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Comparison of semiologies between tilt-induced psychogenic nonsyncopal collapse and psychogenic nonepileptic seizures☆

Geoffrey L. Heyer *, Dara V.F. Albert, Amanda Weber, Satyanarayana Gedela, Jorge Vidaurre

[a] Division of Pediatric Neurology, Nationwide Children's Hospital, The Ohio State University, Columbus, OH, USA
[b] Department of Pediatrics, The Ohio State University, Columbus, OH, USA
[c] Department of Neurology, The Ohio State University, Columbus, OH, USA

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ABSTRACT

We sought to characterize the clinical features of tilt-induced psychogenic nonsyncopal collapse (PNSC) from a cohort of young patients and to compare the semiologies between PNSC and EEG-confirmed psychogenic nonepileptic seizures (PNES). A PNSC diagnosis was made if a clinical event occurred during tilt-table testing that the patient regarded as fainting, but neither hypotension nor EEG changes were present. A diagnosis of PNSC was made in 17.6% of all patients referred during the 15-month study period. Cohorts with psychogenic nonsyncopal collapse ($n = 40$) and PNES ($n = 40$) did not differ in age (15.5 ± 2.2 versus 14.6 ± 2.7, $p = .11$) or female gender (80% versus 72.5%, $p = .43$). Psychogenic nonsyncopal collapse events were briefer than PNES events (median: 45 versus 201.5 s, $p < .001$). Negative motor signs (head drop, body limpness) predominated in PNSC (85% versus 20%, $p < .001$), while the positive motor signs of convulsion occurred more often with PNES (90% versus 30%, $p < .001$). Behavioral arrest (25% versus 32.5%, $p = .46$) and eye closure (85% versus 72.5%, $p = .21$) did not differ between PNSC and PNES. Patients with PNSC were more likely to be tearful before (30% versus 7.5%, $p = .02$) and after (62.5% versus 7.5%, $p < .001$) an event. In conclusion, although overlap exists, the features of PNSC generally appear similar to neurally mediated syncope, while the features of PNES generally appear similar to epileptic seizures. Psychogenic nonsyncopal collapse and PNES likely represent similar disorders that differ primarily by clinical semiologies and referral patterns.

1. Introduction

Psychogenic nonepileptic seizures (PNES) are paroxysmal alterations in behavior, movement, sensation, or arousal that resemble epileptic seizures but arise through involuntary or unconscious processes that have a psychological basis and do not have corresponding abnormal electrical discharges in the brain. By convention, the term has come to imply a disorder in which seizures are the main clinical presentation [1]. It is generally thought that patients with PNES do not deliberately feign their attacks [1]. When psychogenic episodes resemble syncope spells more so than seizures, they have been referred to as psychogenic pseudosyncope [2–9]. Other terms including psychiatric syncope [10,11] and hysterical fainting [12] have also been used. Throughout the remainder of this manuscript, we use the term psychogenic nonsyncopal collapse (PNSC) to describe paroxysmal alterations in behavior, movement, sensation, or arousal that resemble syncope but do not have corresponding hypotension or electroencephalographic (EEG) changes. We recommend using this terminology instead of psychogenic pseudosyncope because PNSC describes what the events are, as well as what they are not, while avoiding the phrase 'pseudo' which may be considered pejorative [13]. Since both PNES and PNSC are thought to represent functional neurological symptom disorders (conversion disorders), the similarities in terminology also underscore their presumptive shared etiologies.

While much has been published about PNES and the clinical signs that help to distinguish psychogenic spells from epileptic seizures, few reports exist about the clinical manifestations of PNSC. Tannemaat et al. provide one of the most thorough PNSC descriptions to date, comparing tilt-induced psychogenic events with tilt-induced neurally mediated syncope [2]. Several clinical features appeared to differentiate the patients with PNSC from the patients with syncope including longer event durations, abrupt head drops, eye closure, sliding down the tilt table during events, and the absence of jerking movements. Blood pressure and heart rate increased before and during PNSC events, which further distinguished psychogenic spells from syncope [2]. Hubsch et al. demonstrated that some patients referred for refractory

Abbreviations: EEG, electroencephalography; HUT, head-upright tilt; PNES, psychogenic nonepileptic seizure; PNSC, psychogenic nonsyncopal collapse.

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* Corresponding author at: Nationwide Children's Hospital and The Ohio State University, 700 Children's Drive, ED-5, Columbus, OH 43205, USA. Tel.: +1 614 722 4625; fax: +1 614 722 4633.
E-mail address: geoffrey.heyer@nationwidechildrens.org (G.L. Heyer).

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epilepsy and diagnosed with PNES also have clinical manifestations that resemble syncope [4]. The authors analyzed 22 clinical variables from PNES to define distinct semiologies; 16.9% of patients had a 'pseudosyncope' semiology described as an abrupt onset of brief loss of responsiveness without vocalizations and with limited abnormal movements [4]. Despite these efforts, functional neurological symptom disorders that resemble syncope remain a source of misdiagnosis [6], potentially leading to inappropriate and costly diagnostic testing and improper treatment. The clinical features of PNSC and PNES have not been directly compared.

Accordingly, we sought to characterize the clinical semiologies of tilt-induced PNSC from a cohort of young patients and to compare them with EEG-confirmed PNES recorded from a similarly aged cohort. We hypothesized that the clinical features would differ between groups according to their respective referral diagnoses, meaning that PNSC would resemble syncope more so than seizures, and PNES would resemble seizures more so than syncope. We also expected some overlap in clinical manifestations between groups. Understanding the potential differences between PNSC and PNES, as well as the potential similarities, will improve clinical recognition and diagnosis of these functional neurological symptom disorders, particularly among youth.

2. Materials and methods

2.1. Patients

We conducted a prospective observational study of sequential patients referred to a pediatric neurology-based clinic for head-upright tilt (HUT) testing with video-EEG monitoring between January 2015 and March 2016. Reasons for referral included refractory syncope, transient loss of consciousness of unclear etiology, and persistent orthostatic symptoms (e.g., lightheadedness, blackout spells, 'near syncope') with or without loss of consciousness. Study inclusion criteria were normal cardiac evaluation (minimally including 12-lead electrocardiogram and cardiac exam) and the diagnosis of PNSC. A PNSC diagnosis was made when a clinical event occurred during orthostatic challenge that the patient regarded as fainting, but hypotension did not occur, and the EEG did not change. In all cases, the patient and a parent who was present during testing confirmed that the captured event was typical of the events that prompted the clinical referral. Psychogenic nonsyncopal collapse spells that occurred immediately before or continued beyond neurally mediated syncope or had any associated hypotension were excluded (see below). The protocol allowed for all patient ages, given their referral to a pediatric neurology-based clinic and their ability to tolerate HUT testing.

A similarly aged cohort of patients diagnosed with PNES was identified from a video-EEG database consisting of routine and long-term EEG studies. Inclusion criteria for subjects with PNES were adequate video resolution and framing to characterize the PNES semiology, at least 30 s of video prior to the event onset, and confirmation in the clinical chart that the EEG event both represented the spells of concern and resulted in a PNES diagnosis.

Allocation of patients into the groups with PNSC and PNES was based solely on the referral patterns: patients who were referred for evaluation of syncope but were found to have a psychogenic spell were diagnosed with PNSC; those referred for evaluation of epilepsy but were found to have a psychogenic spell were diagnosed with PNES.

The study was approved by the Institutional Review Board at Nationwide Children's Hospital.

2.2. Protocol

All medicines that could affect orthostatic tolerance were discontinued ≥5 half-lives prior to HUT. Video-EEG (Comet AS-40, GRASS Systems, Warwick, Rhode Island, USA) was synchronized with continuous heart rate and blood pressure monitoring (Portapres, Finapres Medical Systems, Amsterdam, Netherlands). Following 30 min of recumbency, patients were tilted upright (70°) for up to 45 min.

Several descriptive features of fainting raise suspicion of PNSC: frequent spells, nonresponse to treatment, lack of prodromal symptoms, inability to abort spells, change in fainting character, prolonged episodes, unusual triggers, and atypical episode descriptions [2,6]. When PNSC was suspected, additional maneuvers were added to the testing protocol in an attempt to elicit spells. For example, if no event occurred during routine HUT testing, a series of up to five standing challenges (rapid standing from a seated position for up to 2 min) were performed. One patient had a history of fainting when she raised her arms above her head; following normal HUT testing, arm-raising maneuvers while seated upright successfully elicited a PNSC episode. If neurally mediated syncope or substantial hypotension occurred during HUT testing when PNSC was suspected, the testing was repeated with abdominal and lower-extremity compression to prevent hypotension [14]. If more than one PNSC event occurred, the single spell that best represented the events of concern (based on patient and parent report) was analyzed. Patients were asked to report all symptoms immediately with symptom onset. Clinical signs were recorded in real-time and confirmed by video review.

Similarly aged patients with PNES were identified at the same institution by searching an electronic record database containing routine and long-term video-EEG files. The patient's charts were reviewed for confirmation of the diagnosis, and the semiologic features were tabulated during group review of the videos. Majority consensus was used to determine inclusion of a clinical feature.

For both PNSC and PNES, we defined event onset as the period of apparent change in alertness or the onset of motor or vocal changes that dominated the clinical event. The signs and symptoms that occurred prior to the event onset were designated as the prodrome, yet we recognize that the distinction is purely semantic as all features of a psychogenic event represent the functional neurological symptom disorder. Recovery was defined in two ways: (1) the first sign of apparent alertness or halting of motor or vocal changes and (2) the apparent return to functional baseline.

2.3. Statistical analysis

Several semiologic features related to prodrome, event, and recovery were compared across groups. The features assessed were determined by author consensus a priori. The chi-square test or Fisher's exact test was used to compare categorical variables, and Student's t-test or the Mann–Whitney U-test was used to compare continuous variables. When more than two categorical variables were analyzed, the degrees of freedom were listed along with the p-values. All statistical analyses were performed using SPSS Version 22 (SPSS Inc., Chicago, IL, USA). The significance threshold was set at 5%.

3. Results

3.1. Descriptive and demographic features

In total, 80 patients were identified, 40 with PNSC and 40 with PNES. Patient ages across cohorts ranged from 9 to 22 years. Cohorts with PNSC and PNES did not differ by age (15.5 ± 2.2 versus 14.6 ± 2.7, $p = .11$) or female gender (80% versus 72.5%, $p = .43$). The 40 patients with PNSC represented 17.6% of all HUT tests performed during the study period. The reasons for referral for patients diagnosed with PNSC included refractory syncope ($n = 36$), postural tachycardia syndrome with syncope ($n = 3$), and a single episode of transient loss of consciousness of unclear etiology ($n = 1$). Thirteen patients (32.5%) with PNSC also had neurally mediated syncope demonstrated on prior HUT testing ($n = 2$) or during the PNSC evaluation ($n = 11$). Among those with syncope during the PNSC evaluation, five had combined