

Epilepsy

Introduction

Jimmy Holder, MD, PhD presented on “Epilepsy and EEG”. His presentation provided an overview of seizures, epilepsy, and electroencephalography (EEG) in both ASD and PMS.

A seizure can be defined as a transient disruption in brain functioning due to abnormal and/or excessive electrical charge, whereas epilepsy can be defined as more than one unprovoked seizure. The evaluation of seizures (or epilepsy) is typically completed with outpatient EEGs, which measure brainwave activities. In addition, outpatient magnetic resonance imaging (MRI) also can be completed to examine any potential structural brain differences that may provoke a seizure. Treatment for seizures typically includes pharmacological intervention with a class of drugs known as anti-epileptics.

There are a variety of types of seizures, all of which have been reported in individuals with PMS. Absence seizures are the most common among individuals with PMS and are characterized by 10-15 seconds of staring. Motor stereotypies may or may not be present during absence seizures. Complex partial seizures involve longer staring spells than absence seizures, other eye deviations, and may evolve into a generalized seizure. Atonic seizures are commonly referred to as “drop attack” seizures due to sudden loss of motor tone and control, which often result in the individual falling. In contrast, tonic seizures are characterized by an increase in muscle tone. Tonic-clonic seizures are characterized by both an increase in muscle tone as well as rhythmic motor behavior. Lastly, myoclonic seizures result in sudden jerky body movements. Myoclonic seizures are reportedly rare in PMS. In addition, status epilepticus may occur in individuals with PMS. Status epilepticus is a state of continual and/or recurrent seizure, which may have profound consequences on behavioral and cognitive functioning, including death. Furthermore, parents should be aware of Sudden Unexpected Death in Epilepsy (SUDEP), a fatal result of epilepsy. SUDEP may occur within minutes or hours of the seizure, and most common in adolescents and young adults. SUDEP is extremely rare and of unknown etiology.

Seizures and epilepsy occur within 1-1.5% of the typical population. Among individuals with ASD, epilepsy occurs within approximately 24% of affected individuals with comorbid intellectual disability (ID) and approximately 9% of affected individuals without comorbid ID. The estimated prevalence of seizures in individuals with PMS ranges from 14-70% based upon retrospective studies and approximately 40% based upon a prospective study. The prevalence of seizures in PMS reportedly increases with age. Only one study has examined EEG profiles and prevalence of seizure type in individuals

with PMS. Of the six patients examined, three were diagnosed with epilepsy; however, no signature or common profile of seizures in individuals with PMS was identified. Similarly, no consistent profile of EEG abnormalities has been reported in individuals with ASD. In a recent natural history study conducted at Texas Children’s Hospital, it was reported that approximately 46% of individuals with PMS have a lifetime history of at least one seizure with an average age of onset of 5.2 years old. Total number of seizures ranged from 1 lifetime seizure to hundreds per day. The most typical type of seizure for individual with PMS was reported to be atypical absence seizures. Additionally, 20% of individuals in the study had a history of status epilepticus and 18% had a diagnosis of Lennox-Gastaut Syndrome, a rare and difficult-to-treat form of epilepsy. Among children in the study, approximately two-thirds demonstrated abnormal EEG patterns with at least one-fifth of these individuals not having epilepsy. A total of sixteen different medications were used to treat seizures and epilepsy in this patient population. No pharmacological treatment appeared to be preferred or ideal.

Identified Problems

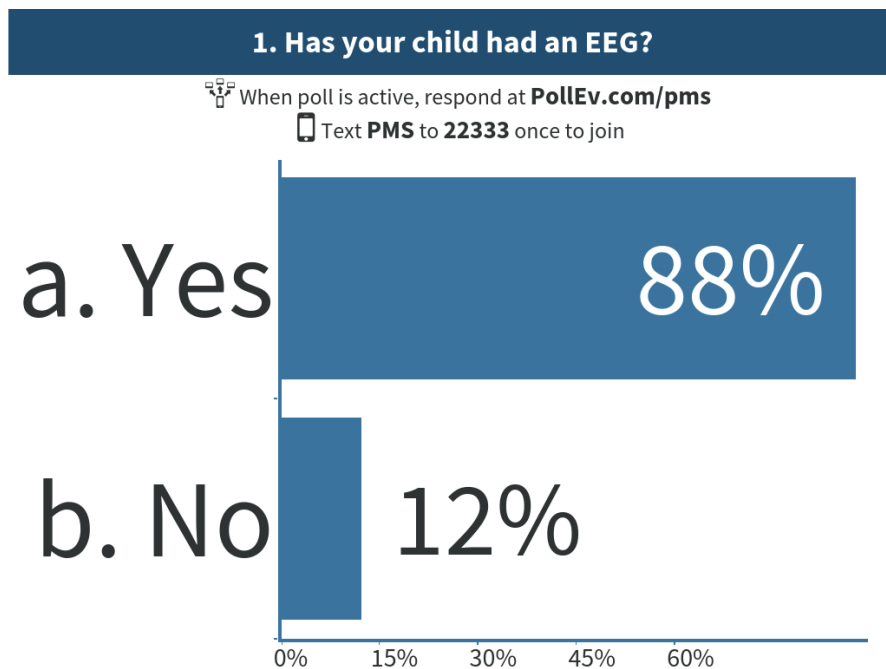
1. Identifying if and when my child has a seizure is difficult.

Based upon the Group and Panel discussions, parents overwhelmingly endorsed having difficulties related to identifying whether their children were having seizures or not. Estimated ranking of concern for parents was 4.8 out of 5, and at least 53 parents identified this as a primary concern. Because absence seizures may be mistaken and/or misidentified as “staring spells”, parents indicated that they considered themselves ill-equipped to distinguish between seizure activity and “typical” behavior. For example, one parent expressed, “I’m concerned that I might not be able to differentiate between behavior and an actual seizure”. Furthermore, parents expressed concerns regarding relaying information about potential seizure activity to their children’s general practitioner or other medical provider. For example, several parents noted that they were “not sure if [they] would get the doctor to believe [them]” if they shared seizure-like behaviors in their children. Parents sought advice on how to speak with their children’s practitioners about seizure concerns. Lastly, parents noted concerns regarding the ability to identify seizures at night. For instance, one parent expressed being “scared to death” that his/her child will have a seizure while sleeping.

2. Using EEGs to determine seizure activity is costly, time-consuming, and difficult for my child with PMS. Is an EEG study necessary and/or are their alternatives? How reliable are the results?

The use of an EEG is the primary method to determine seizure and abnormal EEG activity in individuals. Although the Poll Everywhere data suggests that approximately 88% of parents surveyed have a child who completed an EEG study (see Question 1 graph below), during the Group and Panel discussions, parents identified numerous questions regarding the utility, validity, and necessity of an EEG for their children. Based upon available survey data, the purpose of these EEGs was unclear. For

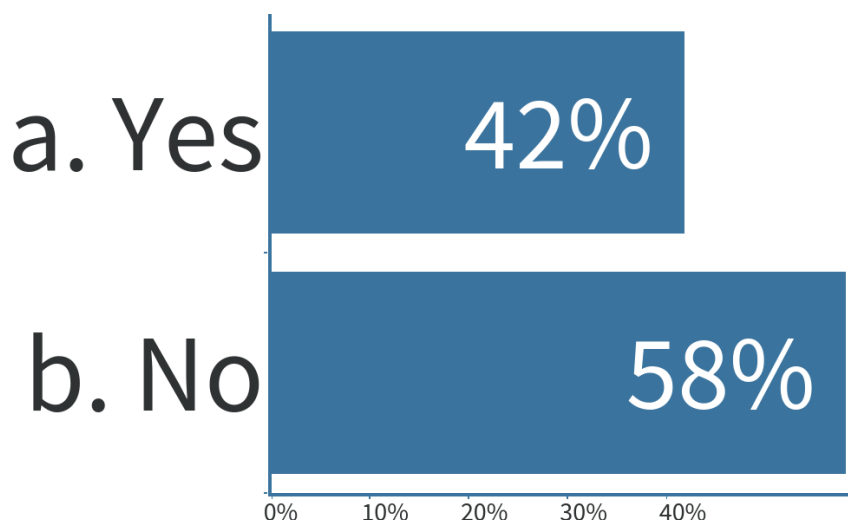
example, in addition to identifying suspected seizure activity, EEGs also may be conducted during a diagnostic work-up from a neurologist or developmental pediatrician or as part of a sleep study or research protocol. Thus, although there seems to be a high percentage of children who have completed EEGs, parents continue to have questions about their child receiving EEGs. It is possible that a portion of these questions may be specifically related to overnight EEGs as only 42% of parents indicated that their child received an overnight EEG (see Question 2 graph below). Additionally, several parents also noted that they were interested in their children completing an overnight EEG, but their neurologist did not support this.



2. Has your child had an overnight EEG?

When poll is active, respond at PollEv.com/pms

Text **PMS** to **22333** once to join



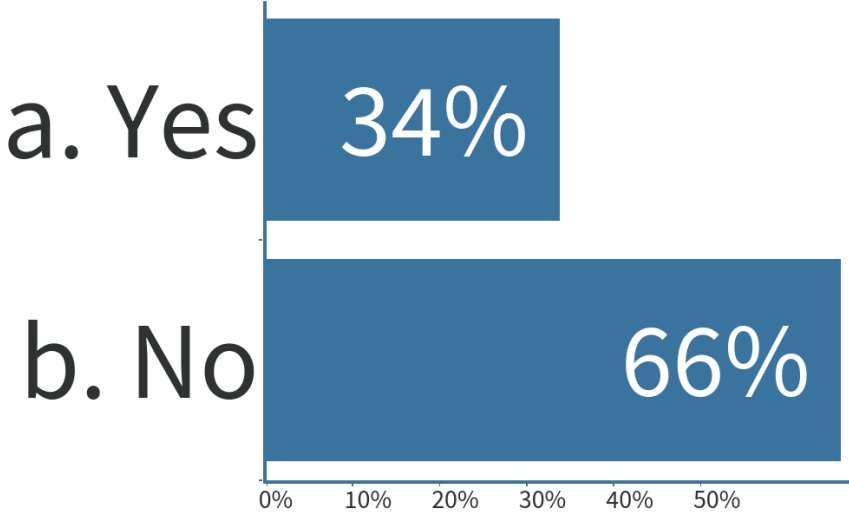
3. Pharmacological treatment for my child's seizures is daunting and not always effective. Additionally, the use alternative methods (e.g., medicinal marijuana, dietary changes) is unclear.

The Poll Everywhere survey indicated that approximately 34% of parents have a child who is taking medications for epilepsy (see Question 3 graph below); however, it is uncertain whether the remaining 66% of children are not taking medications because the children do not have epilepsy, are not prescribed medication, or are using alternative non-pharmacological methods to treat epilepsy. Parents also expressed concerns regarding the “right time to medicate” in the presence of abnormal EEG findings without documented seizure activity or epilepsy. As Dr. Holder indicated in his presentation, there is controversy among physicians whether it is appropriate or not to prescribe medication for abnormal EEG results without seizure activity being indicated. Furthermore, multiple parents shared their experiences of “medication cocktails” over the course of their children’s lifetimes for the treatment of epilepsy. They noted the use of multiple medications and frequent changes in medications that were not always effective and occasionally had negative side effects. In addition to the use of medications for the treatment of epilepsy, parents also indicated concerns and questions regarding the use of alternative methods to treat epilepsy, including medicinal marijuana and diet. The Poll Everywhere survey indicated that 6% of parents have a child who has tried cannabidiol (CBD), a cannabis compound most commonly used for medicinal purposes (see Question 4 graph below). During the Group discussion, several parents expressed their desire to know more about medicinal use of marijuana for the treatment of epilepsy in their child. For example, one parent noted, “I would want to hear about medical marijuana, it would probably be helpful in a lot of ways outside of just

seizures”. The use of CBD was the primary discussion point during the Panel discussion; however, based upon Group discussion documentation, only approximately 9 parents indicated that this was a concern, and it ranked relatively low as a concern (2.4 out of 5). In addition, several parents questioned the extent to which dietary changes could improve epilepsy by reducing the severity and frequency of seizures. Parents who addressed this concern ranked it as a relatively high concern (4 out of 5). Additionally, a few parents shared anecdotal evidence for support of dietary changes on epilepsy in their children.

3. Does your child take any medications for epilepsy?

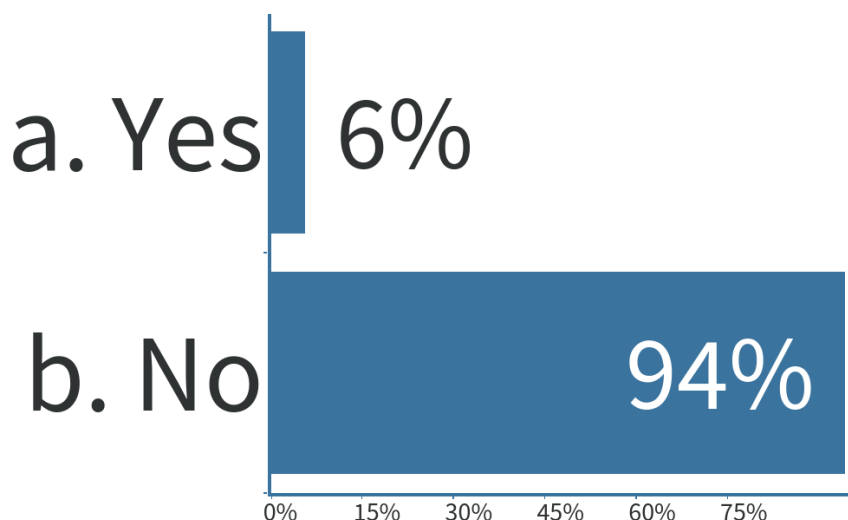
When poll is active, respond at [PollEv.com/pms](https://poll-ev.com/pms)
Text **PMS** to **22333** once to join



4. Has your child tried CBD(cannabidiol)

When poll is active, respond at PollEv.com/pms

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Proposed Solutions

1. Development of guide for parents and caregivers detailing seizure types, symptoms, and treatment in PMS.

Guidelines and charts for the identification of seizures are readily available for the general public online. However, despite the usefulness of these available tools, the identification of seizure activity can be more difficult within the PMS population due to the complexity of behavioral and physiological symptoms of this syndrome. Existing guidelines that detail possible symptoms of each seizure type, necessary steps to take for the safety of the child, and cautions for each seizure type should be expanded upon for this population. For example, as part of this seizure guideline it should include a flow chart that helps parents and caregivers determine the appropriate solutions (e.g., call to doctor versus hospital visit). Furthermore, an interactive form of this guideline should be available to parents that includes videos examples of each seizure type. Information regarding what behavior may be expected from individuals with PMS that are not seizures (e.g., staring spells) also should be included in these guidelines. Although this guide should be lay-friendly, it also will be important for health providers to be familiar with this guide so that parents/caregivers can share information and so that health providers are educated about the presence of seizures in PMS. As such, it would be beneficial for the guideline to include scripts on how to discuss seizure concerns with doctors and other health care providers.

2. Development of practice parameters regarding EEG testing for individuals with PMS.

Consensus regarding the use of baseline EEG testing for individuals with PMS should be established among experts within the field. Although medical providers may conduct EEGs as part of their “standard of care”, it is important for medical providers across fields, institutions, and countries to achieve consensus regarding the utility of initial EEG testing. Similarly, consensus guidelines and practice parameters should be established regarding the use of EEG testing when seizures are suspected or previously determined. Details within these parameters should include, but not be limited to: when/why to conduct baseline and/or overnight EEGs, frequency of follow-up, methods of collection. These guidelines should be established by leaders in the field and supported by research. These guidelines also may follow similar guidelines for general populations, but may need to be revised for this specific population. The practice parameters primarily will be tool for medical providers; however, it should be written in lay-friendly terms so that parents and caregivers of individuals with ASD also may access and help inform clinical decisions. As such, the practice parameters should be published in a parent tool-kit/guideline format for the use of families. Since families have indicated that that have been previously been “brushed off” by medical providers regarding their interests in their children receiving EEGs, the establishment of guidelines and publication of practice parameters may help inform important medical decisions regarding EEGs. The establishment of practice parameters should be mindful of benefits/costs as well as potential to increase insurance coverage if EEG testing is deemed a necessity.

3. Increased research regarding treatment of seizures in individuals with PMS.

First, a review of literature and existing data should be conducted regarding the types and effectiveness of seizure treatment for individuals with PMS. Second, because there have been no evidence-based research studies examining treatment of seizures in individuals with PMS, it would be recommended. By examining existing literature, data, and conducting more rigorous studies, medical providers and parents may be more informed regarding usefulness of specific pharmacological treatments. For example, certain medications may be better able to treat seizures in individuals with PMS than the general population, and vice-versa. Side effects within this special population also should be assessed and documented, as it is possible that individuals with PMS may be more or less prone to certain side effects. Third, alternative methods to traditional anti-epileptic medications should be examined thoroughly, but cautiously, as these methods may be harmful or even lethal. Practice parameters and published guidelines for parents (see Proposed Solution 2) should include outcomes from this research and indicate any necessary warnings regarding alternative treatments.