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Indications and yield of ambulatory EEG recordings

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ABSTRACT

Objective. To study the yield of prolonged ambulatory electroencephalogram (aEEG). **Methods.** A retrospective chart review of all patients who underwent aEEG studies between 2013 and 2017 was performed. Reasons for aEEG were classified into five categories: detection of interictal epileptiform discharges (IEDs), capturing clinical events, detection of unrecognized seizures, monitoring IEDs during treatment, and unclassifiable. Ambulatory EEG reports were reviewed to evaluate whether the study answered the clinical question.

Results. A total of 1,264 patients were included. Forty studies were excluded for incomplete data and 234 for being a repeat study. The average number of recording days was 1.57 ± 0.73 . Based on initial clinical evaluation, patients carried the following presumptive diagnosis: 61% epilepsy, 11% single unprovoked or acute symptomatic seizure and 28% non-epileptic paroxysmal events (PEs). Overall, focal IEDs were seen in 16.1% of studies, generalized IEDs in 10.8%, focal seizures in 4.1%, and generalized seizures in 1.9%. The most frequent reason for ordering aEEG was to detect IEDs for diagnostic purposes (48.1%). For this indication, additional information was provided by the aEEG in 19.1% of cases (58.6% focal IEDs, 33.5% generalized IEDs, 7.9% seizures without IEDs). Ambulatory EEG was ordered with the intent to capture and characterize clinical events in 18.9%, mostly in patients who reported daily or weekly events. In these, aEEG captured either epileptic seizures or PEs in 102 (42.7%) of the studies (83.3% PEs, 16.7% epileptic seizures). Ambulatory EEG was ordered to evaluate unrecognized seizures in 17.8% of patients, and electrographic seizures were identified in 13.3% of these studies. Significance. The yield of aEEG varies based on the indication for the study. Ambulatory EEG can be a useful tool for recording IEDs in the outpatient setting and in a select group of patients to capture clinical events or unrecognized seizures.

Key words: ambulatory electroencephalogram; prolonged electroencephalogram; seizures; epilepsy; diagnostic yield; interictal epileptiform discharges

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Electroencephalogram (EEG) is an important diagnostic tool for epilepsy evaluation, assessment of treatment response, and characterization of habitual events. The diagnostic yield of routine EEG to capture IEDs is only 12-44% and improved by the presence of sleep [1, 2]. Prolonged EEGs are an alternative to serial EEGs to increase diagnostic yield [3]. Inpatient long-term video-EEG in the

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epilepsy monitoring unit (EMU) has been the diagnostic gold standard for characterization of patients' events and for a definite diagnosis, facilitated by medication taper and proper staffing to assure safety and allow seizure testing. However, the EMU has many disadvantages including the need for inpatient admission which can disrupt patients' lives, high cost, long waiting times, and is typically reserved for patients with longstanding intractable seizures [4, 5].

In recent years, the use of prolonged ambulatory EEG (aEEG) monitoring has increased given the advancements in technology. Ambulatory EEG can be helpful in the diagnosis of an epilepsy syndrome after an inconclusive routine EEG and can be used to characterize frequent events, which do not require medication taper [6]. Additionally, aEEG can be helpful in evaluating patients' response to treatment and support management decisions prior to medication taper [6, 7].

There is scarce knowledge on the different indications and diagnostic yield of aEEG as a complementary diagnostic tool in a tertiary epilepsy center. Thus, we aimed to describe the different reasons for ordering aEEGs and the diagnostic yield for each indication.

Methods

Participants

This was a single-center, retrospective cohort study performed at Northwestern Memorial Hospital, a tertiary care center in Chicago, IL. All participants were >18 years old; no children were included in this study. All prolonged (> 24 hours) aEEGs read at our center between January 1, 2013 and December 31, 2017 were included in the study. Ambulatory EEG studies were either performed at our outpatient laboratory or through outside agencies. If a patient had multiple aEEGs during the study period, only the first aEEG was included in the study in order to minimize any sampling bias. Additionally, studies with incomplete clinical data were excluded. The Northwestern University Institutional Review Board approved this study. The need for consent was waived due to the retrospective nature of the project.

Electroencephalogram

Ambulatory EEGs were obtained by using 19 scalp electrodes placed according to the international 10-20 system as well as an EKG channel. Patients were given a push button and instructed to use it if they experienced their habitual events. Additionally, patients were given a log to document the time and nature of their events. Ambulatory EEGs were obtained using either Nihon Kohden (Tokyo, Japan), Lifelines iEEG (Hants, UK), or Digi Cloud Viewer version 4.0 (Digi, Hopkins, MN) acquisition systems. All studies were reviewed by a clinical neurophysiology and/or epilepsy board-certified physician at our institution. EEGs were completely reviewed at 10 seconds per page, on bipolar montage, with other montages available for review and verification, and studies were classified as normal or abnormal. Abnormal studies were separated into non-epileptiform findings (regional, lateralized or generalized slowing and asymmetry), epileptiform findings (regional or generalized discharges), electrographic seizure activity (focal or generalized), and paroxysmal events (PEs) with no EEG change.

Data analysis

The majority of patients were seen by a board-certified epilepsy specialist at our tertiary epilepsy center. Patients' charts were reviewed and the following information was extracted for each patient: sex, age at time of seizure onset, age at time of the study, clinical diagnosis prior to aEEG, frequency of events, number of anti-seizure medications, results of previous EEGs and MRI, and duration of aEEG. Charts were reviewed and the reason for ordering the aEEG was classified into five categories:

- interictal epileptiform discharges (IEDs) to diagnose the epilepsy syndrome;
- capturing clinical events;
- detection of unrecognized seizures (to better understand seizure burden in uncontrolled patients or to detect unrecognized seizures in patients reporting to be seizure-free);
- monitoring IEDs during treatment (quantification of known IEDs or prior to medication discontinuation);
- and unclassifiable reason for the study. Ambulatory EEG reports were reviewed to evaluate whether the study answered the clinical question.

Statistical analyses

Continuous variables were summarized using means and standard deviations and categorical variables as frequencies and percentages. Student's t-test estimated associations between continuous variables of equal variances, and Welch's t-test estimated associations between continuous variables of unequal variances. Chi square test estimated associations between categorical variables, and Fisher's exact test was used to estimate associations between categorical variables with expected frequencies of less than 5. Stata version 16 (College Station, TX) was used for all statistical analyses.

Data availability

Anonymized data is available on request from a qualified investigator.

Results

Patient selection and demographics

A total of 1,538 studies were performed during the study period. Forty studies were excluded for incomplete data and 234 for being a repeat study (*supplementary figure 1*). A total of 1,264 patients (1,983 recording days) were included. The number of average recording days was 1.57 ± 0.73 . *Table 1* shows patient demographics, as well as clinical diagnosis

prior to obtaining the aEEG, seizure frequency, and number of anti-seizure medications (ASMs). The number of patients who were on ASMs did not differ significantly according to indication (*table 1*).

Indications and diagnostic yield based on study indication

The most frequent indication for aEEG was evaluating for IEDs for diagnostic purposes (n=608, 48.1%) (*supplementary figure 1*). Of those 608 patients, 339 (55.8%) had a normal routine EEG prior to their aEEG. The second most common indication was characterization of frequent clinical events (n=239; 18.9%), followed by detection of unrecognized seizures (n=225; 17.8%), and lastly quantification of epileptiform discharges (n=183; 14.5%). Nine

▼ **Table 1.** Demographics and clinical diagnosis of the entire cohort (*n*=1,264 patients).

| Sex (female) | 58.7% (742) |
|--|-----------------------------------|
| Age at seizure onset * | Average 34.4 years ± 20.9 (0-90) |
| Age at time of aEEG study | Average 43.7 years ± 17.8 (15-93) |
| Epilepsy classification prior to aEEG study | |
| Focal epilepsy | 34.1% (431) |
| Generalized epilepsy | 11.4% (144) |
| Multifocal, symptomatic generalized | 2.2% (28) |
| Epilepsy, unclassifiable | 13.3% (168) |
| Paroxysmal events, syncope | 28.0% (354) |
| Single (likely epileptic) unprovoked seizure | 5.2% (66) |
| Acute symptomatic seizures or status | 5.8% (73) |
| Seizure frequency | |
| Seizure-free/single seizure | 38.0% (481) |
| Daily | 7.7% (97) |
| Weekly | 11.1% (140) |
| Monthly | 18.8% (238) |
| Yearly | 11.4% (144) |
| Less than yearly | 4.2% (53) |
| Unclear | 8.8% (111) |
| Number ASMs | Average: 1.1 ± 1.0 (0-6) |
| ASM by indication | On ASM; total: 726 (62%) p <0.001 |
| ED detection | 382 (63%) |
| Characterization of clinical events | 145 (60.7%) |
| Detection of unrecognized seizures | 217 (96%) |
| IED monitoring | 172 (94%) |

ASM: antiseizure medication; IED: interictal epileptiform discharge. * if stated "childhood", estimated to be age 8; if stated "infancy", estimated to be 0; the age of eight patients was unknown.



Figure 1. Breakdown of abnormal ambulatory EEG results by indication. Each graph depicts the breakdown of all abnormal results noted on aEEG for each indication. (A) IED detection; (B) characterization of clinical events; (C) detection of unrecognized seizures; (D) IED monitoring. The red box in each graph shows the diagnostic findings (*i.e.* the number of studies that answered the clinical question). (Gen: generalized; IED: interictal epileptiform discharges; PE: paroxysmal events).

(0.7%) of the studies had no clear indication noted in the chart.

In all the studies ordered (1,264), IEDs were seen in 340 studies (26.9%; focal IEDs in 203 [16.1%]) and generalized IEDs in 137 (10.8%)). Electrographic seizures were seen in 76 studies (6%; focal seizures in 52 [4.1%]), generalized seizures in 24 [1.9%]) and paroxysmal events without EEG correlate were captured in 155 patients (12.3%). Overall, of the 1,264 studies, 476 (37.7%) studies were positive, *i.e.* the study revealed IEDs, epileptic seizures, or PE, alone or in combination. We found that our overall yield for aEEG, to answer the specific clinical question, *i.e.* detecting IEDs, capturing clinical events, and evaluating for unrecognized seizures, was 23.1%.

Interictal epileptiform discharges for diagnosis

In the 608 studies ordered to detect IEDs for diagnosis, 116 (19.1%) yielded positive results, defined as a study showing IEDs and/or EEG seizures. In 45 patients, habitual paroxysmal events were recorded without interictal or ictal EEG changes. *Figure 1A* depicts the breakdown of all abnormal findings noted on aEEG

ordered for this indication. *Table 2* shows characteristics of patients who had diagnostic studies and those who did not. Patients with a positive study tended to be younger at onset of spells (27.8 vs. 37.9 years of age) and at the time of study (36.3 vs. 44.2 years of age). The yield for capturing IEDs varied based on the provisional diagnosis prior to aEEG: 39 out of 133 patients (29.3%) with suspected focal epilepsy had IEDs, 19 out of 30 (63.3%) with suspected generalized epilepsy, 33 out of 135 with unclassifiable epilepsy (24.4%), and 15 out of 87 with a single unprovoked, provoked or acute symptomatic seizure (17.2%).

• Change in diagnosis after aEEG

Figure 2A indicates the change in diagnosis after aEEG was performed to capture IED. In 133 patients with a presumed diagnosis of focal epilepsy prior to aEEG, diagnosis was confirmed in 38 (28.6%) and changed to generalized epilepsy in one patient (0.75%). Of 30 patients with presumed generalized epilepsy, the diagnosis was confirmed in 16 patients (53.3%) and changed to focal epilepsy in three patients (10%). Of the 135 patients with unclassifiable epilepsy, aEEG aided in the diagnosis in 33 patients (24.4%): 19 were diagnosed with focal epilepsy and 14 with generalized

▼ **Table 2.** Demographics and clinical information for patients referred for aEEG for the evaluation of IEDs (*n*=608; 48.1%).

| | Diagnostic (<i>n</i> =116) | Non-diagnostic (<i>n</i> =492) | <i>p</i> value |
|-----------------------------|-----------------------------|---------------------------------|----------------|
| Sex (female) | 56.9% (66) | 58.1% (286) | 0.809 |
| Age at onset | 27.8±18.1* | 37.9±20.1 | <0.001 |
| Age at study | 36.3±16.8 | 44.2±17.7 | <0.001 |
| Duration of epilepsy * | 8.5±11.6 | 6.4±10.7 | 0.079 |
| Frequency of events | | | 0.060 |
| Seizure-free/single seizure | 36.2% (42) | 40.4% (199) | |
| Daily | 1.7% (2) | 5.9% (29) | |
| Weekly | 6.9% (8) | 5.7% (28) | |
| Monthly | 29.3% (34) | 18.1% (89) | |
| Yearly | 14.7% (17) | 13.4% (66) | |
| Less than yearly | 6.0% (7) | 6.7% (33) | |
| Unclear | 5.2% (6) | 9.8% (48) | |
| Epilepsy classification | | | <0.001 |
| Focal | 33.6% (39) | 19.1% (94) | |
| IGE | 16.4% (19) | 2.3% (11) | |
| Multifocal/SGE | 0% (0) | 0.4% (2) | |
| Unclassifiable | 28.5% (33) | 20.7% (102) | |
| PE/syncope | 8.6% (10) | 42.9% (211) | |
| Single unprovoked | 9.5% (11) | 7.7% (38) | |
| Acute symptomatic | 3.4% (4) | 6.9% (34) | |
| Number of AEDs | 1.1±0.76 | 0.75±0.78 | <0.001 |

* age at onset unknown in four patients.



Figure 2. Change in diagnosis after aEEG was performed to capture IEDs (A), and for event capture (B). The x-axis shows the presumed diagnosis prior to aEEG, and the y-axis depicts % of confirmatory and non-confirmatory findings (Gen: generalized; IED: interictal epileptiform discharge; MF: multifocal epilepsy; PE: paroxysmal event; SGE: symptomatic generalized epilepsy; Sz: seizure; Unc: unclassified epilepsy).

epilepsy. Of the 49 patients with a single unprovoked seizure, aEEG aided in making an epilepsy diagnosis in 11 patients (22.4%): six were diagnosed with focal epilepsy, and five with generalized epilepsy. Of the 38 patients with acute symptomatic or provoked seizures, four (10.5%) of the aEEGs showed a predisposition for epilepsy: two studies showed focal IEDs and two studies showed generalized IEDs.

In 221 patients with presumed paroxysmal events, 10 (4.5%) had EEG findings supportive of epilepsy after the aEEG study. Of these, six had focal IEDs, two had focal IEDs and focal seizures, one had a focal seizure but no IEDs, and one had generalized IEDs. In nine out of those 10 patients, additional information was available during follow-up visits to confirm a diagnosis of epilepsy. Only one patient was suspected to have non-epileptic events despite the presence of IEDs on aEEG.

Characterization of clinical events

In 239 patients (18.9%), aEEG was ordered to characterize the patients' frequent clinical events. Ambulatory EEG recorded a clinical event of interest in 102 studies (42.7%) (*supplementary table 1*). The most common finding was paroxysmal events without EEG change seen in 86 studies (36%). *Figure 1B* depicts the breakdown of all abnormal findings noted on aEEG ordered for this indication.

We found a statistically significant difference in the seizure frequency overall between those who had diagnostic tests and those who did not (*supplementary table 1*). In patients who had diagnostic studies, 65 patients (63.7%) reported daily or weekly seizures, compared to 60 (43.8%) of those who had a non-diagnostic test. Overall, in patients who had aEEG ordered to capture events, 52.3% of patients reported daily or weekly events. In contrast, only 18.8% of the whole cohort of patients and 11.0% of patients who had an aEEG to evaluate IEDs reported daily or weekly events.

• Change in diagnosis after aEEG

Figure 2B indicates the change in diagnosis after aEEG was performed for event capture. Patients with presumed PEs represented the largest cohort (123 patients out of 239 patients). Out of 123 patients with suspected PEs, 51 (41.5%) had the diagnosis confirmed after recording their events and six (4.9%) had the diagnosis changed to focal epilepsy (four had focal IEDs and two had focal IEDs and focal seizures). One hundred patients with presumed epilepsy were sent for event capture. Of the 73 patients with suspected focal epilepsy, 13 (17.8%) had their diagnosis confirmed (eight had focal IEDs and focal seizures, one had focal seizures only, and four had focal IEDs only), one (1.4%) had the diagnosis changed to generalized epilepsy after seeing generalized IEDs, and 11 (15.1%)

changed from focal epilepsy to PEs after recording their events on aEEG with no EEG correlate. Of 27 patients with presumed generalized or multifocal epilepsy, 11 (40.7%) had their diagnosis confirmed (three had seizures and generalized IEDs, seven had generalized IEDs only, and one had seizures only). Of the 11 patients with unclassifiable epilepsy, three (27.3%) were diagnosed with focal epilepsy (one had focal seizures and IEDs and two had focal IEDs only) and two (18.2%) had their diagnosis changed from epilepsy to non-epileptic events after capturing their habitual spells.

Detection of unrecognized seizures

Out of 225 patients who underwent aEEG to evaluate unrecognized seizures, EEG seizures were seen in 30 studies (13.3%) (*table 3*). *Figure 1C* depicts the breakdown of all abnormal findings noted on aEEG ordered for this indication. The yield was higher in patients with suspected generalized or multifocal epilepsy: of 34 patients, nine (26.5%) studies recorded seizures. Of the 166 patients with presumed focal epilepsy, seizures were seen in 20 (12.0%) studies. Only four electrographic seizures were seen in the 99 patients who were reportedly seizure-free (4%).

Monitoring IEDs during treatment

Ambulatory EEG was ordered to assess IEDs during treatment with ASMs in 183 patients. This included patients prior to medication discontinuation with seizures in remission or after an acute symptomatic seizure, or to assess response of treatment on IEDs (e.g. clearance for driving in patients with generalized epilepsy). Self-reported seizure freedom was common in this group (112 patients; 61.2%). Ambulatory EEG did not show IEDs in 103 patients (56.3%); in the remaining 80 patients (43.7%), IEDs were captured, and in 10 of those patients, seizures were also recorded. *Figure 1D* depicts the breakdown of all abnormal findings noted on aEEG ordered for this indication.

Seventy-five patients (41%) had a confirmed diagnosis of generalized epilepsy; of those, 50 (66.7%) had IEDs captured on aEEG. Fifty-seven (31.1%) patients were diagnosed with focal epilepsy; of those, 19 (33.3%) had IEDs on aEEG. Twenty-four (13.1%) patients had an acute symptomatic seizure; of those, IEDs were captured in four (16.7%).

Unclassifiable reason for the study

Of the nine studies that had no clear indication noted in the chart, one study recorded a PE, one study recorded a PE and IEDs, and the remaining seven studies were normal.

Discussion

Prolonged aEEG provides a cost effective and convenient alternative to repeat outpatient EEGs and prolonged inpatient EEG monitoring, particularly for patients with a new diagnosis of epilepsy or with a history of frequent events. This is a large-scale study that describes the various indications for ordering aEEG and their yield.

We found that our overall yield for aEEG, to answer the clinical question, *i.e.* detecting IEDs, capturing clinical events, and evaluating for unrecognized seizures, was 23.1%. This yield is lower than that reported in previously published studies, at 68-72% [5, 8]. This could be due to multiple factors, including the smaller sample size in these studies compared to our large sample size of 1,264 patients. Additionally, the average recording time was shorter in our study (average: 37.7 hours) compared to 72-96 hours in one study [8]. Furthermore, we reported yield by indication, rather than the overall positive results reported in some studies [8]. Dash et al. demonstrated a yield of 72%; in their study, however, 57% of their patients were on ASMs at the time of the study compared to 72.9% of our patient population, which could have contributed to the lower yield [8]. In addition, their patient population reported frequent events, occurring at least monthly, with an average of 14.8 events per month [8]. In our study, 53.6% of the patients reported either a single event, seizure freedom, yearly seizures, or less than yearly events. It is important to note that given the retrospective nature of the study, the detection rates in our cohort do not reflect true specificity and sensitivity and should not be interpreted as such. Additionally, our patient cohort was diverse, with some patients being on ASMs, and many having single or infrequent events. Evaluating for true specificity and sensitivity of aEEG by indication is best achieved by a prospective trial in a uniform population.

In our cohort, the most common indication for ordering aEEG was for diagnostic purposes, to evaluate IEDs. For this indication, aEEG showed IEDs in 19.1% of the studies ordered, similar to a recently published study showing a yield of 18% [9]. The likelihood of capturing IEDs varied based on the suspected epilepsy diagnosis prior to aEEG, with the highest yield found for generalized epilepsy. We also noted that a large percentage (42.9%) of patients who had non-diagnostic studies had a clinically low suspicion for having epileptic events prior to aEEG, compared to only 8.6% in the group with a diagnostic study. It is important to note that epilepsy is a clinical diagnosis and should not rely only on normal or "abnormal" test results due to the risk of having "over-reads" of EEGs [10-12]. Over-reading of IEDs on aEEG can result in erroneous epilepsy diagnosis which can be difficult to reverse, and thus an abnormal EEG read should be interpreted within the clinical context [11, 13]. In our cohort, only 10 out of 221 patients with suspected non-epileptic events had IEDs captured on aEEG and epilepsy diagnosis was corroborated by further testing in nine out of these 10 patients, leaving only one patient with a "false positive" aEEG. This demonstrates the low incidence of over-reading EEGs at a tertiary center where readers have extensive EEG fellowship training. In addition, it is important to note that a very small percentage of patients with IEDs on their EEG may not develop epilepsy, which again highlights the importance of the clinical history and the need for caution interpreting "abnormal" aEEG results [14, 15]. Our study highlights one of the advantages for the diagnostic use of aEEG over repeat outpatient EEGs in that it allows capturing seizures, even in the absence of interictal abnormalities (as seen in 1.5% of our patients), resulting in a definitive diagnosis.

A first unprovoked seizure can result in psychological burden to patients. Patients' and physicians' decision on medical management depends largely on the estimated recurrence risk. Previous studies showed that aEEG increases the yield of detecting IEDs after a normal routine [16]. In our cohort, aEEG captured IEDs in 22.4% of patients with first unprovoked seizures, aiding in making an epilepsy diagnosis and influencing treatment plan. This yield is lower than the previously reported yield of 40% [16]. This difference could be due to the different patient populations as our cohort included adults only [16].

While the most common indication for aEEG is for diagnostic purpose, we found the highest yield for aEEG in characterizing clinical events in patients with frequent spells suspected to be non-epileptic. For this indication, aEEG provided crucial clinical information in about half the referred cases, similar to recently published data [9]. The higher yield for this indication stems from patient selection where more than half of the patients referred for aEEG for this indication reported daily or weekly events (as compared to 18.8% of the entire cohort). The majority of our studies were done without associated video, however, we found that a patient diary was sufficient to make the diagnosis. For rare clinical events, smart phone videos are a useful tool and preferable over event capture with aEEG. A recent study demonstrated that interpretation of smart phone videos by experts increases the accuracy of final diagnosis for both epileptic and non-epileptic events [17]. We noted that the yield to capture events was lower in patients with suspected focal epilepsy compared to those with suspected non-epileptic events. Thus, in patients with suspected focal epilepsy, aEEG can be a useful first step. However, in many patients, admission to an epilepsy monitoring unit for proper testing and tapering of ASMs is warranted, particularly for a pre-surgical evaluation. Ambulatory EEG was ordered to evaluate unrecognized seizures in two distinct populations:

- in patients who reported improvement in seizure frequency or seizure freedom with clinical suspicion that they were not aware of all their seizures in the past; and
- patients who reported frequent clinical seizures in order to better evaluate seizure burden.

We found a low overall yield for detecting seizures for this indication, and seizures were only captured in 13.3% of the studies. In patients who reported being seizure-free or having yearly or less than yearly seizures, aEEG captured seizures in 3.9% of the patients. This is problematic given that many of these patients desire clearance to drive or for occupational safety and aEEG might not be the ideal way to confirm true seizure freedom. Ultimately, a long-term seizure detection device would be the ideal goal [18]. In contrast, aEEG aided in evaluating seizure burden and capturing seizures in 53.8% of patients who reported daily or weekly seizures. In this population, more seizures were captured in patients with generalized or multifocal epilepsy.

Limitations

This study has multiple limitations: first, it was a single-center study and reflects the ordering practice of one cohort of physicians, which can introduce selection bias. Second, follow-up data was not collected, and thus we cannot comment on how the findings from the aEEG study affected clinical care after the study. Deciding whether aEEG resulted in change in medical management is best suitable for a prospective study. Third, our study only included adult patients; inclusion of children could result in different detection rates than reported in our adult cohort. Fourth, aEEG has an increased susceptibility to artifacts (chewing, scratching, tooth brushing) that can limit EEG interpretation or result in over-reading of EEG [19]. Our studies were all read entirely by expert physicians who are board-certified in clinical

▼ **Table 3.** Demographics and clinical information for patients referred for aEEG to evaluate for unrecognized seizures (*n*=225).

| | Diagnostic (n=30) | Non-diagnostic (n=195) | ρ value |
|-----------------------------|-------------------|------------------------|--------------|
| Sex (female) | 56.7% (17) | 54.4% (106) | 0.813 |
| Age at onset | 23.1±18.3 | 35.6±22.0 | 0.001 |
| Age at study | 39.5±17.6 | 47.7±17.9 | 0.019 |
| Duration of epilepsy | 16.4±14.3 | 12.1±13.7 | 0.131 |
| Frequency of events | | | <0.001 |
| Seizure free/Single seizure | 13.3% (4) | 48.7% (95) | |
| Daily | 13.3% (4) | 0% (0) | |
| Weekly | 33.4% (10) | 6.2% (12) | |
| Monthly | 26.7% (8) | 22.1% (43) | |
| Yearly | 3.3% (1) | 13.8% (27) | |
| Less than yearly | 0% (0) | 1.0% (2) | |
| Unclear | 10.0% (3) | 8.2% (16) | |
| Epilepsy classification | | | 0.238 |
| Focal | 66.7% (20) | 74.9% (146) | |
| IGE | 16.7% (5) | 8.7% (17) | |
| Multifocal/SGE | 13.3% (4) | 4.1% (8) | |
| PE/syncope | 0% (0) | 1.5% (3) | |
| Single unprovoked | 0% (0) | 1.5% (3) | |
| Acute symptomatic | 0% (0) | 5.2% (10) | |
| Unclassifiable | 3.3% (1) | 4.1% (8) | |
| Number of AEDs | 2.1±1.1 | 1.7±1.0 | 0.060 |

neurophysiology/epilepsy. Caution should be taken to generalize our findings to studies read by a less trained reader. Fifth, most of our studies were done without associated video. While we found that a patient diary was sufficient to make the diagnosis, there could be added value and detection rate if video were included with all aEEG studies. Sixth. all our studies were performed with standard 10-20 electrodes, and the yield could have been different with the addition of subtemporal electrodes. Finally, we acknowledge that some seizure types do not have a clear scalp EEG correlate (for example, cingulate and orbitofrontal seizures). Thus, a lack of EEG correlate for these patients can be misleading and a clinical and/or video correlation is needed for a diagnosis.

Conclusion

Ambulatory EEG can be a useful tool for capturing IEDs and characterizing frequent clinical events in the outpatient setting without medication withdrawal, given appropriate patient selection. For patients with negative studies or for surgical planning, admission to the epilepsy monitoring unit for safe tapering of seizure medication and appropriate ictal clinical testing may be preferred.

Supplementary data.

Supplementary figure and table are available on the www.epi-lepticdisorders.com website.

Disclosures.

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References

1. Baldin E, Hauser WA, Buchhalter JR, Hesdorffer DC, Ottman R. Yield of epileptiform EEG anormalities in incidente unprovoked seizures: a populations-based study. *Epilepsia* 2014; 55(9): 1389-98.

2. Burkholder DB, Britton JW, Rajasekaran V, Fabris RR, Cherian PJ, Kelly-Williams KM, *et al.* Routine vs extended outpatient EEG for the detection of interictal epileptiform discharges. *Neurology* 2016; 86(16): 1524-30.

3. Modur PN, Rigdon B. Diagnostic yield of sequential routine EEG and extended outpatient video-EEG monitoring. *Clinical Neurophysiol* 2008; 119(1): 190-6. 4. Cascino GD. Video-EEG monitoring in adults. *Epilepsia* 2002; 43: 80-93.

5. Dash D, Hernandez-Ronquillo L, Moien-Afshari F, Tellez-Zenteno JF. Ambulatory EEG: a cost-effective alternative to inpatient video-EEG in adult patients. *Epileptic Disord* 2012; 14(3): 290-7.

6. Seneviratne U, Mohamed A, Cook M, D'Souza W. The utility of ambulatory electroencephalography in routine clinical practice: a critical review. *Epilepsy Res* 2013; 105(1–2): 1-12.

7. Stefan H, Kreiselmeyer G, Kasper B, Graf W, Pauli E, Kurzbuch K, *et al.* Objective quantification of seizure frequency and treatment success via long-term outpatient video-EEG monitoring: a feasibility study. *Seizure* 2011; 20(2): 97-100.

8. Faulkner HJ, Arima H, Mohamed A. The utility of prolonged outpatient ambulatory EEG. *Seizure* 2012; 21(7): 491–5.

9. Syed TU, LaFrance WC Jr, Loddenkemper T, Benbadis S, Slater JD, El-Atrache R, *et al*. Outcome of ambulatory video-EEG monitoring in a ~10,000 patient nationwide cohort. *Seizure* 2019; 66: 104-11.

10. Benbadis SR, Lin, K. Errors in EEG interpretation and misdiagnosis of epilepsy: which EEG patterns are overread? *Eur Neurol* 2008; 59(5): 267-71.

11. Amin U, Benbadis SR. The role of EEG in the erroneous diagnosis of epilepsy. *J Clin Neurophysiol* 2019; 36(4): 294-7.

12. Kang JY, Krauss GL. Normal variants are commonly overread as interictal epileptiform abnormalities. *J Clin Neurophysiol* 2019; 36(4): 257-63.

13. Worrell GA, Lagerlund TD, Buchhalter JR. Role and limitations of routine and ambulatory scalp electroencephalography in diagnosing and managing seizures. *Mayo Clinic Proc* 2002; 77(9): 991-8.

14. Gregory RP, Oates T, Merry RTG. Electroencephalogram epileptiform abnormalities in candidates for aircrew training. *Electroenceph Clin Neurophysiol* 1993; 86(1): 75-7.

15. Sam MC, So EL. Significance of epileptiform discharges in patients without epilepsy in the community. *Epilepsia* 2001; 42(10): 1273-8.

16. Geut I, Weenink S, Knottnerus ILH, van Putten MJAM. Detecting interictal discharges in first seizure patients: ambulatory EEG or EEG after sleep deprivation? *Seizure* 2017; 51: 52-4.

17. Tatum WO, Hirsch LJ, Gelfand MA, Acton EK, LaFrance WC Jr, Duckrow RB, *et al.* Assessment of the predictive value of outpatient smartphone videos for diagnosis of epileptic seizures. *JAMA Neurol* 2020; 32224(5): 593-600.

18. Weisdorf S, Duun-Henriksen J, Kjeldsen MJ, Poulsen FR, Gangstad SW, Kjaer TW. Ultra-long-term subcutaneous home monitoring of epilepsy- 490 days of EEG from nine patients. *Epilepsia* 2019; 60(11): 2204-14.

19. Seneviratne UDW. Ambulatory EEG. *Handb Clin Neurol* 2019: 161-70.

TEST YOURSELF

(1) What are some of the different indications for ambulatory EEG?

(2) What is the most common indication for ambulatory EEG?

(3) Which indication is associated with the highest yield?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".