Epilepsy Currents
2021, Vol. 21(3) 173-174

DOI: 10.1177/1535759721994807
journals.sagepub.com/home/epi
SAGE

Closing the Diagnostic Gap in Epilepsy: Recognizing More Than Just Motor Seizures

Focal Nonmotor Versus Motor Seizures: The Impact on Diagnostic Delay in Focal Epilepsy

Pellinen J, Tafuro E, Yang A, et al. *Epilepsia*. 2020;61(12):2643-2652. doi:10.1111/epi.16707

Objective: To test the hypothesis that people with focal epilepsy experience diagnostic delays that may be associated with preventable morbidity, particularly when seizures have only nonmotor symptoms, we compared time to diagnosis, injuries, and motor vehicle accidents (MVAs) in people with focal nonmotor versus focal seizures with motor involvement at epilepsy onset. Methods: This retrospective study analyzed the enrollment data from the Human Epilepsy Project, which enrolled participants between 2012 and 2017 across 34 sites in the United States, Canada, Europe, and Australia, within 4 months of treatment for focal epilepsy. A total of 447 participants were grouped by initial seizure semiology (focal nonmotor or focal with motor involvement) to compare time to diagnosis and prediagnostic injuries including MVAs. Results: Demographic characteristics were similar between groups. There were 246 (55%) participants with nonmotor seizures and 201 (45%) participants with motor seizures at epilepsy onset. Median time to diagnosis from first seizure was 10 times longer in patients with nonmotor seizures compared to motor seizures at onset ($P < .001$). The number and severity of injuries were similar between groups. However, 82.6% of MVAs occurred in patients with undiagnosed nonmotor seizures. Significance: This study identifies reasons for delayed diagnosis and consequences of delay in patients with new-onset focal epilepsy, highlighting a treatment gap that is particularly significant in patients who experience nonmotor seizures at epilepsy onset.

Commentary

The treatment gap in epilepsy is well recognized. Lack of antiseizure medication treatment leads to increased health care utilization and injuries,[1] and physicians are increasingly aware of the mortality risk in those with uncontrolled seizures.[2] Among patients who receive treatment, clinicians and researchers consistently find that one-third of epilepsy patients have drug resistance.[3] As a result, we have seen an increased drive to aggressively evaluate patients for epilepsy surgery using intracranial EEG,[4] and a rapid rate of novel drug development. But what about the patients who haven't made it to the stage of receiving a proper diagnosis, let alone the right treatment? The recognition of this diagnostic gap has led to the creation of "First Seizure Clinics" aimed at rapid evaluation of patients referred for a first lifetime seizure. About a third of those referred to such clinics had in hindsight a prior history of seizures, which had not yet led to a diagnosis of epilepsy.[1,5] One study highlighted nonconvulsive initial seizures and socioeconomic disadvantage as factors associated with delays in diagnosis.[6]

The weight and impact of the former factor on diagnostic delays sinks in with the recent findings of Pellinen et al.[7] In a rigorous multicenter prospective observational study of new-onset focal epilepsy, the authors examined the seizure characteristics associated with diagnostic delays and the impact of untreated seizures prior to diagnosis. Patients were recruited within 4 months of initial treatment for a new diagnosis of focal epilepsy, underwent a structured seizure semiology interview, and retrospectively completed a seizure diary. Seizures were then classified as motor or nonmotor, based on the presence of any observable component, by 2 independent reviewers who reached complete concordance. The authors then correlated seizure characteristics (motor, or "observable," versus nonmotor) with time to diagnosis. Patients with nonmotor seizures prior to motor seizures had a 10-fold delay in obtaining a diagnosis, with a median time of over one and a half years from their first seizure to receiving a diagnosis of epilepsy. Among those with nonmotor seizures, two-thirds eventually experienced a motor seizure, which then led to a diagnosis within a median time of only two weeks. About 80% of the motor vehicle accidents (MVAs) reported prior to a diagnosis of epilepsy occurred among those with undiagnosed nonmotor seizures. In their discussion, the authors calculated an estimate of MVAs that may be occurring yearly as a result of undiagnosed nonmotor focal seizures. Using the known incidence of focal epilepsy, distribution of age of onset (compared to driving age),

and this study's data, they came to the astonishing figure of 1816 MVAs every year in the United States. Although this study does not investigate other factors likely to play a significant role in diagnostic delays, such a social determinants of health, the weight of the impact of seizure characteristics on time to diagnosis is striking. Nonmotor seizures are therefore strongly correlated with significant delays in diagnosis and there is a serious risk associated with that delay.

Where should one focus interventions to improve the diagnosis of nonmotor seizures? Underrecognition of nonmotor seizures can come from 2 sources: patients and their physicians. Pellinen et al examined the role of the latter through an analysis of the outcomes of emergency department (ED) visits in the same multicenter cohort of newly diagnosed focal epilepsy.[8] They found that the majority of those with nonmotor seizures presented to an ED after their first motor seizure, but that in those with prior nonmotor seizures, that history was elicited by the ED physician in only one-fifth of cases. Diagnostic and referral patterns were no different between those with motor seizures and a prior history of nonmotor seizures and those first lifetime motor seizure—the same number (a little over a third) received an antiseizure medication prescription, and a high but not perfect number were admitted or referred to neurology, which indicates that ED physicians manage first lifetime seizures and epilepsy similarly. Only a minority of patients presented to the ED for a nonmotor seizure (6% with a first lifetime nonmotor seizure, 5% with multiple nonmotor seizures), making it difficult to assess how effectively ED physicians diagnose and treat isolated nonmotor compared to motor seizures. It is possible that patients with nonmotor seizures had sought medical care elsewhere (eg, their primary care provider). A qualitative study investigating the public's knowledge on nonmotor seizure signs and symptoms and likelihood of seeking care for such symptoms would likely shed light on patient-specific reasons for diagnostic delays. If one were to confirm that patient underrecognition is a significant factor, how does one reach the public and increase awareness of broad presentations of seizures, beyond convulsions?

Diagnostic gaps are not unique to epilepsy. Perhaps one of the most successful areas of neurology in which diagnostic delays were reduced is stroke neurology. Public awareness campaigns have led to increased ambulance calls by focusing on improving recognition of stroke symptoms through simple mnemonics and emphasizing the importance of calling an ambulance right away.[9] Mass media campaigns have not always been successful though, sometimes producing inconsistent and short-lived effects on health behaviors from campaigns with poor research of the target group and episodic interventions with negative messaging.[10] One can imagine a campaign using an elegant and brief outline of seizure signs and symptoms (beyond "shaking all over"), using various delivery methods for different age groups, and highlighting a positive message of treatment response in the majority of those diagnosed with epilepsy. As a clinical and research community, our efforts should go beyond the one-third of epilepsy patients who continue to have seizures to reach the high number of patients who could join the two-thirds seizure-free group but remain without a diagnosis for sometimes years and suffer preventable injuries.

By Claude Steriade

ORCID iD

Claude Steriade https://orcid.org/0000-0001-6799-9005

References

1. Kalilani L, Faught E, Kim H, et al. Assessment and effect of a gap between new-onset epilepsy diagnosis and treatment in the US. *Neurology*. 2019;92(19):e2197-e208.
2. Devinsky O, Spruill T, Thurman D, Friedman D. Recognizing and preventing epilepsy-related mortality: a call for action. *Neurology*. 2016;86(8):779-786.
3. Chen Z, Brodie MJ, Liew D, Kwan P. Treatment outcomes in patients with newly diagnosed epilepsy treated with established and new antiepileptic drugs: a 30-year longitudinal cohort study. *JAMA Neurol*. 2018;75(3):279-286.
4. Jehi L, Friedman D, Carlson C, et al. The evolution of epilepsy surgery between 1991 and 2011 in nine major epilepsy centers across the United States, Germany, and Australia. *Epilepsia*. 2015;56(10):1526-1533.
5. Jackson A, Teo L, Seneviratne U. Challenges in the first seizure clinic for adult patients with epilepsy. *Epileptic Disord*. 2016; 18(3):305-314.
6. Firkin AL, Marco DJ, Saya S, et al. Mind the gap: multiple events and lengthy delays before presentation with a "first seizure". *Epilepsia*. 2015;56(10):1534-1541.
7. Pellinen J, Tafuro E, Yang A, et al. Focal nonmotor versus motor seizures: the impact on diagnostic delay in focal epilepsy. *Epilepsia*. 2020;61(12):2643-2652.
8. Pellinen J, Tafuro E, Baehr A, et al. The impact of clinical seizure characteristics on recognition and treatment of new-onset focal epilepsy in emergency departments. *Acad Emerg Med*. 2020. doi: 10.1111/acem.14114
9. Bray JE, Mosley I, Bailey M, Barger B, Bladin C. Stroke public awareness campaigns have increased ambulance dispatches for stroke in Melbourne, Australia. *Stroke*. 2011; 42(8):2154-2157.
10. Wakefield MA, Loken B, Hornik RC. Use of mass media campaigns to change health behaviour. *Lancet*. 2010;376(9748): 1261-1271.