



Patients with psychogenic nonepileptic seizures report more severe migraine than patients with epilepsy



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ABSTRACT

Purpose: Clinical observations suggest that psychogenic non-epileptic seizure (PNES) patients often have severe migraine, more severe than epilepsy patients. Investigations into migraine characteristics in patients with PNES are lacking. In this study we tested the hypothesis that, compared to epilepsy patients, PNES patients have more severe migraine, with more frequent and longer duration attacks that cause greater disability.

Method: In this observational study, 633 patients with video-EEG proven epilepsy or PNES were identified from the Mayo Clinic Epilepsy Monitoring Unit database. Contacted patients were screened for migraine via a validated questionnaire, and when present, data regarding migraine characteristics were collected. Two-sample *t*-tests, chi square analyses, and Mann–Whitney *U* tests were used to compare migraine characteristics in PNES patients to those of epilepsy patients.

Results: Data from 43 PNES patients with migraine and 29 epilepsy patients with migraine were available. Compared to epilepsy patients, PNES patients reported having more frequent headaches (mean 15.1 ± 9.8 vs. 8.1 ± 6.6 headache days/month, $p < .001$), more frequent migraine attacks (mean 6.5 ± 6.3 vs. 3.8 ± 4.1 migraines/month, $p = .028$), longer duration migraines (mean 39.5 ± 28.3 vs. 27.3 ± 20.1 h, $p = .035$), and more frequently had non-visual migraine auras (78.6% vs. 46.7% of patients with migraine auras, $p = .033$). Migraine-related disability scores were not different between PNES and epilepsy patients (median 39, interquartile range 89 vs. 25, interquartile range 60.6, $p = .15$).

Conclusion: Compared to epilepsy patients with migraine, PNES patients with migraine report having a more severe form of migraine with more frequent and longer duration attacks that are more commonly associated with non-visual migraine auras.

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1. Introduction

Epilepsy and migraine are co-morbid neurologic disorders that may share some similar underlying pathogenic mechanisms. Individuals with epilepsy are over two times more likely to have migraine compared to people without epilepsy and people with migraine are over two times more likely to have epilepsy compared to people without migraine [1]. Young adults with migraine have a 1.85 adjusted hazard ratio of subsequently developing epilepsy, compared to their peers without migraine [2]. Genetic and environmental factors are likely the cause of such comorbidity

[3]. Migraine may precipitate epileptic seizures, epileptic seizures may induce post-ictal migraine, and rarely, a migraine-like headache is the most prominent manifestation of an epileptic seizure [4].

While there have been several investigations into the relationship between migraine and epilepsy, a potential link between psychogenic non-epileptic seizures (PNES) and migraine has not been extensively evaluated. However, a recent study found that the presence of migraine increases the likelihood of a patient with seizures having PNES as opposed to epilepsy alone [5]. Based upon our clinical experience managing patients who have PNES, we hypothesized that migraine is common in these patients and that patients with PNES have migraine that is more severe (i.e. more frequent attacks, longer attack duration, greater migraine-related disability) and more treatment refractory compared to patients who have epilepsy and migraine. The objective of this study was to

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compare migraine characteristics in patients who have migraine and video-EEG diagnosed PNES to migraine characteristics in patients who have migraine and video-EEG diagnosed epilepsy. Confirming a link between PNES and migraine and determining the severity of migraine in patients with PNES could establish a need for screening PNES patients for the presence of migraine.

2. Methods

This study was approved by the Mayo Clinic Institutional Review Board (IRB). Since participation in this study was considered to pose minimal risks to subjects, verbal consent only (as opposed to written consent) was considered sufficient for collection of data over the telephone. However, collected data could only be used for this study if subjects signed and returned HIPAA authorization forms.

Patients were identified from an existing clinical database of patients who had been evaluated in the Mayo Clinic Epilepsy Monitoring Unit (EMU) between 2008 and 2014. The database was used to identify patients who were at least 18 years of age and who received an EMU discharge diagnosis of PNES or epilepsy. Patients were excluded from this study if they had an uncertain diagnosis at discharge or if they were diagnosed with both PNES and epilepsy.

We attempted to make telephone contact with all patients who met these inclusion and exclusion criteria. Since our goal was to contact and enroll all eligible patients, no power analysis was performed for determination of sample size. After verbal consent was obtained, subjects were screened for the presence of migraine using ID Migraine, a validated 3-item questionnaire that has a sensitivity of .81 (95% CI, .77–.85), a specificity of .75 (95% CI, .64–.84), and positive predictive value of .93 (95% CI, 89.9–95.8) for the diagnosis of migraine [6]. Subjects who screened in for migraine (gave an affirmative response on 2 of 3 questions) were then asked additional questions about their migraine and seizures through the use of standardized questionnaires and a standardized interview. These additional data included patient demographics (i.e. age and sex), migraine characteristics (i.e. headache frequency, headache duration, headache severity, presence and symptoms of migraine aura), migraine-related disability (via the Migraine Disability Assessment Scale [MIDAS]), and timing of migraines in relation to their non-epileptic or epileptic seizures (i.e. no temporal relationship, migraines start before seizures, seizures start before migraines) [7]. Subjects were also asked about their current and past use of migraine treatments. Subjects who had used migraine therapies selected their current and past therapies from a comprehensive list created by the Mayo Clinic Headache Center that was read to them.

Data were analyzed within SPSS (version 22.0, Armonk, NY; IBM Corp.). Descriptive statistics were used to report data and two-sample *t*-tests, chi-squared tests and Mann–Whitney *U* tests were used for comparing PNES and epilepsy subjects. Uncorrected *p*-values <.05 were considered significant.

3. Results (Table 1)

3.1. Subjects

The EMU database contained 633 patients (Fig. 1). Of these 633 patients, 205 patients were consented for participation. This population included 88 patients with PNES and 117 with epilepsy. Fifty-three of the 88 patients with PNES (60.2%) had migraine as determined by their ID-Migraine answers and additional clinical information collected during the subsequent interview. Forty-five of the 117 epilepsy patients (38.5%) had

migraine. Twenty-two patients were excluded due to a mixed diagnosis of PNES and epilepsy. Ten PNES patients and 16 epilepsy patients did not return their HIPAA forms and thus their data is not included in further analyses. Therefore, data from 72 subjects (43 with PNES and 29 with epilepsy) were available for this study. The flow diagram in Fig. 1 illustrates enrollment.

Twelve subjects were male and 60 were female, with no differences in sex distribution between PNES and epilepsy groups ($p = .77$). Subject ages ranged between 20 years and 82 years in the PNES group and between 21 years and 78 years in the epilepsy group. On average, PNES subjects were slightly older than epilepsy subjects (47.0 years \pm 13.2 years vs. 40.2 years \pm 13.4 years, $p = .039$).

3.2. Headache and migraine frequency, pain intensity and duration

PNES patients reported having more frequent headaches than patients with epilepsy (15.1 \pm 9.8 headache days per month vs. 8.1 \pm 6.6 headache days per month, $p < .001$). PNES patients also reported having more frequent migraine attacks than patients with epilepsy (6.5 \pm 6.3 migraine attacks per month vs. 3.8 \pm 4.1 migraine attacks per month, $p = .028$). There were no differences in average headache intensity between the PNES and epilepsy groups (6.6 \pm 2.1 on a scale from 0 (no pain) to 10 (most severe pain) vs. 6.8 \pm 1.8, $p = .74$). Patients with PNES reported longer duration migraines (when untreated) compared to patients with epilepsy (39.5 \pm 28.3 h vs. 27.3 \pm 20.1 h, $p = .035$).

3.3. Migraine aura status and characteristics

Migraine auras were reported by 28 of 43 (65.1%) PNES patients and 15 of 29 (51.7%) epilepsy patients ($p = .26$). Visual aura symptoms were the most common aura symptom in PNES (25 of 28 patients with migraine aura [89.3%]) and epilepsy groups (11 out of 15 patients with migraine aura [73.3%]). Non-visual aura symptoms including sensory, motor and language symptoms were more commonly reported in the PNES group (22 of 28 patients [78.6%]) compared to epilepsy patients (7 of 15 patients [46.7%]) ($p = .033$).

3.4. Migraine treatments

At the time of the interview, 17 of 43 (39.5%) PNES patients considered themselves to be taking a migraine prophylactic medication compared to 5 of 29 (17.2%) epilepsy patients who considered themselves to be taking a migraine prophylactic medication ($p = .58$). Twenty four of forty three (55.8%) PNES patients and 11 of 29 (37.9%) epilepsy patients had been prescribed a migraine abortive medication ($p = .58$). The total number of abortive medications (prescription + over-the-counter) ever used by PNES patients averaged 2.7 (\pm 1.6), compared to 3.5 (\pm 4) for epilepsy patients ($p = .25$). This included .86 (\pm .95) prescription abortive medications in the PNES group and 1.6 (\pm 3.6) prescription abortive medications in the epilepsy group ($p = .29$). The total number of prophylactic therapies (prescription + non-prescription) ever tried by PNES patients averaged 1.9 (\pm 1.7) compared to 1.8 (\pm 2.7) for epilepsy patients ($p = .83$). The total number of prescription prophylactic medications ever tried averaged .88 (\pm 1.14) for PNES patients and .72 (\pm 1.6) for patients with epilepsy ($p = .64$). Twenty-three of 43 (53.5%) PNES patients and 22 of 29 (75.9%) epilepsy patients felt that their migraines were adequately treated ($p = .054$). Nineteen of 43 (44.2%) PNES patients had never been prescribed a medication to abort migraines and 19 of 43 (44.2%) PNES patients considered themselves to have never been prescribed a migraine prophylactic medication.

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