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Optimal recording duration of ambulatory EEG (aEEG)

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1. Introduction

Ambulatory electroencephalography (aEEG) has been established as a useful tool for differentiating epileptic versus non-epileptic attacks (Lawley et al., 2016, 2015) and is a viable alternative to inpatient video EEG (vEEG) which requires admission (Kandler et al., 2017). It is a cost-effective technique with high diagnostic yield especially for quantifying seizure activity (Dash et al., 2012). With the advent of increased electronic storage capacity in recent years, the duration of aEEG recordings can be increased to 72 h. The diagnostic yield of aEEG with differing durations between 24–72 h has rarely been analyzed (Faulkner et al., 2012a; Tolchin et al., 2017). Our primary aim is to measure the overall capture rate of aEEG to detect epileptiform discharges or seizures at 1, 2, or 3 days of recording. Our secondary aim is to determine how frequently the diagnosis or management was changed as a function of recording duration. We suspected that the yield of aEEG declines after 2 days of recording.

2. Methods

2.1. Study population

At the Stanford Comprehensive Epilepsy Center, a total of 358 consecutive adult aEEG procedure notes for routine clinical care from 2010 to 2017 were retrospectively collected and filtered by a software program. A chart review was performed on each aEEG to investigate indications for the procedure and how the aEEG results directly changed management. AEEG was conducted using the standard 10–20 electrode placement and recorded for at least 20 h. If a patient had multiple aEEGs, only the first one was examined. We then retrospectively reviewed and separated the aEEGs into 3 categories by duration: 1 day (20–30 h), 2 days (30–50 h), and 3 days (50–76 h).

2.2. Variables and definitions

Chart review of the clinical encounter prior to the aEEG was assessed to determine whether the patient had an established diagnosis of epilepsy, established by board-certified epileptologists using the ILAE criteria (Fisher et al., 2014). Indications for the aEEG were tabulated.

For the primary aim of this study, we determined the proportion of the studies which detected epileptic seizures or epileptiform discharges for each of the 3 categories of aEEG durations. A study containing epileptic seizures or epileptiform discharges would qualify as one positive study. For the secondary aim, we counted cases whereby aEEG led to a change in diagnosis and/or management. We reviewed the progress notes, telephone encounters, and patient messages immediately after the aEEG was completed and noted any direct changes in diagnosis and/or management. Direct changes included increased dosages of current anti-seizure drug(s) (ASD), started new ASD, admitted the patient to the hospital, or changed the pre-surgical workup. We also counted cases where epilepsy was newly diagnosed in patients based on aEEG who were not suspected of having epilepsy prior to the recording. We counted cases of detecting non-epileptic events of interest on the aEEG that were not associated with an ictal pattern. Negative studies were aEEGs without any epileptic discharges or seizures detected. Note that this study analyzed the cumulative conclusion of each recording, not by each day of recording independently. In other words, except for the time of seizure onset, we did not analyze if any diagnostic

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information was present in the first 1 or 2 days of a 3 day study.

2.3. Statistical analysis

All analyses were performed using RStudio version 1.0.153 (RStudio 2017, Boston, MA) and Microsoft Excel 14.0 (Microsoft 2010, Redmond, WA). Descriptive statistics including means and standard deviations were determined. A Cochran-Armitage Linear Trend Test (Armitage, 1955) was used to ascertain significant trends with the increasing duration of the recordings. This test is used in categorical data analysis to assess for the presence of an association between a variable with two categories and an ordinal variable with 3 categories (in our case). A p-value of less than 0.05 was regarded as significant.

3. Results

3.1. Description of demographics

Between 2010–2017, 358 consecutive adult patients with ages ranging from 18 to 87 underwent aEEG for routine clinical care. Abnormal aEEGs were reported in 46.6% demonstrating slowing, epileptiform discharges, or epileptic seizures. About half (53.4%) of aEEGs were performed on patients with known epilepsy. Indications included better characterization and diagnosis of events of interest (67.6%), detecting subclinical seizures (14.3%), risk stratification for driving (3.1%), medication dosage adjustment (8.1%), classification of seizure type (4.8%), and additional pre-surgical workup (1.1%).

3.2. Detection of epilepsy

Epileptiform discharges or epileptic seizures were detected in 101/358 records (28%). The yield of epileptiform discharges for each duration interval was 28%, 25%, and 24% for 20–30 h (n = 141 studies), 30–50 (n = 123), and 50–76 (n = 94) respectively. Epileptic seizures were detected in 11%, 7%, and 10% for 20–30 h (n = 141 studies), 30–50 (n = 123), and 50–76 (n = 94) respectively. There was no significant difference in the detection of epileptiform abnormalities between the 3 categories of duration. Combining both seizures and epileptiform discharges resulted in a yield of 33%, 25%, and 26% for 20–30, 30–50, and 50–76 h studies. Across all 3 categories, the yield was not significantly different when detecting any electrophysiological abnormality, whether it was seizure or epileptiform discharge (Table 1). The average time from starting the aEEG recording to detecting the first electroclinical seizure was 1376 min (22.9 h) and 1136 min (18.9 h) in 30–50 (n = 8) and 50–76 (n = 8) hour studies (Fig. 1). The yield of detecting any electroclinical seizures and nonepileptic event of interest, epileptic or non-epileptic was 28%, 24%, and 35% for 20–30, 30–50, and 50–76 h studies.

3.3. Description of trend analysis

The indications for all aEEGs were analyzed and tabulated in Table 2. Two statistically significant trends were observed: (i) Longer recordings were ordered for characterizing new events ($p < 0.0004$).

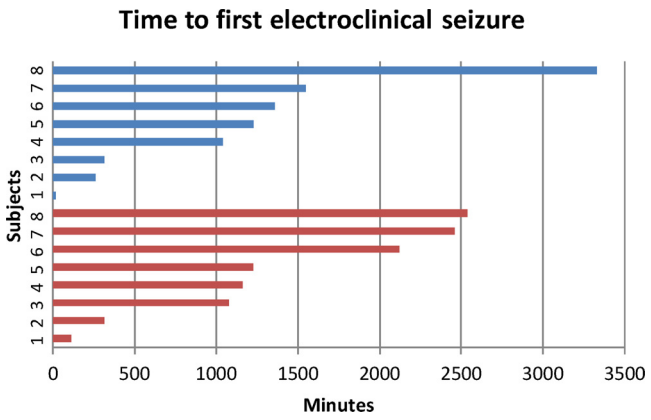

Fig. 1. This figure shows that amount of minutes from the start of the aEEG recording to the first electroclinical seizure detected. The red bar represents 2-day studies. The blue bars represent 3-day studies. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

Table 2
Indications for Studies.

	Hours of AEEG recording			
	24–30	30–50	50–80	P
Epilepsy known prior to aEEG acquisition	49.65%	52.85%	59.57%	0.1422
For detecting new events	57.45%	71.54%	77.66%	0.0004
For subclinical seizures	10.64%	20.33%	11.70%	0.6102
For medication adjustments	13.48%	4.88%	4.26%	0.0033

(ii) Shorter recordings were ordered for guidance of medication dosage ($p < 0.0033$).

AEEG directly led to a change in management in 28%, 17%, and 36% of 20–30 h (n = 141 studies), 30–50 (n = 123), and 50–76 (n = 94) respectively, but did not reach statistical significance (Table 3). Likewise, the subset of positive aEEGs (n = 101) directly led to a change in diagnosis or management in 50%, 28%, and 64% of 20–30 h (n = 46 studies), 30–50 (n = 31), and 50–76 (n = 24) respectively, but did not reach statistical significance.

Longer recordings were also associated with a statistically significant increasing trend in detecting non-epileptic events ($p < 0.03$). Similarly, in the subset of positive aEEGs, longer recordings were associated with a statistically significant increasing trend in detecting non-epileptic events ($p < 0.009$). The average time from starting the aEEG recording to detecting the first non-epileptic event was 1136 min (18.9 h) and 1576 min (26.3 h) in 30–50 (n = 20) and 50–76 (n = 26) hour studies respectively. Note that not all events were timed and are thus not included in these calculations. Longer recordings in all aEEGS were associated with a significantly decreasing trend in detection of newly diagnosed epilepsy ($p < 0.009$), with similar findings in the subset of positive aEEGs ($p < 0.016$). When non-epileptic events were

Table 1
Proportion of Studies with Epilepsy.

	Hours of AEEG recording			
	24–30	30–50	50–80	p
Sample size	141	123	94	
Abnormal studies	51.06%	47.15%	41.49%	0.1522
Studies with seizures	10.64%	7.32%	9.57%	0.7031
Studies with epileptiform discharges	28.37%	25.20%	24.47%	0.4840
Studies positive for patterns of epilepsy	32.62%	25.20%	25.53%	0.1992

Table 3
Management changes.

	Hours of AEEG recording			
	24–30	30–50	50–80	p
Increased medications	4.96%	4.88%	11.70%	0.0294
Started new medications	7.09%	3.25%	5.32%	0.4600
Admit to hospital	2.13%	0.81%	2.13%	0.9129
New diagnosis of epilepsy	5.67%	3.25%	0.00%	0.0091
Changes in surgical management	2.13%	0.00%	0.00%	0.0588

combined with changes in management, there was a significantly increasing trend of both in longer recordings ($p < 0.029$).

We found that in positive aEEGs, the longer durations were associated with increasing the dosage of ASDs ($p < 0.006$) as a direct result of the procedure. We did not observe a significant trend of starting new ASDs among positive aEEGs that were longer in duration.

Of the negative aEEGs (n = 257), longer recordings were associated with a significant trend of patients who had epilepsy known prior to the recording ($p < 0.036$). A significant trend ($p < 0.003$) of longer recordings were performed for characterizing new events that the ordering physician was unsure if they were seizures. A significantly larger proportion of shorter negative aEEGs were ordered for medication dosage adjustments ($p < 0.002$).

The overall yield of seizures, epileptiform discharges, and confirmed events that were not epileptic was 70 (49.7%), 51 (41.5%), and 48 (51.1%) in 20–30 (n = 141), 30–50 (n = 123), and 50–76 (n = 94) hour studies respectively.

4. Discussion

The present study demonstrates that epileptiform discharges or epileptic seizures were present in roughly 28% of the aEEGs regardless of the duration. This is a similar finding compared to other studies. Faulkner et al. (2012a) analyzed 324 aEEGs lasting 4–5 days and found that 36% showed epileptiform dischargesIn another study (Faulkner et al., 2012b), epileptiform discharges were recorded in 44% of patients within 4 h, 58% within 8 h, 85% within 24 h and 95% within 48 h. Thus this study recommended 48 h studies, but in our study, we did not find that longer aEEG recording > 24 h significantly increased the yield of detecting epileptic seizures or epileptiform discharges. We questioned if a 24 h aEEG was ordered because the patient had more frequent seizures to begin with and if ordering physician may have thought that a shorter recording was sufficient. Therefore, we tracked when seizures occurred in 2 day and 3 day studies. We found that the first electroclinical seizure occurred on average within 24 h. Interpretation must be done with caution as the sample size for these cases was small and the variation among time to first seizure was quite large. Based on Fig. 1, there are outliers with seizures well beyond 24 h. Perhaps, if seizures absolutely needed to be captured, a 48 h study would be a reasonable choice. Frequency of clinical seizures would influence the duration of aEEG but this was not investigated in this study.

Longer duration aEEGs were associated with a higher percentage of patients with known epilepsy before confirming on the aEEG recording, but this trend was not statistically significant. This may be because longer duration aEEGs were ordered to characterize new events, which were unlike the patients' typical seizures. A statistically significant larger percentage of patients had longer duration aEEGs for events of uncertain etiology (psychogenic non-epileptic events (PNEE) versus epileptic seizures). Therefore, longer aEEGs were often ordered for patients with established epilepsy but with events that may or may not be seizures.

Another statistically significant indication for shorter aEEG was for medication adjustments. Oftentimes, aEEG is used for determining epileptiform discharge burden by counting the amount of these discharges in a given time period. Thus the aEEG is an objective metric for counting seizures and assaying ASD effectiveness especially in poor historians. We found that a larger proportion of 1 day aEEGs were used to make medication adjustments because perhaps, clinicians believed that aEEGs longer than 24 h would not provide any additional information regarding epileptiform discharge burden.

We found a statistically significant trend of increasing ASD dosages but not adding new medications with longer aEEGs. While increasing medications for seizures or for a large amount of epileptiform discharges is an expected management change, the significantly increasing trend observed in longer duration aEEGs was not clear. Also, we did not observe an increased amount of seizures or epileptiform discharges across aEEGs of different durations. The trend of increasing medications could be related to the severity of epilepsy and not necessarily just from the presence of a positive aEEG. There was actually proportionally less patients with prior known epilepsy included in longer recordings, but the severity of the particular seizures or the actual epileptiform discharge rate was not investigated in this study.

Table 4
Nonepileptic Events and seizures.

	Hours of AEEG recording			
	24–30	30–50	50–80	p
Studies with seizures	10.64%	7.32%	9.57%	0.7031
Detected events	17.73%	16.26%	28.72%	0.0295
Confirmed seizures of interest	7.80%	7.32%	8.51%	0.8678
Seizures and events combined	27.66%	23.58%	35.11%	0.2862

New diagnoses of epilepsy were significantly made in 1 day studies. In other words, we tracked patients who had a low suspicion of seizures who underwent an aEEG, but were found to have epileptiform discharges or seizures. These unexpected positive tests were counted for each duration. The clinicians might have ordered shorter studies to primarily screen these patients for epilepsy. However, the proportion of patients with a low suspicion of epilepsy was not significantly different across the various durations of aEEGs.

Longer aEEGs were associated with a significantly larger proportion of capturing non-epileptic events (Table 4). A limitation of aEEG is that sensory focal aware seizures are frequently below the sensitivity for scalp EEG detection. Additionally, no video was available to further delineate nonepileptic events. However, the majority of these cases was described with a motor component and is expected to have some associated EEG changes. This statistically significant trend was also observed in the cohort of positive aEEGs but not in the cohort of negative aEEGs. Another group (Dash et al., 2012) demonstrated that 31% of 101 aEEGs (mostly 24 h) had detected nonepileptic events which is a similar proportion to our 72 h studies. Patients who have epilepsy had longer aEEGs performed, most likely due to new behaviors. Interestingly, the average latency of capturing a non-epileptic event in 72 h studies was 26 h. Thus, longer aEEGs (> 24 h) are especially useful for characterizing new events in patients with epilepsy and capturing non-epileptic events.

We found that the overall yield for capturing epileptic or non-epileptic spells of interest was about one-third of the records overall. Another study (Dash et al., 2012) in a younger set of patients found that 72% of aEEGs captured epileptic or nonepileptic spells. This is similar to a study (Kandler et al., 2017) which had a yield of 74% in 41 video aEEGs. We expected our yield to be lower because our study sought to characterize only spells that were previously described in the preceding note prior to the aEEG recording. Other described spells during the aEEG recording were not included in this study. A study (Tolchin et al., 2017) of 24–72 h aEEGs in elderly patients yielded 37% with epileptiform discharges, epileptic seizures, or typical non-epileptic event. They also concluded that longer aEEGs have a higher yield in capturing typical non-epileptic events.

Inherent limitations of this study include the retrospective nature, selection bias, tertiary referral center, and the subjective nature of interpretation. There is also an indication bias whereby empiric treatment is given to patients with higher clinical suspicion of epileptic seizures often before the aEEG is performed. The data points for changes in diagnosis and/or management are more subjective. Note that for days 1, 2, and 3, aEEG changed management in 28%, 17% and 36% of cases. While longer recordings were associated with more changes in management, this finding was not significant. However, when we include the new diagnosis of nonepileptic events as a change management, then longer recordings are significantly associated. The caveat is that we did not track how the diagnosis of nonepileptic events affected

management in progress notes subsequent to the aEEG. Another limitation is that a negative aEEG may affect management by providing reassurance that the patients' new events are indeed not epileptic seizures, but there was no reliable measure of this outcome on chart review.

5. Conclusion

Theyield of aEEG for epileptiform discharges or seizures is not significantly increased regardless of the duration. Detection of seizures usually occurred within the first 24 h of recording. If aEEGs are ordered for detecting epileptiform abnormalities, 24 h is sufficient. However, if aEEGs are ordered for characterizing suspected events, a 72 h study has a higher rate of capture.

Declaration of interest

None.

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