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The clinical utility of ambulatory EEG in childhood

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ABSTRACT

Purpose: To evaluate the clinical utility of the ambulatory electroencephalogram (AEEG) in children.
Method: Data from 199 consecutive referrals for a paediatric AEEG were reviewed retrospectively. Information was gathered on various aspects of the referral process, the characteristics of the children referred and the reasons for referral. Clinical utility was calculated as the percentage of cases in which the investigation provided useful information with respect to the question asked of the test.
Results: The AEEG was useful in 64.8% cases overall. In 51.4% of cases the reason for referral was to capture events, however the test was only useful in 42.6% of these. The most common reason for an unsuccessful investigation was failure to capture events (55.6%). Suspected encephalopathy with status epilepticus during sleep (ESES) was the indication in a substantial number of cases (38.6%), and the investigation was useful in most of these (97.5%). Technical issues were only responsible for 7 (9.7%) of unsuccessful studies.
Conclusion: The paediatric AEEG was useful in two thirds of patients. Failure to capture events appears to be the most significant limiting factor. The AEEG is very useful in investigating suspected ESES.

1. Introduction

The electroencephalogram (EEG) has an important role in the assessment of paroxysmal disorders. The routine EEG is the most frequently used type, however since the duration of the recording is short (typically around 20 min), and interictal EEG is often normal in patients with epilepsy, the usefulness of the technique has limitations. In a recent meta-analysis, the sensitivity of a routine EEG after a first unprovoked seizure was only 17.3 (7.9, 33.8) % in adults and 57.8 (49.7, 65.6) % in children. [1]

The diagnostic yield can be increased by repeated routine EEG recordings [2], by employing activation techniques (sleep deprivation, hyperventilation, photic stimulation) or else by more prolonged and overnight recordings, since epileptic discharges are often triggered by sleep [3]. The International League Against Epilepsy lists a number of situations where long-term EEG monitoring is indicated, including the following: 1) Detection, characterisation and quantification of ictal events, 2) Differential diagnosis between epileptic and non-epileptic events, 3) Diurnal/circadian variation in occurrence of paroxysmal EEG changes, 4) Effects of drug interventions, 5) Pre-surgical evaluation (video telemetry only). [4]

Video telemetry (VT) is a method that is considered the gold standard [5] as it has the advantage of a synchronous video recording during the EEG. Ambulatory EEG (AEEG) only consists of a prolonged EEG recording, so it may be difficult to interpret the EEG changes without an accompanying video. The AEEG has a number of advantages in comparison to VT – lower cost [6], outpatient setting, convenience and shorter waiting lists. The disadvantages of AEEG include difficulty managing technical issues that arise at home, inability to reduce antiepileptic medication safely to trigger events [5], and the fact that some seizures may not be associated with surface EEG changes and would not be picked up on AEEG, while VT would capture these on video [7].

Prolonged EEG monitoring increases the diagnostic yield compared to routine EEG [8], with the largest studies reporting clinically useful information in 72% (n = 101), 68% (n = 324), and 74.4% (n = 344), and ability to capture events in 40.6%, 52% and 48.3% [9,10,11] respectively. There is difficulty in comparing or pooling data from these studies, as there is significant heterogeneity in patient selection, duration of recordings and definition of clinical usefulness [6]. In addition, most of the studies so far relate either to a mixed-age population or to the adult population only, while studies on the usefulness of prolonged EEG studies in children are scarce.

Existing studies in children have varied in their estimates of clinical utility of the test, ranging from 30 to 89% [12–17]. Selection criteria

Abbreviations: AEEG, ambulatory electroencephalogram; VT, video telemetry; ESES, encephalopathy with status epilepticus during sleep

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and study design differ, with some studies having very small samples, applying stringent selection criteria, or analysing data prospectively with a potential risk of selection bias. The two more recent studies by Wirrell et al [15] and Hussain et al [16] prospectively analysed data from 64 and 100 consecutive AEEG studies and found that it answered the clinical question in 73% and 71% respectively.

2. Methods

Data was collected from 199 consecutive AEEG recordings. This involved all AEEG studies performed between June 2016 and August 2017 in the EEG department of the Royal Hospital for Children in Glasgow. This tertiary referral centre serves a population of around 2.7 million, covering the majority of the West of Scotland.

The recordings were done using a 16-channel system with the international 10–20 electrode placement. The standard procedure for the ambulatory EEG recording consisted of electrode attachment in the EEG department, followed by a 1-day period of continuous EEG recording in the outpatient setting and electrode removal the next day in the EEG department. In a small number of cases the recording continued for two days. The child and their parents were provided with a diary to record the child's activities as well as any events observed. In addition, they were asked to press a button marker each time an event occurred.

Reasons for referral were categorised into four groups: 1) to capture events, 2) suspected encephalopathy with status epilepticus during sleep (ESES), 3) to aid with syndromic diagnosis, 4) other. The AEEG investigation was deemed useful if the clinical question asked was answered by it.

For the purposes of this study, the data were obtained by reviewing the referral forms and letters, the EEG reports and relevant electronic patient records.

3. Results

Data from 199 children were included in this study. Table 1 contains demographic data and information on the EEG recordings.

Some recordings were affected by technical issues (Table 2). Overall, clinical interpretation was marred because of technical difficulties in only 7/199 (3.5%) cases.

Clinical utility (i.e. whether the question posed was answered) was calculated overall and also for each of the four subgroups divided by the reason for referral (Table 3).

Among unsuccessful AEEG studies, the reasons for failure are shown in Table 4. Further, Table 4 includes information on reasons for failure of the test for the subgroup where the indication for referral was to capture events.

In the subgroup where the indication for referral was 'to capture events', further information was gathered on the nature of the events captured. An event was recorded in 53/108 (49.1%) cases. Of these, typical events were recorded in 43 (39.8%) cases. In 8 of these, though a typical event was captured, the test was not regarded as useful: in 6 cases it was felt a video was needed to identify the nature of events, and in 2 cases technical issues marred interpretation. Conversely, in 11 cases no events were captured, however the referring clinician felt that the test provided useful information because syndromic features were present on the AEEG or they were reassured by a normal sleeping pattern. The investigation was therefore useful in 46/108 cases.

The referral forms were further reviewed for information on frequency of events (Table 5). In those patients where events were occurring at least 3 times a week, the test was found useful in 27/57 (47.4%) cases. Where frequency of events was less than 3 times a week, the test was useful in 9/29 (31.0%) cases. Frequency of events was not recorded in the clinical records in 22 (20.4%) cases and not recorded on the referral form in 48 (44.4% cases).

In the subgroup where the indication for referral was suspected ESES, the detailed reasons for referral are included in Table 6. AEEG studies done for this indication provided useful information in 79/81

Table 1
Demographic data and recording information.

	(N = 199)
Age, *years*	
Mean	7.9
Median	8
Range	5 months–19 years
Gender, *n* (%)	
Male	124 (62.3)
Female	75 (37.7)
Referral to recording time, *days*	
Mean	60
Mean	62
Range	0–259
Urgent referrals, *n (%)*	8 (4.0)
Previous EEG recording, *n (%)*	
Any	160 (80.4)
AEEG	56 (28.1)
VT	20 (10.1)
Established diagnosis of epilepsy[a], *n (%)*	128 (64.3)
More than 1 reason for referral, *n (%)*	11 (5.5)
Recording duration, *hours*	
Median	23
Mean	22.1
Range	19 min –48 h
≥48 hours, *n (%)*	4 (2.0)

[a] Made on clinical grounds and supported by EEG findings.

Table 2
Technical issues affecting the recordings.

Technical issue	n (%)
Total number of technical issues	124
Movement artefact	49 (39.5)
Accidental presses of the event marker	34 (27.4)
Diary not returned	14 (11.3)
Electrode detachment	11 (8.9)
Button not pressed during events or no correlation between presses and events	10 (8.1)
Uncooperative/did not tolerate procedure	3 (2.4)
Equipment failure	3 (2.4)
Recordings affected	98/199 (49.2)
Marred clinical interpretation	7/199 (3.5)

Table 3
Clinical utility of the AEEG.

Clinical question answered, N = 199	n (%)
Yes	129 (64.8)
No	65 (32.7)
Partially	5 (2.5)
Clinical question answered, by indication for referral[a] N = 210	**n (%)**
To capture events	108 (51.4)
Yes	46 (42.6)
No	62 (57.4)
Suspected ESES	81 (38.6)
Yes	79 (97.5)
No	2 (2.5)
Aid syndromic diagnosis	13 (6.2)
Yes	7 (53.8)
No	6 (46.2)
Other	8 (3.8)
Yes	6 (75)
No	2 (25)

[a] Some referrals were done for more than one reason, therefore the total number of cases in this Table is 210, whereas the number of referrals overall is 199.

Table 4
Reasons for the test not providing useful information.

Reasons for question not answered by the test	Overall Cases/72[a] (%)	Indication: to capture events Cases/62 (%)
No events captured	40 (55.6)	40 (64.5)
Video required to interpret EEG changes	10 (13.9)	9 (14.5)
Atypical event only	7 (9.7)	7 (11.3)
Technical issues	7 (9.7)	5 (8.1)
Absence of epileptiform abnormalities/ Did not aid syndromic diagnosis	6 (8.3)	
Other	2 (2.8)	1 (1.6)

[a] This includes cases with more than 1 indication for the AEEG where question was only partially answered or not answered for either of the indications.

Table 5
Recorded nature and frequency of events in the subgroup where 'to capture events' was the indication for referral.

Recorded frequency of events (N = 108)	n (%)	Clinically useful, n (%)
≥ 1x/day	45 (41.7)	21 (46.7)
≥ 3x/week	12 (11.1)	6 (50.0)
1-2x/week	11 (10.2)	3 (25.0)
1x/2 weeks	5 (4.6)	1 (25.0)
< 1x/month (infrequent)	13 (12.0)	5 (38.5)
No information	22 (20.4)	10 (45.5)

Table 6
Specific reasons for referral in the subgroup suspected ESES.

Reason for referral (n = 81)	Cases (%)
Learning and memory difficulties	25 (30.9)
Response to treatment of ESES	14 (17.3)
Specific language regression	13 (16.0)
Isolated behavioural change	12 (14.8)
Previous ESES	8 (9.9)
Rolandic epilepsy	3 (3.7)
Family history	2 (2.5)
Other	4 (4.9)

(97.5%) cases. The 2 unsuccessful studies failed because the patients did not tolerate the procedure.

In the subgroup where the indication was to aid syndromic diagnosis, the different suspected syndromes were: rolandic epilepsy (5, 38.5%), genetic generalised epilepsy (4, 30.8%), genetic focal epilepsy (1, 7.7%), and further unspecified (3, 23.1%).

The remaining 8 cases did not fall into any of the categories of indication for referral and were classified as 'other'. For example, this group included patients in whom the referring clinician wanted to assess response to treatment or evaluate background EEG abnormalities varying throughout the day in a child with GLUT1 deficiency.

4. Discussion

The AEEG was found clinically useful in 129 (64.8%) cases in this study and this is comparable to the smaller studies by Hussain et al [16] (n = 100), and Wirrell et al [15] (n = 64), where the clinical usefulness achieved was 71% and 73% respectively. However, since these were both prospective studies, the accepted referrals might have been influenced by selection bias and therefore only patients who were more likely to have a positive AEEG recording might have been included. Alix et al [17] conducted a retrospective study and reported a very similar clinical utility of 63%, however the sample was small (n = 30) and the findings may have been skewed because the study only selected patients who underwent a subsequent VT as well. Foley et al [12] (n = 84) and Olson et al [13] (n = 167) found higher clinical usefulness in their studies – 86% and 89% respectively - however patients were only included if they were experiencing events at least three times a week. Moreover, Olson et al only assessed the ability to capture events, which is not equivalent to clinical utility. This was also demonstrated in another study by Saravanan et al [14] (n = 54), where events were captured in 57% cases, but this was clinically helpful in only 52% of these, giving a low overall utility of 30%. Patients were only included in this study if they were experiencing events on most days. The minimum recording duration was 48 h; therefore, the clinical utility was lower than expected.

In our study a high proportion (48.6%) of referrals for an AEEG were for reasons other than 'to capture events'. These other reasons include: suspected ESES (38.6%), to aid with syndromic diagnosis (6.2%) and for other reasons (3.8%). This differs from previously published studies, where the vast majority of referrals (88–100%) were made to capture events and to distinguish if events are epileptic or not [13–17]. Suspected ESES was only specifically mentioned as a reason for referral in two studies [16,17], and represented only a small proportion of the referrals (2–7%). It has been suggested that if there is a high suspicion of ESES, patients should preferentially be investigated with a prolonged sleep recording [18], since continuous spike and wave features may not be present for the whole duration of slow-wave sleep [19]. The findings in this study suggest that the AEEG is clinically useful in the vast majority of patients investigated for suspected ESES (97.5%). The reasons why ESES was suspected in the referred patients are listed in Table 4. The most common reason was learning and memory difficulties (25 cases, 30.9%). Three children with rolandic epilepsy and no clinical evidence of congitive or behavioural abnormalities had AEEG requested to look for ESES. Two children with autism, learning disability and epilepsy had AEEG requested as they have siblings with *GRIN2A* gene pathogenic variants associated with autism and ESES.

Even though this study demonstrates that AEEG is a useful tool overall, still in 32.7% of cases the results were clinically unhelpful. Understanding the reasons for the test failure may help to improve the clinical utility of the test. It is interesting to note that when cases were split into subgroups based on the reason for referral, the lowest clinical utility was achieved in the group where the indication was to capture events – only 42.6% of recordings in this category were clinically helpful. In the majority of those that failed, the reason was that no events were captured (64.5%). Previously it has been suggested that to increase the diagnostic yield of the AEEG, the frequency of events prior to the test should be at least 3 times a week [12,13], or perhaps even daily [16]. In the present study, less than half of the cases had such frequent events, perhaps explaining why clinical utility was so low for this subgroup. In fact, in the subgroup of patients where events were occurring less than 3 times a week, the clinical utility was reduced to 31.0%. Moreover, frequency of events was not adequately recorded on the referral form in almost half of the cases, which was surprising given that it is important to know whether events are occurring reasonably frequently if the AEEG is expected to capture them. However, while having the information on frequency of events is important, it may be

that by applying stringent inclusion criteria some will be denied a potentially useful investigation. Each referral should therefore be made within the specific clinical context, taking frequency of events into consideration. In fact, in the subgroup of patients where events were recorded as occurring at least 3 times a week, the clinical utility was still only 47.4%, suggesting that other reasons for not being able to record events may be more relevant.

One such reason could be change in frequency of events in the time between referral made and the AEEG study actually taking place. Referrals are often made several months in advance (in this study, the mean time between referral and recording was 62 days) and frequency of events may change in that time so that an AEEG study is no longer warranted. In another study, telephone checks 7 days prior to the study taking place reduced the number of cases where no events were recorded by half [16].

In addition, it is interesting to note that technical issues were in general not associated with unsuccessful AEEG studies – only in 7/72 (9.7%) cases of unsuccessful AEEG could this be attributed to technical issues. This is often listed as a disadvantage of the AEEG [5], however this study demonstrates that technical difficulties are rarely a significant problem with home EEG recordings.

In this study, the majority of recordings were performed over 24 h (mean 22.1 h, median 23 h). A 48-h recording was only done in four cases. The overall clinical utility was 64.8%. This is comparable to studies with a mixed-age population where a large number of recordings was done over 72–96 h, and where clinical utility of 68–72% was achieved [9,10]. The results from this study suggest that it may be unnecessary to perform long recordings in children apart from in very selected cases, as they are unlikely to significantly increase the diagnostic yield.

4.1. Strengths & limitations

A major strength of this study is its large sample (the three most recent related studies had a sample of 64 [15], 100 [16] and 30 [17]). Consecutive EEG studies were reviewed in a non-selective way, and since in this centre there are no published criteria for a referral for AEEG, this provided an opportunity to review the effectiveness of the actual clinical practice.

In addition, clinical usefulness was evaluated based on the ability of the study to answer the clinical question posed rather than by the number of cases where events were captured. This is a more accurate way to establish clinical utility, as in some cases even if events are captured the study may still be unhelpful (e.g. because of artefact marring), and equally sometimes no events might be captured but the recording still provides a useful answer (e.g. electrographic evidence of an epilepsy syndrome). Unfortunately, some studies only focused on the ability of the test to capture events (e.g. Olson et at [13]) making it difficult to compare the results.

In some respects, the study is limited by its design – this was a retrospective study which, while revealing useful information related to the efficiency of the clinical practice, also means that the data used was of variable quality and lacked standardisation, particularly because referrals were received from a number of hospitals/centres using different referral methods.

4.2. Recommendations for practice

With the recent developments in the area of home video ambulatory EEG [20–22], it may be that the use of ambulatory EEG without a video recording will decline, particularly for the cases where children are being investigated to capture events.

So far home video EEG seems to be comparable to inpatient video telemetry with respect to clinical utility as well as technological challenges [21,22]. Lawley et al [20] and Kandler et al [21] found that video AEEG was clinically useful in 67% and 73% respectively. Carlson et al [22] conducted the only study in a purely paediatric population to date and found similar results - home video telemetry was clinically useful in 70% of cases.

The AEEG is still likely to be used in clinical practice, and as shown in this study, is particularly useful for investigation of suspected ESES and perhaps also to aid with syndromic diagnosis (even though the numbers were small). It is reassuring that the AEEG is clinically useful in about two thirds of patients being referred.

There are several recommendations that could potentially lead to an increased diagnostic yield from AEEG studies. Information on the referral forms should be comprehensive, particularly in reference to the frequency of events in question. This may help the clinician to reconsider if the investigation is truly likely to capture events. In addition, clarity of referral forms will likely also help the technician and neurophysiologist with the interpretation of the EEG recording. It may be worth introducing telephone checks a few days prior to the AEEG study, to confirm that events are still occurring at a reasonable frequency.

5. Conclusion

This study demonstrates that ambulatory EEG recordings in children are clinically useful in two thirds of cases. They are the least useful for capturing events, however this is also the most common indication for an AEEG referral. The most frequent reason for a failed AEEG investigation is that no events are captured. The AEEG is very useful when investigating suspected ESES. Technical issues are only rarely responsible for failed investigations.

Declarations of interest

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