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Predictors of 6-month and 3-year outcomes after psychological intervention for psychogenic non epileptic seizures.

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Abstract

Purpose

To determine outcome and its predictors following psychological intervention in people with Psychogenic Non-Epileptic Seizures (PNES)

Methods

Prospective audit of 89 consecutive patients. PNES were recorded at baseline (initial psychology appointment), at 6 months and 3 years post the initial appointment. Six-month data was obtained by face-to-face interview, while 3-year data was obtained by contacting general practitioners and by postal survey.

Results

Eight patients had stopped having PNES at the first appointment and were discharged. At 6-month follow up 43/81 patients (53.1%) were free of seizures. Predictors of cessation of seizures were: patient employed (OR 4.48, $p=0.004$), short waiting time for intervention (OR 0.94, $p=0.018$), the patient feeling they had some control over the seizures (OR 3.30, $p=0.021$), and an internal locus of control ((OR 7.46, $p=0.001$). Outcomes at 3 years based on patient report were available in 32/81 patients (36%). 11/32 patients reported being free of seizures. 50/65 patients were not accessing any healthcare for seizures. There were no significant predictors of either outcome among the variables collected.

Conclusion

Just over half of our patients reported being free of seizures following intervention. Being employed predicted good outcome, but the best predictor of being seizure free at 6 months was having an internal locus of control. This may be useful practically and requires further study. No good predictors of long-term outcome were found, possibly because of loss to follow up.

Introduction

There is relatively little published evidence to guide the use of therapeutic interventions in psychogenic non-epileptic seizures (PNES). Communication of the diagnosis may be associated with improvement or resolution in a proportion of cases (Buchanan & Snars, 1993, Farias et al., 2003, McKenzie et al., 2010, Duncan et al, 2011). There are no RCT data to support this as a therapeutic effect, but in many patients the PNES do stop in close temporal association with the conversation (Duncan et al 2011), making a causal relationship likely. There is some RCT evidence that withdrawal of AED improves healthcare utilisation, but no clear evidence that the PNES themselves are improved (Oto et al., 2010). Psychological therapy of different kinds has been widely used (LaFrance et al., 2008), though positive RCT evidence for effectiveness has been limited to two relatively small trials, both of CBT approaches (LaFrance et al., 2014, Goldstein et al., 2013). An RCT of antidepressant medication was negative (LaFrance et al., 2010). One larger observational study of the results of brief augmented psychodynamic interpersonal therapy, found that 25% of 66 patients reported that they were free of PNES after 3.5 years (Mayor et al., 2010).

One particular difficulty using RCT methodology in PNES is that a large initial patient population may yield only a small number of outcomes (Oto et al., 2010, LaFrance 2014). This is all the more problematic as PNES populations appear to be heterogeneous in terms of potential causal factors, psychological and medical background (Selkirk et al., 2008, Duncan & Oto, 2008, Duncan et al., 2006, Hingray et al., 2010). Psychotherapists and psychologists treating PNES may have a feeling for which patients might engage and improve. It may therefore be helpful to determine any such predictors and to explore factors on which they may be based. Determining predictors of outcome in observational studies may also be helpful in the subsequent design of RCTs and in interpretation of their data. We have therefore analysed the data from an audit of the results of a psychological intervention to determine which of a range of baseline variables might predict outcome.

Methods

All patients who were referred for psychological intervention to a specialist service for PNES during the year from 1st October 2008 and who attended their first appointment were included. All had a confirmed diagnosis of PNES, based on clinical evaluation, plus in all cases video EEG recording of events or ambulatory EEG recording of events with good clinical descriptions. The diagnosis was communicated in a semi-standardised way (Duncan 2010), and anticonvulsant medication was withdrawn where appropriate. All patients were referred for psychological intervention, with the exceptions of patients whose PNES had already ceased, patients who did not accept the diagnosis and patients who declined psychological intervention. Psychological intervention included an initial triage appointment with one of four clinical psychologists, where clinical information was gathered, a psychological formulation was generated. Patients were offered a maximum of 10 sessions. Therapeutic targets were identified and agreed with patients and one or more of a range of interventions were chosen (see Table 1). We extracted a range of potentially predictive variables from the case record and the psychologists' semi-standardised triage assessment.

Table 1

Protocol for psychological intervention in patients with PNES

Triage:

Patient thoughts on diagnosis and potential treatment (locus of control, attributions, perceived responsibility for recovery)

Seizure occurrence, response to seizures (seizure description, frequency, hospital contact, medication)

Onset factors (home, work and life events in the months prior to onset)

Current circumstances (home, family, work, pastimes, social support)

Past history (other illness, traumatic events, long term life history)

Treatment:

Treatment approach was based on a psychological formulation developed with the patient. The broad outline of treatment covered: psychoeducation to patients and family to develop understanding of PNES and awareness of triggers - both external and internal; considering the context that may both prevent and perpetuate attacks and identifying the attack prodromal phase and how to take remedial action. While the models used were integrative and varied according to the formulation, intervention was predominantly delivered in a CBT framework; other approaches were used on a case by case basis (see below).

Session 1: assessment and formulation

Sessions 2-10: interventions are used according to treatment targets that emerge from formulation.

1. When social factors predominate in cause and maintenance:

Family therapy

Interpersonal therapy

Social interventions

2. When internal thought processes / personal conscious behaviour predominate in cause and maintenance:

Cognitive behavior therapy

Behavioural management advice

3. When internal conflicts such as grief or reaction to past trauma predominate in cause and maintenance:

Mindfulness and compassionate mind

Acceptance and commitment therapy

Counselling

Focused analytic therapy

Dialectical behavior therapy

4. When physiological states, current health problems or habitual reactions to these problems predominate in cause and maintenance:

Psychological treatment for sleep dysregulation

Cognitive assessment remediation

Behavioural management advice

One hundred and two patients were sent an appointment to see a psychologist, of whom 89 attended the triage appointment, and of whom 81 attended triage plus at least one further appointment. They included 72 women (80.9%). Their mean age was 38.7 (± 15.6) years, and mean duration of PNES history was 6.2 (± 7.49) years. Nine patients (10.1%) had additional epilepsy, 6 (6.7%) had mild learning disability, 58 (65.1%) had other health problems, 20 (22.5%) had past or present other medically unexplained symptoms other than PNES, 44 (54.3%) had a previous psychiatric diagnosis, and 70 (78.6%) reported antecedent psychological trauma (in 21 (25.9%) this was sexual or physical abuse). Reported seizure frequency ranged from 1 – 180 per month, mean 22.3 \pm 30.4. The average decile score obtained using the Scottish Index of Multiple Deprivation (<http://www.scotland.gov.uk/Topics/Statistics/SIMD>) was 3.5, with 56 patients in the first 4 deciles, indicating that our sample predominantly came from the lower half of the socio-economic scale.

Baseline variables were: demographic data, age at onset of PNES, duration of history, diagnostic delay, hospital anxiety and depression scale (HADS), patient agreement with diagnosis, whether the psychologist could formulate a problem and whether the patient agreed with the formulation. Our psychologists felt that they could predict success, so they agreed to record their predictions, and to record a series of factors that they felt influenced their prediction. These factors were: Whether the patient was employed or had a career, whether they felt their attacks could be helped, whether they felt they had a degree of control over their attacks, whether the patient had an internal locus of control, whether the patient lived with his or her family, whether the patient had other medically unexplained symptoms. We also recorded whether the patient had engaged with therapy, and whether the psychologist predicted good outcome. All these factors were elicited or estimated clinically by the psychologist and were recorded as binary measures.

Seizure outcomes at 6 months post triage were acquired at face to face interview with the neurologist. Patients reporting no seizures for two months were recorded as 'seizure free', this being the longest period we could practically use in the time frame of the follow up. Where patients did not attend this appointment, or had been discharged from treatment before 6 months and did not attend neurological review (44 patients), the last report was carried forward. All patients in Scotland are attached to a named family doctor, who acts as a central point for organising care and acts as a gateway to specialist services, and who receives reports from all secondary care presentations. From family doctors we requested data relating to presentation to medical services over 6 months for the year ending September 2012 (range 3-4 years

post treatment, mean follow-up 3.2 years). At the same time we also sent out a short questionnaire that included a question on whether or not the patient considered him or herself free of PNES.

Statistical analysis

Statistical analysis was carried out using SPSS v21. The Chi squared test was used to evaluate between-groups 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 ($p < 0.1$) were considered for entry into the model. Where screening for co-linearity 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 ($p < 0.05$) 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.

The West of Scotland Research Ethics Committee confirmed the status of the study as an audit, and did not require formal review. The authors report no conflicts of interest.

Results

At triage, 8/89 patients (9%) had already stopped having PNES, and were sent no further appointments. Overall, 81/89 patients (91.0%) attended triage plus at least one further appointment. Only 50/89 patients (56.2%) attended all appointments sent out (range 1 - 10), and 76.9% of appointments were attended overall. Waiting time for the triage appointment ranged from 1-32 weeks. Among those patients who became seizure-free, mean waiting time was 13.4 ± 8.5 weeks, whereas for those who did not become seizure free within 6 months it was 17.1 ± 8.5 weeks ($p = 0.031$). Waiting time was also less for those patients who were employed (12.2 ± 8.6 weeks vs. 17.0 ± 9.0 weeks, $p = 0.015$).

Outcome at 6 months

At the time of the last appointment within 6 months after triage 43/81 patients (53.1%) reported that their seizures had stopped for the last two months. Patients attended a median 4.9 appointments (range 1-10). Sessions were planned fortnightly, but in the event there was considerable variation from this for clinical and other reasons (e.g. non-attendance or rescheduling by patients). Seizure outcome was based on last observation carried forward (locf) in 44 patients, after a median 2.7 (range 1-6) attended appointments. Outcomes were not significantly different between the locf group and the rest of the patients (23/44 were seizure free, vs. 20/37, $p=0.873$). When tested using binary logistic regression, number of appointments attended did not predict outcome.

A list of variables that significantly predicted seizure freedom at 6 months appears in Table 1. These variables are presented as single factors rather than combined in models, as most co-varied significantly. Predictive variables were: the patient was currently employed (OR 4.48 (1.63 - 2.35), $p=0.004$), the waiting time before psychological intervention was short ((OR 0.94 (0.90 - 0.99), $p=0.018$), the psychologist predicted a good outcome (OR 3.18 (1.34 - 7.57), $p=0.009$), the patient believed that the seizures could be helped (OR 3.86 (1.60 - 9.35), $p=0.003$), the patient felt he/she had some control over his/her seizures (OR 3.30 (1.20 - 9.09), $p=0.021$), and the psychologist estimated that the patient had an internal locus of control ((OR 7.46 (2.62 - 21.28), $p<0.001$). Unsurprisingly, a post hoc judgment that the patient had engaged with therapy also predicted a good result (OR 4.73 (1.93 - 11.63), $p=0.001$). The best predictor, whether the psychologist felt the patient had an internal locus of control, predicted the outcome in 70.5% of cases. No other variable had significant predictive value.

Table 2

Variables predicting good PNES seizure outcome at 6 months.

Variable	OR	c.i.	p	% cases predicted
Patient employed	4.48	1.63 - 2.35	0.004	65.5
Waiting time for psychology	0.94	0.90-0.99	0.018	n/a
Psychologist predicts good result	3.18	1.34 - 7.57	0.009	65.1
Psychologist predicts patient will engage with therapy	3.92	1.57 - 9.80	0.003	65.2
Patient believes attacks can be helped	3.86	1.60 - 9.35	0.003	66.3
Patient can control attacks	3.30	1.20 - 9.09	0.021	61.8

Internal locus of control	7.46	2.62 - 21.28	< 0.001	70.5
Patient engaged with intervention	4.73	1.93 - 11.63	0.001	68.5

Outcomes at 3-4 years

We had information from the family doctor in 65/89 patients (73.0%). Of these patients 50 (77.0%, or 56.2% of the total sample) had no attendances in the previous 6 months at primary or secondary care for seizures.

Only 32 patients (36.0%) responded to our survey. Of these patients 11 (34.4%) reported being free of seizures. In 16/32 patients, the reply to the survey matched the outcome recorded at 6 months. Eleven patients who recorded being free of seizures at 6 months reported not being free of seizures at 3 years, and 5 patients who reported not being seizure free at 6 months reported being seizure free at 3 years.

No variables in our baseline dataset predicted either attendance at family doctors or hospital at three years, nor patient report of being free of PNES at three years. To test whether the lack of predictors of patient reported outcome at three years was an effect of reduction in patient numbers, we repeated our BLR analysis of relationship between baseline variables and outcome at 6 months, but only on the subset of patients who responded to the survey at 3 years. This resulted in the loss of all but one of the predictors (whether or not the patient was judged to have engaged with therapy). Therefore, it seems likely that the loss of predictive value of factors such as employment and internal locus of control could be explained largely or entirely by loss of cases.

There were no significant differences in any baseline or outcome variable among the four psychologists. There were no significant differences in baseline variables between patients in whom we had data and in whom we did not, either for patient report of family doctor data.

Discussion

Overall, the results of our short psychological intervention appeared reasonably good in the short term, with approximately half of all patients reporting cessation of their seizures. In the longer term, and within the limitations of data from a reduced proportion of patients, outcomes were less good, with only 34.4% of patients reporting that they were free of seizures. This is rather similar to the results of the study of Mayor et al. (2010), who found that 25% of their patients considered themselves free of seizures at 3.5 years. Unsurprisingly, given that patients who remitted before psychological intervention began were effectively excluded, these results are somewhat poorer than those we reported for a broader sample (McKenzie et al., 2010). Longer term healthcare utilisation in the present sample was better, nonetheless, with most patients not accessing any type of healthcare for their seizures. Given that the information depended on the response of the family doctor rather than the patient, our healthcare utilization data is unlikely to be affected by patient response bias. Interpreting survey data based on whether or not the patient considers him or herself 'seizure free' is not straightforward even when a time period is specified (Duncan et al., 2014). However, it may be useful to compare previous data generated in a similar way (e.g. Reuber et al., 2003).

Obtaining longer term follow up data based on patient report in patients with PNES is challenging. Our experience was similar to that in previous studies in which conclusions are based on subsets of patients who self-select by attending appointments or by responding to surveys (Meierkord et al., 1991, Lancman et al., 1993, Selwa et al., 2000, Reuber et al., 2003). Thus, our 3-year patient-report data is based on small numbers, limiting the degree to which we were able to examine associations with baseline and other data. In studies of PNES, outcome measures themselves pose some difficulties. Relying on patient report of 'seizure freedom' is problematic for two reasons. Firstly, in the longer term a large proportion of cases are lost to follow up (Meierkord et al., 1991, Lancman et al., 1993, Selwa et al., 2000, Reuber et al., 2003), reducing the power of the study and inducing potential bias. Secondly, there appears to be considerable variation in what a patient might understand by 'free of seizures' (Duncan et al., 2014), so that the question needs to be combined

with a question on timing of last seizure or on seizure frequency. Data obtained 'face to face' with corroboration from a caregiver might be best, but no study has yet succeeded in obtaining long term outcome data in this way from a high proportion of patients. Healthcare utilization measures appear to dissociate from patient seizure report, suggesting that some patients retain some seizures, but do not seek healthcare for them. This may nonetheless be an important aspect of outcome, the more so as it may be that the frequency of PNES appears to reduce over time in this patient group (Duncan et al., 2014)). One might measure disability in some way, by asking about employment or state benefit support, but in a patient population who are likely to have other medical or medically unexplained reasons for economic inactivity (Ettinger et al., 1999, Duncan et al., 2006, Selkirk et al., 2008), it is unclear what symptom or illness is responsible for the unemployment, so that this outcome may relate to a disorder other than PNES.

Like previous cohorts studied by our group (e.g. cohort from McKenzie et al., 2010, unpublished data) our patients were from the lower half of the socio-economic spectrum. Within the ranges found in this study and in our previous studies, socio-economic status did not predict outcome. The predictors we did find were in most cases unsurprising. Those who did well early believed that they had some control over their PNES and that their PNES could be helped. Those who the psychologists identified as having an internal locus of control did well, as did those who were employed. Employment has previously been identified as a strong predictor of good outcome, both generally and especially after psychotherapy (McKenzie et al., 2010, Duncan et al., 2010, Mayor et al., 2010). Exploration of this effect would be a potentially fruitful direction for future research. Our psychological predictive variables were based on the estimation of the psychologist, rather than on recognised research instruments. This means that it is possible that the relationship we found between employment and internal locus of control, for example, might have been because psychologists were influenced in their judgment of locus of control by whether or not the patient was employed, or that they felt for some other reason that outcome was likely to be good. Given that most of the predictive factors co-varied, it looks possible that they did in fact capture the same effect, the most likely and interesting candidate for which would be locus of control. A prospective study using formal determination of locus of control and other variables would be required to confirm or refute this. Similarly, having found that psychologists do seem to be able to predict outcome to a degree, it would potentially be helpful in future research to explore which factors allow them to make this prediction.

We found that patients seen by the psychologist soon after diagnosis did better. This may have been due to an interaction with employment and locus of control, as patients who were employed were prioritised by the psychologists. Thus, while it is attractive to believe that 'rapid response' psychological intervention might be more effective than delayed intervention, our data could not be said to positively support this. The fact that number of appointments did not predict outcome was not surprising, as therapy might be curtailed for reasons associated with either bad or good outcome.

The design of an RCT to test the effectiveness of psychological therapy is difficult, and meaningful patient or therapist blinding is probably not practically possible. The limited RCT data generated thus far has tested CBT type therapies, which are relatively easy to define and circumscribe. Analytic therapies require tailoring to individual patients and practically could only be tested as 'black boxes'. Such therapies can be highly successful in individual patients, which is probably why many centres continue to use them, despite lack of supporting group-level data. The development of better predictive data from formal prospective studies may allow better identification of patients likely to benefit.

The status of this study as an audit meant that we could not acquire data on the wider PNES population from which our sample was drawn. We studied only that subset of patients who were referred for and attended a psychology appointment, i.e. those whose PNES did not remit after communication of the diagnosis, and who were willing and motivated enough to accept a referral to psychological services, and to attend for evaluation and at least to some extent for therapy. In this respect, our patient population was 'realistic', and was that part of the PNES population who are likely to undergo psychological intervention at many centres. Thus, our results may give an approximate estimate of the maximum group-level benefit one might potentially obtain in an RCT in this selected patient population. The fact that we had patient-reported outcomes in only a subset of patients may have induced further bias, albeit we detected no obvious differences between responders and non-responders.

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