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Prevalence and distribution of MRI abnormalities in patients with psychogenic nonepileptic events

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ABSTRACT

Introduction: Both structural and functional abnormalities have been reported in patients with psychogenic nonepileptic events (PNEEs), although no truly consistent abnormalities have been found.
Methods: We retrospectively identified patients discharged from our EMU with video-EEG diagnoses of epileptic seizures, PNEEs, epileptic seizures plus PNEEs, interictal epileptiform abnormalities only, and nondiagnostic admissions. We then collected brain MRI results for analysis.
Results: We found significant brain MRI abnormalities in 33.8% of patients with PNEEs, clearly higher than the rate of brain MRI abnormalities in the healthy population. In addition, we found statistically significant differences in the locations of brain MRI abnormalities in patients with epileptic seizures (more frequently temporal) versus PNEEs (more frequently multifocal).
Conclusion: This multifocal nature of abnormalities in patients with psychogenic nonepileptic events may help to explain the underlying pathophysiology as it relates to psychiatric disorders which are so frequently comorbid with PNEEs.

1. Introduction

Psychogenic nonepileptic events (PNEEs) are paroxysmal spells that resemble epileptic seizures without correlating epileptiform abnormalities or clinical evidence for epilepsy. Association with psychosocial and psychologic mechanisms are usually seen, including sexual and/or physical abuse, posttraumatic stress disorder, dissociation disorder, somatization disorder, personality disorder, poor coping mechanisms, depression, panic disorder, and chronic anxiety disorder [1]. An association with past head injury is also seen, with as many as 32% of patients with PNEEs having a documented history of head trauma [2]. Psychogenic nonepileptic events are very commonly encountered in neurologic practice. This is especially true in epilepsy monitoring units (EMUs) at large academic referral centers where PNEEs can account for up to 39% of admitted patients [3]. Despite their widespread prevalence, the pathophysiology and anatomic substrate of PNEEs is currently not well understood.

Previous studies have looked for structural imaging abnormalities in attempts to explain the pathophysiology of nonepileptic events. It has been reported that no consistent structural or functional imaging abnormalities are present in patients with PNEEs [4].The overall prevalence of imaging abnormalities in patients with PNEEs has been reported to be as low as 17% [5] and as high as 86.4% [6]. A better designed study by Reuber et al. found imaging abnormalities in 27% of 74 patients studied with PNEEs [7]. Limitations to the first two studies, likely responsible for the discrepancy in prevalence, include small sample sizes (18 and 22 patients respectively), some patients in the group with PNEE without video-EEG monitoring, and probably clinically insignificant imaging abnormalities such as developmental venous malformations, venous angiomas, arachnoid cysts, aneurysm, and "white matter lesions". Nevertheless, these studies suggest that the prevalence of imaging abnormalities in PNEEs is higher than what is seen in the healthy population where intracranial abnormalities are incidentally noted in 4.8% [8] to 13.6% [9] of healthy individuals.

Other studies have investigated laterality of imaging abnormalities seen in PNEEs. It has been observed in the past that conversion symptoms are more commonly present on the left side of the body [10], so investigators have tried to implicate right hemisphere pathology in PNEEs. Devinsky et al. actually found that right-sided abnormalities (structural or functional as defined by abnormal imaging and EEG respectively) were more frequently seen in patients with PNEEs and PNEEs plus epilepsy than what would be expected by chance, though the sample size of both groups were low including 22 and 38 patients respectively [6]. Reuber et al. investigated this with a larger sample size by comparing patients with PNEEs plus epilepsy to patients with only epilepsy [11], and patients with PNEEs plus epilepsy to patients with only PNEEs [7], but was unable to find a significant difference in the lateralization of imaging abnormalities. Ristić et al. analyzed MRIs

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of patients with PNEEs and healthy controls and found that as opposed to abnormalities on the right, patients with PNEEs had increased cortical thickness in the left insula, bilateral medial orbital frontal cortex, and left lateral orbital frontal cortex compared with healthy controls [12].

Functional studies including interictal single photon emission computerized tomography (SPECT), diffusion tensor imaging (DTI), high-density EEG (HDEEG), and functional MRI (fMRI) have also been used to investigate abnormalities in PNEEs. Findings from interictal SPECT in patients with PNEEs include increased relative cerebral blood flow in the right precuneus and right posterior cingulate gyrus as well as decreased relative cerebral blood flow in the right amygdala [13]. Results from DTI in patients with PNEEs suggest altered white matter connectivity involving the left corona radiata, left internal and external capsules, left superior temporal gyrus, and left uncinate fasciculus [14]. Using HDEEG, patients with PNEEs have been found to have a decrease in lagged functional connectivity between the basal ganglia and paralimbic, prefrontal, temporal parietal, and occipital regions suggestive of decoupling in corticosubcortical networks [15]. Finally, fMRI and measured fractional amplitude of low-frequency fluctuations (fALFF) have shown increased fALFF in the dorsolateral prefrontal cortex and parietal cortices along with decreased fALFF in the inferior frontal gyrus suggesting abnormalities in neuronal synchrony in patients with PNEEs [16].

It is clear that truly no *consistent* structural or functional abnormalities have been verified in patients with PNEEs, but structural imaging abnormalities appear to be more prevalent compared with the healthy population. We sought to improve on previous studies focused on imaging abnormalities in PNEEs to better determine prevalence as well as investigate the actual location of abnormality as opposed to simple laterality. Obtaining a large sample size, assuring correct VEEG diagnosis, and excluding clinically insignificant structural abnormalities in our analysis were critical elements in our study.

2. Methods

We retrospectively identified all adult patients discharged from our EMU from July 1, 2009 to June 30, 2011. The patients were then stratified into groups based on their VEEG diagnosis. The five groups identified were: epilepsy (ES), psychogenic nonepileptic events (PNEEs), both epilepsy and psychogenic nonepileptic events (ES + PNEE), interictal epileptiform discharges only (IEDs), and nondiagnostic admissions (nondiagnostic). The semiology of psychogenic nonepileptic events was recorded and categorized as follows: major convulsions (including full body movements or movements involving all extremities), minor convulsions (including unilateral movements or mild bilateral arm movements such as hand flapping/trembling), nonconvulsive (including unresponsiveness with at most mild chewing or eye blinks), and subjective (including report of sensory or psychic symptoms/auras).

Next, the patients' charts were reviewed for brain MRI results. At our institution, images were obtained using T1 and T2 sequences in coronal, sagittal, and axial planes in addition to FLAIR, diffusion weighted imaging, gradient echo, and postcontrast T1 imaging as dictated by individual study protocol. Results at our institution were reviewed by board certified neuroradiologists. Magnetic resonance imaging results from outside institutions were also included. All abnormalities were recorded but only abnormalities felt to be clinically significant were included in our analysis. This resulted in the exclusion of nonspecific white matter T2/FLAIR abnormalities suggestive of chronic microvascular ischemic changes, developmental venous anomalies, and arachnoid cysts. Abnormalities were then sorted by location: frontal, temporal, parietal, occipital, brainstem, cerebellum, and multifocal. Abnormalities were considered multifocal if they included two or more locations or were seen diffusely. Data were then analyzed for statistical significance. The study protocol was reviewed and approved by the Medical University of South Carolina's Institutional Review Board for human research.

3. Results

A total of 339 patients were discharged from our EMU during the specified 2-year period including 123 patients in the group with ES, 112 in the group with PNEE, 22 in the group with ES + PNEE, 29 in the group with IED, and 53 in the nondiagnostic group. Magnetic resonance imaging results were available for 111 patients in the group with ES, 68 in the group with PNEE, 19 in the group with ES + PNEE, 26 in the group with IED, and 32 in the nondiagnostic group. There were significant MRI abnormalities in 64 patients in the group with ES (57.7%), 23 in the group with PNEE (33.8%), 9 in the group with ES + PNEE (47.4%), 12 in the group with IED (46.2%), and 15 in the nondiagnostic group (46.9%) (Table 1). The most common brain MRI abnormalities observed in each group can be seen in Table 2. Some etiologies of the T2 hyperintensities seen in the group with PNEE included: encephalitis, metastases, possible vasculitis, and postsurgical changes from past ventriculoperitoneal shunt. Fig. 1 shows MRI imaging from selected patients in the group with PNEE.

In the 112 patients included in the group with PNEE, 539 total psychogenic nonepileptic events were captured. The semiologies of these events were as follows: 40% major convulsions, 34% minor convulsions, 16% nonconvulsive, and 10% subjective. In the 23 patients included in the group with PNEE with abnormalities on brain MRI, 97 total psychogenic nonepileptic events were captured with semiologies as follows: 40% major convulsions, 20% minor convulsions, 20% nonconvulsive, and 20% subjective.

Further analysis was done on patients in the group with ES and group with PNEE to examine the location of significant MRI abnormalities. Table 3 shows the number and relative percentage of total abnormalities in each location. Temporal lobe abnormalities were significantly more frequent for ES than for PNEEs ($p = 0.003$). Multifocal abnormalities were significantly more frequent for PNEEs ($p = 0.018$). The remaining locations showed no significant difference between the two groups.

4. Discussion

Our results show that the prevalence of significant brain MRI abnormalities in patients with PNEEs is greater than the reported prevalence of significant brain MRI abnormalities found incidentally in the healthy population [8,9]. We found that 33.8% of patients with PNEEs who underwent brain MRI had significant abnormalities, which falls within the range of past studies that have documented the presence of imaging abnormalities in PNEEs to be from 17 to 86.4% [5–7]. A possible limitation of our study is that only 68 patients out of 112 with PNEEs had a brain MRI scan performed, as this was a retrospective study. An additional limitation to our study is that a healthy control group could not be studied for comparison, and the prevalence of brain MRI abnormalities in the healthy population was determined from past literature. In any case, 26 out of 112 total patients with PNEEs (20.5%) had a significant brain MRI abnormality identified. That prevalence rate is almost double the rate of incidental brain abnormalities in the healthy population [8,9].

In addition, we found a statistically significant difference in the location of MRI abnormalities in patients with PNEEs versus those with epilepsy. As expected, 57.8% of abnormalities were temporal in the group with epilepsy, significantly more than the group with PNEE (21.7%).

Table 1
Number of patients identified in each group as well as number of patients with MRIs available and number/percentage of significant MRI abnormalities.

	Total patients	Patients with MRIs	Number of abnormalities (%)
ES	123	111	64 (57.7)
PNEE	112	68	23 (33.8)
ES + PNEE	22	19	9 (47.4)
IED	29	26	12 (46.2)
Nondiagnostic	53	32	15 (46.9)