Epilepsy & Behavior 41 (2014) 140–143

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Brief Communication

Long-term outcome of psychogenic nonepileptic seizures: The role of induction by suggestion ☆

Orsola Gambini [a,1], Benedetta Demartini [a,*,1], Valentina Chiesa [b,1], Katherine Turner [b,1], Valentina Barbieri [a,1], Maria Paola Canevini [b,1]

[a] Cattedra di Psichiatria, Dipartimento di Scienze della Salute, Università degli Studi di Milano, Italy
[b] UO Neurologia 2, Centro Epilessia, A.O. San Paolo, Dipartimento di Scienze della Salute, Università degli Studi di Milano, Via A. Di Rudinì, 8, 20142 Milan, Italy

ARTICLE INFO

Article history:
Received 26 June 2014
Revised 19 August 2014
Accepted 27 September 2014
Available online 23 October 2014

Keywords:
Psychogenic nonepileptic seizure
Induction by suggestion
Outcome
Prognosis

ABSTRACT

Purpose: The aims of our retrospective observational study were to evaluate the long-term outcome of PNESs after communication of the diagnosis and to define predictors of good outcome.
Method: Twenty-seven consecutive patients with a certain diagnosis of psychogenic nonepileptic seizures (PNESs) were included in the study. Follow-up information was obtained from each participant through a questionnaire designed for the study. Regarding seizure frequency, the patients were asked to report how many seizures they had experienced on average every month before the communication of the diagnosis and after it.
Results: After the communication of the diagnosis, the median seizure frequency had dropped to 4 every month ($p < 0.001$). Seventeen participants (63%) were seizure-free at follow-up, and a further five (18.5%) showed a greater than 50% improvement in seizure frequency. Regarding the predictive value of clinical and sociodemographic variables for PNES global outcome, the factors gender, education, economic status, interval of time from onset, comorbidity with epilepsy, psychiatric history, mental retardation, psychological therapy, psychiatric therapy, and the presence of stressful and traumatic events were not related to prognosis; the only factor associated with a better outcome was the diagnosis made after the induction of PNESs by suggestion ($p = 0.000$, $\chi^2 = 4.654$).
Conclusion: A substantial majority of our patients became seizure-free with communication of the diagnosis as the only intervention. The use of the induction by suggestion test was an important predictor of good outcome.

1. Introduction

Psychogenic nonepileptic seizures (PNESs) can be defined as paroxysmal events that resemble or can be mistaken for epilepsy, without being associated with abnormal electrical activity in the brain [1]. Psychogenic nonepileptic seizures represent a puzzling clinical condition for which etiology, evidence-based treatments, and outcomes are not yet defined. Subjects with PNESs constitute a heterogeneous group; nevertheless, the majority of them fulfill the Diagnostic and Statistical Manual of Mental Disorders — fourth edition, text revision (DSM-IV-TR) criteria for conversion disorders. In addition, a high percentage of patients affected by PNESs present a comorbid mood or anxiety disorder; according to recent studies, mood and anxiety disorders have been found in more than 50% of cases [2], posttraumatic stress disorders in up to 100% [3], and cluster A and B personality disorders in up to 40% [4].

The first step in PNES management is diagnosis, for which video-electroencephalography (video-EEG) remains the gold standard; in their recent study, Syed et al. suggested that video-EEG, combined with the patient's history, has a very high sensitivity and specificity [5]. In addition to video-EEG, induction by suggestion has previously been reported to be effective in the diagnosis of PNESs. In the study by Lancman et al., the sensitivity of the induction test, which consisted in placing a colored patch imbibed in alcohol on the neck of the patients, was 77.4%, the specificity 100%, the positive predictive value 100%, and the negative predictive value 48.7% [6].

A second important step in PNES management resides in the communication of the diagnosis. Recently, Mayor et al. showed how communicating the diagnosis in a clear and supportive manner is the only intervention required to stop PNESs in at least 15–30% of cases [7]. Nevertheless, they did not identify specific predictors of good response to the sole communication of the diagnosis.

☆ This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.
* Corresponding author at: Cattedra di Psichiatria, Dipartimento di Scienze della Salute, Università degli Studi di Milano, AO San Paolo, Via A. Di Rudinì, 8, 20142 Milan, Italy. Tel.: +39 3496375759.
E-mail address: bennidemartini@hotmail.it (B. Demartini).
[1] Each author has contributed in all the following: 1) conception and design, acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published.

http://dx.doi.org/10.1016/j.yebeh.2014.09.076
1525-5050/

After the diagnosis of PNESs and its communication to the patient, treatment options are presented. To date, no official guidelines for the treatment of PNESs are available. Psychological treatment and pharmacotherapy (mainly antidepressants) are widely used, but data regarding their efficacy are limited and not consistent. Efficacy of cognitive–behavioral therapy, which is the most used approach among psychotherapies, has been recently evaluated in two pilot randomized controlled studies [8,9]: Goldstein et al. found a significant reduction in seizure frequency at the end of the treatment period, but no changes were found in most of the psychological outcomes [8]; LaFrance et al. reported a significant improvement in a range of clinical and psychological factors at the end of the treatment [9]. However, neither study evaluated the long-term outcome of the psychological approach. Concerning pharmacotherapy, different drugs have been anecdotally used, but only a small controlled trial on sertraline, whose results are of partial efficacy, has been conducted [10].

Another controversial issue on PNESs concerns outcome and outcome measures. Among the outcome measures, PNES frequency after diagnosis and/or therapeutic program is often evaluated. However, recent studies showed how the reduction or cessation of seizures is useful as an objective clinical outcome measure but often do not correlate with psychosocial recovery or quality of life [11–13]. Data concerning outcome (assessed by the reduction of seizures) are often controversial and are mainly limited to the short term. Overall, prognosis of PNESs appears to be poor. The majority of studies found that 40% or less of patients with PNESs achieve seizure remission in the follow-up period [14–16]. The largest study ($n = 260$) [14] found that just 38% of patients were seizure-free 6–12 months after diagnosis. In one of the studies with the longest follow-up, Reuber et al. [15] found that 71% of patients were still having seizures 1–10 years after diagnosis. Nevertheless, long-term outcomes of PNESs after diagnosis have been rarely evaluated.

The aims of our retrospective observational study were to evaluate the long-term outcome of PNESs after diagnosis communication and to define predictors of good outcome.

2. Methods

Between October 2013 and February 2014, 27 consecutive patients with a certain diagnosis of PNESs seen at our Regional Epilepsy Center for follow-up were included in a retrospective outcome study. The original number of patients was 36, but nine of them have not been included because they were not reachable at the time of the present study. In order to focus on the long-term outcome, we recruited patients who had received the diagnosis at least 1 year before (in all cases, the diagnosis had been communicated by one of the authors). The following criteria were selected: age of 18–60 years, normal IQ, and no or mild intellectual disabilities. Twelve out of the 27 patients have also been previously enrolled in one of our previous studies [17].

All patients had given their written informed consent for the study. The Ethics Committee of San Paolo Hospital reviewed and approved the study protocol.

The diagnosis of PNESs was made on the basis of the consensus of at least two epilepsy specialists based on the patients' clinical history and video-EEG monitoring. When no episode was registered during the video-EEG monitoring, an induction by suggestion test was also performed.

The induction was carried out using a standardized protocol, according to Lancman et al. [6].

Patients with PNESs with a history of possible additional epileptic seizures were eligible to take part but only if the two seizure types could be distinguished clearly by the patients and caregivers.

2.1. Assessment

All subjects were assessed by a psychiatrist at the Regional Epilepsy Center at the time of the PNES evaluation or diagnosis. Each patient received a psychiatric assessment as follows. Diagnoses were made according to DSM-IV-TR criteria. All patients were evaluated using the Italian version of the SCID-I and SCID-II interview. Subjects were also interviewed about stressful and traumatic life events from childhood to present in the context of a nonstandardized interview.

Follow-up information was obtained from each participant through a questionnaire designed for the study (Table 1). Seizure frequency data were collected retrospectively in one-month intervals for the duration of the follow-up period: patients were asked to report how many seizures they had experienced on average every month before the communication of the diagnosis and after it, relying on their seizure diaries (for patients with intellectual disabilities, seizure diaries were kept by caregivers). Patients who had experienced no seizures in this period of time were classed as “seizure-free”.

2.2. Statistical analysis

Statistical analysis was performed using SPSS version 21 (Statistical Package for the Social Sciences).

Categorical or ordinal variables were compared using the χ^2 test, the Mann–Whitney U test, or the Kruskal–Wallis test where appropriate; continuous variables were compared using Student's t-test or one-way analysis of variance after applying Levene's test for equality of variance. If the variance was unequal, nonparametric tests were performed. Simultaneous logistic regression models were used to evaluate the ability of independent variables to predict outcomes.

Seizure outcome data were expressed as a percentage of improvement in seizure frequency from before the communication of the diagnosis to follow-up (a 50% improvement represented 50% fewer seizures at follow-up).

3. Results

Twenty-seven patients (21 females [77.8%]; mean age: 43.9 years [SD, 12.1 years]) took part in the study. Patients' demographic and clinical characteristics are shown in Table 2. Thirteen patients (48.1%) did not have PNESs during the video-EEG monitoring; subsequently, they underwent the induction test. Two patients (7.4%) underwent further investigations after the communication of the diagnosis, which consisted in brain MRI for both of them.

Before the communication of the diagnosis, the median seizure frequency of the whole group was 11 per month. After the communication of the diagnosis [a mean of 21 months (SD, 12.1 months, range: 14–38 months)], the median seizure frequency had dropped to 4 per month (significant difference; $p < 0.001$). Seventeen participants (63%) were seizure-free at follow-up, and a further five (18.5%) showed a greater than 50% improvement in seizure frequency.

The predictive value of a range of clinical and sociodemographic variables for PNES global outcome is summarized in Table 3: the factors gender, education, economic status, interval of time from onset, comorbidity with epilepsy, psychiatric history, mental retardation, psychological therapy, psychiatric therapy, and the presence of stressful and traumatic events were not related to prognosis; the only factor associated with a better outcome was the diagnosis made after the induction of PNESs by suggestion ($p = 0.000$, $\chi^2 = 4.654$): all 13 patients who received the induction of PNESs by suggestion were seizure-free at follow-up; this finding was independent from all the

Table 1
Questions of the standardized interview designed for the study.

1. How many months ago did you receive the diagnosis of PNESs?
2. How many PNESs every three months did you have before the communication of the diagnosis?
3. How many PNESs did you have in the last three months?
4. Did you receive any specific treatment for PNESs? If yes, specify.
5. After the diagnosis of PNESs, did you have any other investigation?