HHS Public Access

Author manuscript

Epilepsy Behav. Author manuscript; available in PMC 2022 February 01.

Published in final edited form as:

Epilepsy Behav. ; 115: 107696. doi:10.1016/j.yebeh.2020.107696.

Reliability of additional reported seizure manifestations to identify dissociative seizures

Wesley T. Kerr[1,2,3], **Xingruo Zhang**[1], **Emily A. Janio**[3], **Amir H. Karimi**[1], **Corinne H. Allas**[1], **Ishita Dubey**[1], **Siddhika S. Sreenivasan**[1], **Janar Bauirjan**[1], **Shannon R. D'Ambrosio**[1], **Mona Al Banna**[1], **Andrew Y. Cho**[4], **Jerome Engel Jr.**[1,4,5,6], **Mark S. Cohen**[1,4,7], **Jamie D. Feusner**[3], **John M. Stern**[1]

[1]Department of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, California, USA

[2]Department of Biomathematics, David Geffen School of Medicine at UCLA, Los Angeles, California, USA

[3]Department of Psychiatry and Biobehavioral Sciences, University of California Los Angeles, Los Angeles, California, USA

[4]Department of Neurobiology, David Geffen School of Medicine at UCLA, Los Angeles, California, USA

[5]Brain Research Institute, University of California Los Angeles, Los Angeles, California, USA

[6]Departments of Radiology, Psychology, Biomedical Physics, and Bioengineering, University of California Los Angeles, Los Angeles, California, USA

[7]California NanoSystems Institute, University of California Los Angeles, Los Angeles, California, USA

Abstract

Purpose: Descriptions of seizure manifestations (SM), or semiology, can help localize the symptomatogenic zone and subsequently included brain regions involved in epileptic seizures, as well as identify patients with dissociative seizures (DS). Patients and witnesses are not trained observers, so these descriptions may vary from expert review of seizure video recordings of seizures. To better understand how reported factors can help identify patients with DS or epileptic seizures (ES), we evaluated the associations between more than 30 SMs and diagnosis using standardized interviews.

Corresponding Author: Wesley T. Kerr, M.D., Ph.D., 710 Westwood Plaza, Suite 1-240, Box 951769, Los Angeles, California, 90095, WesleyTK@g.UCLA.edu, Phone: (310) 825 5745, Fax: (310) 206 4733.

6.Conflicts & Ethical Publication:

Drs. Engel, Stern, Kerr and Al Banna have clinical practices that include the diagnosis and treatment of patients with epilepsy and non-epileptic seizures. 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.

Methods: Based on patient- and observer-reported data from 490 patients with diagnoses documented by video-electoencephalography, we compared the rate of each SM in five mutually exclusive groups: epileptic seizures (ES), DS, physiologic seizure-like events (PSLE), mixed DS and ES, and inconclusive testing.

Results: In addition to SMs that we described in a prior manuscript, the following were associated with DS: light triggers, emotional stress trigger, pre-ictal and post-ictal headache, post-ictal muscle soreness, and ictal sensory symptoms.

The following were associated with ES: triggered by missing medication, aura of déjà vu, and leftward eye deviation. There were numerous manifestations separately associated with mixed ES and DS.

Conclusions: Reported SM can help identify patients with DS, but no manifestation is pathognomonic for either ES or DS. Patients with mixed ES and DS reported factors divergent from both ES-alone and DS-alone.

Keywords

psychogenic nonepileptic seizures; functional seizures; semiology; symptomatogenic zone

1. Introduction:

A core element of the clinical history for patients with seizures is eliciting a description of seizure manifestations (SM) from the patient and any available witnesses. In patients with epileptic seizures (ES), this assists in hypothesized seizure classification and neuroanatomic localization of the symptomatogenic zone, defined as the area of cortex that, when activated by epileptiform activity, produces ictal symptoms [1]. In addition, this description can help identify patients with dissociative seizures (DS), which also are known as functional seizures or psychogenic nonepileptic seizures (PNES) [2-4]. While the exact mechanism of DS is unknown, these seizures most commonly reflect abnormally prominent, involuntary physical manifestations of chronic and, in some cases, acute psychological stressors [5-7]. Identifying patients with DS early can lead to triage towards cognitive behavioral therapy designed for DS, or potentially psychodynamic therapy, and avoidance of adverse effects of antiseizure medication and intubation for prolonged dissociative seizures [8-10].

While reported SM are not as reliable as video recordings, especially with concomitant electroencephalography (EEG), evidence-based decision support tools have been developed that have 70-85% accuracy in differentiating patients with DS from ES [11-16]. In our prior work, we evaluated more than 30 reported manifestations based on retrospective chart review and were unable to evaluate the diagnostic value of additional manifestations due to lack of reporting [17]. In this prospective evaluation, patients underwent a standardized interview during admission for video-EEG monitoring (VEM) that specifically inquired about additional SMs (Table 1).

Specifically, we characterized seizure triggers; types of aura, eye movements and head movements; the specific words used to describe the movements; and description of the post-ictal symptoms. By evaluating the extent to which each reported factor was associated with

DS, ES, or mixed ES plus DS, we aimed to improve clinician's understanding and interpretation of patients' and caregivers' reports. A clinical purpose of interpreting reported SMs is to determine if the patient has probable DS and warrants further confirmation of diagnosis with ictal VEM prior to prescribing another antiseizure medications [18-20], therefore we focus on characterizing the patient as a whole, as compared to each individual seizure type that a patient may experience.

2. Methods:

Our patient population includes all patients admitted to an adult vEEG monitoring unit from May 2015 to December 2019. Diagnosis was based on expert clinical opinion and met the International League Against Epilepsy definition of "documented" based on the available clinical history, physical exam, vEEG, structural and diffusion MRI, FDG-PET, MEG and SPECT [18]. We placed patients in five mutually exclusive categories: DS, ES, mixed DS plus ES, physiologic seizure-like events (PSLE), and inconclusive monitoring. Our statistical modeling recognizes that these are heterogeneous populations, but the prediction of subtypes is outside the scope of this investigation. In contrast to non-epileptic seizures caused by dissociation, we define PSLE as non-epileptic seizures caused by non-psychological factors including syncope, complex migraines, dementia, and movement disorders [21]. We use mixed seizures only when referring to patients with both DS and ES. As suggested by our results, we keep mixed seizures and DS separate because their SMs were described differently and treatment protocols are different [22]. There were no patients with PSLE and ES.

Inconclusive monitoring occurred when a patient did not have occurrences of their characteristic events to determine a diagnosis for all types of seizures. Inclusion of these patients reduces selection bias while not otherwise affecting the conclusions regarding the other diagnostic categories. Publication of data from these patients with uncertain diagnoses promotes data transparency and hypothesis generation. However, because our data pertains to patients for whom video-EEG was conclusive, our results may not generalize to patients for whom video-EEG would not be conclusive.

Patients underwent a standardized interview with a trained non-neurologist interviewer (EAJ, SRD, MA, JB, CHA, AK) or WTK within 48 hours of the vEEG admission. No information from the health record, beyond age and sex, was used to supplement the history. Age was recorded at the time of the standardized interview. The standardized interview was conducted in the patient's private hospital room and available caregivers, family, or friends were not dismissed, mirroring a typical neurological interview. The structure of this interview mirrored the Center for Medicare Services billing requirements of an initial neurological history without the physical exam and included sections on medical comorbidities, medications, epilepsy risk factors, head trauma, psychological trauma, family history, allergies, quality of life, and peri-ictal manifestations [17, 23-25]. Caregivers and loved ones were dismissed for questions regarding psychological trauma and suicidal ideation. Peri-ictal manifestations were elicited by asking the patient to describe their typical seizure from start to finish. After this open question, the interviewer would clarify details that were not otherwise specified. As many patients were amnestic of their seizures, no

distinction was made between details or descriptions provided by the patient and caregivers. When patients and caregivers disagreed, although this was rare, we used the patients' report. In total, this detailed standardized interview takes between 15 and 90 minutes.

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 are at SeizureDisorderCenterResearchGroup.org.

2.1. Description of Seizure Manifestations

We included each SM that was described for at least 1 type of seizure that the patient had. For example, an individual patient could report eye closure in one type of seizures and, simultaneously, eye opening during another type of seizure. In this case, patients would be recorded to have both. Therefore, SM were analyzed per patient and were not analyzed per patient and seizure type. This reflects the perspective that clinicians look to diagnose the patient, as compared to diagnosing each seizure type. While there are clear and clinically important exceptions to this (e.g. tuberous sclerosis complex or Lennox-Gastaut Syndrome), it is uncommon for patients to have multifocal epilepsy, generalized-onset and focal-onset epilepsy, or mixed ES and DS. For patients with mixed ES and DS, we report our results to better understand this complex population.

Seizure manifestations indicators were selected based on previous literature and factors not evaluated in our previous retrospective dataset (Table 1, [17]). Briefly, we describe why each SM was included.

Versive head and eye movements are a reliable lateralizing features for focal ES [26]. In discussion of other eye and head movements, we also evaluated other common reports including upward eye movements, rolling eye movements. Upward eye movements were described similarly to versive eye movements but were directed upward. Eye rolling included motion of the eyes that was not forced or versive. Other descriptions of eye movements were coded as eye movements without additional specifications. Eye closure has been associated with DS [17, 27-34], so we evaluated the converse, eye opening, as well as the rapid alternation between opening and closing, which was termed fluttering [11]. Staring was commonly described during seizures but was not included previously. Similarly, we evaluated ictal lapse of awareness according to the current definitions for epileptic seizures [35]. To reference the literature describing preserved awareness with bilateral movements, we added factors describing bilateral movements as compared to unilateral movements. We found that the physical description of seizures was difficult to analyze, so we included multiple words that were commonly used by patients including stiffening, shaking, and flailing. Although we did not hear these descriptions often, we also added characterization of sensory symptoms of tingling, numbness, and dizziness. To add to the prior evaluation of injury from seizure [36], we also evaluated if the patient falls during seizure.

In addition to ictal features, we evaluated peri-ictal features describing the events immediately before or after ictus, as well as the triggers or factors associated with ictus. An electrographic feature of DS is absence of post-ictal EEG changes [37, 38], so we included clinical post-ictal features of confusion or fatigue, muscle soreness, and headache. We also

further evaluated the aura to include typical limbic auras of epigastric rising, déjà vu, and scents other than metallic tastes. Our prior work evaluated metallic tastes [17]. Due to the observation that epileptic scents likely are unpleasant, we specified if the scent of an aura was pleasant or unpleasant. To further characterize incontinence that has been discussed previously [17, 39-41], we added aura of urinary urgency that may localize to insula or temporal lobe epilepsy [42].

2.2. Statistical Modeling

We evaluated the population-level differences in each reported seizure manifestation using pairwise comparison of each diagnostic group using either linear or log-linear heteroskedastic t-tests or Fisher exact tests. When a manifestation was reported in no patients in a group, the binomial exact confidence intervals were calculated assuming that "one half" of a patient in that group reported the factor. This provides the most conservative comparison between groups by assuming the highest potential prevalence that would be rounded down to the actual observed prevalence. The purpose of this analysis was to highlight specific clinical features that clinicians may consider in diagnostic and decision-making situations, rather than quantitatively determining the predictive ability of any feature. Thus, we did not apply a correction for multiple statistical tests [43-45]. Some patients and caregivers were unable to quantify seizure duration, seizure frequency, or age of onset of seizures. For population-level analysis, we excluded patients with missing entries that pertained to the factor modeled in that regression.

3. Results:

In our sample of 490 patients, 77 had DS alone (16% of total), 16 had mixed DS and ES (3% of total, 17% of all patients with DS or DS and ES), 19 had PSLE (4% of total, 20% of patients with DS or PSLE), and 241 had ES alone (49% of total). Of the patients with ES, 105 (44%) had temporal lobe ES, 22 (9%) had frontal lobe ES, 89 (37%) had other or poorly localized focal onsets, 15 (6%) had generalized-onset ES, 3 (1.2%) had both focal and generalized-onset ES, 2 (0.8%) had other epileptic syndromes, and 47 (20%) had ES with unclear localization. Table 2 summarizes the number of patients in each diagnostic group.

Patients with PSLE included paroxysmal kinesigenic dyskinesia, other dyskinesia, complex migraines, syncope with and without dysautonomia, orthostatic tremor, sleep myoclonus, obstructive sleep apnea, Tourette's syndrome, behavioral events in nonverbal or otherwise intellectually disabled patients, and non-epileptic vertigo or dizziness.

The univariate odds ratios of factors that were significantly different between patients with DS and ES are illustrated in Figure 1. The population level prevalence of each patient-reported factor is summarized in Supplementary Table 1. Seizure duration and seizure frequency were missing in 9% and 5% of patients, respectively.

For patients with ES, the average time from seizure onset to VEM was 18 years (95% linear confidence interval (CI): 16-21 years; median 15, interquartile range (IQR) 6-26 years). For patients with DS, the average time to VEM was 8.6 years (95% CI: 6-11 years; median 4,

IQR 1.25-11.5 years). For patients with mixed seizures, the average time to VEM was 23 years (95% CI: 13-33 years; median 21.5, IQR 5-38 years).

The seizure manifestations that were more common in DS compared to ES included seizure trigger involving light (19% DS, 16% ES, p=0.09); seizures triggered by emotional stress (27% DS, 19% ES, p=0.02), aura of headache (16% DS, 7% ES, p=0.005), ictal numbness (19% DS, 7% ES, p=0.004), ictal tingling (19% DS, 8% ES, p=0.01), ictal dizziness (16% DS, 7% ES, p=0.04), post-ictal muscle soreness (61% DS, 38% ES, p=0.0005), and post-ictal headache (62% DS, 49% ES, p=0.04).

The seizure manifestations that were more common in ES compared to DS included seizures triggered by missing medications (19% DS, 41% ES, p=0.01), aura of déjà vu (1.2% DS, 12% ES, p=0.01), and leftward eye deviation (0% DS, 19% ES, p=0.009).

The seizure manifestations that in the limited number of patients with mixed seizures that differed from those with DS or ES included more seizure types (average 3 mixed, 1.7 DS, 1.7 ES, $p_{mixedvsDS}$=0.0008, $p_{mixedvsES}$=0.0006), injury from seizure (81% mixed, 39% DS, 45% ES, $p_{mixedvsDS}$=0.002, $p_{mixedvsES}$=0.008), ictal muscle jerks (50% mixed, 15% DS, 11% ES, $p_{mixedvsDS}$=0.005, $p_{mixedvsES}$=0.0003), ictal incontinence (63% mixed, 26% DS, 33% ES, $p_{mixedvsDS}$=0.07, $p_{mixedvsES}$=0.03), ictal numbness (25% mixed, 7% ES, $p_{mixedvsES}$=0.04), ictal head movements (62% mixed, 36% ES, $p_{mixedvsES}$=0.06), ictal leftward head movement (25% mixed, 5% DS, 11% ES, $p_{mixedvsDS}$=0.03), ictal side to side head movements (25% mixed, 9% DS, 7% ES, $p_{mixedvsES}$=0.03), ictal staring (69% mixed, 38% DS, 39% ES, $p_{mixedvsDS}$=0.03, $p_{mixedvsES}$=0.03), ictal leftward eye movements (13% mixed, 0% DS, 7% ES, $p_{mixedvsDS}$=0.03), ictal cry or scream (38% mixed, 13% DS, 21% ES, $p_{mixedvsDS}$=0.03).

In comparison to our prior retrospective work, this prospective dataset independently confirmed differences in the prevalence or value of the following patient-reported SM: seizure duration (average 2:48 min:sec DS, 1:28 ES, p=0.0092), seizures directly from sleep (44% DS, 57% ES, p=0.07), limb automatisms (4% DS, 16% ES, p=0.006), and eye closure (23% DS, 9% ES, p=0.006).

The following factors did not significantly differ between patients with DS, mixed, or ES: catamenial seizures; trigger of loud noises; trigger of stress, trigger of alcohol, the presence of any aura, an epigastric rising aura, aura of fear or anxiety, an aura involving a scent or taste, falling during seizures, ictal amnesia, ictal aphasia, oral injury during seizure, tonic-clonic movements, stiffening, shaking, flailing, hallucinations, hip thrusting, rightward head movements, any eye movements, rightward eye movements, eyes rolling upwards, eye fluttering, eye opening, ictal freezing, and post-ictal confusion or fatigue.

4. Discussion:

These results provide meaningful data to assist clinicians in interpreting many reported seizure manifestations, even though we did not address all of the hundreds of seizure manifestations that were potentially suggestive of DS. While some SMs can raise the likelihood of DS, none fully excluded ES, therefore the diagnosis of DS or ES should not

rely on the reporting of a single SM suggestive of DS. Instead, the experienced clinician should consider the totality of SMs as well as other data to formulate a diagnosis and provide suggestions for evaluation and management. We also address the difficult population of patients with mixed DS and ES.

A significant portion of functional neurological disorders (FNDs) includes an element of physical pain. The increased reports of pre- and post-ictal headache as well as post-ictal muscle soreness could reflect this phenomenon. In other series, pre-ictal headache was present in 16% (n=258, [46]) and 87% (n=63, [28]) of patients with DS, and is considered rare in epilepsy [47]. When it occurs in temporal lobe epilepsy, pre-ictal migraine is ipsilateral [48]. In contrast, post-ictal headache was common in both populations including 49% of patients with ES. Therefore, while both pre- and post-ictal headache were more common in DS than ES, our results suggest that timing matters: the positive predictive value of pre-ictal headache (92%, 95% CI 89-96%) was higher than that of post-ictal headache (51%, 95% CI 45-58%).

This differential rate of pain also translates to post-ictal muscle soreness. Even though dissociative seizures tend to be longer [17], the quantitative pattern of muscle involvement can be different from either focal, focal-to-bilateral and generalized or bilateral epileptic seizures [49-52]. Serum studies of anion gap, leukocytosis, creatine kinase and other objective markers of muscle fatigue suggest that ES produce more metabolic demand than DS [53-56], but these results are inconsistent. However, even though a similar percent of patients with DS and ES noted bilateral motor involvement, patients with DS perceived increased muscle soreness after seizures. This parallels a consistent finding in FND that patients' perception and description of the severity of their symptoms may be higher than suggested from objective physiological measures [57-61].

Similarly, sensory symptoms are subjective. While the ictal sensory symptoms of tingling, numbness and dizziness were present in less than 20% of patients with DS, they were present in less than 10% of patients with ES. Dizziness was the second most common aura in DS [46] and, when seen in 9% of epilepsy in other meta-analyses, ictal dizziness localized to the temporal lobe or temporal-parietal-occipital junction [62]. The temporo-parietal junction has been implicated in functional movement disorders and dissociative seizures [63-66]. Similarly, ictal paresthesias and numbness are reported in a minority of DS and, when rarely present in epilepsy, localize to the parietal lobe or insula [67-70]. This association of sensory symptoms with DS mirrors our prior finding that sensory hallucinations were more common in DS than ES, although that difference was not statistically different in this dataset (13% DS versus 8% ES, p=0.18). Therefore, while ictal sensory symptoms are rare, they may raise suspicion for DS.

The ability to recognize and successfully cope with stressors is a key part of the mechanism of DS and other functional neurological disorders [71, 72]. However, psychological and physiologic stress also reduce seizure threshold on patients with epilepsy [73-76]. This was reflected in our results by the dichotomy between seizures triggered by general stress as compared to emotional stressors, in particular. General stress triggering seizures was common in both groups (57% DS versus 49% ES, p=0.24), but stressful emotional triggers

were more prevalent in DS (32% versus 19%, p=0.02), as has been described elsewhere [77]. In our experience, patients needed to be prompted to recognize this difference, therefore providers can follow up a reported trigger of stress by asking about emotional stress in particular.

This type of dichotomy also was seen regarding eye movements. While it is not diagnostic in isolation, ictal eye closure is established to be suggestive of DS [17, 27-34]. Some of this literature refers to “forced eye closure” but we found that without a video, patients and caregivers had difficulty understanding the difference between forced and unforced eye closure and tended to state that all ictal eye closure was forced. Logically, one would presume that the converse—ictal eye opening—would suggest ES, as had been shown in a single 120-patient series [11]. However, ictal eye opening, fluttering, rolling and upward deviation were all nondiagnostic in our dataset (all p-values>0.14).

Another typical finding in focal to bilateral epileptic seizures is versive movements that typically include forced eye and head deviation to one side [26]. While patient and caregiver reports had difficulty differentiating forced versus unforced version, we observed that leftward eye or head movements were quite rare in DS (0% and 5%, respectively) and were present in a minority of patients with ES (7% and 7%, respectively). Nonintuitively, this difference was not present for rightward eye or head movements and was not correlated with handedness (data not shown). While eye deviation towards the ground, termed geotropic, has been reported in DS [78], lateral head and eye version similar to that seen in focal ES have not been described in DS previously.

Other findings suggestive of limbic onset focal to bilateral epileptic seizures were more reliable indicators of ES. Specifically, an aura of déjà vu and simple limb automatisms were not uncommon in patients with ES (12% and 16%, respectively), and were rare in patients with DS (3% and 4%, respectively).

This finding that typical limbic behaviors suggested epilepsy reflects the increased prevalence of limbic epilepsy in our VEM dataset and also reflects the intuitive concept that if a patient’s seizure manifestation closely resembles that of a particular epilepsy syndrome or localization, then the seizures might be more likely to be epilepsy. However, the prevalence of these specific epilepsy syndromes is low so that even in our large, unselected, consecutive series of patients with VEM, there was insufficient data to evaluate specific collections of seizure manifestations in a data-driven fashion.

While we had limited data from the complex population of patients with mixed DS and ES, the data we have suggested that this population may be different from patients with DS alone or ES alone. To a certain extent, some of the manifestations that were suggestive of DS in our dataset were even more prevalent in mixed seizures. In addition to these manifestations, side to side head movements and muscle jerks, as compared to tonic-clonic movements, have previously been described as suggestive of DS and were more common in mixed seizures [14, 71, 79-82], but were not observed to be different between DS alone and ES alone. Conversely, the leftward head and eye version that was suggestive of ES were even more common in mixed seizures. Further, manifestations that were typically associated with

ES in prior literature also were exceptionally common in mixed seizures, even if they were not different between DS and ES in our dataset, including injury from seizure, ictal incontinence, and ictal scream. This mixed ictal manifestation in mixed seizures reflects that the average patient had 3 seizure types, whereas patients with DS alone or ES alone reported 1 to 2 seizure types. The rate of ictal staring was very prevalent in mixed seizures (69%), suggesting that this last seizure type may in part include more bland seizures.

This divergence of the interpretation of these seizure manifestations suggests that patients with these difficult to interpret descriptions and multiple seizure types should be evaluated further, likely with VEM. This would suggest that these complex patients should be referred earlier, but the median time from seizure onset to VEM in mixed seizures was 21.5 years, which was longer than patients with either DS or ES (4 and 15 years, respectively). This may reflect a reluctance to refer patients with medication-resistant epilepsy for an epilepsy surgery evaluation of epilepsy, when they also have DS, even though they can be good surgical candidates [83].

While this dataset includes a wide range of ages, many patients and localizations of epilepsy, our data pertains just to adults with DS and ES. The descriptions of seizure manifestation were provided by a combination of the patient and any available witnesses. While this may differ from separate descriptions of the patient and witnesses [16], but our approach mirrors a typical clinical encounter. Our approach of an initial open question followed by specific questions balances an open, patient-centered clinical approach with the need for reliable data for research. As suggested by conversation analysis across cultures, patients with epilepsy more readily provide specific details regarding their seizures, as compared to patients with dissociative seizures who tend to focus on the environment and impact of their seizures [84-87]. Therefore, this prospective design can overcome some limitations inherent to deriving specific factors from chart review of patients with dissociative seizures, while also addressing the difference in communication patterns between patients with epilepsy and dissociative seizures.

The seizure manifestations of children and adolescents with seizures is different from adults [39]. Therefore, we caution the generalization of our results to younger patients. Further, the differential diagnosis of seizures with atypical behaviors focuses primarily on frontal lobe epilepsy (FLE). However, the prevalence of FLE is low even compared to the prevalence of DS, even in our larger dataset (Of all 490 unique admissions, 4.4% (22) were FLE and 16% (77) were DS). Therefore, it remains difficult to distinguish between patients with DS and FLE in the absence of direct observation of the seizure by a seizure specialist with or without concomitant EEG.

The single-variable associations that we discussed used data to provide helpful information to interpret clinically reported peri-ictal manifestations of DS, ES, and mixed seizures, but we caution that these insights are qualitative and only indirectly comment on the underlying pathophysiology of these conditions. While associative studies provide a short list of candidate findings, interventional or other mechanistic studies are needed to demonstrate causal links between findings and DS, ES, or mixed seizures.

Additionally, unlike some of our prior work [17, 23-25, 88], we did not evaluate how these factors can be applied to diagnose individual patients with seizures. Future work is needed to evaluate how these population-level differences can be integrated with other information from patients to reliably diagnose individual patients. Population-level differences do not always translate to reliable individual-level predictions [24]. The diagnosis of seizure-like events is complex because clinicians must consider ES, DS, mixed ES plus DS, as well as PSLE. In comparison to ES and DS, patients with mixed seizures or PSLE are relatively rare in video-EEG datasets, and substantially more data is needed to accurately differentiate these clinically important populations [22]. This is particularly challenging for patients with PSLE who needed video-EEG for diagnosis because of the wide heterogeneity of observed etiologies. However, due to this heterogeneity, it is particularly difficult to interpret SMs in this population. We report data on these populations to facilitate future meta-analyses and multicenter studies that could build a large enough sample to characterize patients with mixed seizures or PSLE.

Just as patients with PSLE are diagnostically heterogeneous, individual patients may experience multiple seizure types. This analysis focused on diagnosing patients instead of individual seizure types. Differentiation of the epileptic from dissociative seizures in a patient with mixed seizures is particularly important, but this analytical level of complexity was outside the scope of this work.

4.4 Conclusions

No reported seizure manifestation is pathognomonic for DS. Ictal sensory symptoms and both pre-ictal and post-ictal headache were more common in patients with DS than ES. Conversely, an aura of déjà vu and, intriguingly, leftward but not rightward eye deviation was very uncommon in patients with DS and was present in some patients with ES. The seizure manifestation of patients with mixed seizures appears quite different from both DS and ES in isolation. Based on the limited predictive value, reported seizure manifestation can suggest “probable” DS; further diagnostic evaluation including observation of the seizures by a seizure specialist is needed to guide treatment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

The authors thank Kirk Shattuck, Marc Nuwer, and Edward P. Lau for organization support, access to the data, and technical support. This work was supported by the NIH R25 NS065723, UCLA-California Institute of Technology Medical Scientist Training Program (NIH T32 GM08042), the William M. Keck Foundation, research grants to JE (NS03310 & NS080181), the UCLA Departments of Psychiatry & Biobehavioral Sciences and Biomathematics.

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Highlights:

- Pre-ictal headache was more specific for dissociative seizures (DS) than post-ictal headache.
- Ictal sensory symptoms and seizures triggered by emotional stress were associated with DS.
- Epileptic seizures (ES) were associated with déjà vu, left eye deviation and missed medications.
- Patients with both ES and DS reported seizure manifestations different from ES-alone and DS-alone

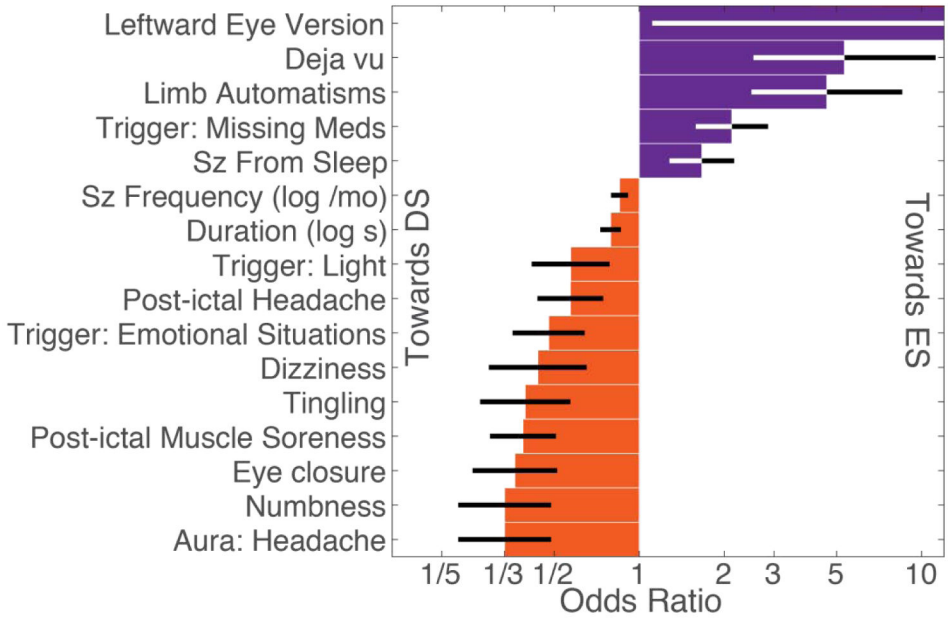

Figure 1:

Patient reported seizure manifestations (SM) with different prevalence between patients with DS and ES (α<0.10, uncorrected). SMs are ordered based on magnitude. Black and white error bars reflect standard error plotted on a scale of log-odds ratios with tick labels reflecting odds ratios. Leftward eye version was only reported in ES, therefore significance was as determined by a Fisher exact test. Abbreviations: seizure (sz), month (mo), second (s).

Table 1:

List of all the seizure manifestations that we evaluated. Tabs indicate specifications within a category. Abbreviations: medications (meds), movements (mvmts), number (#), seizure (sz).

Seizure Manifestations		
Seizure Duration	Sz From Sleep	Head mvmts
Sz Freq	Falling	Left Version
# Sz Types	Lapse of Awareness	Right Version
# Limbs Moving	Dialeptic	Side-to-side
Injury from Sz	Maximum Intensity at Onset	Staring
Trigger: Sleep Dep		Eye mvmts
Catamenial	Amnesia	Left Version
Trigger: Light	Aphasia	Right Version
Trigger: Food	Oral injury	Upwards
Trigger: Missing Meds	Muscle jerks	Rolling
Trigger: Loud Noises	Tonic-clonic mvmts	Fluttering
Trigger: Stress	Whole Body mvmts	Eye closure
Trigger: Emotional Stress	Part Body mvmts	Eye opening
Trigger: Alcohol	Stiffening	Freezing
Aura	Shaking	Ictal Cry
Headache	Flailing	Ictal Anxiety
Urinary Urge	Numbness	Post-ictal Confusion Or Fatigue
Epigastric Rising	Tingling	
Anxiety	Dizziness	Post-ictal Muscle
Déjà vu	Hallucinations	Soreness
Scent	Incontinence	Post-ictal Headache
Pleasant	Limb Automatisms	
Unpleasant	Oral Automatisms	
Metallic	Hip thrusting	

Table 2:

The number and percent of patients based on seizure etiology. Horizontal bars separate classes of diagnoses and tabs indicate specification within a category. For patients with ES, we include a breakdown of the localization of epilepsy and the percent (%) contribution of each subgroup to the total sample of patients with ES. Similarly, we calculate the relative proportion of patients with DS who have ES (Mixed DS and ES) and who do not have ES (DS-alone).

Diagnosis	Number	% Total	% of Class
Dissociative Seizures (DS)	77	16.	83.
Mixed DS and ES	16	3.3	17.
Inconclusive Monitoring	137	28.	
PSLE	19	3.9	
Epileptic Seizures (ES)	241	49.	
Generalized	15	3.1	6.
Frontal lobe	22	4.5	9.
Temporal lobe	105	21.	44.
Parietal lobe	2	0.4	0.8
Occipital lobe	3	0.6	1.2
Other Focal or Multifocal	61	12.4	25.
Focal unclear localization	28	5.7	12.
Focal and Generalized	3	0.6	1.2
Other Epilepsy Syndrome	2	0.4	0.8
Not otherwise specified	47	9.6	20.