reported that a more threatening view of the illness was associated with lower mental ($rho = 0.7$, $p = 0.001$) and physical ($rho = 0.44$, $p = 0.001$) HRQoL components.

In summary, there is evidence to suggest illness perceptions have a significant relationship with HRQoL in individuals with medical disorders including epilepsy and PNES. However, the relationship or predictive value of the individual components of illness perceptions on HRQoL has not been studied extensively or compared directly in adult samples of patients with epilepsy or PNES. Factors determining HRQoL in chronic disorders, such as epilepsy and PNES, can provide insight into patients' subjective illness experience and the nature of the disorder [31].

The first aim of the present study was to explore and compare the condition and psychological profile of patients with epilepsy on the one hand, and those with PNES on the other. Understanding the differences between the two conditions can highlight potential targets for treatment, as well as offer implications for making a differential diagnosis and prognosis. We hypothesized that patients with PNES would report higher scores on anxiety and depression and a lower HRQoL. Patients would also hold different beliefs about their condition including the perceived threat.

The second aim was more specifically to investigate the relationship and determine the predictive power of a range of factors on HRQoL: psychological factors (illness perceptions and psychological distress) and condition-related features (seizure duration, frequency, and severity). In light of the fact that prior research has reported inconsistencies between the association of demographic factors (age, gender and education) and HRQoL, we also investigated this as a potential factor.

Our study tested the hypothesis that there is a significant correlation between HRQoL and psychological variables in patients with epilepsy and those with PNES. Secondly, we expected that psychological variables would account for the largest variance in HRQoL in both conditions.

2. Methods

2.1. Patients

Patients were recruited from outpatient neurology clinics at the Royal Hallamshire Hospital, Sheffield (UK). To maximize recruitment, patients were also recruited from membership-led organizations for individuals who experience seizures (see acknowledgements for the list of organizations). Recruitment took place between October 2015 and July 2016. All patients were either from the UK (89.7%) or the United States (10.3%). This dataset was collected in the context of a randomized control trial investigating the effects of a writing intervention for patients with seizure disorders. The data presented in this study have been extracted from patients' baseline measures. The North of Scotland Research Ethics Committee granted ethical approval for this study.

Patients were included in the present study if they: were over the age of 18 years; had experienced at least one seizure in the last twelve months; had a diagnosis of epilepsy or PNES (patients with comorbid epilepsy and PNES were excluded); were able to provide informed consent and complete a demographic and clinical questionnaire without help (i.e. have a sufficient understanding of English and no recognized learning difficulties). Patients recruited through membership-led organizations were asked to self-report their diagnosis: epilepsy or PNES (patients were not eligible if they were currently undergoing clinical investigations to obtain a seizure diagnosis or if there was any doubt about the diagnosis).

All self-reported diagnoses of patients recruited at the Royal Hallamshire Hospital were confirmed by review of the hospital records. Patients were only included if they had a clear diagnosis of either epilepsy or PNES formulated by a Consultant Neurologist on the basis of all available clinical evidence (sometimes but not always including video-EEG recorded habitual seizures). When possible, confirmation of the self-reported diagnoses of patients recruited through membership-led organizations was sought from their General Practitioner (GP). However, patients were not excluded if GPs failed to respond to our requests for diagnostic confirmation.

A sample size calculation revealed that using the alpha level ($p = 0.05$), with 90% power, and a correlation of at least 0.5, that a sample size of 31 was required (>0.5 is classified as a strong relationship). The data from 45 patients with PNES and 62 patients with epilepsy were analysed.

2.2. Recruitment

This was a cross-sectional study. Patients recruited from outpatient neurology clinics were sent a participant information sheet at least 48 h before their appointment with a Consultant Neurologist. On the day of their appointment, the patient was approached in the waiting room by G.R. and invited to take part in the study. Patients who agreed to take part were asked to complete a set of self-report measures. Patients recruited from membership-led organizations replied to an advert for a study of a writing intervention designed to help patients with seizure disorders. The patient then contacted G.R. who gained written informed consent and provided access to an online form where patients could complete the self-report measures.

2.3. Measures

2.3.1. Demographic and medical information

This included age, gender, years in education, current diagnosis (PNES, epilepsy), duration since seizure onset, and the date of their last seizure.

2.3.2. Anxiety

The Generalized Anxiety Disorder (GAD-7) instrument is a seven-item scale used as a screening tool and severity measure of mild (score of 5–9), moderate [10–14], and severe anxiety (>15). Patients are asked to report on a four-item Likert scale (Not at all, Several days, More than half the days, Nearly every day) how often they have been bothered by anxiety-related problems over the past two weeks. The GAD-7 has been validated in patients with epilepsy [32] and has been used in patients with PNES [33].

2.3.3. Depression

The Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) is a six-item scale measuring major depression in people with seizures. Patients are asked to report on a four-item Likert scale (Always or Often, Sometimes, Rarely, Never) how best depression-related statements describes them over the last two weeks. Scoring above the cutoff of 15 suggests a major depressive episode. The NDDI-E has been validated in patients with epilepsy [34] and PNES [35].

2.3.4. Illness perceptions

The Brief Illness Perception Questionnaire (B-IPQ) is a nine-item scale assessing a patient's cognitive and emotional representation of illness. Patients are asked to answer questions regarding: consequences, time-line, personal control, treatment control, symptoms, concern, understanding, and emotional representation using a ten-item Likert scale. As recommended by the scoring instructions, the relevant items were reverse-coded and the eight items were added to compute a total score (illness perception total, epilepsy $\alpha = 0.75$, PNES $\alpha = 0.67$). In all items, a higher score represents a more threatening view of the condition. The B-IPQ has been used in patients with epilepsy [36] and PNES [30].

2.3.5. HRQoL

The NEWQOL-6D [37] is a six-item HRQoL measure specifically developed for patients with seizures. Patients are asked questions across six domains: worry about attacks, depression, memory, concentration, control of events, and stigma. Each question has an option of four possible responses. A higher score represents better HRQoL.

2.3.6. Seizures frequency and severity

The Liverpool Seizure Severity Scale (LSSS-3) is a twelve-item self-report questionnaire asking patients about their experiences of seizure frequency in the past year, and the severity of their seizures in the last four weeks. It is scored from 0 to 100 with higher scores reflecting greater seizure severity. The LSSS has been shown to have good internal consistency ($\alpha = 0.72$–0.96) in patients with epilepsy [38] and has been used in patients with PNES [26].

2.4. Data analysis

Shapiro-Wilk test demonstrated that HRQoL scores were not normally distributed in either condition; therefore, differences in sample characteristics were examined using chi-square or Mann-Whitney *U* test (pairwise comparisons) as appropriate. To examine if there were significant differences between clinic and membership-led organizations recruits; patients were compared on demographic, condition-related, and psychological variables as a function of recruitment method.

Preliminary analyses were carried out using Spearman's rank correlation coefficient investigating the relationship between HRQoL and demographic, condition-related, and psychological variables. Next, a four-stage hierarchical multiple regression analysis was conducted on these variables with HRQoL as the dependent variable. None of the correlations exceeded 0.8 and the collinearity statistics (tolerance and VIF) were all within accepted limits; therefore, the assumption of multicollinearity was met. To reduce the number of variables in the regression model, any variable that was not significantly correlated with HRQoL in both conditions was omitted. For the same reason, as anxiety and depression were strongly correlated in both PNES ($rho = 0.71$, $p < 0.001$) and epilepsy ($rho = 0.66$, $p < 0.001$), the two scores were combined to compute a new variable named psychological distress (epilepsy $\alpha = 0.75$, PNES $\alpha = 0.76$). This approach is in line with previous studies by Shallcross et al. [39] and Rizou et al. [29]. Consistent with other studies investigating the predictive value of illness perceptions on HRQoL [29,40,41], demographic variables were entered at stage one, condition variables at stage two, psychological distress was entered at stage three, and the different components of illness perception were entered at stage four. The data met the assumption of independent errors (Durbin-Watson value, epilepsy = 1.98, PNES = 1.7). Due to the modest sample size, in the regression analysis missing scores were replaced with the mean (one patient with PNES was excluded at this stage of the analysis due to missing more than >20% of scores across all measures). An alpha value of 0.05 was used for all statistical analysis. All data were analysed using SPSS 23.

3. Results

3.1. Clinic vs. membership-led organization recruits

Overall, 31 of the 62 patients with epilepsy and 11 of the 45 patients with PNES were recruited from outpatient neurology clinics. In patients with epilepsy, there were no significant differences on any condition, demographic or psychological variable between clinic and membership-led organization recruits (i.e. patients with consultant-confirmed diagnoses and those with consultant unconfirmed diagnoses). In patients with PNES, those recruited from neurological clinics reported lower on scores of anxiety ($U = 109.5$, $p = 0.039$), were more concerned about their condition ($U = 110.5$, $p = 0.04$), and reported having a better understanding of their disorder ($U = 85.5$, $p = 0.016$).

3.2. Epilepsy vs. PNES profile

The demographic, condition-related, and psychological profile of patients with epilepsy and patients with PNES are shown in Table 1. The two patient groups were matched on age and education; however, a difference was observed in gender.

Table 1
Mann-Whitney-U analysis and chi-square test. Scores reflect median (IQR) unless otherwise stated.

	Epilepsy	PNES	*P* value
Demographic variables			
Female	69.4%	91.1%	0.005
Age (years)	39.5 (22)	38 (22)	0.32
Education (years)	15 (5)	15 (5)	0.57
Condition variables			
Duration (years)	17 (21.5)	3.3 (6.75)	<0.001
Frequency (last 4 weeks)	2 (3)	14.5 (35.25)	<0.001
Severity of seizures	50 (62)	50 (30)	0.53
Psychological variables			
HRQoL	0.765 (0.22)	0.68 (0.2)	0.01
Psychological distress	19.5 (13.5)	27 (17.75)	<0.001
Depression	14 (7)	18 (5.75)	<0.001
Score > 15	43.5% (27)	75.6% (35)	
Anxiety	5 (8)	9 (12)	0.001
None (0–4)	43.5% (27)	17.8% (8)	
Mild (5–9)	29% (18)	33.3% (15)	
Moderate (10–14)	14.5% (9)	13.3% (6)	
Severe (>15)	13% (8)	35.6% (16)	
Illness perception total	47 (20.25)	55 (16.25)	0.001
Consequences	6 (3)	8 (3)	<0.001
Timeline	10 (3)	8 (3)	0.06
Personal control	6 (5)	7 (4)	0.15
Treatment control	4 (3)	6 (6)	0.04
Symptoms	6 (4)	8 (4)	<0.001
Concern	7 (3)	8 (5)	0.008
Understanding	3 (4)	3 (6)	0.4
Emotional representation	7 (4)	8 (4)	0.02

Patients with PNES reported a greater number of seizures within the last four weeks. Those with epilepsy had experienced seizures for longer. There was no difference in self-reported seizure severity.

Patients with epilepsy reported greater HRQoL than those with PNES. Compared to those with epilepsy, patients with PNES scored higher on the subscales of depression (with over three-quarters of patients with PNES scoring above the cutoff score of 15 suggesting current major depression) and anxiety (with 35.6% of patients with PNES scoring above the cutoff of 15 suggesting severe anxiety).

Compared to those with PNES, patients with epilepsy perceived their condition as: having less severe consequences on their life, causing a fewer number of symptoms and were less concerned, associated with a lower negative emotional experience, and less threatening overall. Both patient groups thought of their condition as chronic and reported that they possessed a good understanding of their condition.

3.3. Correlates of HRQoL

Bivariate correlation analyses were conducted to examine the relationship between HRQoL and demographic, condition-related, and psychological variables (Table 2). In epilepsy, all psychological variables were negatively associated with HRQoL. In addition, HRQoL was correlated with seizure frequency and severity and education. In PNES, all psychological variables, with the exception of treatment control, were negatively associated with HRQoL. In contrast to the epilepsy group, no demographic or condition variables were significantly associated with HRQoL in PNES.

3.4. Predictors of HRQoL

A hierarchical multiple regression analysis of epilepsy with HRQoL as the dependent variable revealed that at stage one, education and gender explained 12.6% of the variance ($p = 0.02$). Condition factors were added second, explaining a further 2.5% ($p = 0.44$). Psychological distress was added next, accounting for the largest variance, 27% ($p < 0.001$). Finally, the different components of the B-IPQ were added explaining 23.1% ($p < 0.001$), of which, symptoms and consequences were the strongest predictors of HRQoL. The final model accounted for 65.3% of variance (Table 3).

Table 2

Spearman's rank correlation coefficient between HRQoL and demographic, condition-related, and psychological variables.

	Epilepsy	PNES
Demographic variables		
Gender	−0.24	−0.09
Age	0.19	0.11
Education	0.28*	0.27
Condition variables		
Duration	−0.06	0.06
Frequency	−0.38**	−0.22
Severity of seizures	−0.29*	−0.16
Psychological variables		
Psychological distress	−0.55***	−0.58***
Depression	−0.56***	−0.54***
Anxiety	−0.52***	−0.57***
Illness perception total	−0.63***	−0.42**
Consequences	−0.57***	−0.28
Timeline	−0.38**	−0.32*
Personal control	−0.38**	−0.31*
Treatment control	−0.21	0.18
Symptoms	−0.57***	−0.14
Concern	−0.34**	−0.55***
Understanding	−0.06	−0.23
Emotional representation	−0.56***	−0.54***

* $p = 0.05$.
** $p = 0.01$.
*** $p < 0.001$.

Table 3

Summary of hierarchical multiple regression analysis for variables predicting HRQoL in patients with epilepsy. Scores reflect standardized coefficient beta.

	Model 1	Model 2	Model 3	Model 4
Demographic variables				
Gender	−0.23	−0.18	−0.2	−0.21***
Education	0.26*	0.22	0.16	0.06
Condition variables				
Frequency		−0.08	−0.02	0.01
Severity of seizures		−0.14	−0.9	−0.05
Psychological variables				
Psychological distress			−0.53***	−0.45***
Illness perception total				
Consequences				−0.31*
Timeline				0.008
Personal control				−0.1
Symptoms				−0.27*
Concern				0.2
Emotional representation				−0.07
R^2 model	0.13	0.15	0.42	0.65
R^2 change	0.13	0.03	0.27	0.23
F change	4.27*	0.85	26.2***	5.55***

* $p = 0.05$.
** $p = 0.01$.
*** $p < 0.001$.

The same analysis was performed in the PNES group (Table 4). The final model accounted for 61.9% of the variance. At stage one, demographic factors explained 3% of the variance ($p = 0.53$). At stage two, condition factors accounted for a further 10.9% ($p = 0.1$). Psychological distress accounted for 24.8% ($p < 0.001$) and at stage four, illness perceptions accounted for 23.3% ($p = 0.02$), with personal control as a significant predictor of HRQoL.

4. Discussion

This study examined the differences, relationship, and predictive value of demographic, condition-related, and psychological factors, including illness perceptions, on HRQoL in patients with epilepsy or PNES.

As in previous studies, patients with epilepsy reported higher HRQoL and scored lower on measures of depression and anxiety than those with PNES. In terms of illness perceptions, patients with epilepsy considered their condition as less threatening, more likely to be controlled by personal ($p = 0.15$) and treatment factors, having fewer

Table 4

Summary of hierarchical multiple regression analysis for variables predicting HRQoL in patients with PNES. Scores reflect standardized coefficient beta.

	Model 1	Model 2	Model 3	Model 4
Demographic variables				
Gender	−0.04	0.002	0.04	0.07
Education	0.17	0.2	0.07	0.12
Condition variables				
Frequency		−0.31*	−0.09	−0.11
Severity of seizures		−0.1	−0.01	0.07
Psychological variables				
Psychological distress			−0.57***	−0.4**
Illness perception total				
Consequences				0.02
Timeline				−0.22
Personal control				−0.32*
Symptoms				0.28
Concern				−0.18
Emotional representation				−0.19
R^2 model	0.03	0.14	0.39	0.62
R^2 change	0.03	0.11	0.25	0.23
F change	0.64	2.46	15.41***	3.24*

* $p = 0.05$.
** $p = 0.01$.
*** $p < 0.001$.

consequences on their life, causing fewer of their symptoms, and having a lower emotional impact than those with PNES. Despite the fact that patients with epilepsy reported a greater duration since seizure onset (17 years compared to 3.3 years in PNES, $p < 0.001$), no significant difference was found in the perceived timeline, with both patient groups viewing their condition as chronic.

Surprisingly, on the group level, patients with PNES reported having a good understanding of their disorder, the level of which did not differ from that reported by patients with epilepsy ($p = 0.4$). This finding conflicts with previous quantitative and qualitative research [10,26]. It is possible that this inconsistency is the consequence of differences in the populations studied, for example, patients recruited from undergoing video-electroencephalography for diagnosis vs. outpatients with a confirmed diagnosis. The fact that in the current study, patients with PNES recruited from clinics scored higher on subjective understanding compared to those recruited from membership-led organizations indicates differences between the patient populations. Additionally, the data in the current study were collected from individuals who volunteered to take part in a psychological writing intervention, and therefore, may mean that the participants were more aware of the importance of psychological factors on symptom manifestation. Finally, it is conceivable that this mode of recruitment introduced different selection biases in the PNES and epilepsy groups; for instance, in terms of intellectual capacity, but both groups were matched on years of education and no participants had a recognized learning difficulty.

Our results are in line with a recent systematic review that reported seizure frequency is associated with HRQoL in patients with epilepsy [14]. This is in contrast to patients with PNES where no such association has been demonstrated [15]. The cause of this difference between the two conditions is not clear. Perhaps epileptic seizures have a more direct emotional, psychological, physical, social, and financial impact on the individual whereas seizures are only one manifestation of a more pervasive psychosocial disorder in patients with PNES [42,43]. Additionally, in patients with PNES, there are several possible casual factors that may negatively impact HRQoL, but which may not be directly connected to seizure frequency (e.g. lack of treatment, delayed diagnosis, attachment and interpersonal problems) [15,44]. In contrast, there is some evidence to suggest that patients with PNES who are seizure-free score higher on HRQoL measures. Nevertheless, the current evidence supports the notion that seizure remission alone should not be the only outcome of treatment for PNES as symptoms of psychopathology and reduced HRQoL may continue following a reduction in the frequency of nonepileptic seizures [43,45].

Our results are in line with the current evidence suggesting that psychological factors account for a larger variance of HRQoL in both epilepsy and PNES when compared to condition-related factors (i.e. seizure frequency and severity) and demographic variables. Depression and anxiety are generally reported as the strongest predictors; however, our findings demonstrate that illness perceptions account for almost as much of the variance as psychological distress.

This finding highlights the importance of targeting patients' beliefs about their condition when designing and implementing patient-centered treatment pathways for those who experience epileptic or nonepileptic seizures. Our findings support those of a study in patients with functional neurological symptoms by Sharpe et al. [46] involving 716 patients who had been referred to neurology clinics presenting with symptoms unexplained or somewhat explained by organic causes. They found that patients' expectation of non-recovery more than doubled the odds of a poor outcome at a one-year follow-up (odds ratio 2.04). More specific to seizure disorders, several studies investigating the feasibility and effectiveness of a psycho-educational intervention in patients with PNES that aimed to improve patients' illness beliefs (e.g. educate patients about the cause, triggers, and perpetuating factors) have suggested that this approach to an intervention can help reduce seizure frequency [47,48].

Examination of the regression analyses provides evidence to suggest that not all illness perceptions are significant predictors of HRQoL. Notwithstanding the fact that each component was investigated using only one question, after psychological distress, demographic, and clinical factors were controlled for, the final model showed that believing the condition has seriously affected their life and attributing a greater number of symptoms is associated with lower HRQoL. The implications of this finding are somewhat limited as the nature of these symptoms (i.e. organic or functional) or their consequences are unknown. However, as illness perceptions account for a larger variance of HRQoL when compared to seizure frequency and severity, these findings do support treatment pathways involving psychological interventions used in conjunction with anti-epileptic medication for epilepsy, and thus addressing the full spectrum of challenges associated with the condition and not just the seizures, which are only one of its manifestations [1,49].

In PNES, the final model of the multiple regression analysis suggests that better HRQoL is associated with the belief in greater personal control over the condition. The impact of self-control in PNES has been documented previously; for example, Stone et al. [12] found that patients with recent onset PNES ($n = 20$) experienced a more external locus of control than those who had just been diagnosed with epilepsy ($n = 20$, $p < 0.001$). Patients with PNES would therefore be more likely to perceive events as unpredictable and out of their control. Fairclough et al. [50] qualitatively analyzed the transcripts of twelve patients with PNES who were interviewed about their perceived treatment needs. The authors found that patients with PNES experienced a lack of control over their seizures as distressing and that “control” was perceived as an important treatment target.

4.1. Limitations

The study has a number of limitations. We did not examine patients' ideas about the etiology of their seizures although perceptions of the causes of their seizures form a key part of their illness representations. This has particular relevance for PNES as patients often reject psychological explanations and consider their condition as having physical causes [26,27]. In fact, evidence from qualitative studies in patients with PNES suggest that patients beliefs about the etiology of their condition can have an important influence on treatment acceptance and adherence, and prognosis as the failure to accept a biopsychosocial account of the diagnosis can lead to outright rejection of psychological treatment [51]. Similarly, patients with PNES who accept psychosocial factors are more hopeful for change with this form of therapy [50].

Although we attempted to confirm seizure diagnoses using the medical records for UK patients who were recruited via membership-led organizations, we cannot guarantee that such diagnoses were made using a gold-standard approach [52]. In addition, differences were found in patients with PNES on several psychological factors between clinic and membership-led organization recruits; though recruiting patients in this way means that we have data from a sample that will have had access to a wide range of different medical care providers and resources. This may make the findings more generalisable than if patients had been recruited from a single center.

As the study was cross-sectional in design, we are unable to argue causality. The conclusions from this research would have been stronger if the predictive power of illness perceptions (and indeed, the other psychological and condition-related factors) had been investigated longitudinally, for example, pre- and post-diagnosis or pre- and post-treatment.

4.2. Conclusion

Despite these limitations, our findings demonstrate that patients with epilepsy report a higher HRQoL and lower levels of depression and anxiety than those with PNES. Based on the analysis of an adequately powered sample size of patients recruited from outpatient neurology clinics and membership-led organizations, this study shows that psychological factors, including illness perceptions, accounted for a larger variance of HRQoL in both PNES and epilepsy than condition-related and demographic factors. While this study confirms prior research demonstrating that anxiety and depression are key predictors of HRQoL, this study also shows that illness perceptions account for almost as much of the variance in HRQoL. A better understanding of the determinants of HRQoL is important for the design of patient-centered treatment pathways for patients with epileptic or nonepileptic seizures.

Competing interests

None declared.

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References

[1] NICE. The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. London: National Institute for Health and Care Excellence; 2015.
[2] Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia 2014;55(4):475–82.
[3] Brown RJ, Reuber M. Towards an integrative theory of psychogenic non- epileptic seizures (PNES). Clin Psychol Rev 2016;47:55–70.
[4] Angus-Leppan H. Diagnosing epilepsy in neurology clinics: a prospective study. Seizure 2008;17(5):431–6.
[5] Al Marzooqi SM, Baker GA, Reilly J, Salmon P. The perceived health status of people with psychologically derived non-epileptic attack disorder and epilepsy: a comparative study. Seizure Eur J Epilepsy 2004;13(2):71–5.
[6] Jacoby A, Snape D, Baker GA. Epilepsy and social identity: the stigma of a chronic neurological disorder. Lancet Neurol 2005;4(3):171–8.
[7] Wyatt C, Laraway A, Weatherhead S. The experience of adjusting to a diagnosis of non-epileptic attack disorder (NEAD) and the subsequent process of psychological therapy. Seizure Eur J Epilepsy 2014;23(9):799–807.
[8] Tellez-Zenteno JF, Patten SB, Williams J, Jetté N, Wiebe S. Psychiatric comorbidity in epilepsy: a population-based analysis. Epilepsia 2007;48(12):2336–44.
[9] Brown RJ, Reuber M. Psychological and psychiatric aspects of psychogenic non-epileptic seizures (PNES): a systematic review. Clin Psychol Rev 2016;45:157–82.
[10] Rawlings GH, Reuber M. What patients say about living with psychogenic nonepileptic seizures: a systematic synthesis of qualitative studies. Seizure Eur J Epilepsy 2016;41:100–11.
[11] Reuber M, Rawlings G. Nonepileptic seizures - subjective phenomena. In: Hallett M, Stone J, Carson A, editors. Handbook of clinical neurology. Functional neurological disorders. 139. Elsevier; 2016. p. 283–96.
[12] Stone J, Binzer M, Sharpe M. Illness beliefs and locus of control - a comparison of patients with pseudoseizures and epilepsy. J Psychosom Res 2004;57(6):541–7.
[13] Reuber M, Elger CE. Psychogenic nonepileptic seizures: review and update. Epilepsy Behav 2003;4(3):205–16.
[14] Taylor RS, Sander JW, Taylor RJ, Baker GA. Predictors of health- related quality of life and costs in adults with epilepsy: a systematic review. Epilepsia 2011;52(12):2168–80.
[15] Jones B, Reuber M, Norman P. Correlates of health- related quality of life in adults with psychogenic nonepileptic seizures: a systematic review. Epilepsia 2016; 57(2):171–81.
[16] Broadbent E, Wilkes C, Koschwanez H, Weinman J, Norton S, Petrie KJ. A systematic review and meta- analysis of the Brief Illness Perception Questionnaire. Psychol Health 2015;30(11):1361–85.
[17] Leventhal H, Diefenbach M, Leventhal E. Illness cognition: using common sense to understand treatment adherence and affect cognition interactions. Cogn Ther Res 1992;16(2):143–63.
[18] Weinman J, Petrie KJ. Illness perceptions: a new paradigm for psychosomatics? J Psychosom Res 1997;42(2):113–6.
[19] Leventhal H, Brissette I, Leventhal E. The common sense model of self regulation of health and illness. In: Cameron L, Leventhal H, editors. The self regulation of health and illness behaviour. New York: Routledge; 2003.
[20] Weinman J, Petrie K, Moss-morris R, Horne R. The illness perception questionnaire: a new method for assessing the cognitive representation of illness. Psychol Health 1996;11(3):431–45.
[21] Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. J Psychosom Res 2006;60(6):631–7.
[22] Goldstein LH, Holland L, Soteriou H, Mellers JDC. Illness representations, coping styles and mood in adults with epilepsy. Epilepsy Res 2005;67(1):1–11.
[23] Brown I, Sheeran P, Reuber M. Enhancing antiepileptic drug adherence: a randomized controlled trial. Epilepsy Behav 2009;16(4):634–9.
[24] Worsely C, Whitehead K, Kandler R, Reuber M. Illness perceptions of health care workers in relation to epileptic and psychogenic nonepileptic seizures. Epilepsy Behav 2011;20(4):668–73.
[25] Whitehead K, Reuber M. Illness perceptions of neurologists and psychiatrists in relation to epilepsy and nonepileptic attack disorder. Seizure 2012;21(2):104–9.
[26] Whitehead K, Kandler R, Reuber M. Patients' and neurologists' perception of epilepsy and psychogenic nonepileptic seizures. Epilepsia 2013;54(4):708–17.
[27] Ludwig L, Whitehead K, Sharpe M, Reuber M, Stone J. Differences in illness perceptions between patients with non- epileptic seizures and functional limb weakness. J Psychosom Res 2015;79(3):246–9.
[28] Whitehead K, Stone J, Norman P, Sharpe M, Reuber M. Differences in relatives' and patients' illness perceptions in functional neurological symptom disorders compared with neurological diseases. Epilepsy Behav 2015;42:159–64.
[29] Rizou I, De Gucht V, Papavasiliou A, Maes S. Illness perceptions determine psychological distress and quality of life in youngsters with epilepsy. Epilepsy Behav 2015;46:144–50.
[30] Novakova B, Howlett S, Baker R, Reuber M. Emotion processing and psychogenic non-epileptic seizures: a cross-sectional comparison of patients and healthy controls. Seizure Eur J Epilepsy 2015;29:4–10.
[31] Lawton G, Mayor R, Howlett S, Reuber M. Psychogenic nonepileptic seizures and health- related quality of life: the relationship with psychological distress and other physical symptoms. Epilepsy Behav 2009;14(1):167–71.
[32] Seo J, Cho Y, Lee SJ, Lee J, Kim J, Moon H, et al. Validation of the Generalized Anxiety Disorder- 7 in people with epilepsy: a MEPSY study. Epilepsy Behav 2014;35:59–63.
[33] Chen J, Caller TA, Mecchella J, Thakur D, Homa K, Finn CT, et al. Reducing severity of comorbid psychiatric symptoms in an epilepsy clinic using a colocation model: results of a pilot intervention. Epilepsy Behav 2014;39:92–6.
[34] Cole AJ. New screening tool for identifying major depression in patients with epilepsy. Nat Clin Pract Neurol 2006;2(12):656–7.
[35] Williams HE, Bagary M. Using the Neurological Disorders Depression Inventory for Epilepsy (NDDI- E) in patients with psychogenic non- epileptic seizures (PNES). Epilepsy Behav 2012;24:191.
[36] Jan S, Martiniuk Alexandra L, Glozier Nicholas S, Hackett Maree L, Anderson CS. Sydney epilepsy incidence study to measure illness consequences: the SESIMIC observational epilepsy study protocol. BMC Neurol 2011;11(1):3.
[37] Mulhern B, Rowen D, Jacoby A, Marson T, Snape D, Hughes D, et al. The development of a QALY measure for epilepsy: NEWQOL- 6D. Epilepsy Behav 2012;24(1):36–43.
[38] Baker GA, Smith DF, Jacoby A, Hayes JA, Chadwick DW. Liverpool Seizure Severity Scale revisited. Seizure 1998;7(3):201.
[39] Shallcross AJ, Becker DA, Singh A, Friedman D, Montesdeoca J, French J, et al. Illness perceptions mediate the relationship between depression and quality of life in patients with epilepsy. Epilepsia 2015;56(11) [e186-e90].
[40] Rochelle TL, Fidler H. The importance of illness perceptions, quality of life and psychological status in patients with ulcerative colitis and Crohn's disease. J Health Psychol 2013;18(7):972–83.
[41] Kotsis K, Hyphantis T, Voulgari PV, Tsifetaki N, Drosos AA, Carvalho A. Illness perceptions and psychological distress associated with physical health-related quality of life in primary Sjögrens syndrome compared to systemic lupus erythematosus and rheumatoid arthritis. Rheumatol Int 2014;34(12):1671–81.
[42] Kerr C, Nixon A, Angalakuditi M. The impact of epilepsy on children and adult patients' lives: development of a conceptual model from qualitative literature. Seizure Eur J Epilepsy 2011;20(10):764–74.
[43] Reuber M, Mitchell AJ, Howlett S, Elger CE. Measuring outcome in psychogenic nonepileptic seizures: how relevant is seizure remission? Epilepsia 2005;46(11): 1788–95.
[44] Jones B, Norman P, Reuber M. Attachment style, relationship quality, and psychological distress in patients with psychogenic non-epileptic seizures versus epilepsy. Epilepsy Behav 2017;66:120–26.
[45] Reuber M, House A. Treating patients with psychogenic non- epileptic seizures. Curr Opin Neurol 2002;15(2):207–11.
[46] Sharpe M, Stone J, Hibberd C, Warlow C, Duncan R, Coleman R, et al. Neurology outpatients with symptoms unexplained by disease: illness beliefs and financial benefits predict 1- year outcome. Psychol Med 2010;40(4):689–98.
[47] Mayor R, Brown RJ, Cock H, House A, Howlett S, Singhal S, et al. Short- term outcome of psychogenic non- epileptic seizures after communication of the diagnosis. Epilepsy Behav 2012;25(4):676–81.
[48] Mayor R, Brown RJ, Cock H, House A, Howlett S, Smith P, et al. A feasibility study of a brief psycho-educational intervention for psychogenic nonepileptic seizures. Seizure 2013;22(9):760–5.
[49] Dewhurst E, Novakova B, Reuber M. A prospective service evaluation of acceptance and commitment therapy for patients with refractory epilepsy. Epilepsy Behav 2015;46:234–41.
[50] Fairclough G, Fox J, Mercer G, Reuber M, Brown RJ. Understanding the perceived treatment needs of patients with psychogenic nonepileptic seizures. Epilepsy Behav 2013;31:295–303.
[51] Thompson R, Isaac C, Rowse G, Tooth C, Reuber M. What is it like to receive a diagnosis of nonepileptic seizures? Epilepsy Behav 2009;14(3):508–15.
[52] Lafrance W, Baker G, Duncan R, Goldstein LH, Reuber M. Minimum requirements for the diagnosis of psychogenic nonepileptic seizures: a staged approach a report from the International League Against Epilepsy Nonepileptic Seizures Task Force. Epilepsia 2013;54(11):2005–18.