HIGH SCHOOL EDITION
Journal of Student Research
Volume 11 Issue 3 (2022)

# Seizures on the Spectrum: A Study of Non-Epileptic Seizures in Autistic Children

Haylie McKinney[1], Dr. DeeDee Montgomery[2#] and Jillian Runser[2#]

[1]Independence High School
[2]Williamson County Schools
[#]Advisor

## ABSTRACT

This study aimed to analyze data from McWilliams et. al. (2019) to answer the research question, is there a correlation between non-epileptic seizures and autism spectrum disorder that could suggest a cause of non-epileptic seizures in autistic children? A quantitative method and explorative approach were used for the inquiry process of correlational research. Furthermore, a one-proportion z test was used to study the correlation between the population of autistic patients and the occurrence of non-epileptic seizures. The results of this test found a significant statistical correlation between autism spectrum disorder and non-epileptic seizures (p=8.01e-35, z=12.3). In addition, a gap in research on the differences between autistic females and males with non-epileptic seizures was studied using a chi-square test. However, the test found no significant difference in the rate of occurrence of seizures in autistic patients (p=0.85, x=0.0397). Further research will need to be done to determine qualitative differences between the sexes.

## Introduction

In the United Kingdom (UK), one in six children have a probable mental disability. These mental disabilities can lead to a special type of psychogenic seizure (Rawlings et al., 2021). This means that up to one sixth of a population could develop a seizure disorder. Non-epileptic seizures (NES) are recurrent seizures that do not show up on an electroencephalogram (EEG) — a test that studies brain activity and often used to study seizures — and cannot be diagnosed as epileptic (Wright & Zvartua-Hind, 2012). These non-epileptic seizures have multiple suspected causes, including psychological stress, genetics, and trauma. In a recent UK study of 59 patients with non-epileptic seizures, 10 (or 16.9%) had been diagnosed with Autism Spectrum Disorder (ASD) (McWilliams et al., 2019). However, the national average of ASD in the UK is 1-2%. This percentage of autistic children and young adults in the study is significant and cause for concern. While this pattern has been identified, there is a gap in research on the differences between autistic females and males with NES.

Autism is a developmental disability that affects communication. It is often characterized by resistance to changes in routine and the environment and unusual responses to stimuli (Pennington et al., 2014). These characteristics make children more likely to become overwhelmed by external stimulation. Contrary to what is typically seen in the ASD research field, the autistic community prefers identity-first language. While person-first and identity-first were used interchangeably in this study, identity-first language was preferred and used more often (ASAN, 2022). Assuming that the non-epileptic seizures are caused by stress and not trauma or genetics, ASD could create a heightened chance of psychological stress that could trigger a seizure. The goal of testing this hypothesis was to determine what causes a stress-induced non-epileptic seizure and compare it to the psychogenic, or psychological and non-physical, effects of ASD. The relationship between the two could suggest NES as a potential indicator of autism, and a found cause of NES in autistic children could lay the pathway for future therapies and treatments, eliminating the need for unnecessary epilepsy drugs. All of this has been done through answering the question, is there a correlation between NES and ASD that could suggest a cause of NES in autistic children?

## Literature Review

### *Types of Non-Epileptic Seizures*

The types of seizures outlined in this research are non-epileptic seizures (NES) and psychogenic non-epileptic seizures (PNES). These are distinct from epileptic seizures because NES seizures, unlike epileptic seizures, are not caused by disrupted electrical brain activity (Epilepsy Society, 2020). In fact, one in five patients diagnosed with epilepsy are found to actually have NES. These seizures can be caused by something physical, such as low blood pressure or a problem with the heart. However, the most common type of NES is caused by someone's reaction to thoughts or feelings that affect them physically; these are called dissociative seizures, or PNES.

PNES occurs subconsciously and cannot be controlled by the person having them (Epilepsy Society, 2020). When an individual goes through a traumatic event, they can repress their memories to cope. These distressing, repressed memories can be triggered by an emotionally stressful situation. The emotional stress caused by triggered memories and stressful situations overwhelm the brain and causes a PNES. Due to the nature of ASD causing hypersensitivity, this research is assuming the seizures potentially caused by ASD are psychogenic.

### *Autism Spectrum Disorder*

Autism Spectrum Disorder is defined as a neurodivergent disorder that affects "verbal and nonverbal communication and social interaction" (Pennington et al., 2014). It is often associated with repetitive movements, resistance to changes or routine, and heightened responses to sensory stimulation (Pennington et al., 2014).

According to a study conducted by Chanyound Ko and others (2016), ASD has been addressed as prevalent in 15-47% of epileptic cases. The study looked at the medical records of 182 participants, 22 of which had both ASD and epilepsy. They then took a group of 44 patients with only autism that had similar ages, genders, and IQs to the group of 22 children. They found that the group of individuals with both ASD and epilepsy were "significantly more impaired" than the group with only ASD with social functioning. The study hypothesizes epilepsy plays a factor in producing autistic symptoms.

There is little known about individuals who have PNES and an intellectual disability. An intellectual disability (ID) is a condition "characterized by limitations in cognitive, social, and practical skills" (Rawlings et al., 2021). While ID has been identified as a factor in developing PNES, it is often overlooked in research. Rawlings and others' (2021) paper identified clinical differences in PNES in patients with and without ID. However, due to a lack of research, there is limited evidence on the connection between the two.

Emotional differences between female and male patients have been recently observed. A study by Minyoung Jung and others (2015) looked to see if these differences occurred in response to brain networks. Resting-state functional magnetic resonance imaging (fMRI) was studied in a group of 42 females (ages 18-30) and 43 males (ages 20-29). Significant differences were found in default mode network (DMN) brain regions. In addition, a negative correlation between DMN in the prefrontal cortex and autism quotient scores (AQs) was found in males. However, this same correlation was not found in females. This suggests a biological and neurological difference between autistic male and female patients. Since seizure activity happens in the brain, this study hypothesized that there is a difference between autistic female and male patients with NES.

### *Influences and Advancements*

The study of psychogenic non-epileptic seizures (PNES) is a relatively new field — most papers being published within the last decade. A study conducted at the Epilepsy Center at the Marshall University School of Medicine looked at epileptic episodes using a video electroencephalography (VEEG) to identify PNES (Dipali et al., 2020). It found that most PNES patients were older than 45, females, obese, single/separated/divorced/widowed, low education, unemployed, or having a physical or psychiatric illness. This adds evidence of "the sociodemographic and sociocultural variability of PNES".

Recently, advancements have been made in determining a connection between NES and autism. One case report in support of the connection is a 10 year-old Japanese girl with undiagnosed autism who developed PNES while getting treatment for childhood epilepsy (Miyawaki et al., 2016). She reported hypersensitivity to sound and interpersonal conflicts that were caused by deficits in communication. This could suggest hypersensitivity was the cause of her PNES.

Neural network instability is hypothesized to be connected to PNES (Radmanesh et al., 2020). The resting state EEGs of 141 children (35 with PNES, 31 with another functional neurological disorder, and 75 healthy controls) were used to examine connectivity in neural networks. In the EEGs, the children with PNES were shown to have increased physiological arousal, which could suggest a heightened sensitivity to stimulation. While the study primarily focused on functional neurological disorder, the results could be related to ASD.

A study conducted in the UK worked to identify a connection between autism and NES. This study focused on 59 children and young adults with NES; it found that five of the patients had diagnosed ASD and another five were diagnosed after the trial (McWilliams, Reilly, Gupta, et al., 2019). In addition, autistic patients with NES were significantly more likely to have tics or attention-deficit hyperactivity disorder (ADHD), compared to patients without ASD. These patients were also more likely to have psychiatric comorbidity, including PTSD, anxiety disorders, and OCD. Patients also reported having physical symptoms after their seizures: headache, weakness, changes in vision, memory loss, and vomiting. This research could suggest a link between physical and physiological symptoms. However, the study did not find a conclusive connection between autism and NES.

### *Significance*

When it comes to children, NES is often neglected and patients are only accessed by pediatrics or child mental health (McWilliams, Reilly, & Heyman, 2017). This neglect has resulted in children receiving inadequate treatment. A child could be misdiagnosed with epilepsy and given unnecessary anti-epileptic drugs. However, the ideal treatment for NES is not drugs but behavioral therapy. Monitoring a child for NES after an autism diagnosis would allow for the proper treatment if seizures started to develop. In addition, re-evaluating cases of autistic children with epilepsy could provide an adequate care pathway for the child.

Damiani et. al. (2020) tested the hypothesis that autism symptoms can be onset by epilepsy through looking at a group of 20 adults. To limit discrepancies, this group was between the ages of 20-55, all suffering from a severe intellectual disability (ID), and all living in a rural farming community. The researchers were primarily looking for the association between epilepsy and regressive ASD — where they found an initial trend — and secondarily looking for differences in behavioral profiles. In addition, the study found subjects with regressive ASD or epilepsy had shown worse behavioral profiles. The results of this study suggest associations between epilepsy and ASD.

### *Conclusion*

Due to the similar symptoms of epilepsy and NES causing the misdiagnosis of NES as epilepsy, there can be an assumption that the association between epilepsy and ASD can be related to NES and ASD. This association should suggest a screening for autism when a child is diagnosed with NES or PNES. In addition, autistic children should be monitored for the development of seizures. Research has been done in studying epilepsy in ASD, NES in children, and ASD in children. However, no research has been done on the differences between female and male children who have autism and PNES. This gap in research will be evaluated over the duration of this study.

## Methods

This study was conducted using a correlational method with a quantitative approach. The purpose of this study was to make progress towards future causational studies. In addition, this study looked to compare the variable of autism with the variable of seizures. For these reasons, this study was conducted with the correlational method. A

quantitative approach was used for measurement as opposed to a mixed method approach because the researcher did not have access to qualitative patient files. This meant characteristics and symptoms between patients could not be compared. Access to patient files could lead to future research on the qualitative aspects of NES and autism. These could include how patients exhibit different symptoms and the potential causes behind them. However, the bounds of the researcher and purpose of the study require a quantitative analysis. The researcher found that this method and approach were vital to answering the research question, is there a correlation between NES and ASD that could suggest a cause of NES in autistic children?

## *Approach*

Due to the researcher's lack of access to new patient data, the data sample from the McWilliams et. al. study (2019) was reanalyzed for the purpose of this study. The McWilliams study was focused on co-morbidity and analyzed data through a T Test, but this study used a chi square test and a one proportion z test for analysis. Significant differences between female and male patients — as described in this study's gap — were studied with a chi square test. In addition, the one proportion z test was used to test the phenomenon of NES occurring in autistic children and the hypothesis of a correlation. A table of sample data from the McWilliams et. al. study (2019) is included as figure 1.

**Features of patients with and without ASD**

| | Total (n=59) | ASD (n=10) | No ASD (n=49)[a] | p-value |
|---|---|---|---|---|
| sex female | 37 (62.7%) | 6 (60.0%) | 31 (63.3%) | 0.557 |
| epilepsy | 22 (37.3%) | 3 (30.0%) | 19 (38.8%) | 0.406 |
| age of first non-epileptic seizure (years; range, standard deviation) | 12.5 (5.4-17.5, 2.6) | 11.8 (7.2-15.0, 2.7) | 12.7 (5.4-17.5, 2.5) | 0.291 |
| co-morbid psychiatric illness (any) | 30 (50.1%) | 7 (70.0%) | 23 (46.9%) | 0.184 |
| ADHD | 5 (8.5%) | 3 (30.0%) | 2 (4.1%) | 0.030* |
| tic disorder (any) | 3 (5.1%) | 3 (30.0%) | 0 | 0.004* |
| intellectual disability | 4 (6.8%) | 2 (20.0%) | 2 (4.1%) | 0.068 |

[a]except age, where n=45 *statistically significant

**Figure 1.** Features of patients with and without ASD, McWilliams et al., 2019. This figure shows the breakdown of the population used in this study. It includes comorbidity rates in the sample.

The chi square test was run through a calculator statistical program. The test compared the groups of male and female patients with how many had ASD in each group. For example, the square included 37 female patients with NES, 6 of which were autistic and had NES. In addition, it included the 22 male patients with NES and the 4 who had both NES and autism. These findings would suggest if there is a quantitative distinction between female and male patients. However, this does not include distinctions between qualitative differences. Therefore, the results of the quantitative study will not be enough to fully distinguish or not distinguish male and female patients. A recreated mixed method approach will be required for proper correlational comparisons between patients. This study assessed if females or males were more likely to have both NES and autism.

The one proportion z test was run to find the probability non-epileptic seizures occur in autistic children by chance. The program used n = sample size and x = total number of autistic children with NES in the sample. The parameters included $p_0$: 0.01 and a proportion $p_0 \neq 0$. The sample size used was 59 patients with NES and the group of 10 autistic children in the sample of non-epileptic seizures. The results of this test determined if there is a quantitative correlation between non-epileptic seizures and autism spectrum disorder.

## *Sample Selection*

The study used data from a similar study because both were looking at correlations between NES and autism. While McWilliam and others' study (2019) included other neurodevelopmental co-morbidities, this study focused

specifically on the group of NES patients who had autism. The relatively small sample size was a result of the limited number of patients who have NES. Information was gathered from a database of children with NES that was diagnosed between 2012 and 2016. The sample was selected from the criteria that a patient was under the age of 18 and confirmation of NES diagnosis from a clinical assessment. A team with a psychiatrist, psychologist, and neurologist was used for assessing the sample. While diagnosis with a vEEG is ideal, it was not used for diagnosis in all cases selected. All patient participants were accessed for confirmation of NES diagnosis by the clinical team of the McWilliam and others' study (2019).

## *Population*

According to McWilliams et. al. (2019), this data was collected at the Great Ormond Street Hospital, London, UK. Ethnicity and income were not included in the data. However, demographics can be assumed to resemble the demographics of the hospital in 2019. These demographics were collected from a 2020 data report reflecting 2019 care. Patient race and ethnic inpatient demographics were taken from a graph included in the report. These numbers were not explicitly stated and were estimated by the researcher. Inpatient demographics include approximately 9,500 patients from a white background (49% of the patient population), 2,500 patients from an asian background, 1,100 from a black background, 800 from a mixed background, and 18-21% of the population is unspecified. The patient race and ethnicity outpatient demographics appear to reflect the same as inpatient percentage wise, with higher numerical groups. When recreating the study, information of patient demographics from access to medical records will provide more accurate results specific to the studied region.

Demographics gathered from the data directly include sex and age. The data set had 59 total patients, 62.7% of which were female (n=37). The age of first non-epileptic seizure was 12.5 and ranged from 5.4-17.5 years. This study is focusing on the female and male populations of the sample. The data also included other psychiatric details of the population including but limited to ADHD, tic disorders, intellectual disabilities, anxiety disorder, PTSD, and OCD. However, this data was irrelevant to the purpose of this study and was not included in any tests. It must be noted that these co-morbidities could affect results in recreation of this study. Figure 2 will be included to give a more detailed representation of co-morbidities in the sample.

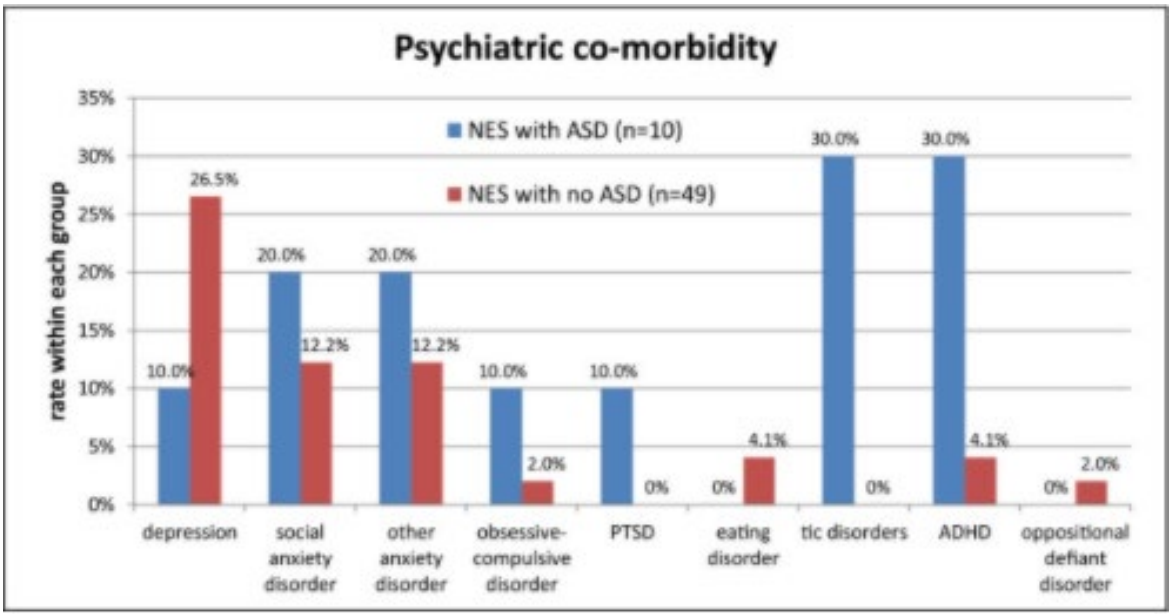


**Figure 2**. Psychiatric co-morbidity, McWilliams et al., 2019. Blue lines indicate autistic patients with NES and red lines indicate patients with NES and no ASD. This figure shows the breakdown of comorbidities in the patient population.

## Results

The purpose of this study was to answer the question, is there a correlation between NES and ASD that could suggest the cause of NES in autistic children, through the approach of explaining the connection with quantitative tests. In addition, the study intended to investigate a gap in the research field of differences in female and male autistic children with NES. In summary, the results of a chi square and one proportion z tests found that there was no significant quantitative relationship between female and male patients. However, the tests did find a significant probability in the correlation between NES and ASD (p=8.01e-35). The tests, results, analysis, and further implications and limitations were evaluated over the course of this section.

### *Limitations*

Before discussion of findings, it is important to identify limitations that could have changed the outcomes of the results. The most prominent limitation was sample size. Due to the small percentage of the population that is affected by ASD, the initial population was smaller. In addition, due to difficult diagnosis of non-epileptic seizures, the sample size was limited. This combination led to a small sample size which could not accurately represent the population as a whole. In addition, the data used was not original and was taken from a peer reviewed, credible preexisting study (McWilliams et. al., 2019). Since the data was being used for a comorbidity study, it has the potential to inaccurately represent the population as a whole. The data could also be subject to bias because it was taken for the purpose of a different study. Having a larger, more generalized, population could produce a more accurate conclusion. Finally, population demographics were taken from the patient demographics of the hospital where the McWilliams et. al. (2019) study was conducted. While these demographics provide a good estimate of the sample, differences in patterns between sample demographics and hospital demographics could result in different results if recreated. These limitations could have created a less accurate data set which could have, in turn, altered the results of the study.

### *Chi Square Test*

The gap in research this study tried to fill was a difference between autistic male and female children with NES. The chi square test, as previously mentioned, was used to study quantitative differences between female and male patients with NES and ASD. Chi value for the test was measured to be 0.0397, and the probability value was found to be 0.8457 (p=0.85). The low chi value reflects that it is unlikely that one sex is affected more than the other. A low standard deviation is also identified from this value, which reflects that it is unusual for a population to defer from this pattern. This further provides evidence that female and male children have similar affectance rates. Furthermore, the high probability value suggests it is statistically improbable that the rates of female and male children are not the same or similar (p>0.5). These results mean that it is unlikely an outside factor is determining whether more females and males have both NES and ASD. This high p value and low chi value point to a negative test — a test that does not support a hypothesis. Therefore, the hypothesis in a numerical difference between the two groups has been concluded to be untrue. According to the data, females and males suffer from both non-epileptic seizures and autism at a random rate. Additionally, this rate does not change based on gender.

### *One Proportion Z Test*

The focus of this study was to answer the research question, is there a correlation between NES and ASD that could suggest a cause of NES in autistic children? To answer this question, a one proportion z test was used to find a numerical correlation between NES and ASD. The test had the given parameters of $p_0$: 0.01, $p_0 \neq 0$, and 10 NES patients in the population (n=59) who also had autism. The results of the test were taken from a Texas Institute version 84 calculator (Ti-84). The test resulted in a z score of 12.312 and a probability value of 8.01e-35. The z value reflects standard deviation. The high standard deviation reflects that the data can fluctuate without being a statistical abnormality. The probability value of 8.01e-35 is a statistically significant result. The value reflects the chance that an

outside factor caused patients to have both NES and ASD. The extremely low value reveals that it can be proven that NES and ASD are correlated.

To make sure results were consistent, the same process was repeated for the subgroups of females and males. The second test used 6 autistic females with NES and the total female population with NES (n=37). The test concluded with similar results to the first test, with a z score of 9.302 and a probability value of 1.3e-20. Lastly, a test was made with the male population (n=22) — with 4 autistic males having non-epileptic seizures. Again, similar results were found (z=8.1 and p=5.57e-17). The similar results for the main test and two subtests are evidence that the results are consistent. These results are consolidated into table 1. This effectively proves the hypothesis that there is a correlation between NES and ASD that could result in causation for one another.

**Table 1.** One-proportion z test results. This table shows the results and populations used for the three different one-proportion z tests.

| 1-Proportion Z Test | Paitients with NES | NES and Autism | Z Score | Probability Value |
|---|---|---|---|---|
| Total | 59 | 10 | 12.3125 | 8.01E-35 |
| Female | 37 | 6 | 9.30229 | 1.40E-20 |
| Male | 22 | 4 | 8.09959 | 5.57E-16 |

### *Implications*

This study concluded that there is a significant correlation between non-epileptic seizures and autism spectrum disorder. This conclusion can lead to future causational studies in the field. Since this study is correlational, an explanatory approach was used to explain the connection between NES and ASD patients. In addition, the chi square test evaluated that female and male children get both seizures and autism at the same rates. Since there is already research in differences between autistic females and males, a similar result could occur when discussing the population with NES. Further research should be done in types of seizures and triggers for autistic female and male children. Due to the limitations of this study, further research regarding affectance rates should be evaluated. This can lead to future research and hypotheses about the relationship between gender and NES in autistic children.

## Conclusion

This study was focused on answering the question, is there a correlation between NES and ASD that could suggest a cause of NES in autistic children? In addition to finding a correlation between NES and ASD, this study also focused on filling the gap in differences between autistic females and males with NES. It was hypothesized that ASD heightens a person's neurological response to stimuli. This increase in stimuli was thought to trigger the non-epileptic seizures. In order to begin research into this hypothesis, it had to be determined that the two groups were correlated. This correlation was studied through the testing and analysis of one-proportion z-tests. These tests found a probable correlation between NES and ASD. Causation was not able to be determined by the resources available to this study; therefore, future research will need to be conducted by organizations with access to patient participants and medical and psychological professionals.

The implications in this study will provide more adequate diagnosis, screening, monitoring, and treatment for the patients affected with both. An autistic patient should be monitored for the development of NES. In addition, autistic patients who also experience seizures should see a non-epileptic seizure specialist to avoid misdiagnosis and improper treatment. Patients with non-epileptic seizures receive behavioral therapy, while patients with epilepsy receive anti-epileptic drugs. These are two vastly different approaches to treatment, so it is important to use a patient's medical history with ASD to avoid misdiagnosis. Children diagnosed with NES or PNES should be screened for

autism. The correlation could relate NES to an indicator of autism, therefore, children could be diagnosed and receive support earlier.

There was no existing research in the field of NES in ASD about the differences between females and males. It was hypothesized that there would be behavioral and numerical differences between the groups because of the known knowledge of differences between autistic females and males. However, through statistical analysis of data in a pre-existing study, it was found that there is no difference between the rates of females and males who have been diagnosed with NES and ASD. Since the data was taken from a pre-existing study, it cannot be fully concluded that there are no differences. However, this data still adds valuable knowledge in the relationships between autistic females and males affected by NES. Assuming the data is valid, psychological differences between autistic males and females have no impact on the development of seizures. This could be the result of both sexes being affected by similar rates of overstimulation. This would mean that sex does not play a factor in how autistic individuals process stimuli. Future research will be required to determine with certainty the accuracy of the results found.

Qualitative findings were not able to be researched in this study. While contact was made to autism and seizure specialists, anonymous patient information was not able to be released to the researcher due to the Health Insurance Portability and Accountability Act of 1996 (HIPAA) — a federal law that prevents medical information from being disclosed without patient consent. Future analysis of patient symptoms, behavior, and medical tests would provide a more conclusive look into the connections and causation between NES and ASD.

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