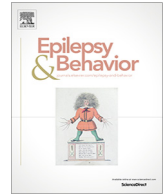




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Brief Communication

Psychogenic nonepileptic seizures during the COVID-19 pandemic in New York City – A distinct response from the epilepsy experience

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ABSTRACT

Although psychogenic nonepileptic seizures (PNES) are a common neurologic condition, there remains a paucity of literature on the COVID-19 pandemic's effect on these patients. Using a cross-sectional questionnaire study, our group examined the experience of patients with PNES at a single Comprehensive Epilepsy Center in New York City, the epicenter of the initial COVID-19 outbreak in the United States. Among our cohort of 18 subjects with PNES, 22.2% reported an improvement in seizure control during the peak of the COVID-19 pandemic in New York City. Compared to the cohort of subjects with epilepsy without PNES, subjects with PNES were significantly more likely to report an improvement ($p = 0.033$). Our findings signal that sleep and stress may be relevant variables in both conditions that should be further investigated and potentially intervened upon. Larger dedicated studies of patients with PNES are needed to understand the impact of the pandemic's widespread societal effects on these patients.

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1. Introduction

There is a rapidly growing body of literature on the COVID-19 pandemic's impact on patients with chronic neurologic conditions. This includes the direct impact of infection with the novel SARS-CoV-2 virus as well as the wide-reaching societal effects of the pandemic. This global crisis has had a profound psychological impact, perhaps more severe in people with seizures [1,2]. We previously published on our patients with epilepsy and their self-reported seizure control during the initial surge, and found that 17.5% of subjects in our cohort reported worsened seizure control [3]. Patients with more frequent seizures at baseline were more susceptible to worsening, and increased stress as well as barriers to care appeared to play significant roles in their deterioration.

As a Comprehensive Epilepsy Center in New York City, the epicenter of the initial COVID-19 outbreak in the United States in the Spring of 2020, our group is in a unique position to also examine the experience of patients with psychogenic nonepileptic seizures (PNES) or functional seizures during the pandemic. We hypothesized that patients with PNES may have a distinct experience during the pandemic from that of patients with epilepsy without concurrent PNES in terms of event frequency.

Neurologists, and particularly epileptologists, frequently diagnose patients with PNES. To date, there remains a paucity of literature on the COVID-19 pandemic's effect on patients with PNES and other functional neurologic disorders (FND). A preliminary study of eight patients with PNES and ten with functional movement disorders suggested that subjects with functional movement disorders experienced greater psychological distress compared to those with PNES [4]. A cross-sectional study from Brazil found that 28% of patients with PNES reported increased frequency of PNES during the pandemic, and higher anxiety and depression scores were associated with this deterioration [5].

2. Materials and methods

We performed a prior cross-sectional questionnaire study of adult patients with epilepsy at a single urban Comprehensive Epilepsy Center (Montefiore Medical Center), as previously described [3]. Informed consent was obtained via telephone, and then subjects could choose to complete the one-time survey via telephone or secure online platform (REDCap). The study and remote telephone consent process were approved by the Einstein/Montefiore Institutional Review Board.

The current study focuses on adult patients with PNES, who had a scheduled follow-up appointment with a neurologist (seizure/epilepsy specialist) at our institution between 3/1/2020 and 5/31/2020, regardless of whether their visit was completed, canceled, or rescheduled. This time range was chosen because it rep-

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resents the peak of the COVID-19 pandemic in New York City. Inclusion criteria were that patients must have a diagnosis of seizures, be established patients at the Comprehensive Epilepsy Center at Montefiore, and must be able to complete a questionnaire independently in either English or Spanish. The questionnaire consisted of four sections: seizure control at baseline, seizure control during the pandemic, seizure precipitants, and stress and access to care during the pandemic. Seizure control was assessed qualitatively and quantitatively. Subjects were not asked to distinguish between the frequency of their PNES and epileptic seizures. Subjects were asked whether they felt the pandemic had worsened their stress levels, and then in a separate question whether it had worsened their sleep. Responses were categorical: yes, no, or I'm not sure/prefer not to answer. Demographic and neurologic history information was obtained from the subjects' medical records. Of the 1212 scheduled visits, 693 patients were eligible, of whom 201 completed the questionnaire. Eighteen subjects who completed the survey had documented PNES (captured on continuous video-EEG at our institution) [6]. All eligible patients were contacted and questionnaires completed in June, 2020.

Data were analyzed using SPSS v27 to determine any statistically significant associations between the variables and change in seizure control. Associations between patient-perceived worsening seizure control and continuous variables were tested for significance using a Mann-Whitney U test. Categorical variables were tested for significance using a Fisher's exact test or a Pearson Chi-square test.

3. Results

3.1. Background and demographics

There were a total of 18 patients with PNES studied. The subjects' demographic and neurologic history data are presented in Table 1. Among the subjects with PNES, the median age was 48, and 17/18 subjects identified as female (94%). In terms of racial and ethnic background, nine identified as Hispanic (50%), five as Black/African American (27.8%), one as "Other" (5.6%), and three declined to answer (16.7%). Only one subject with PNES completed

the survey in Spanish. As both cohorts completed the same questionnaire, we also compared the subjects with PNES to the larger cohort of patients with epilepsy without concurrent PNES. Compared to subjects with epilepsy without concurrent PNES (Table 1), subjects with PNES were significantly more likely to be female (94.4% vs 68.8%, $p = 0.022$). Otherwise there were no significant demographic differences. Five subjects with PNES had a history of concurrent epilepsy with electroclinical seizures also captured on continuous video-EEG at our institution. Median duration of PNES was 18 years.

3.2. PNES and seizure control during COVID-19 pandemic

Among the 18 subjects with PNES, four reported improved PNES control during the peak of the COVID-19 pandemic in New York City, two reported worsening, and twelve reported no change. Compared to the cohort of subjects with epilepsy without PNES, subjects with PNES were significantly more likely to report an improvement (22.2% vs. 7.3%, $p = 0.033$) (Table 1). When asked to elaborate how their PNES had improved, three subjects reported fewer events and one stated that her attacks had become less severe. Both subjects who reported a deterioration stated that they had more frequent attacks and one also reported a new semiology and "more intense convulsion."

3.3. Variables associated with PNES and seizure control

Within the cohort of subjects with PNES, there was no significant demographic difference among subjects who reported improved versus stable or worsened PNES control (Table 2). There was also no significant difference in terms of duration of PNES or rate of concurrent epilepsy among the groups. Among the five subjects with concurrent epilepsy, two reported improved control, one reported worsening, and two reported no change. In this cohort, 75% of subjects with improved PNES control had stress and poor sleep as one of their usual seizure triggers, opposed to 50% and 35.7%, respectively, for patients who reported stable or worsened PNES control; however, this did not reach statistical significance (Table 2). None of the other variables associated with reported

Table 1
Subjects with PNES with or without epilepsy vs. respondents with epilepsy without PNES.

Reported change	PNES subjects with or without concurrent epilepsy (18)	Subjects with epilepsy without concurrent PNES (177)	p-value
Improved seizure control	22.2% (4)	7.3% (13)	0.033
Age – median (years)	48 (range 28–66)	47	0.469
Gender – female	94.4% (17)	68.4% (121)	0.022
Duration of epilepsy or PNES in years (median)	18 (range 2–37)	15 (range 0–64)	0.941
Median average monthly seizure rate 2019	1.04 (range 0–6.5)	0.08 (range 0–≥10)	0.022
Jan & Feb 2020	0.0 (range 0–4)	0.0 (range 0–≥10)	0.774
Mar, Apr, May 2020	0.17 (range 0–4)	0.0 (range 0–≥10)	0.261
Typical seizure triggers			
Stress	55.6% (10)	31.1% (55)	0.036
Poor sleep	44.4% (8)	12.4% (22)	<0.001
Headache/migraine	16.7% (3)	7.9% (14)	0.210
Infection	0.0% (0)	2.8% (5)	0.470
Missed medications	33.3% (6)	18.1% (32)	0.120
Menstrual cycle/period	5.6% (1)	4.5% (8)	0.842
Other	22.2% (4)	19.8% (35)	0.805
I have no clear triggers	22.2% (4)	35% (62)	0.274
Increased/worsened stress due to the COVID-19 pandemic	55.6% (10)	55.4% (98)	0.988
Worse sleep due to the COVID-19 pandemic	50.0% (9)	42.9% (76)	0.645
Worse epilepsy care during the COVID-19 pandemic	22.2% (4)	16.9% (30)	0.847
Patient canceled a Neurology appointment	16.7% (3)	18.6% (33)	0.198
Neurologist canceled an appointment	27.8% (5)	27.7% (49)	0.564

Table 2
Variables associated with reported improved PNES control vs. stable or worsened during the COVID-19 pandemic.

Variable	Patients who reported improved PNES control (4)	Patients who reported stable or worsened PNES control (14)	p-value
Age – median (years)	49.5	48	0.798
Gender – female	75% (3)	100% (14)	0.222
Duration of PNES in years (median)	21 (range 2–32)	18 (range 3–37)	1.0
Concurrent epilepsy	50% (2)	21.4% (3)	0.533
Presumed COVID-19	25% (1)	0	
Typical seizure triggers			
Stress	75% (3)	50% (7)	0.588
Poor sleep	75% (3)	35.7% (5)	0.275
Headache/migraine	25% (1)	14.3% (2)	1.00
Infection	0	0	n/a
Missed medications	25% (1)	35.7% (5)	1.00
Menstrual cycle/period	0	7.1% (1)	1.00
Other	25% (1)	21.4% (3)	1.00
I have no clear triggers	0	28.6% (4)	0.524
Increased/worsened stress due to the COVID-19 pandemic	50% (2)	57.1% (8)	1.00
Worse sleep due to the COVID-19 pandemic	25% (1)	57.1% (8)	0.366
Worse epilepsy care during the COVID-19 pandemic	25% (1)	21.4% (3)	0.857
Patient canceled a Neurology appointment	0	21.4% (3)	0.416
Neurologist canceled an appointment	25% (1)	28.6% (4)	0.603

improved PNES control vs. stable or worsened reached statistical significance, likely due to the small sample size.

Among these 18 subjects, only one reported suspected COVID-19 illness during this time period. That subject was never tested and reported improved seizure control during this three-month period.

Subjects with PNES were significantly more likely than the subjects with epilepsy (without concurrent PNES) to report that stress and poor sleep were their typical seizure precipitants (55.6% vs 31.1%, $p = 0.036$, and 44.4% vs. 12.4%, $p < 0.001$, respectively). There was no significant difference in reported increased stress or worsened sleep related to the pandemic or in access to neurologic care.

4. Discussion

Among our cohort of subjects with PNES, 22.2% reported an improvement in seizure control during the peak of the COVID-19 pandemic in New York City. Subjects with PNES with or without concurrent epilepsy were significantly more likely than our cohort of subjects with epilepsy to report improved control during this three-month time period. The only other dedicated study to date of patients with PNES during the pandemic did not report the percentage of patients that improved, but rather grouped the improved and unchanged subjects together and compared them to the cohort that experienced PNES worsening [5].

Comparing the subjects with PNES to the subjects with epilepsy without concurrent PNES provides some clues about this unique subset of patients with PNES who improved amidst extenuating circumstances. There may be a subset of patients with PNES for whom spending significantly more time at home limited exposure to stressful settings or specific PNES triggers. Compared to patients with epilepsy without concurrent PNES, perhaps some subjects with PNES disproportionately benefitted from additional sleep and other healthy lifestyle habits related to the closure of schools and workplaces. Other studies have demonstrated that patients with PNES are more likely than those with epilepsy to report poor sleep quality and meet clinical criteria for insomnia, so they may have derived greater benefit from additional sleep [7,8]. Our subjects with PNES were also significantly more likely to identify lack of sleep, as well as stress, as typically provoking events. The rela-

tionship between sleep and PNES control during this ongoing global crisis should be further investigated.

Though there was no significant difference in access to neurologic care, the questionnaire did not ask about access to psychiatrists and other behavioral health providers. Access to psychiatric care and therapists during the pandemic, especially during this initial peak before telehealth platforms were well-established, is another potential contributor to be further explored. Appointments are less likely to be canceled now that there are established telehealth platforms and neurologists and psychiatrists are no longer being redeployed to COVID-19 units. Furthermore, live video visits appear to be an effective way to deliver care to patients with PNES and may be associated with improved appointment adherence [9].

We recognize the limitations of this study, including the small sample size. The questionnaire study was designed to examine the experience of patients with epilepsy during the pandemic [3]. With a larger cohort of subjects with PNES, associations between patient-perceived improved PNES control and some variables could reach statistical significance. A larger sample size as well as standardized anxiety and depression screening tools could better delineate the potential impact of stress and mood symptoms on changes in PNES control during this global crisis. In addition, assessing anxiety and depression could allow one to try to further determine how mood symptoms directly impact PNES control and indirectly do so by affecting sleep. A future study distinctly asking subjects whether their sleep and/or stress improved would allow for better understanding of why some subjects experienced fewer seizures.

Five of the eighteen subjects in our cohort have concurrent epilepsy, including two of the four subjects who reported improved seizure control. Another limitation of this study is that subjects were not asked to distinguish between the frequency of their PNES and epileptic seizures, though in many cases it would be extremely difficult to confidently differentiate based on self-report in patients with both conditions. Ideally future studies would focus on patients with PNES without concurrent epilepsy.

Lastly, the changes in PNES control may also in part reflect fluctuations in PNES unrelated to the pandemic. There are limitations of self-reported retrospective seizure or PNES counts. Many patients do not consistently document their events, and recall bias

is inevitable. Despite these limitations, this study suggests that subjects with PNES had a distinct experience during the pandemic.

5. Conclusions

We find the differences between our subjects with PNES compared to those with epilepsy without concurrent PNES during the peak of the COVID-19 pandemic to be striking. While the subjects with epilepsy in our center tended toward worsened seizure control [3], more of the subjects with PNES tended toward improved nonepileptic seizure control, highlighting these episodic disorders' distinct physiologies and precipitants. Psychogenic nonepileptic seizures represent a relatively common neurologic condition, and larger dedicated studies of patients with PNES are needed to understand the impact of SARS-CoV-2 infection as well as the pandemic's widespread societal effects on these patients. Our findings signal that sleep and stress may be relevant variables in both conditions that should be further investigated and potentially intervened upon. Given the minimal literature emerging regarding the experience of patients with PNES during the pandemic, we anticipate that sharing these early findings from our PNES subset will stimulate further exploration into this important area. We must strive for a greater understanding of our patients with PNES and their experiences and unique needs related to this ongoing global health and societal crisis. Prospective diary studies collecting data on episodes of PNES are needed to expand upon this study and clarify the rates of worsened and improved PNES control as the pandemic continues.

6. Disclosure of conflicts of interest

Dr. Sheryl R. Haut is serving as a consultant for Nile.

The other co-authors do not have conflicts of interest to disclose.

7. Ethical publication statements

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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