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Clinical characterization of the pre-ictal state in the pediatric population: A caretaker's perspective

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ABSTRACT

The unpredictability of seizures causes distress to patients with epilepsy and their caretakers. To date, no studies have explored seizure prediction specifically in the pediatric population. If the period of time preceding a seizure can be reliably identified, either by child or caretaker, there may be a role for pre-emptive interventions. The aim of this study was to investigate caretaker seizure prediction. A questionnaire was distributed to caretakers of patients with epilepsy. The patients were 0–21 years old and experienced ≥1 seizure within the past year. We excluded patients with non-epileptic seizures or daily seizures. One hundred and fifty of 240 questionnaires met criteria. Of these, 32 (21.6%) caretakers indicated a positive report of seizure prediction. Age of seizure onset was earlier in the positive predictive group (3.3 ± 3.3 years) than in the non-predictor group (5.3 ± 4.8 years) ($p = 0.01$). The most common pre-ictal symptoms reported were being tired, hazy look, and sleepiness. A total of 76.6% of caretakers reported at least one seizure precipitant. The prevalence of positive caretaker seizure prediction in this study is similar to that of seizure self-prediction in adult studies. These findings will be used to design prospective online or electronic diary studies to further investigate the caretaker's, as well as children's, perspectives on seizure prediction. We anticipate that this investigation may lead to novel treatments during times of high seizure risk.

1. Introduction

The unpredictability of seizures causes distress to patients with epilepsy and their caretakers. This distress likely reflects medical issues such as physical risk, and psychosocial issues such as lost school or work, interrupted plans, and stigma. If seizures were predictable, the element of uncertainty would be reduced or eliminated, and opportunities would present for pre-emptive therapy.

Many clinicians note that patients or caregivers will often report the ability to predict an impending seizure up to hours to days before the actual event. Clinical seizure prediction may be based on awareness of pre-ictal symptoms and/or seizure precipitants. There are several studies investigating clinical seizure prediction in the adult population, with mixed results. Few studies have shown that patients are able to make accurate seizure self-prediction [1,2]. To date, there have been no studies exploring clinical seizure prediction specifically in the pediatric population.

Pre-ictal symptoms have been referred to as prodromes, premonitory symptoms, or warning symptoms. They represent the subjective experiences of patients preceding a seizure. Rates of 6–47% of epilepsy patients with pre-ictal symptoms have been reported [3–6]. Symptoms such as irritable mood, headache, "funny feeling," dizziness, visual changes, and concentration difficulties, among others have been identified. Seizure precipitants, or triggers, are factors shown to increase the probability of subsequent seizure occurrence. These include circadian or catamenial patterns, sleep deprivation, stress or other emotional factors, alcohol use, or medication non-adherence [7]. In the general population, up to 90% of patients with epilepsy identified at least one seizure precipitant [8].

To date, most studies have focused on the patient's experience, but of course epilepsy impacts caretakers as well. Caretakers often influence the decisions of patients with epilepsy or make them on their behalf. There is little research investigating others' perceptions of clinical seizure prediction. The difficulty in observer's perceptions of predicting seizures is that only outward changes can be detected, whereas most of the pre-ictal symptoms and some seizure precipitants require awareness of the internal state, felt only by the person experiencing the seizure. However, it is possible that an observer who is able to closely monitor the person with seizures for significant periods, such as a parent, may be able to similarly predict seizures [9].

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In this study, we examined clinical seizure prediction as reported by the caretakers of children with epilepsy. We hypothesized that the percentage of caretakers who are able to predict seizures would be similar to the adult studies, and that these caretakers could report pre-ictal symptoms and seizure precipitants in the child they care for. The goal of this study was to collect baseline data, which we hope to use in the future to design more definitive studies on clinical seizure prediction in the pediatric population.

2. Methods

2.1. Participants

This study was conducted at the Children's Hospital At Montefiore (CHAM) between February 2014 and December 2015. An anonymous questionnaire was distributed to caretakers of patients with epilepsy. Typically, about 1000 pediatric epilepsy patients are seen per year by the pediatric epilepsy service. Around 75% have Medicaid or Medicaid managed care, and the remainder with private insurance. The population comprises mostly of African American and Hispanic patients, with a smaller percentage of White, Asian, and other races. Subjects received a full explanation of the research protocol. Willingness to complete the questionnaire served as informed consent. We included patients up to the age of 21 who experienced at least one seizure within the past year and who were being seen in the outpatient neurology clinic, were hospitalized as an inpatient, or were in the epilepsy monitoring unit. We excluded patients with non-epileptic seizures or daily seizures.

The study was approved by the institutional review board.

2.2. Data collection

The questionnaire was developed to assess for caretaker seizure prediction, pre-ictal symptoms, and seizure precipitants. It consisted of multiple choice questions, as well as the option to add additional information. Demographic information included current age, age of seizure onset, seizure frequency, epilepsy syndrome, and seizure type (supplementary material).

Prediction questions included: 1. "Do you know when your child is going to have a seizure day?" (yes, no, sometimes), 2. "Can you predict that your child is going to have a seizure?" (yes, no, sometimes), 3. "How far in advance can you predict your child's seizures?" (range of choices from <5 min up to 24 h before a seizure). Caretakers who endorsed a prediction time >5 min indicated pre-ictal symptoms. All caretakers were given the option to indicate precipitants. The list of pre-ictal symptoms and seizure precipitants was compiled from previous clinical seizure prediction studies [1,6–8,10]. The questionnaire was validated in 20 subjects to assess the quality and understanding of the questions, and appropriateness of answer choices.

2.3. Statistical analysis

SPSS was utilized for analysis. The prevalence of reported clinical seizure prediction among caretakers was determined as a percent of positive report from the total questionnaires administered.

Reported clinical seizure prediction was considered as a dichotomous outcome. The associations between making a positive report of seizure prediction and continuous variables, including age of patient, age of seizure onset, and duration of epilepsy, were tested for significance using a Student's t-test if assumptions were met, or Mann Whitney U-test. The associations between making a positive report of seizure prediction and categorical variables such as gender of patient, frequency of seizures, epilepsy syndrome, seizure type, and seizure precipitants were tested for significance using Pearson's chi square test.

Reported pre-ictal symptoms and seizure precipitants were collected in a descriptive manner. The association between each pre-ictal symptom and seizure type (focal versus generalized seizure) was tested for significance using Pearson's chi square test. The association between the number of pre-ictal symptoms and seizure type (focal versus generalized seizure) was tested for significance using a Student's t-test if assumptions were met, or Mann Whitney U-test.

3. Results

3.1. Study sample

Two hundred and forty questionnaires were returned, of which 150 met the criteria. Those surveys which were eliminated either did not meet inclusion and exclusion criteria, or were not correctly or completely filled out. On two of these questionnaires, the question of whether or not the caretaker was able to predict their child's seizures was not answered, and therefore excluded from analyses using positive caretaker predictors. The characteristics of all eligible patients including mean age, gender, mean age of seizure onset and duration of epilepsy, seizure frequency, epilepsy syndrome, and seizure type can be found in Table 1.

3.2. Positive caretaker predictors

We considered that a positive seizure prediction would have to precede the seizure by >5 min, in order to exclude auras. Of the eligible patients, 32 (21.6%) of their caretakers indicated a positive report of seizure prediction. Demographic variables, duration of epilepsy, frequency of seizures, epilepsy syndrome, and seizure type did not differ significantly between the overall population and subgroup of predictors. Age of seizure onset was found to be significantly different ($p = 0.01$), with positive prediction associated with an earlier age of seizure onset

Table 1
Patient characteristics and factors relating to seizure prediction.

	Population characteristics (N = 150)	Positive caretaker predictor (N = 32)
	Value (mean ± standard deviation)	
Age (years)	10.3 ± 5.8	10.2 ± 5.4
Age of onset (years)	4.9 ± 4.7	3.3 ± 3.3*
Duration of epilepsy (years)	5.4 ± 5	6.9 ± 5.5
	Value (% of population)	
Gender (male/female)	55.3/44.7	59.4/40.6
Seizure frequency		
1×/year	12	15.6
≥2×/year	47.4	46.9
≥1×/month	27.3	31.2
≥1×/week	13.3	6.3
Epilepsy syndrome		
Generalized	31.3	26.1
Absence	13.3	20.0
Infantile spasms	3.3	0
Lennox Gastaut syndrome	2.7	50.0
Juvenile myoclonic epilepsy	3.3	0
Benign Rolandic epilepsy	4.0	0
Frontal lobe epilepsy	2.7	25.0
Temporal lobe epilepsy	4.0	33.3
Dravet syndrome	2.0	33.3
Myoclonic-astatic	0.7	100
Other	0.7	0
Seizure type		
Generalized tonic-clonic	33.3	26.5
Absence	15.3	21.7
Focal dyscognitive	40.0	25.4
Focal without dyscognitive features	4.7	14.3
Focal evolving bilaterally	22.7	20.6
Myoclonic	26.7	30.0
Tonic	17.3	34.6
Atonic	6.0	33.3

* $p = 0.01$ – mean age of seizure onset was lower for positive predictors (3.3 years ± 3.3) when compared to negative predictors (5.3 years ± 4.8).