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Epilepsy, dissociative seizures, and mixed: associations with time to video-EEG

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Abstract

Purpose: Video-electroencephalographic monitoring (VEM) is a core component to the diagnosis and evaluation of epilepsy and dissociative seizures (DS)—also known as functional or psychogenic seizures—but VEM evaluation often occurs later than recommended. To understand why delays occur, we compared how patient-reported clinical factors were associated with time from first seizure to VEM (TVEM) in patients with epilepsy, DS or mixed.

Methods: We acquired data from 1245 consecutive patients with epilepsy, VEM-documented DS or mixed epilepsy and DS. We used multivariate log-normal regression with recursive feature elimination (RFE) to evaluate which of 76 clinical factors interacting with patients' diagnoses were associated with TVEM.

Results: The mean and median TVEM were 14.6 years and 10 years, respectively (IQR 3–23 years). In the multivariate RFE model, the factors associated with longer TVEM in all patients included unemployment and not student status, more antiseizure medications (current and past),

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6. Conflicts of Interest & Ethical Publication:

Drs. Engel, Stern, and Kerr have clinical responsibilities that include the diagnosis and treatment of patients with epilepsy and non-epileptic seizures. Drs. Engel, Stern and Kerr have received speaking fees and honoraria for articles on this topic. The remaining authors have no declared conflicts of interest. 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.

concussion, and ictal behavior suggestive of temporal lobe epilepsy. Average TVEM was shorter for DS than epilepsy, particularly for patients with depression, anxiety, migraines, and eye closure. Average TVEM was longer specifically for patients with DS taking more medications, more seizure types, non-metastatic cancer, and with other psychiatric comorbidities.

Conclusions: In all patients with seizures, trials of numerous antiseizure medications, unemployment and non-student status was associated with longer TVEM. These associations highlight a disconnect between International League Against Epilepsy practice parameters and observed referral patterns in epilepsy. In patients with dissociative seizures, some but not all factors classically associated with DS reduced TVEM.

Keywords

functional seizures; psychogenic nonepileptic seizures (PNES, PNEA); drug resistant epilepsy; healthcare triage

1. Introduction:

Video-electroencephalographic monitoring (VEM) is critical to the evaluation and treatment of patients with medication resistant epilepsy, defined by failure of two adequate trials of tolerated, appropriately-chosen antiseizure medications (ASM) at appropriate doses [1, 2]. While some studies demonstrated that early surgical therapy for epilepsy may be more effective, the time from first seizure to VEM (TVEM) remains around 20 years and VEM remains underutilized [3–20]. For comparison, it typically takes 9 years to meet the definition of medication resistant epilepsy [13].

In addition to consideration of surgery, VEM identifies patients with physiologic seizure-like events or dissociative seizures (also called psychogenic nonepileptic seizures or functional seizures [21–24]), which were identified in 6% of patients referred for presurgical evaluation [25]. Of all patients who undergo VEM, 20–30% are found to have dissociative seizures [25, 26]. For patients diagnosed with dissociative seizures, shorter TVEM has been associated with improved quality of life, decreased seizure severity, and decreased healthcare utilization [27–31].

Prior literature has evaluated the many factors related to the TVEM in patients with medication resistant epilepsy (see [15] for review), however there has not been a direct comparison of the factors associated with TVEM in patients with epilepsy to patients with dissociative seizures or both diagnoses. In this study, we evaluate how patient-reported clinical factors acquired during a typical neurological interview were associated with TVEM at a comprehensive epilepsy center. While some associations with TVEM will be unique in epilepsy as compared to dissociative seizures, prior to VEM, the diagnosis of dissociative seizures is uncertain, therefore we hypothesized that some factors would be common across all patients. The goal of this study is to identify key factors that are associated with delay so that future studies can better understand how to reduce TVEM in patients with epilepsy, dissociative seizures, and both.

2. Methods:

2.1 Patient Population

Our patient sample included consecutive patients with epilepsy, dissociative seizures, and both types of seizures admitted to the UCLA adult VEM unit from January 2006 to December 2019. We refer to patients with both types of seizures as “mixed” seizures. Other centers may refer to these patients as “dual diagnosis.” These represent at least two distinct types of seizures, as compared to patients with epileptic seizures with functional elaboration [32, 33]. We excluded patients for whom there were insufficient typical events during VEM to characterize all seizure types in each patient. If patients were re-admitted after an initial inconclusive monitoring, TVEM was based on the time to first VEM. Diagnoses of dissociative seizures met the International League Against Epilepsy (ILAE) criteria for documented [24] and all epilepsy diagnoses were based on expert clinical opinion based on the available clinical history, physical exam, VEM, structural MRI, FDG-PET, MEG and SPECT. Other aspects of this dataset have been published elsewhere [25, 26, 34–39].

We defined the time from first seizure to VEM (TVEM) based on the onset of repeated unprovoked seizures and excluded remote isolated and provoked seizures (e.g. childhood febrile seizures, seizures from alcohol withdrawal). Due to the time it took for patients with epilepsy to develop medication resistant epilepsy, we use the term “time from first seizure” to VEM (TVEM) instead of delay to VEM. In contrast, for patients with dissociative seizures, time to VEM typically represents a diagnostic delay. Median time from first encounter at our center to VEM was less than 6 months, therefore we do not report delays within our center (data not shown).

Records from patients were acquired through retrospective chart review or prospective interview. Chart review focused on the earliest, single neurologist’s note that described the patient’s seizures, comorbidities, medication history and allergies. The specific factors that were evaluated in these notes are listed in Supplemental Table 1. Prospective interview occurred during the first 48 hours of VEM and was conducted by a trained non-neurologist or the first author (WTK). Formal psychiatric assessment was not routine; therefore, our data reflect patient-reported or neurologist-documented comorbidities.

2.2 Statistical Modeling

As suggested by prior studies’ [40–44], it was clear that TVEM was exponentially distributed (Figure 1), therefore we used log-linear multivariate regression to evaluate the association of each factor with TVEM. This was appropriate because the residuals of the log-normal model of TVEM were substantially more normal than the linear model (results not shown). This multivariate model included all 76 studied factors plus two interaction terms of all 76 factors with the diagnosis of dissociative seizures and mixed epileptic and dissociative seizures (Supplemental Table 1). We excluded any factor that was not observed in at least 10 patients of a specific type. Epilepsy was considered the reference diagnosis in the regression. We log-transformed seizure frequency and seizure duration. For variables other than TVEM, missing data that had values but were not documented (e.g. seizure frequency) were imputed based on trends in the retrospective dataset not including the

patient's diagnosis using multiple imputation with 20 independent datasets [45, 46]. Rare missing data in the prospective data was filled in based on retrospective trends. Other missing data that was not specifically documented in the patients' histories (e.g. head injury, ictal incontinence, sexual abuse) were assumed to be absent.

To reduce this multivariate model to an interpretable size, we used recursive feature elimination (RFE) to sequentially exclude the single factor with the largest p-value until the largest p-value was less than 5% [47]. The significance of each factor was based on a combination of the between and within-imputation variance [45, 46].

All patients consented for the use of their records in research, and the UCLA Institutional Review Board approved this study. This work is consistent with Declaration of Helsinki. De-identified raw data and code for this study is available on Mendeley Data.

3. Results:

TVEM was documented for 1245 of 1295 (96%) patients who underwent VEM during the time period. In total, 873 patients had epilepsy, 361 had dissociative seizures and 61 had mixed seizures. During the same time period, 273 patients had inconclusive monitoring and 49 patients were diagnosed with physiologic seizure-like events. For patients with epilepsy, 78% had tried at least 2 antiseizure medications either currently or in the past. Seizure duration was missing in 23% (205/873), 27% (97/361), and 30% (18/61) of patients with epilepsy, dissociative seizures, and mixed seizures, respectively. Seizure frequency was missing in 16% (141/873), 19% (67/361), and 20% (12/61) of patients with epilepsy, dissociative seizures, and mixed seizures, respectively.

Among all patients, the mean TVEM was 14.6 years with a median of 10 years, minimum of 1 day and maximum of 67 years, and interquartile range of 3 to 23 years. Due to the exponential pattern in TVEM, our regressions focused on log-TVEM, which had a robust mean of 6.3 years (1.8 log-years, SE 1.87 log-years). Table 1 summarizes these statistics and the rates of antiseizure medication (ASM) treatment by diagnostic group. The distribution of TVEM is illustrated in Figure 1.

Of the 76 factors studied, there were 30 factors and interactions selected by the regression model with p less than 5% (Figure 2 and Supplemental Table 2), of which 13 were associated with TVEM in all patients, 14 in dissociative seizures, and 3 in mixed seizures. This selected model accounted for significantly more variation than an intercept model (Chi-squared deviance difference, 31 degrees of freedom, $p < 10^{-100}$). The full model accounted for significantly more variation than the selected model (deviance test, 154 degrees of freedom, $p = 3 \times 10^{-8}$).

We illustrate the associations with TVEM in Figure 2. All associations not specifically listed below were not significant ($p > 0.05$). There were no factors with both a significant main effect in all patients and an interaction effect in either dissociative seizures or mixed seizures ($p > 0.05$), with the exception of active employment or student status, which was associated with longer TVEM in all patients ($p = 0.04$) and even longer TVEM in patients with

dissociative seizures ($p=5\times 10^{-5}$). Summary statistics for all models are displayed in Supplementary Table 1.

3.1 All patients with seizures

The factors that were significantly associated with longer TVEM in all patients included more prior ASMs (0.07 log-years per medication, standard error (SE) 0.02, $p=6\times 10^{-6}$), more current ASMs (0.12 log-years per medication, SE 0.03, $p=0.0001$), more supplements (0.10 log-years per supplement, SE 0.03, $p=0.004$), hypertension (0.74 log-years, SE 0.14, $p=9\times 10^{-8}$), history of concussion (0.41 log-years, SE 0.10, $p=4\times 10^{-5}$), a seizure trigger of stress (0.24 log-years, SE 0.09, $p=0.008$), and ictal behaviors commonly seen in temporal lobe epilepsy including oral automatisms (0.32 log-years, SE 0.13, $p=0.01$), any aura (0.18 log-years, SE 0.08, $p=0.03$), and seizures where the only symptom was impaired awareness (0.19 log-years, SE 0.09, $p=0.03$). Factors associated with shorter TVEM in all patients included higher seizure frequency (0.08 log-years per log-seizure/month, SE 0.02, $p=0.0008$), current employment or student status (0.19 log-years, SE 0.10, $p=0.04$), older age of onset (0.05 log-year of delay per year of age, SE 0.003, $p=4\times 10^{-83}$), and an external event thought to precipitate the onset of seizure disorder (0.26 log-years, SE 0.10, $p=0.01$).

3.2 Patients with Dissociative Seizures

Patients with dissociative seizures had shorter delay to diagnosis (TVEM) than patients with epilepsy or mixed epilepsy and DS (0.48 log-years, SE 0.22, $p=0.03$). Longer delays to VEM were associated with more non-ASM and non-psychiatric medications (0.08 log-years per medication, SE 0.02, SE=0.0003), more types of seizures (0.25 log-years per seizure type, SE 0.09, $p=0.004$), nonmetastatic cancer (0.98 log-years, SE 0.44, $p=0.025$), seizure trigger of sleep deprivation (0.55 log-years, SE 0.22, $p=0.01$), and maximal seizure severity at seizure onset (0.55 log-years, SE 0.22, $p=0.01$). Factors associated with shorter delay included a comorbidity of depression (0.65 log-years, SE 0.23, $p=0.06$), anxiety (0.59 log-years, SE 0.025, $p=0.02$), migraines (0.79 log-years, SE 0.18, $p=2\times 10^{-5}$), gastro-esophageal reflux or ulcers (0.88 log-years, SE 0.25, $p=0.0005$); current employment or student status (0.78 log-years, SE 0.19, $p=5\times 10^{-5}$); current smoking (0.90 log-years, SE 0.23, $p=0.0001$); and ictal behavior of eye closure (0.55 log-years, SE 0.21, $p=0.01$) and head movements (0.49 log-years, SE 0.19, $p=0.009$).

3.3 Patients with Mixed Epilepsy and Dissociative Seizures

While there were relatively fewer patients with mixed seizures, there were 3 factors associated with delay to VEM. Longer delay was associated with longer seizures (0.23 log-years per log-seconds, SE 0.07, $p=0.001$) and an external event thought to precipitate the onset of seizure disorder (1.27 log-years, SE 0.47, $p=0.006$). Shorter delay was associated with more seizure types (0.80 log-years per type, SE 0.17, $p=5\times 10^{-6}$).

4. Discussion:

These data continue to demonstrate that TVEM likely includes unnecessary delays in patients with all types of seizures. The TVEM is comparable to other comprehensive epilepsy centers in the US and internationally [5, 6, 13] and has been consistent for decades

despite efforts to educate referring providers of the direct and indirect benefits of referrals to a comprehensive epilepsy center for medication-resistant epilepsy [10, 17, 48], and the increased awareness of and treatment options for dissociative seizures [24, 49]. By understanding the associations with longer TVEM that were common to all patients, as well as unique for dissociative seizures, future efforts for intervention can be targeted towards patients that may not be referred in timely manner with the goal of improving seizure frequency, quality of life and healthcare costs for patients with high risk of morbidity and mortality from both epileptic and dissociative seizures [3, 28, 48–60].

This analysis identified a large number of patient-reported clinical factors associated with TVEM in patients with epileptic and dissociative seizures. This array of associations reflects the complexity of these patients. While we do not discuss each individual association, this discussion aims to place the observed associations in the context of prior literature and demonstrate how this analysis builds upon prior knowledge.

4.1 Associations in all patients

Prior to VEM, the etiology or localization of seizures is uncertain. Therefore, these associations may apply to patients with epilepsy, dissociative seizure, or both. In multivariate regression models, reference diagnosis of epilepsy was chosen, and we evaluated if these associations varied in patients with dissociative seizures or mixed seizures. When no significant change in these associations were seen in those comparative populations, these associations apply to all patients, irrespective of diagnosis. However, because providers typically assume that patients have epilepsy prior to VEM, we place these associations in the context of the evaluation of epilepsy. With the exception of employment or student status, the associations we discuss below were not significantly different in patients with epilepsy as compared to dissociative seizures or mixed seizures.

The ILAE and American Academy of Neurology (AAN) Practice Parameter recommends that patients who were failed by 2 ASMs should be evaluated at a comprehensive epilepsy center unless they are seizure free [60–62]. Medication-resistant epilepsy is defined by continued seizures despite adequate trials of 2 appropriate ASMs [2]. Patients who had tried more ASMs in the past and, more so, patients who were on higher degrees of polytherapy had longer TVEM. While our definition of “past” ASM was subtly different from “failed” ASM, our data suggest that further trials of ineffective or intolerated medications contribute to delays. Berg and colleagues showed that it takes an average of 9 years to fail two ASMs [13], but a survey of Canadian neurologists showed that 48.6% incorrectly defined medication resistant epilepsy, often requiring failure of 3 or even more ASMs and a minimum seizure frequency [63]. While the ILAE and AAN have extensively improved education of neurologists about the vast benefits of and therefore recommendation of prompt referral, these associations and the consistently long TVEM across decades suggest that this education may not have impacted the knowledge or practice of some neurologists [10, 17] or that there may be other important barriers to timely VEM.

This dichotomy between practice parameters and our associations extends to ictal behavior. Auras, oral automatisms and seizures in which the only symptom was impaired awareness were associated with temporal lobe epilepsy, which has the best evidence for the efficacy of

surgical intervention [1, 3, 8, 64–67]. For these patients, the diagnosis of temporal lobe epilepsy may have been clear, therefore providers may have appropriately waited until patients met the definition for medication resistant epilepsy to refer for VEM. Unfortunately, this only accounts for an estimated 9 of the median 17 years of TVEM [13], suggesting that there may be delays to referral.

Alternatively, these ictal behaviors may reflect patients that were less likely to have frequent bilateral or generalized tonic-clonic seizures [68]. Patients typically present for initial evaluation after tonic-clonic seizures, as compared to non-motor seizures [69], therefore patient’s and provider’s perception of the urgency of referral to VEM may be driven by tonic-clonic seizures, as compared to more subtle non-motor seizures. This may be driven by the knowledge that patients with tonic-clonic seizures have an increased risk for sudden unexpected death in epilepsy (SUDEP) [70]. Similarly, patients with higher seizure frequency have increased risk for SUDEP [70], and also had shorter TVEM.

This dichotomy could be addressed by provider and patient education that emphasize that patients with both motor and non-motor seizures with any non-zero seizure frequency should be evaluated at a comprehensive epilepsy center to address all aspects of their seizures, comorbidities and quality of life, including but not limited to, surgical evaluation [10, 12]. In particular, the difference between our database and prior literature highlights this broad indication for referral. While the majority of prior literature about time to VEM in epilepsy focuses on patients who eventually undergo surgical treatment, our population includes a broader population of patients including surgical candidates who undergo surgery, surgical candidates who opt to not undergo surgery, non-surgical candidates with medication-resistant epilepsy, and patients with epilepsy that were not medication-resistant (Table 1). For patients with epilepsy, we use the term, “time” to VEM, instead of “delay” to VEM to reflect that the time prior to development of medication-resistant epilepsy should not be considered a delay in care.

Especially in the United States, access to healthcare is a critical barrier to appropriate care [71, 72]. While patients who were employed or a student had shorter TVEM, those who were both unemployed and not students had longer TVEM. Medical insurance in the United States is frequently tied to employment, therefore this association with employment may reflect patients with private insurance, as compared to public insurance [9, 73]. Similarly, students typically are young enough to be covered under their parents’ insurance or are provided private healthcare from their educational institution [74, 75]. These delays in VEM in unemployed, uninsured, or underinsured patients may be due to cost-conscious policies. While the initial cost of VEM and epilepsy surgery is high, this evaluation results in a net savings within 3 years because of the improved seizure frequency, reduced antiseizure medication use, and other healthcare utilization [1]. While not evaluated in our study, patients with private insurance had greater access to epilepsy surgery in prior studies [9, 73]. While we did not evaluate race in our study, Englot and colleagues also demonstrated that white patients were more likely to have surgery, suggesting that racism and other social determinants of health can contribute to delays [9, 76].

The purpose of a referral to a comprehensive epilepsy center can be to provide additional services, including but not limited to surgical interventions. [10, 12]. However, patients with hypertension had longer TVEM and were almost exclusively older than 40 years old, which may represent perceived increased surgical risk, despite the studies showing efficacy of epilepsy surgery in patients older than 60 years old [77]. In addition to surgery, comprehensive epilepsy centers can evaluate for non-epileptic seizures, address common comorbidities, perform neuropsychological evaluations, and can discuss newer ASMs as well as non-surgical therapies. Therefore, we encourage referrals based on ILAE guidelines irrespective of their perceived candidacy for surgical therapy.

4.2 Associations in patients with dissociative seizures

A major cause of apparent medication-resistant seizures was dissociative seizures and other non-epileptic conditions, with 53% of patients with dissociative seizures having continued seizures after taking at least 2 ASMs. While diagnostic evaluation prior to VEM can increase the likelihood of dissociative seizures, substantial inaccuracies in diagnoses based on clinical information, ictal video-without-EEG, and non-ictal EEG that varied with level of training of the seizure observer have been demonstrated [24, 78–80]. Therefore, even though the diagnosis of dissociative seizures is less certain prior to ictal VEM [24], there is often a suspicion for this diagnosis and these patients represent a unique population.

Even though unemployment and non-student status was associated with longer TVEM in all patients, the significant interaction term suggests that it was associated with even longer delays in dissociative seizures. This may reflect further decreased access to healthcare in these patients with dissociative seizures [81], irrespective of absolute seizure burden. In addition to being unemployed more often than patients with epilepsy [35], patients with dissociative seizures may be more dependent on loved ones and other social services to access healthcare [82], potentially leading to delays to time and resource-intensive evaluation at a comprehensive epilepsy center. This increased impact of dissociative seizures as compared to epilepsy has been seen on prior comparisons of social functional status and quality of life [83–88]. In addition, there may be a stigma of healthcare providers against patients disabled by dissociative seizures [81, 89–91]. This stigma and lack of understanding for appropriate diagnosis and treatment are evidenced by patient reports stating: “The [emergency room] doctor threw water on my face when he thought I was mid-episode [...] I flinched, he loudly proclaimed, ‘She’s a faker. Discharge her’” or “He was not interested in me as I only had [non-epileptic seizures] and not epilepsy and that I brought it on and can control it, which I can’t” [89].

The associations with shorter delay to VEM primarily were factors associated with the diagnosis of dissociative seizures, therefore this may represent the level of suspicion for dissociative seizures prior to VEM. In particular, depression, anxiety, migraines, ictal eye closure, and ictal head movements were known associations with dissociative seizures [26, 34, 37]. Conversely, although rare, patients with non-metastatic cancer may be perceived as low risk for functional neurological symptoms due to their established medical disease, leading to longer delays to VEM more similar to patients with epilepsy [43]. Improved

screening for and knowledge of factors associated with dissociative seizures through standardized clinical histories or questionnaires may facilitate shorter delays [26, 92–94].

The relationship between concussion and seizures is complex. We found that concussion was associated with longer delays to VEM in all patients, but not specifically in patients with dissociative seizures. In our prior work with this dataset, we showed that concussion was more common in dissociative seizures [26, 35]. When viewed in combination, this replicates an association between concussion and longer delay to VEM in dissociative seizures by Asadi-Pooya and colleagues [42].

We observed further complexity in interpreting the pattern of psychiatric comorbidities. While the overall number of psychiatric comorbidities was associated with longer delays to VEM, depression or anxiety were associated with shorter delays in patients with dissociative, but not epileptic, seizures. Depression and anxiety are commonly experienced by patients with epilepsy [95], therefore neurologists may be familiar with and comfortable treating patients with these conditions. However, patients with other psychiatric conditions including but not limited to post-traumatic stress disorder, obsessive compulsive disorders, bipolar disorder and schizophrenia frequently have barriers to accessing healthcare for seizures and other physical conditions [96–100].

4.3 Associations in patients with mixed epileptic and dissociative seizures

The smaller and clinically important population of patients with mixed seizures typically is excluded from studies, leading to limited characterization of these patients. Additionally, due to comorbid pathologies, it can be difficult to interpret findings because referral for VEM may be for diagnosis and characterization of seizures, for pre-surgical evaluation of epilepsy, or both. Therefore, it was expected that, due to a comparatively small sample size, we did not observe many unique associations in patients with mixed seizures, and the interpretation of the associations we did see are unclear.

Even though patients with mixed seizures had more seizure types in this dataset [34], patients with mixed seizures who had more seizure types than other patients with mixed seizures had shorter TVEM. This suggests that more complex patients were appropriately referred earlier. In contrast, patients with isolated dissociative seizures with more seizure types had longer TVEM.

This contradiction of observed associations also extends to epilepsy. Patients with epilepsy who reported an event precipitating their seizures (e.g. head trauma) had shorter TVEM. However, patients with mixed seizures and the same history had substantially longer TVEM.

These difficult to interpret differences in associations between mixed seizures and patients with either epileptic or dissociative seizures highlights the unique clinical challenges in the diagnosis and treatment of these patients. While many studies exclude this complex population [101], we favor inclusion of these patients so that we and others can characterize this important group in meta-analyses and other future work.

4.4 Limitations and Future Directions

There are a number of limitations to our data-driven approach that focused on a subset of patient-reported factors. The factors that we evaluated focused primarily on the information that providers use to identify dissociative and epileptic seizures and did not evaluate patient-focused factors, racial factors, social determinants of health, factors about referring providers, the reason for referral, prior EEG results, and neuroimaging findings. It is unclear if these unmeasured factors differ between patients with epilepsy and dissociative seizures [102–104]. We emphasize the non-surgical impact of a comprehensive epilepsy center evaluation because patient hesitancy regarding surgical interventions likely plays a large role in delays to referral [19]. The reasons for delays in referral for differential diagnosis of paroxysmal events may differ from delays in referral for presurgical evaluation, but the reason for referral was inconsistently documented in our patients. However, 53% of patients with dissociative seizures met criteria for referral from medication-resistant seizures, therefore we emphasize that the impact of comprehensive epilepsy center evaluation is broad and not limited to surgical evaluation. Patients with dissociative and epileptic seizures are heterogeneous, therefore analysis of meaningful subgroups of patients may identify additional trends.

While our complex results generate hypotheses about the *cause* of delays to VEM, our large, but cross-sectional, study only identifies *associations*. Further work targeting particular associations that we observed would be needed to establish that these associations cause the delays.

Additionally, this data-driven approach aimed to generate a short list of hypotheses for which patient-reported factors were associated with TVEM. The practice of backward selection with recursive feature elimination tends to overestimate the effect of factors and underestimate p-values. Therefore, we focus on qualitative interpretations of associations as compared to quantitative predictions of how TVEM can be predicted.

5. Conclusion:

There are numerous complex factors that contribute to a referral of a patient to VEM. This data driven analysis improves our understanding of factors associated with TVEM both in patients with epilepsy and dissociative seizures. In epilepsy, we further highlight the difference between guidelines and practice parameters and observed outcomes. In dissociative seizures, we demonstrated that medically and psychiatrically complex patients have longer delay to VEM instead of shorter delays. In all patients, shorter TVEM has been associated with improved seizure frequency, better quality of life, and decreased healthcare utilization [3, 28, 48–60], therefore additional measures should be taken to address these delays in care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- There are delays to video-electroencephalographic monitoring for seizures
- Access to healthcare through employment or school shortens delays
- Ictal behavior suggestive of limbic epilepsy had longer delays
- Some factors associated with dissociative seizures had shorter delays

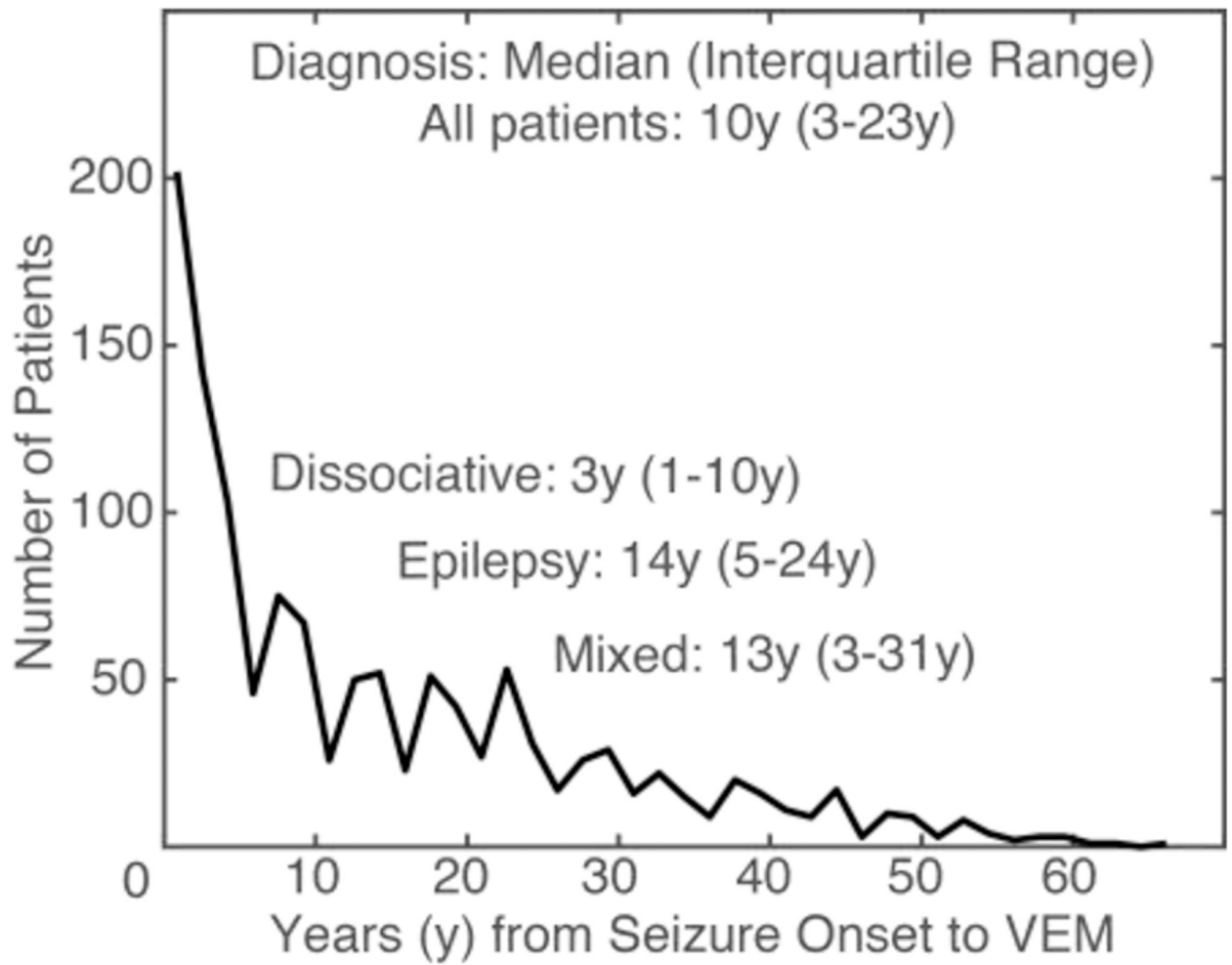


Figure 1:
Distribution of the time to video-EEG monitoring (VEM) in our dataset for all patients.

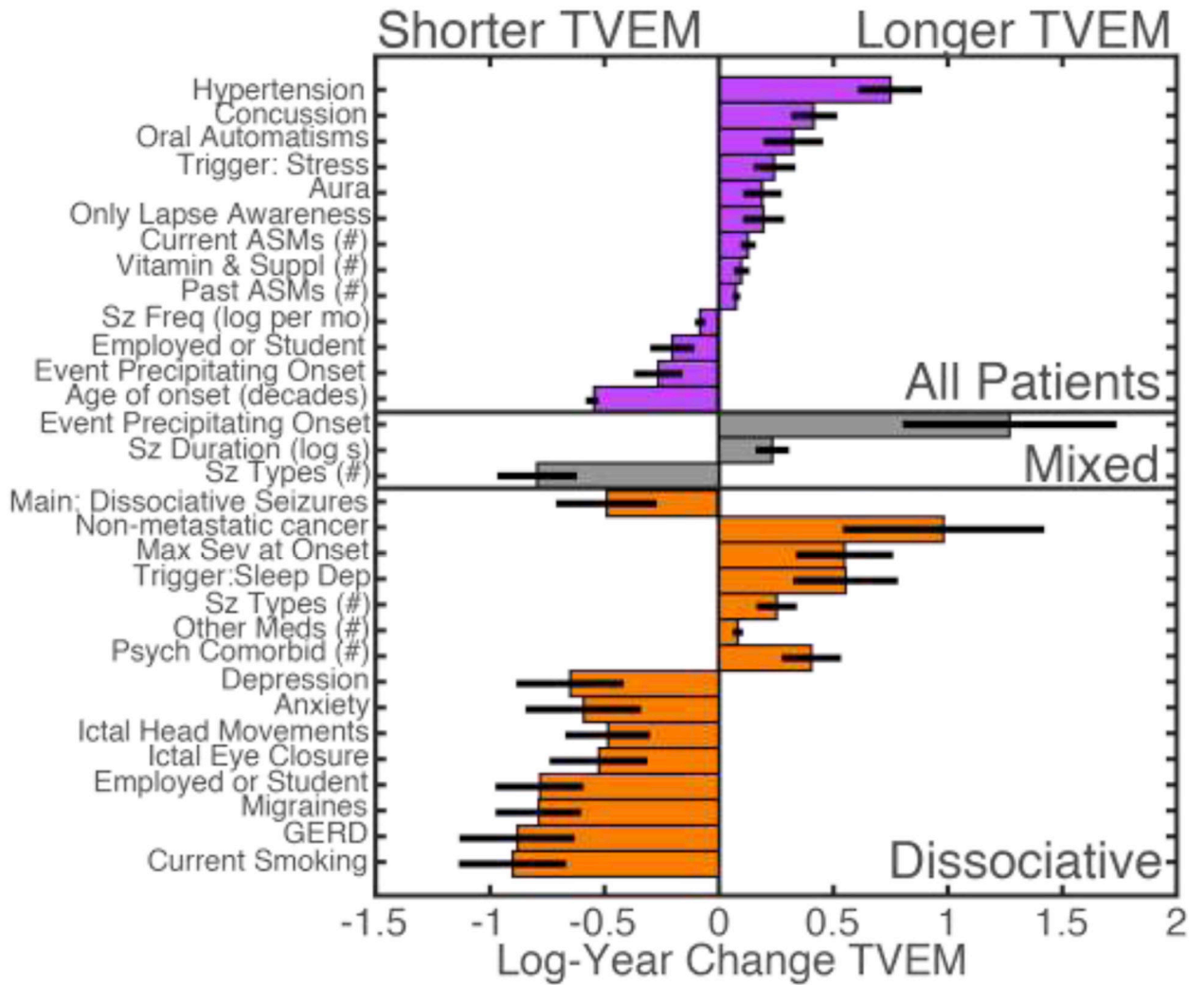


Figure 2: Significant multivariate associations between time to video-EEG monitoring (TVEM) in a recursive feature elimination (RFE) log-regression model ($p < 0.05$). Factors listed in the mixed and dissociative panels had a significant interaction with these diagnoses, in addition to any association observed in all patients. The factor of Main: Dissociative Seizures reflects that conditionally independent of all other factors, a diagnosis of dissociative seizures was associated with shorter TVEM. Error bars reflect Wald standard error. Abbreviations: number (#), antiseizure medications (ASM), seizure (sz), frequency (freq), month (mo), seconds (s), maximum severity (max sev), medications (meds), Gastro-esophageal reflux disorder (GERD).

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Table 1:

Statistics describing the time to video-EEG monitoring (TVEM) and the number of antiseizure medications (ASMs) in each diagnostic group. Robust statistics were calculated on log(TVEM). Two-or-more ASMs was chosen to reflect the definition of medication-resistant epilepsy. Abbreviations: standard deviation (SD), interquartile range (IQR), year (y), number (#), percent (%).

	Statistic	ES	DS	Mixed
TVEM	Mean, y	16.9	8.3	18.7
	SD, y	13.9	11.5	17
	Median, y	14	3	13
	IQR, (y-y)	(5–24)	(1–10)	(3–31)
	Robust mean, log-y (y)	2.2 (9.1)	0.9 (2.5)	2.1 (8.3)
	Robust SD, log-y	1.6	2.1	1.8
Current+ Prior ASMs	Median, #	4	3	5
	IQR, #	(3–7)	(1–5)	(2–7)
	At least 1, %	96%	87%	97%
	2 or more, %	78%	53%	72%