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Brief Communication

Parental consanguinity in patients with psychogenic nonepileptic seizures

Ali A. Asadi-Pooya [a,b,*], Zahra Bahrami [a]

[a] Neuroscience Research Center, Shiraz Medical School, Shiraz University of Medical Sciences, Shiraz, Iran
[b] Jefferson Comprehensive Epilepsy Center, Department of Neurology, Thomas Jefferson University, Philadelphia, PA, USA

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ABSTRACT

Purpose: The aim of this study was to investigate the rate of consanguinity of parents of the patients with psychogenic nonepileptic seizures (PNES). This would provide important information for future studies on the potential genetic bases of PNES.
Methods: In this retrospective study, all patients with PNES, who were studied at Shiraz Comprehensive Epilepsy Center at Shiraz University of Medical Sciences, from 2008 to 2018, were recruited. We categorized the patients as (1) no consanguineous marriage of the parents and (2) with consanguineous marriage of the parents.
Results: Three-hundred and sixteen patients had the data on their parental consanguinity available and were studied. The sex ratio (female:male) of the patients was 1.92 (208:108). Parents of 110 (35%) patients had consanguineous marriage, and parents of 206 (65%) patients did not. Demographic variables, seizure-related variables, PNES-associated factors, and the use of antiepileptic drugs were not significantly associated with parental consanguinity in the patients.
Conclusions: In this study, we observed that more than one-third of the patients with PNES had parental consanguinity. This rate is very similar to the rate of consanguinity in the general population in Iran.

1. Introduction

Psychogenic nonepileptic seizures (PNES) consist of paroxysmal changes in responsiveness, movements, or behavior that seemingly look like epileptic seizures but lack a neurobiological origin similar to that in epileptic seizures and are not associated with electrophysiological epileptiform changes; they are associated with psychological disorders [1]. Genetic factors play a significant role, and heritability is encountered in many psychiatric disorders [2,3]. The role of genetic factors has even been implicated in psychiatric disorders relevant to PNES (e.g., conversion disorders) [4]. In a previous study [5], the authors observed that children of first-cousin consanguineous parents were more than three times as likely to be receiving antidepressant or anxiolytic medications compared with children of nonrelated parents [5]. Since brain connectivity abnormalities have been suggested in the pathophysiology of PNES, it is not irrational to investigate if genetic factors play a role in their pathophysiology [3,6].

Consanguineous marriage (i.e., marriage between relatives) has been considered as a potential risk factor for many genetic disorders; it is a clinical marker for genetic factors playing significant roles in the pathophysiology of medical conditions. To the best of our knowledge, no study has ever investigated the consanguinity (familial marriage) of parents of the patients with PNES. The aim of this study was to investigate the rate of parental consanguinity and its association with PNES. This would provide important information for future studies on the potential genetic bases of PNES. We hypothesized that consanguinity is more prevalent among parents of the patients with PNES compared with that in the general population.

2. Methods and materials

In this retrospective study, all patients with a documented diagnosis of PNES, who were studied at Shiraz Comprehensive Epilepsy Center at Shiraz University of Medical Sciences, from 2008 to 2018, were recruited. The diagnosis was made by clinical assessment and documented by ictal recording during video-electroencephalography (video-EEG) monitoring by the epileptologist.

Age, gender, age at seizure onset, seizure semiology, seizure frequency, and factors potentially predisposing to PNES [history of physical abuse (i.e., corporal punishment or any physical injury resulted from aggressive behavior towards the patient), sexual abuse, child abuse (i.e., neglect, emotional/verbal abuse), dysfunctional family (i.e., divorce, single parent, significant family disputes, etc.), academic failure (school dropout or repeated grades), any medical comorbidities, and family

* Corresponding author at: Neuroscience Research Center, Shiraz Medical School, Shiraz University of Medical Sciences, Shiraz, Iran.
E-mail address: aliasadipooya@yahoo.com (A.A. Asadi-Pooya).

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history of epilepsy] were registered routinely. We categorized the patients as (1) no consanguineous marriage of the parents and (2) with consanguineous marriage of the parents. Demographic variables and relevant clinical variables were summarized descriptively to characterize the study population. Pearson Chi-square, Mann–Whitney, Kolmogorov–Smirnov, and t-test were used for statistical analyses. p value less than 0.05 was considered as significant. This study was conducted with the approval by Shiraz University of Medical Sciences Review Board.

3. Results

During the study period, 325 patients were registered in our database. Three-hundred and sixteen patients had the data on their parental consanguinity available and were studied. The sex ratio (female:male) of the patients was 1.92 (208:108). Parents of 110 (35%) patients had consanguineous marriage, and parents of 206 (65%) patients did not; 79 (25%) parents were first cousins and 31 (10%) were second cousins. Age at onset of PNES was 21 ± 9 years in those with parental consanguinity and 24 ± 10 years in those without such a history ($p = 0.009$). Other demographic variables (i.e., gender), seizure-related variables (i.e., aura, loss of responsiveness, seizure semiology, seizure frequency, urinary incontinence, seizure-related injury, and duration of the condition), PNES-associated factors (i.e., head trauma, history of physical or sexual abuse, dysfunctional family, academic failure, and medical comorbidities), and the use of antiepileptic drugs were not significantly associated with parental consanguinity (all p values were >0.05).

4. Discussion

In this study, we observed that more than one-third of the patients with PNES had parental consanguinity. This rate is very similar to the rate of consanguinity in the general population in Iran; 31–39% in previous studies [7,8]. First- and second-cousin marriages differ significantly for genetic studies. First cousins, but not second, have coinherited one-eighth of their genes from one or more common ancestors. In our study, even the rates of the first and second cousin marriages were similar to those in the general population of Iran [7]. Parental consanguinity did not have any significant associations with the demographic and clinical characteristics of PNES. We do not have any explanation for the observation that age at onset of PNES was earlier in those with parental consanguinity compared with those without such a history. We have to say that the rate of consanguinity that was observed in this study is higher than that in many other cultures. Couples related as second cousins or closer and their progeny account for an estimated 10% of the world population [9]. The highest rates of consanguineous marriage in the world occur in north and sub-Saharan Africa and the Middle East. In these regions, even couples who consider themselves as unrelated may exhibit high levels of genetic similarities, because marriage within tribe or caste boundaries has been a long-established tradition [9]. Therefore, this may have affected the results of our study and may limit the generalizability of the findings to cultures with lower rates of consanguineous marriage.

One should keep in mind that consanguinity is only one aspect of genetics — it is a clinical marker. Despite our observations that could not establish any associations between parental consanguinity and PNES, we have to say that our finding does not exclude the possibility of significance of genetic factors in the pathophysiology of PNES. Exploring any potential genetic basis of PNES could have important clinical implications in formulating better preventative, diagnostic, and therapeutic approaches [6]. Patients with PNES often have comorbidities [e.g., psychiatric comorbidities, including posttraumatic stress disorder (PTSD) and epilepsy] [10–12]. It has been shown that genetic factors play a significant role in many of comorbidities with PNES [3]. However, the most obvious genetically determined risk factor for PNES is probably female gender predominance of the patients [6,13]. This gender difference was very obvious in the current study. The relationship between genetic factors and PNES is multifactorial, if proved to be existent. Well-designed international genetic studies should investigate such relationships. It is also important to remember that PNES is a very heterogeneous condition; this may hamper genetic studies in this condition. The most commonly reported PNES-associated factors include abuse (sexual or physical), traumatic brain injury, and psychiatric comorbidities [1,10]. Often several potential interacting factors may be identified in a patient with PNES [1,10]. Therefore, in designing any genetic study in patients with PNES, many confounding factors should be considered.

This study has some limitations. Most patients with PNES have a coexisting psychiatric disorder that was not documented in this study. In addition, a control group was not included.

Conflict of interest

Ali A. Asadi-Pooya, M.D.: Honoraria from Cobel Daruo; Royalty: Oxford University Press (Book publication). Zahra Bahrami, M.D.: none.

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