Medically unexplained symptoms in patients with PNES: Do they explain poor employment outcome in patients with good seizure outcomes?

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ABSTRACT

Background: Many patients with psychogenic nonepileptic seizures (PNES) have other medically unexplained symptoms (MUS). In order to assess their long-term contribution to ill-health and unemployment, we recorded MUS, employment, healthcare utilization, and seizure outcomes in a cohort of patients with PNES.
Methods: We had complete computerized healthcare records and employment information in 120 patients with PNES, 5–10 years postdiagnosis. We analyzed these data to assess the contribution of MUS to ill-health and to determine whether MUS could explain differences among seizure, employment, and healthcare utilization outcomes in PNES.
Results: At 5–10 years, 41/120 patients (34.2%) were attending primary or secondary care for seizures, 42/120 patients (35.0%) had MUS other than PNES, and 36/120 patients (30.0%) were employed. Unemployment was predicted by age at presentation (OR: 0.90 (0.86–0.94), p < 0.001), presenting to primary or secondary care with seizures (OR: 0.16 (0.05–0.52), p = 0.003), and contact with psychiatric services at 5–10 years (OR: 0.16 (0.05–0.58), p = 0.005). No outcome measures were predicted by additional MUS, though MUS themselves were predicted by psychiatric contact (OR: 2.27 (1.01–5.01), p = 0.048).
Conclusions: Our data suggest that MUS do not contribute independently to unemployment in the population with PNES, whereas psychiatric morbidity appears to do so. Nonetheless, MUS and psychiatric morbidity persist in the long term in a substantial minority of patients with PNES. We found no evidence that seizures in patients whose PNES have resolved are replaced with other MUS.

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1. Introduction

In terms of seizures, outcome in psychogenic nonepileptic seizures (PNES) is generally thought to be poor [1]. Other measures may be important in gauging PNES outcome, however, and may be different from seizure outcome. For example, healthcare utilization outcomes may be good when seizure outcomes are poor [2,3], whereas many individual patients who have good seizure outcomes remain economically inactive over the long term [2,3].

Up to 70% of patients with PNES have additional medically unexplained symptoms (MUS), with disorders such as fibromyalgia and chronic pain receiving particular attention in the literature [1,4,5,6]. It seems possible that these additional MUS contribute significantly to long-term disability associated with PNES, and might help explain discrepancies among seizure, socioeconomic, and healthcare utilization outcomes. In addition to this, individual patients may be reported anecdotally to develop another MUS when PNES resolve. This has sometimes

been interpreted as a 'replacement' effect, the hypothesis being that new MUS in some way fulfill the emotional or psychological role of the PNES. This effect seems not to occur in the short term [7], but may be relevant in the longer term and might also go some way toward explaining discrepancies among PNES outcomes.

We have studied the prevalence of MUS in a cohort of patients with PNES at 5–10 years from diagnosis, to determine whether MUS may explain some of the discrepancies among different PNES outcomes, whether the burden of additional MUS has changed over the long term, and whether there is evidence of a tendency for MUS to become more prevalent in patients whose PNES have resolved.

2. Materials and methods

At 5–10 years from diagnosis, we reported outcome information obtained from family doctors on 188/260 patients with PNES [3]. In 120 of these patients, we had employment data and a complete printout of the patient's practice record, including clinical notes and copies of secondary care correspondence, over the 6-month study period, allowing analysis for MUS other than PNES. The diagnosis of PNES was

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confirmed by video-EEG recording. In order to assess potential selection bias, we compared the present cohort of 120 patients with the 'parent' cohort of 260 from which they were drawn. In the following, the figures in italics refer to the latter, and the p value to the difference between the two: of the 120 patients, 91 (75.8%) (*75.4%, p = 0.793*) were female. Mean age at first attendance at the PNES clinic was 37.2 years (range: 13–73, SD: 13.3) (*37.8, p = 0.863*), mean age at onset of PNES was 30.2 years (range: 10–69, SD: 13.5) (*30.8, p = 0.709*), and median diagnostic delay 3.5 years (range: 0.1–33.0, interquartile range: 4.0) (*3.8, p = 0.850*). Additional epilepsy was present in 16/125 (12.8%) (*10.0%, p = 0.488*), and seven (5.6%) had a mild learning disability (LD) (*8.5%, p = 0.319*). Mean reported seizure frequency at the time of diagnosis was 19.7 (SD: 28.1) per month (*19.6, p = 0.438*). The average decile score obtained using the Scottish Index of Multiple Deprivation (http://www.scotland.gov.uk/Topics/Statistics/SIMD) was 3.8 (*3.8*), indicating that our sample came predominantly from the lower half of the socioeconomic scale.

As in our previous studies [2,7], MUS were pragmatically defined as symptoms sufficiently problematic to have resulted in a referral to secondary care, with negative investigation, which had occasioned consultations in the 6-month study period. We included symptoms attributed to tension headache, irritable bowel syndrome, chronic fatigue, and fibromyalgia. If the family doctor printout included primary or secondary care consultations for symptoms that met these conditions, the patient was recorded as having 'active' MUS.

Our previous work demonstrated incongruence among three long-term (5–10 years) PNES outcome measures [3,8], so in the present study, we analyzed all three: whether or not the patient presented to the family doctor or to the hospital or the Emergency Department with seizures (available in all 120 of the present cohort), whether the patient reported being free of attacks or not, and what the date or month of the last seizure was (these data were dichotomized into last seizure more or less than 6 months before). The latter two measures were obtained by postal survey, for which we obtained responses in 51/120 patients (42.5%). Baseline data were acquired with the approval of the Southern General Hospital Research Ethics Committee. The follow up data were acquired with the approval of the West of Scotland Research Ethics Committee.

3. Statistical analysis

Statistical analysis was carried out using SPSS v21. The chi-squared test was used to evaluate between-group differences. Simultaneous binary logistic regression (BLR) models were used to evaluate the ability of independent variables to predict outcomes. Exploratory bivariate analysis was carried out for each one. Independent variables correlating with outcome variables at the 10% level or less ($p \leq 0.1$) were considered for entry into the model. Where screening for colinearity identified two independent variables correlating at the 30% level ($p = <0.3$) or less, the variable correlating less significantly with the dependent variable was eliminated. The remaining independent variables were entered into an initial model. Independent variables without significant predictive value at the 5% level ($p \leq 0.05$) were then eliminated, and final analysis carried out. Where the number of predictors exceeded that allowed by the number of cases, the excess predictors were eliminated least significant first. In reporting the results of BLR, we have followed the convention of using the term 'predictor', whether the prediction is chronological or one of 'category membership': in the latter case, the variables concerned may not be separated in time.

4. Results

4.1. Employment outcome

At the time of diagnosis, only 25/120 patients (20.8%) were employed. At 5–10 years, only 11 of those patients were still employed,

but a further 25 patients had become employed, so overall, 36/120 patients (30.0%) were employed (p = 0.103) at 5–10 years.

At the time of diagnosis, 9 additional patients described themselves as housewives, and of these, 3 were employed at 5–10 years. Nine additional patients described themselves as students at the time of diagnosis, of whom 4 were employed at 5–10 years.

4.2. PNES outcomes

At the time of diagnosis, all 120 patients reported that they were having seizures and were attending both primary and secondary care for them.

At 5–10 years, only 41/120 patients (34.2%) were accessing medical care for seizures, 23/51 patients (45.1%) reported that they considered themselves free of seizures, and 24/51 patients (47.1%) reported a date of last seizure that was more than 6 months before.

4.3. MUS outcome

At the time of diagnosis, 85/120 patients (70.8%) had active MUS. At 5–10 years, 42/120 patients had active MUS (35.0%, p < 0.001). Of those 42 patients with MUS at 5–10 years, 36 had MUS at baseline.

Only 6 of the 35 patients who had no active MUS at baseline developed them at 5–10 years. Of these, 4/6 were attending medical services for seizures at 5–10 years, and 4/6 reported that they were not 'seizure-free'. Thus, there was no evidence of a better PNES outcome in patients who developed MUS between diagnosis and 5–10 years.

4.4. Binary logistic regression (BLR) analysis — predictors of employment and MUS at 5–10 years

We analyzed for predictive effect the demographic and clinical factors listed in the Materials and methods section, including the presence of comorbid epilepsy and learning disability, and found no predictions of any outcome variable. The best BLR model predicted employment outcome (i.e., that the patient was employed) in 80.8% of cases, and explained 41.5% of variance. The predictors were: age at presentation (OR: 0.90 (0.86–0.94), p < 0.001), presenting to primary or secondary care with seizures (OR: 0.16 (0.05–0.52), p = 0.003), and contact with psychiatric services at 5–10 years (OR: 0.16 (0.05–0.58), p = 0.005). Thus, patients who were older at diagnosis were presenting to medical services with seizures, and patients who had contact with psychiatric services at 5–10 years were less likely to be employed. Of these factors, age at diagnosis was most predictive, alone accounting for 21.4% of variance, with seizure presentation next at 11.1%, then psychiatric contact at 8.2%. Age at onset of attacks and latency to diagnosis were also predictive if entered into the model instead of age at diagnosis, but less so than age at presentation (these three variables covaried, so these could not be entered into the same model). To determine whether the predictive effect of age was an effect of retirement, we repeated the analysis excluding 17 patients who were over 55 at the time of diagnosis, and obtained a marginally less good model, but one in which age at diagnosis remained highly predictive, with an OR of 0.90 (p = 0.003). Neither of the patient report measures, freedom from seizures or last seizure more than 6 months ago, was predictive.

Having active MUS at 5–10 years was predicted by having psychiatric contact at 5–10 years (OR: 2.27, cl 1.01–5.01, p = 0.048), and by a history of sexual abuse given at baseline (OR: 2.05, cl 1.01–4.19, p = 0.048). Medically unexplained symptoms at baseline or at 5–10 years did not predict seizure outcome.

5. Discussion

Our data show that just over one-third of our patients with PNES had accessed primary or secondary medical care for MUS other than PNES