Seizure: European Journal of Epilepsy 66 (2019) 104–111

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Outcome of ambulatory video-EEG monitoring in a ~10,000 patient nationwide cohort

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ARTICLE INFO

Keywords:
EEG
Epilepsy monitoring
Video/EEG use in epilepsy
Ambulatory EEG

ABSTRACT

Purpose: We evaluate outcome of in-home diagnostic ambulatory video-EEG monitoring (AVEM) performed on a nationwide cohort of patients over one calendar year, and we compare our findings with outcomes of inpatient adult and pediatric VEM performed during the same year at two academic epilepsy centers.
Methods: This is a retrospective cohort study. We obtained AVEM outcome data from an independent ambulatory-EEG testing facility. Inpatient VEM data from a 4-bed adult epilepsy center and an 8-bed pediatric epilepsy center were also included. Primary outcome measure was composite percentage of VEM records with epileptiform activity on EEG tracings or at least one video-recorded pushbutton event. We assessed patient-reported symptoms documented in AVEM event diaries.
Results: Of 9221 AVEM recordings performed across 28 states, 62.5% attained primary outcome. At least one patient-activated pushbutton event was captured on video in 54% of AVEM recordings (53.6% in adults, 56.1% in children). Epileptiform activity was reported in 1657 (18.0%) AVEM recordings (1473 [88.9%] only interictal, 9 [0.5%] only ictal, 175 [10.6%] both interictal and ictal). Most common patient-reported symptomatology during AVEM pushbutton events was behavioral/autonomic/emotional in adults and children. Compared to AVEM, inpatient VEM captured more confirmed representative events in adult and pediatric samples.
Conclusions: AVEM is useful for non-urgent diagnostic evaluation of events.

1. Introduction

Despite cost, accessibility, and convenience advantages of diagnostic ambulatory video-EEG monitoring (AVEM) over inpatient VEM, some clinicians tend to favor inpatient VEM even when inpatient level-of-care may not be medically needed, mainly because of two

Abbreviations: VEM, video-EEG monitoring; AVEM, ambulatory video-EEG monitoring

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https://doi.org/10.1016/j.seizure.2019.01.018
Received 30 November 2018; Received in revised form 18 January 2019; Accepted 20 January 2019

concerns, one practical and another technical. First, AVEM may be assumed less likely than inpatient VEM to capture patient events on video because it is more challenging to ensure that patient remains within video-camera field-of-view in an ambulatory setting than in a hospital room. Second, there is concern that EEG-tracings may be more prone to difficult to correct artifact and degradation when VEM is carried out in patient home rather than in hospital, potentially rendering VEM in the ambulatory setting uninterpretable [1].

Prospective AVEM outcome studies have lessened these concerns [2], finding that only 1/101 (< 1.0%) [3] and 1/41 (2.4%) [4] AVEM recordings were un-interpretable, due to artifact, that ambulatory and inpatient VEM were statistically indifferent in their capacity to capture patient events on video (74% ambulatory, 62% inpatient) [4], and that in side-by-side comparison ambulatory and inpatient VEM were overall equally likely to generate results that meaningfully impact clinical decision-making in non-urgent and non-surgical cases (73% ambulatory, 73% inpatient) [4]. However, these and other published AVEM outcome studies [5,6] are limited to single-center investigations with no greater than 502 subjects.

Our present study assesses outcome of diagnostic AVEM performed on a nationwide cohort of patients over one year. We compare our findings with outcome of inpatient adult and pediatric VEM performed during the same year at academic epilepsy centers.

2. Materials and methods

2.1. Study design

This is an a priori designed, retrospective cohort study to assess outcome of diagnostic AVEM. We obtained AVEM outcome and utility data from a single independent diagnostic ambulatory-EEG testing facility (Alliance Family of Companies, Irving, TX) [7] that sets up AVEM in the patient's home. We assessed outcome of inpatient VEM in separate concurrent retrospective adult and pediatric cohorts, to be used as a standard against which AVEM outcome in our study would be compared. For this purpose, we acquired inpatient VEM outcome data for our study from a 4-bed adult epilepsy center (The George Washington University School of Medicine and Health Sciences Epilepsy Center; GWU) and an 8-bed pediatric epilepsy center (Boston Children's Hospital; BCH), each a National Association of Epilepsy Centers (NAEC)-accredited level 4 epilepsy monitoring unit with procedural and technical standards that are described on the NAEC official website [8]. We selected these two epilepsy centers based on need to appropriately represent adult and pediatric subpopulations in our study. Approval from University Hospitals Cleveland Medical Center institutional review board to conduct this study was received.

2.2. Ambulatory video-EEG monitoring

The collaborating ambulatory-EEG testing facility performs AVEM according to a protocol that incorporates for each patient 25 electrodes (23 standard 10–20 EEG, two EKG), a waist worn 200 samples-per-second EEG recording device with built-in patient-activated pushbutton event monitor, two portable video-cameras that are synchronized with EEG recording, and Bluetooth radio hardware for remote real-time monitoring of video and EEG-tracings (Lifelines Trackit MK3). For each patient undergoing AVEM, the facility assigns EEG technologists to each carry out one of three roles, AVEM 'setup', 'remote-monitoring', and 'reading'. 'Setup' technologist resides local to patient and is responsible for setting up AVEM equipment in patient residence. Battery-life permits ˜72 h of continuous AVEM recording, therefore > 72-hour AVEM referrals require that 'setup' technologist rehook AVEM equipment in patient residence every 2–3 days, which typically results in a 3–4 hour break in AVEM recording every ˜72 h. Using referring clinician's notes as a guide, 'setup' technologist interviews patient and caregiver(s) to generate an updated written clinical history relevant to AVEM (e.g., description of events, past medical history, medication list). 'Setup' technologist instructs patient to press pushbutton at onset of each event and maintain a written diary that details each event. 'Setup' technologist positions each of the two video-cameras within patient home according to where patient and cohabitant(s) deem that patient would most often be captured on video. 'Setup' technologist emphasizes to patient and cohabitant(s) the clinical significance of patient remaining as often as possible within video-camera field-of-view, especially during events, explaining its impact on referring clinician's subsequent plan-of-care. To maintain quality of video- and EEG-recording, 'monitoring' technologist remotely logs in to AVEM recording live in real-time for three minutes every two hours via Bluetooth radio connection in order to identify any technical issue (e.g., poor electrode contact, video-camera failure, hardware malfunction), and, if needed, communicates the issue to 'setup' technologist. Facility protocol requires, patient permitting, that 'setup' technologist visit patient residence and resolve any technical issue within two hours of being notified by 'monitoring' technologist. All AVEM studies are interpreted by an ABPN board-certified neurologist who is granted access to entire AVEM recording, all technologist-clipped AVEM files (3–4 minutes every three hours and potential epileptiform discharges), and AVEM technical summary (clinical history, patient event diary, patient "in" or "out" of camera view during events).

2.3. Outcome and clinical utility variables

Abstracted data from the ambulatory-EEG facility documentation (AVEM technical summary and ABPN board-certified neurologist interpretation) pertaining to each AVEM that the facility performed between July 1, 2016 and June 30, 2017 was coded into a priori and supplemental variables that were deemed to most precisely reflect AVEM outcome and clinical utility in our study population. Study investigators at the two collaborating epilepsy centers provided inpatient VEM outcome and clinical utility data that was generated from admissions to each of these two centers during the same year time-span. Three epileptologists (T.U.S., M.T.K., M.Z.K.) as a group reviewed AVEM documentation to determine clinical rationale for each AVEM referral and outcome, and, in line with our study objective, we only included AVEM recordings that at least two of these three epileptologists concurred were referred for diagnostic evaluation of events. Likewise, we only included inpatient VEM referrals that study investigators at the two collaborating epilepsy centers opined were referred for diagnostic evaluation of events. Based on prior AVEM outcome literature [2,3], we a priori defined primary outcome measure of our study as composite percentage of VEM recordings that captured at least one pushbutton event on video-camera or demonstrated epileptiform activity on EEG tracings. With expert opinion that varied as to how to optimally define a clinically meaningful VEM outcome, we defined 12 secondary outcome measures (Fig. 1) that differed in stringency from our primary outcome measure. Two epileptologists (T.U.S., M.T.K) and a medical student (H.A.) compared clinical history with event diary pertaining to each AVEM recording to identify AVEM recordings that captured events that were "representative" of what patient reported during history-taking. Our study design (AVEM report review) precluded use of video-recording or structured patient interview to assess whether recorded events were "representative", and therefore, we anticipated that our results would tend to underestimate our outcome measures that only counted "representative" events. For this reason, we opted to include "representative" events in only secondary, and not primary, outcome measures in our study. Collaborating investigators at the two participating epilepsy centers provided this data for inpatient VEM. Because inpatient VEM technologists are at liberty to demarcate events independent of patient and epileptologist, we counted each technologist-demarcated event captured on video during inpatient VEM as a video-recorded event, but not as a pushbutton event, unless patient concomitantly activated pushbutton.

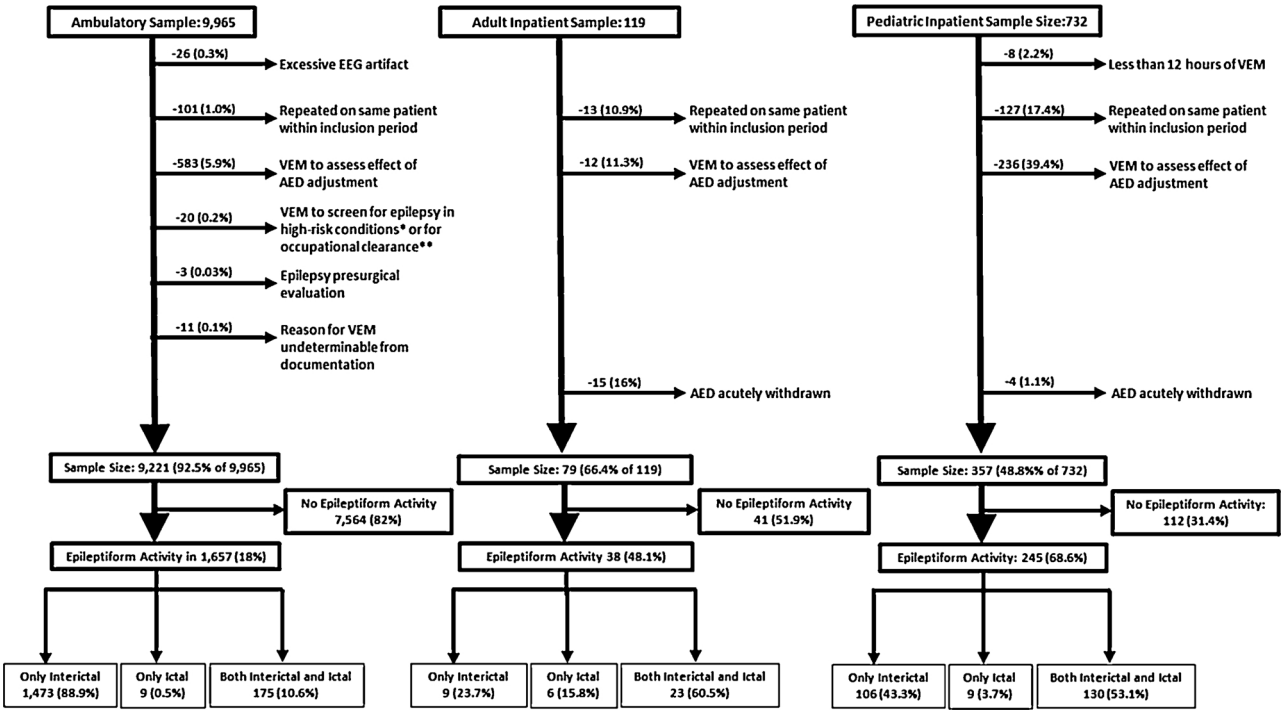

Fig. 1. Ambulatory and inpatient video EEG samples. Ambulatory studies were performed across 28 states (AL, AZ, CA, CO, DC, FL, GA, ID, IL, IN, KS, LA, MD, MI, MO, MS, NC, NJ, NV, OH, OK, PA, SC, TN, TX, UT, VA, WV). Exclusion criteria included 'repeat' studies that were performed multiple times on the same patient during the inclusion period, studies that at least two of three adjudicated epileptologists did not opine were referred for diagnostic evaluation of events, technically unsatisfactory studies due to pervasive EEG artifact (muscle, movement, or electrode), and studies during which antiepileptic medication was acutely reduced/withdrawn for the purpose of bringing on events. Eight pediatric inpatient studies were excluded because duration of recording was < 12 h, opined by the authors not to truly represent 'inpatient' monitoring. *High-risk conditions such as status-post brain tumor resection and tuberous sclerosis. **Occupational reasons such as clearance for pilot license or full-contact sports (boxing, mixed martial arts).

2.4. Statistical analysis

We used nonparametric statistical tests (Fisher's exact test, Mann-Whitney U-test) to generate p-values that were two-tailed, with probability of Type I error (alpha) less than 0.05 considered statistically significant. Application of Bonferroni correction for multiple comparisons yielded critical $p < 0.025$ for each of two primary outcome comparisons (adult and pediatric) and critical $p < 0.002$ for each of 24 secondary outcome comparisons (12 measures, adult and pediatric). All statistical analyses were performed using Stata 15.1 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

IQR - interquartile range. *$p > 0.05$ for adult versus pediatric comparison; all other adult versus pediatric comparisons in table were associated with $p < 0.05$. P-values were generated using Fisher's exact test for categorical (%) variables and Mann-Whitney U-test for continuous (median) variables. In ambulatory sample, 'Adult' refers to ≥18 years of age, and 'Pediatric' refers to < 18 years of age. In inpatient sample, 'Adult' refers to admission to adult epilepsy center (The George Washington University School of Medicine and Health Sciences Epilepsy Center) and 'Pediatric' refers ton admission to npediatric epilepsy center (Boston Children's Hospital).

3. Results

3.1. Outcomes

Fig. 1 shows derivation of AVEM and inpatient VEM study samples, and Table 1 summarizes sample demographics, VEM duration, and number of pushbutton and video-recorded events. AVEM outcomes and comparison with inpatient VEM outcomes are shown in Fig. 2 (adult) and Fig. 3 (pediatric). Primary outcome for AVEM was 62.5% (5,766/9221) when adult and pediatric samples were combined. AVEM outcome was similar to that of inpatient VEM in adults (61.7%, 5,254/8,515 ambulatory; 54.4%, 43/79 inpatient; $p = 0.201$), but lower than that of inpatient VEM in pediatric samples (72.5%, 512/706 ambulatory; 86.3%, 308/357 inpatient; $p < 0.001$). Tables 2 and 3 compare descriptive and outcome variables by age-group (adult/pediatrics) and by VEM modality (ambulatory/inpatient).

Fig. 1 details prevalence of epileptiform activity in our AVEM and inpatient VEM samples. Inpatient VEM demonstrated electrographic seizure more often than AVEM in adult and pediatric subsamples (both $p < 0.001$, Fisher's exact test). Most common cortical localization of EEG epileptiform activity was temporal lobe in adults and generalized in children, in ambulatory and inpatient samples. Proportion of focal versus generalized epileptiform discharges did not differ between ambulatory and inpatient adult samples (85.6% vs. 90.0% focal, 12.5% vs. 10.0% generalized, 1.4% vs. 0.0% both, 0.5% vs. 0.0% unlocalizable; $p = 0.911$); however, in pediatric samples, ambulatory recordings had higher proportion of focal discharges (68.9% vs. 52.7% focal, 28.3% vs. 46.1% generalized, 2.9% vs. 1.2% both; $p < 0.001$).

Of the 4957 AVEM recordings that captured at least one pushbutton event on video, 97.6% (4839) were without electrographic seizure, and 15.1% (730/4839) of these AVEM recordings demonstrated IEDs (interictal epileptiform discharges). In our inpatient adult VEM sample 58.3% (7/12) of recordings that captured at least one pushbutton event on video were with electrographic seizure, and the remaining 41.7% (5/12) were without electrographic seizure (i.e., none of these five recordings was solely with IEDs). In our inpatient pediatric sample 50.8% (125/246) of recordings that captured at least one pushbutton event on video were with electrographic seizure, and 58 (47.9%) of the remaining 121 recordings without electrographic seizure demonstrated only IEDs.

Values are in format: adult sample versus pediatric sample (p-

Table 1
Ambulatory and inpatient video-EEG monitoring samples.

	AVEM			Inpatient VEM	
	All	Adult	Pediatric	Adult	Pediatric
No. (%)	9221 (100.0)	8515 (92.3)	706 (7.7)	79 (100.0)	357 (100.0)
Female sex, No. (%)	5802 (62.9)	5475 (64.3)	327 (46.3)	48 (60.8)	156 (43.7)
Age years, median (IQR)	53 (35-67)	55 (40-68)	11 (7-15)	45 (32-56)	8 (3-13)
No. days VEM, median (IQR)	3 (3-3)	3 (3-3)	3 (2-3)	4 (3-5)	1, (1-2)
No. pushbutton events, median (IQR)	2 (1-7)	2 (0-7)	3 (1-7)	0 (0-0)	3 (0-9)
No. events on video, median (IQR)	1 (0-3)	1 (0-3)*	1 (0-3)*	1 (0-3)	3, (0-13)

IQR - interquartile range. *p > 0.05 for adult versus pediatric comparison; all other adult versus pediatric comparisons in table were associated with p < 0.05. P-values were generated using Fisher's exact test for categorical (%) variables and Mann-Whitney U-test for continuous (median) variables. In ambulatory sample, 'Adult' refers to ≥18 years of age, and 'Pediatric' refers to < 18 years of age. In inpatient sample, 'Adult' refers to admission to adult epilepsy center (The George Washington University School of Medicine and Health Sciences Epilepsy Center) and 'Pediatric' refers to admission to pediatric epilepsy center (Boston Children's Hospital).

value). P-values were generated using Fisher's exact test for percentages and Mann-Whitney U-test for continuous variables. *Simple sensory*, defined as implicating one sensory modality (e.g., tingling, hearing loud noise, bright flashes, abdominal or chest discomfort/pain), *complex sensory*, defined as a subjective experience not limited to a single sensory modality (e.g., altered awareness, euphoria, psychosis, confusion, vertigo), *cognitive/language* (e.g., aphasia, inability to focus, alexia, agraphia, memory lapse), *loss of awareness/consciousness*, *focal motor* defined as any movement or muscle contraction not involving all extremities (e.g., hand, arm, or leg shaking/tremor, muscle twitches, dystonia, "spasms"), *negative motor* defined as paralysis, weakness, or bradykinesia, and *generalized motor* defined as any movement or muscle contraction involving all extremities.

3.2. Patient-reported symptoms during ambulatory Video-EEG monitoring

Pushbutton events occurred in 6926 (75.1%) AVEM recordings, of which 2819 (40.7%) were without description in patient event diary, leaving 4110 (44.6% of sample) ambulatory recordings with patient pushbutton event documentation that could be assessed for symptomatology. In an attempt to summarize and estimate prevalence of patient-reported event symptomatology in a clinically meaningful manner, we assigned each patient-reported symptom in event diaries to one of seven mutually exclusive symptom categories defined using selected International League Against Epilepsy (ILAE 2017) common descriptors of seizure symptoms [9], according to what we deemed would encompass nearly all (> 99%) patient-reported symptoms in our sample. These symptom categories included *sensory*, defined as implicating one sensory modality (e.g., tingling, hearing loud noise, bright flashes, abdominal or chest discomfort/pain), *behavioral/autonomic/emotional* (e.g., altered awareness, euphoria, psychosis, confusion, vertigo), *cognitive* (e.g., aphasia, inability to focus, alexia, agraphia, memory lapse), *loss of awareness/consciousness*, *focal motor* defined as any movement or muscle contraction not involving all extremities (e.g.,

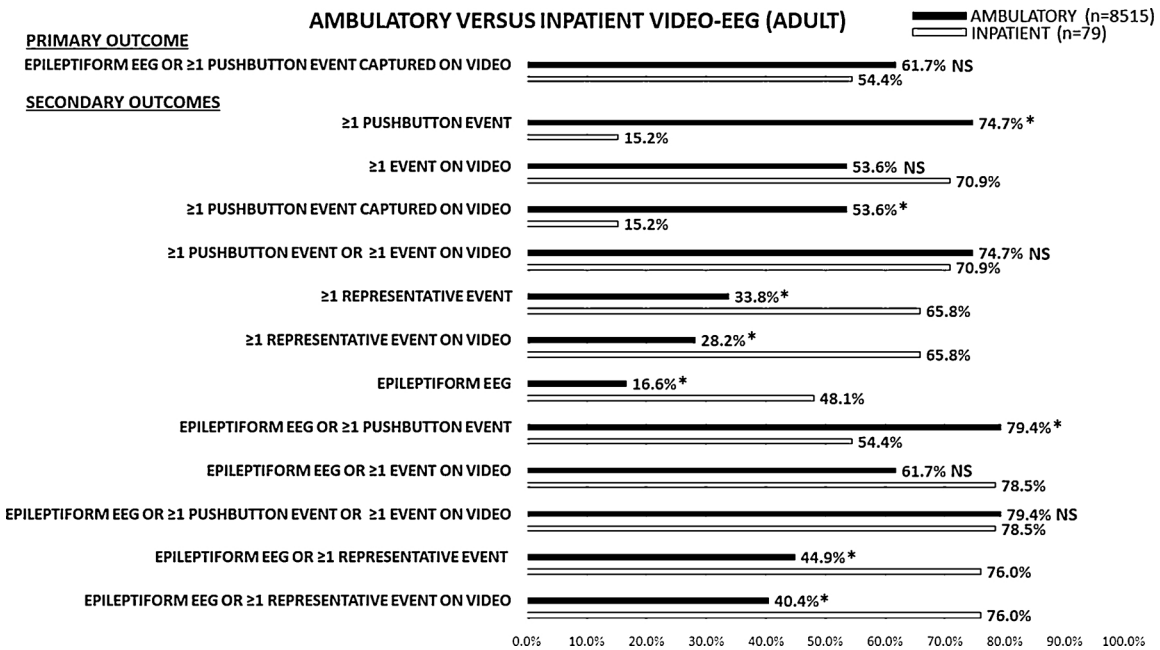

Fig. 2. Outcome of diagnostic ambulatory versus inpatient video-EEG monitoring in pediatric patients. Epileptiform EEG – IEDs (interictal epileptiform discharged) or electrographic seizure reported. Pushbutton event – patient-, family member-, or cohabitant-activated pushbutton. Event on video – patient captured on video during event, including technologist-demarcated event during inpatient video-EEG monitoring. Representative event – patient event diary description shares commonality with clinical history description of events. Events without description in patient event diary were counted as non-representative. Pushbutton events were not counted if accompanying event diary annotation indicated literally that the event was not the patient's habitual event or that the pushbutton was accidental. NS – not statistically significant; *Statistically significant; critical p < 0.025 for primary outcome, p < 0.002 for secondary outcomes; All p-values generated using Fisher's exact test.

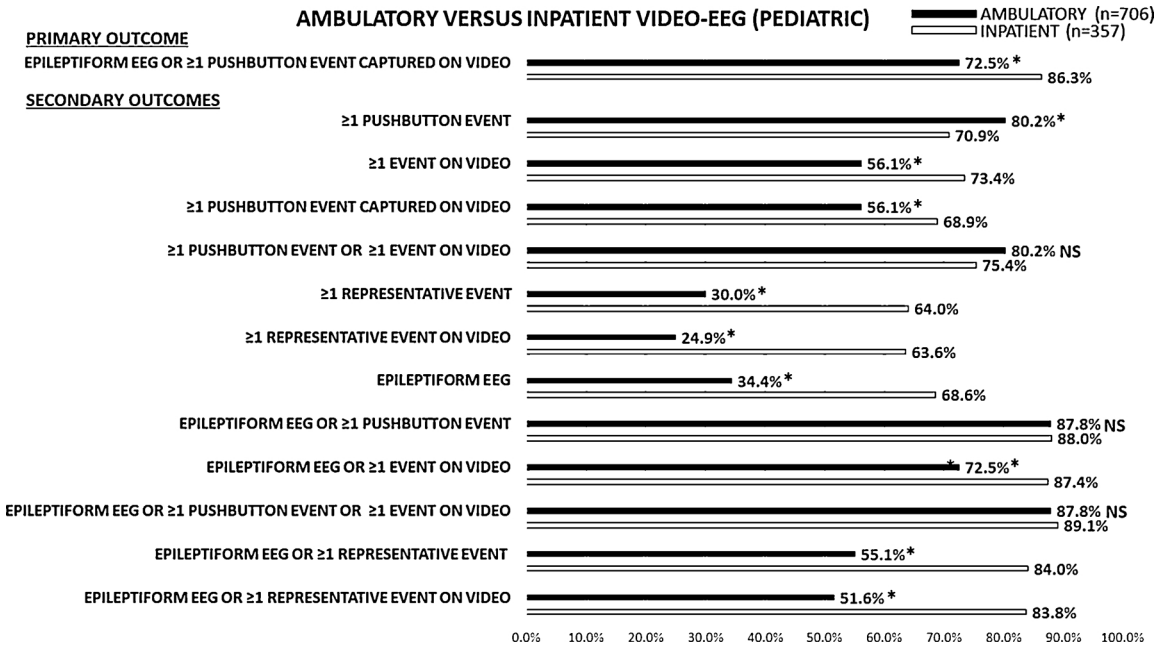

Fig. 3. Outcome of diagnostic ambulatory versus inpatient video-EEG monitoring in pediatric patients. Epileptiform EEG – IEDs (interictal epileptiform discharged) or electrographic seizure reported. Pushbutton event – patient-, family member-, or cohabitant-activated pushbutton. Event on video – patient captured on video during event, including technologist-demarcated event during inpatient video-EEG monitoring. Representative event – patient event diary description shares commonality with clinical history description of events. Events without description in patient event diary were counted as non-representative. Pushbutton events were not counted if accompanying event diary annotation indicated literally that the event was not the patient's habitual event or that the pushbutton was accidental. NS – not statistically significant; *Statistically significant; critical $p < 0.025$ for primary outcome, $p < 0.002$ for secondary outcomes; All p-values generated using Fisher's exact test.

hand, arm, or leg shaking/tremor, muscle twitches, dystonia, "spasms"), *negative motor* defined as paralysis, weakness, or bradykinesia, and *generalized motor* defined as any movement or muscle contraction involving all extremities. A given AVEM event could, therefore, contribute to prevalence of one or more symptom categories. Because our methodology relied on patient event diary descriptions as opposed to epileptologist review of event video-recordings, we were not able to classify AVEM events according to existing epileptic [10] and nonepileptic [11] seizure semiology classifications. Table 3 compares prevalence of each symptom category in AVEM pushbutton events by age-group (adult vs. pediatrics). *Behavioral/autonomic/emotional* was the most prevalent symptom group in AVEM recorded events in adult and pediatric samples. Methodological differences in assessment of event symptomatology between AVEM (patient event diary) and inpatient VEM (epileptologist review of event video-recordings) precluded meaningful statistical comparison of event symptomatology between the two modalities of VEM.

3.3. Post-hoc analysis

We considered post-hoc that demonstration of only IEDs during AVEM, without any video-captured pushbutton events, may be less clinically meaningful if preceded by a routine (≤60 min) EEG that had also been positive for IEDs, or if patient had a documented history of epilepsy prior to AVEM referral. To estimate prevalence of the first of these two scenarios in our ambulatory sample, we sought documentation pertaining to routine EEG performed prior to each AVEM in our sample. We found that 8880 (96.3%) AVEM recordings in our sample had accompanying documentation of a prior routine EEG, of which 1186 (13.4%) were reported as demonstrating IEDs. We determined that of the 743 (8.1%) AVEM recordings that demonstrated only IEDs and did not capture a pushbutton event on video, 314 (42.3%) were preceded by a routine EEG that had also demonstrated IEDs, yielding only a 3.4% (314/9221) prevalence of the first of the above two scenarios in our AVEM sample. In addition, we found that 277 (37.3%) of the 743 ambulatory recordings that demonstrated only IEDs and did not capture at least one pushbutton event were associated with a documented history of epilepsy prior to 'new-onset' or 'breakthrough' events for which AVEM referral had been made, yielding only a 3.0% (277/9221) prevalence of the second of the above two scenarios in our AVEM sample.

Also, post-hoc, we compared symptomatology of video-recorded pushbutton events in AVEM records that were with versus without IEDs, excluding records that demonstrated electrographic seizure. We found that AVEM recordings with only IEDs had 4.1% higher prevalence of *loss of awareness/consciousness* (12.2% vs. 8.1%, $p = 0.005$) and 6.3% lower prevalence of *behavioral/autonomic/emotional* (50.8% vs 57.1%, $p = 0.011$) symptoms in video-recorded pushbutton events than AVEM recordings without any epileptiform activity. Prevalence of each of the remaining five symptom categories did not statistically significantly differ between these two subgroups of ambulatory recordings. Finally, we appreciated post-hoc that age-group stratification of comparisons between VEM modalities was necessary statistically, because our adult AVEM sample was ˜12 times larger than our pediatric AVEM sample, and our adult inpatient VEM sample was ˜5 times smaller than our pediatric inpatient VEM sample.

Finally, post-hoc, we used multivariable logistic regression to re-evaluate statistical significance of primary and secondary outcome measure comparisons between AVEM and inpatient VEM after controlling for patient age (years) and duration (days) of video-EEG monitoring. After controlling for age and monitoring duration our primary outcome comparison between AVEM and inpatient VEM became statistically significant ($p < 0.001$). Additionally, four secondary outcome comparisons changed from nonsignificant to significant (Adult: ≥1 pushbutton event or ≥1 event on video [$p < 0.001$], epileptiform EEG or ≥1 pushbutton event or ≥1 event on video [$p < 0.005$]; Pediatric: epileptiform EEG or ≥1 pushbutton event [$p = 0.026$], epileptiform EEG or ≥1 pushbutton event or ≥1 event on video

Table 2
Ambulatory versus inpatient video-EEG monitoring and adult versus pediatric samples.

Ambulatory versus inpatient video-EEG monitoring	Adult	Pediatric
Sample		
% Women	64.3 vs 60.8 (0.556)	46.3 vs 43.7 (0.434)
Mean age in years	53.6 vs 45.0 (< 0.001)	10.7 vs 8.5 (< 0.001)
Days of monitoring	3.0 vs 4.3 (< 0.001)	2.8 vs 1.8 (< 0.001)
Mean number of pushbutton events	5.6 vs 0.3 (< 0.001)	6.4 vs 9.5 (0.483)
Mean number of events on video	2.6 vs 2.3 (0.045)	2.6 vs 11.9 (< 0.001)
Mean number of pushbutton events per day	1.8 vs 0.1 (< 0.001)	2.4 vs 6.5 (0.011)
Mean number of events on video per day	0.8 vs 0.6 (0.448)	1.0 vs 8.1 (< 0.001)
Outcome measures (%)		
Epileptiform EEG or ≥1 pushbutton captured on video	61.7 vs 54.4 (0.201)	72.5 vs 86.3 (< 0.001)
≥1 pushbutton	74.7 vs 15.2 (< 0.001)	80.2 vs 70.9 (0.001)
≥1 event on video	53.6 vs 70.9 (0.002)	56.1 vs 73.4 (< 0.001)
≥1 pushbutton captured on video	53.6 vs 15.2 (< 0.001)	56.1 vs 68.9 (< 0.001)
≥1 pushbutton or ≥1 event on video	74.7 vs 70.9 (0.436)	80.2 vs 75.4 (0.082)
≥1 representative event	33.8 vs 65.8 (< 0.001)	30.0 vs 64.0 (< 0.001)
≥1 representative event on video	28.2 vs 65.8 (< 0.001)	24.9 vs 63.6 (< 0.001)
Epileptiform EEG	16.6 vs 48.1 (< 0.001)	34.4 vs 68.6 (< 0.001)
Epileptiform EEG or ≥1 pushbutton event	79.4 vs 54.4 (< 0.001)	87.8 vs 88.0 (1.000)
Epileptiform EEG or ≥1 event on video	61.7 vs 78.5 (0.002)	72.5 vs 87.4 (< 0.001)
Epileptiform EEG or ≥1 pushbutton or ≥1 event on video	79.4 vs. 78.5 (0.889)	87.8 vs 89.1 (0.614)
Epileptiform EEG or ≥1 representative event	44.9 vs 76.0 (< 0.001)	55.1 vs 84.0 (< 0.001)
Epileptiform EEG or ≥1 representative event on video	40.4 vs 76.0 (< 0.001)	51.6 vs 83.8 (< 0.001)
Adult versus pediatric video-EEG monitoring	**AVEM**	**Inpatient VEM**
Descriptive variables		
% Women	64.3 vs 46.3 (< 0.001)	60.8 vs 43.7 (0.006)
Mean age in years	53.6 vs 10.7 (< 0.001)	45.0 vs 8.5 (< 0.001)
Days of monitoring	3.0 vs 2.8 (< 0.001)	4.3 vs 1.8 (< 0.001)
Mean number of pushbutton events	5.6 vs 6.4 (0.006)	0.3 vs 9.5 (< 0.001)
Mean number of events on video	2.6 vs 2.6 (0.352)	2.3 vs 11.9 (< 0.001)
Mean number of pushbutton events per day	1.8 vs 2.4 (< 0.001)	0.1 vs 6.5 (< 0.001)
Mean number of events on video per day	0.8 vs 1.0 (0.103)	0.6 vs 8.1 (< 0.001)
Outcome measures (%)		
Epileptiform EEG or ≥1 pushbutton captured on video	61.7 vs 72.5 (< 0.001)	54.4 vs 86.3 (< 0.001)
≥1 pushbutton	74.7 vs 80.2 (0.001)	15.2 vs 70.9 (< 0.001)
≥1 event on video	53.6 vs 56.1 (0.209)	70.9 vs 73.4 (0.675)
≥1 pushbutton captured on video	53.6 vs 56.1 (0.209)	15.2 VS 68.9 (< 0.001)
≥1 pushbutton or ≥1 event on video	74.7 vs 80.2 (0.001)	70.9 vs 75.4 (0.396)
≥1 representative event	33.8 vs 30.0 (0.042)	65.8 vs 64.0 (0.797)
≥1 representative event on video	28.2 vs 24.9 (0.061)	65.8 vs 63.6 (0.796)
Epileptiform EEG	16.6 vs 34.4 (< 0.001)	48.1 vs 68.6 (0.001)
Epileptiform EEG or ≥1 pushbutton event	79.4 vs 87.8 (< 0.001)	54.4 vs 88.0 (< 0.001)
Epileptiform EEG or ≥1 event on video	61.7 vs 72.5 (< 0.001)	78.5 vs 87.4 (0.050)
Epileptiform EEG or ≥1 pushbutton or ≥1 event on video	79.4 vs 87.8 (< 0.001)	78.5 vs 89.1 (0.015)
Epileptiform EEG or ≥1 representative event	44.9 vs 55.1 (< 0.001)	76.0 vs 84.0 (0.101)
Epileptiform EEG or ≥1 representative event on video	40.4 vs 51.6 (< 0.001)	76.0 vs 83.8 (0.105)

P-values were generated using Fisher's exact test for percentages and Mann-Whitney U-test for continuous variables.

Table 3
Event diary symptomatology during ambulatory video-EEG monitoring.

Event diary symptomatology (%)	Adult vs. Pediatric
Sensory	19.7 vs 8.2 (< 0.001)
Behavioral/autonomic/emotional	56.0 vs 39.4 (< 0.001)
Cognitive	10.4 vs 5.3 (0.003)
Loss of awareness/consciousness	7.9 vs 16.9 (< 0.001)
Focal motor	22.4 vs 25.3 (0.237)
Negative motor	3.7 vs 4.4 (0.540)
Generalized motor	6.5 vs 10.0 (< 0.020)

[p < 0.013]), and four comparisons changed from significant to non-significant (Adult: ≥1 event on video [p = 0.247], epileptiform EEG or ≥1 event on video [p = 0.182]; Pediatric: ≥1 pushbutton event [p = 0.784], ≥1 pushbutton event or ≥1 event on video [p = 0.239].

4. Discussion

Our study confirms on a larger scale results of previous studies [2,5] of AVEM utility for non-urgent and non-surgical evaluation of events. Within the limitations of the current methodology AVEM and inpatient VEM appeared similar on selected outcomes, consistent with prior adult [3,4] and pediatric [12,13] VEM studies, although in our study inpatient VEM captured more confirmed “representative” events than AVEM. Nevertheless, absent within-sample temporal sequencing of AVEM followed by inpatient VEM the present study’s capacity to compare usefulness of the two modalities of diagnostic VEM is limited. Other noteworthy limitations of our study include that it is retrospective and that our data was gathered via review of VEM reports, as opposed to review of actual video-EEG recordings. Our primary outcome measure was significantly higher in children than in adults in both modalities of VEM, partly reflecting that children, on average, appear to manifest more events per day of VEM than adults whether monitored in hospital or at home. Parent/caregiver participation in pushbutton activation may also account for higher outcomes in children in our study. Number of events recorded during AVEM in our study was less than that reported in prior studies [3], perhaps reflecting a lower event frequency threshold for including AVEM as part of diagnostic workup in our study population. We opted to use rate of video-recorded events and epileptiform discharges as outcome measures instead of ‘diagnosis’ because due to AVEM documentation deficiencies and

limitations of our study design (no access to video-recordings and post-AVEM clinical notes) diagnosis could not be accurately ascertained, particularly in events without EEG seizure pattern (e.g., simple partial seizures, syncope, panic attacks). On the other hand, successful video-recording of event and knowledge of presence versus absence of EEG epileptiform discharges are elements that can be determined more objectively from AVEM reports, and form the basis for interpreting clinician to make a diagnosis.

In 30.6% of our AVEM sample there was lack of patient documentation to describe at least one pushbutton event, partially explaining why our AVEM outcomes lagged behind our inpatient VEM outcomes by ~30% in virtually all of our outcome measures that considered only 'representative' events. We did not have access to clinician follow-up notes after AVEM, which might have explained what transpired during pushbutton events that were without description in the event diaries. Prior research supports the notion that AVEM and inpatient VEM are not indifferent in their capacity to capture events that are representative of patients' typical events [13]. More importantly, in AVEM, pushbutton activation is patient-driven, whereby patients and caregivers understand that the purpose of wearing electronic headgear for multiple days and having stationary video-camera(s) setup in home is to record paroxysmal events that will subsequently be analyzed by a clinician with expertise in VEM. It follows that patient-activated pushbutton events during AVEM represent paroxysmal events (or symptomatology) which patient has deemed to be of clinical concern and expects subsequent clinician review of the events. In other words, all patient-activated pushbutton events during AVEM, by definition, have clinical value; relying only on patient and eyewitness historical accounts, known to be unreliable [15], would likely underestimate the true "habitual-ness" of an event. Furthermore, patients not documenting symptomatology during an event could well indicate their belief that documentation is unnecessary because the event is, indeed, habitual and representative of what was described to referring clinician during clinical encounter prior to AVEM. Nevertheless, our results may also underscore a need to educate and instruct patients undergoing AVEM and their cohabitants on the importance of proactively participating in documentation of description of pushbutton events. Information bias may have confounded our symptomatology assessment during AVEM, as we characterized AVEM pushbutton event symptomatology in our study using patient self-reported written diary, again, known to be unreliable [6,15,16]. This is typically less of an issue with inpatient VEM, wherein epileptologists and EEG technologists work in conjunction, interacting with patients and employing audio-recording, to characterize pushbutton event symptomatology/semiology.

Consistent with prior literature, we found a low rate (0.3%) of uninterpretable AVEM due to artifact or degradation (muscle > electrode > movement); [3,4,17] however, this result must be interpreted with caution, as it is not to say that the remaining 99.7% of AVEM records in our sample were without artifact or degradation, or were of quality comparable to inpatient VEM. Rather, the remaining 99.7% of AVEM records may have been partially obscured by artifact and degradation, likely more so than expected with inpatient VEM, but only to a degree that still allowed for interpreting neurologist to "confidently" rule out epileptiform discharges. Although remote monitoring every two hours permitted correction of video and electrode malfunction in our AVEM sample, our study design precluded review of event video-recordings to ascertain the impact of remote monitoring on video and EEG quality.

A salient finding in our study is that 98% of AVEM recordings that captured a pushbutton event on video did not demonstrate any EEG seizure pattern, while over half of adult and pediatric inpatient samples that captured a pushbutton event on video demonstrated an EEG correlate to at least one video-recorded event. Moreover, 15% of the ambulatory recordings that were without seizure pattern demonstrated IEDs, 63% of which were without a documented history of epilepsy. In post-hoc analysis event phenomenology did not clinically significantly differ between ambulatory recordings with and without IEDs. It is plausible that nonepileptic events in the context of IEDs could indicate comorbid non-epileptic events and epilepsy [18], or, consistent with higher prevalence of sensory/experiential event phenomenology in our ambulatory sample (see post-hoc analysis), could represent epileptic seizures with an electrographic correlate that is too subtle to be detected by scalp EEG recording [19]. Another possible explanation is that events without EEG correlate, but with IEDs, may not fully represent the epileptic seizures that these patients may have been exhibiting prior to VEM referral, particularly if their epileptic disorder had manifested in a manner that rendered patients unaware of their seizures. Instances in which epileptic seizures may go unnoticed by patients and their cohabitants include, for example, seizures that occur solely during sleep [20], subclinical 'electrographic' seizures [19], or brief non-motor seizures that manifest with amnesia or loss of awareness [21]. In these instances, patients may only report subtler interictal symptoms that per se may not be seizures, but might cue the clinician to consider an underlying epileptic disorder, prompting referral for VEM that subsequently may demonstrate IEDs as the only objective evidence of an underlying epileptic disorder. IEDs reported during AVEM could also result from false-positive EEG interpretation (i.e., overinterpretation) [22], the rate of which is challenging to measure because EEG interpretation is subject to interrater variability, whether ambulatory [17] or inpatient [14], without a truly objective gold-standard with which to compare.

Because inpatient VEM samples in our study were derived from only two epilepsy centers, generalizability of our inpatient VEM outcomes may be limited. Nevertheless, our inpatient VEM outcomes were comparable to outcomes reported in prior studies at other epilepsy centers [23–26]. AVEM documentation in our study sample, particularly clinical histories and event descriptions, lacked the detail and structure akin to inpatient VEM documentation generated at the two collaborating epilepsy centers, a potential source of information bias. For example, frequency of events was missing in 91.5% of our ambulatory sample, and time between last event and onset of VEM recording was not found in 86.8% of our ambulatory sample. Furthermore, we did not have access to follow-up clinician notes to ascertain actual (as opposed to expected) impact of AVEM on clinical decision-making. Although these documentation limitations do not appear to lessen the validity of our study outcomes, these may demonstrate the need to develop national standards for AVEM documentation and reporting.

In summary, AVEM appears to be a useful method for non-urgent and non-surgical evaluation of paroxysmal events, that may be considered when inpatient level-of-care is not medically necessary. AVEM may potentially circumvent some of the high-cost, reduced access, delay, and inconvenience burdens associated with inpatient VEM [1,3]. Moreover, AVEM may be of added benefit to patients who report seizures or events resembling epilepsy that occur in certain environments or with specific triggers that may not be replicated in the hospital setting [27]. Hospital setting may be medically necessary for diagnostic evaluation of events when acute medical intervention is potentially needed (e.g., prolonged seizures), when additional seizure testing is required (such as ictal SPECT, semiology assessment that cannot be reliably performed at home), or when diagnostic plan-of-care includes physician-guided antiepileptic medication reduction in an attempt to bring on a seizure during VEM [28]. Inpatient VEM should remain the accepted gold-standard diagnostic test for evaluating events and should be the mainstay of evaluation at academic epilepsy centers. However, AVEM may be more appropriate for diagnostic assessment of events in community neurology healthcare settings, followed by referral of those found to have an active epileptic disorder to inpatient VEM centers for consideration of a more interactive, audio-recorded, epileptologist-driven video-EEG evaluation of seizures. Bearing in mind potential for EEG overinterpretation, referral to epilepsy centers may particularly be considered when patients with events are diagnosed with epilepsy solely based on AVEM IEDs.

Declaration of interest

Dr. Jeremy D. Slater (J.D.S.) acquired full-time employment as chief medical officer at The Alliance Family of Companies (AFOC), the present study's collaborating ambulatory-EEG testing facility, on January 1, 2018, which was approximately five months after inception of this study, and approximately two months after completion of outcome analysis.

The remaining authors have no conflicts of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

We kindly acknowledge Laura Tahri and her team of EEG technologists at the collaborating ambulatory-EEG facility for facilitating data acquisition for this study.

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