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Using sampled visual EEG review in combination with automated detection software at the EMU

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ABSTRACT

Purpose: Complete visual review of prolonged video-EEG recordings at an EMU (Epilepsy Monitoring Unit) is time consuming and can cause problems in times of paucity of educated personnel. In this study we aimed to show non inferiority for electroclinical diagnosis using sampled review in combination with EEG analysis softreferware (P13 software, Persyst Corporation), in comparison to complete visual review.

Method: Fifty prolonged video-EEG recordings in adults were prospectively evaluated using sampled visual EEG review in combination with automated detection software of the complete EEG record. Visually assessed samples consisted of one hour during wakefulness, one hour during sleep, half an hour of wakefulness after wake-up and all clinical events marked by the individual and/or nurses. The final electro-clinical diagnosis of this new review approach was compared with the electro-clinical diagnosis after complete visual review as presently used.

Results: The electro-clinical diagnosis based on sampled visual review combined with automated detection software did not differ from the diagnosis based on complete visual review. Furthermore, the detection software was able to detect all records containing epileptiform abnormalities and epileptic seizures.

Conclusion: Sampled visual review in combination with automated detection using Persyst 13 is non-inferior to complete visual review for electroclinical diagnosis of prolonged video-EEG at an EMU setting, which makes this approach promising.

1. Introduction

EEG is an important tool in the management of epilepsy. Interictal and ictal findings can help in epilepsy diagnosis, seizure and syndrome classification, epilepsy monitoring and for identifying surgical candidates [1,2].

At an Epilepsy Monitoring Unit (EMU) prolonged video-EEGs are performed, resulting in large datasets. At our centre, technicians visually review the entire EEG recording, aiming at finding all relevant interictal and ictal events for answering the referral question. Subsequently, a clinical neurophysiologist reviews selections made by the technician and provides a final electro-clinical diagnosis. The complete visual data analysis is time-consuming and costly. In times where there is a paucity of technicians, this can cause problems. It is necessary to look for time saving alternatives to review large EEG datasets, without loss of quality.

One approach for saving time is sampled visual review. This approach has hardly been evaluated. One study suggested that the first hour of sleep reliably predicts the occurrence of interictal epileptiform activity for whole recording [3]. Another study showed that sampled review was non-inferior regarding final electro-clinical diagnosis, although a substantial number of events was missed [4].

Another approach is automated EEG analysis, using detection software. These software packages are widely used in ICU settings, but to our knowledge not commonly used at EMUs. There are several reports on automated detection algorithms, although most focus on the algorithm development rather than clinical validation [5]. The Persyst 13 (P13) spike detector is a commercially available software frequently used in the assessment of automated detection software [6–9]. Two studies showed P13 was non-inferior to human mark-up when detecting interictal epileptiform abnormalities [6,7]. Two other studies looked at ictal events. The first study found P13 only correctly identified at least one electrographic seizure in 53 % of ambulatory recordings [8]. The second showed a previous Persyst version (version 11) detected 76 % of electrographic seizure at an EMU setting, but missed most of the myoclonic and focal aware seizures [9].

Our main objective is to determine whether a review approach using a combination of sampled visual review and automated detection software is non-inferior to the conventional method, where the entire EEG is visually reviewed.

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2. Material and methods

Fifty prolonged video-EEG recordings between November 2018 and May 2019 were prospectively included. The only inclusion criterion was a minimum age of 16 years. We excluded presurgical recordings. The analyses of these records were embedded in our usual clinical workflow, so informed consent was not obtained in accordance to local Ethics guideline.

All recordings were performed at our 8-bedded EMU [10]. A Micromed EEG system (Micromed, Mogliano Veneto, Italy) using the standard 10–20 International electrode placement plus F9/F10 and 256 Hz sample frequency was used. During daytime and early evening, individuals were observed by three nurses, positioned at a nearby video footage observation station; at night, two nurses carried out the task [10,11]. During the recording individuals were asked to press the button when experiencing a clinical event.

2.1. Sampled EEG

The sampled EEG contained the first hour of recording during wakefulness including hyperventilation provocation and intermittent photic stimulation, the first hour of sleep and the first half hour after sleep the next morning, which was added due to the circadian distribution of some generalized epilepsies (especially JME). In addition, EEG and video periods around nurse or patient 'push button' marked events were reviewed.

2.2. Automated detection software

The P13 software from Persyst Corporation (P13) was used for the automated spike and seizure detection. Spike detections are clustered per electrode, where maximum amplitude was recorded. It generates 1-second epochs centred around the detected spike, with an average signal per electrode. All single potentially abnormal findings can also be reviewed. Further details can be found in previous literature [12,13]. Regarding seizure detection, the manual states that the algorithm detects ictal patterns with a minimum duration of 11 s. The Persyst software also includes various options for quantitative EEG trends.

2.3. Research protocol

The human experts (HEs) were pairs, in varying combinations, of two clinical neurophysiologists and a physician assistant, all with more than five years of video-EEG reviewing experience. To reduce steep learning effects, the HEs had already practiced using the P13 software before the first review for the study.

The reviewing process consisted of three steps (Fig. 1). As in our normal routine, EEGs were pre-reviewed by EEG technicians. They first made a report of the sampled EEG in step 1, subsequently they reviewed the whole EEG record, and documented additional findings for step 3. For step 1 as well as step 3, video is only reviewed in the period that (1) nurses note a (possible) event, (2) patients use the push button, (3) technicians see a (possible) ictal EEG rhythm and (4) to distinguish an artefact from cerebral activity. Technicians were blinded for the results of step 2 during the whole reviewing process. The HEs first reviewed the sampled EEG in step 1, afterwards reviewed the whole EEG using automated software (step 2), and finally reviewed technicians additional findings in step 3. As with the technicians, the video is only reviewed by the HE's in the above-mentioned periods. After each step the HEs formed an electro-clinical diagnosis, using SCORE terminology [14]. Possible epilepsy was used when only a few, or only ambiguous, interictal epileptiform discharges (IEDs) were seen. Probable epilepsy was used when definite interictal epileptiform activity was seen. Definite epilepsy was used when a record contained one or multiple seizures with electro-encephalographic correlate. The electro-clinical diagnosis in step 3 was regarded as the current best available gold standard.

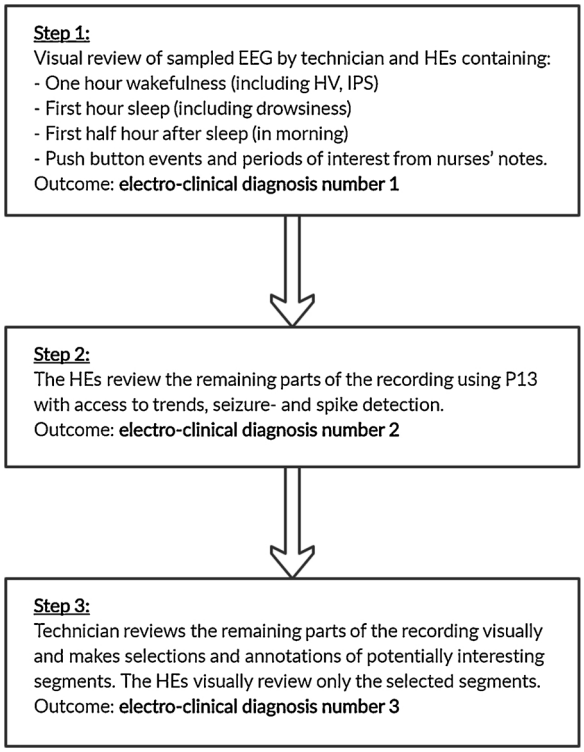

Fig. 1. Research protocol.
HE = human expert; HV = hyperventilation provocation; IPS = intermittent photic stimulation, P13 = Persyst 13.

Furthermore, HEs described the ictal and interictal findings at each step.

2.4. Outcome measures

The primary outcome measure was the difference between the electro-clinical diagnoses in sampled visual review with automated detection (step 2) and the electro-clinical diagnoses in complete visual review (step 3). Secondary outcome measures were the electro-clinical diagnosis for sampled visual review only (step 1), compared to step 3. Furthermore we looked at the occurrence of IEDs, missed seizures by P13 in step 2, false seizure detections by P13 in step 2 and missed seizures by technicians in step 3.

3. Results

A total of 1170 h of video-EEG from 50 records (18 males and 32 females with median age 32 (range 18–73) years) was analysed with a median duration of 23.4 h (range 17.5–44.5 hours). The clinical referral question for the EEGs was presence of interictal epileptiform findings (to support diagnosis or follow-up) in 32 records, classification of epilepsy in 10 records, and event recording in 8 recordings for diagnostic or classification purposes.

3.1. Electro-clinical diagnoses

Table 1 shows the various reported electro-clinical diagnoses in each step. In none of the cases the electro-clinical diagnosis in step 2 differed from the electro-clinical diagnosis in step 3.

The electro-clinical diagnosis reported in step 1 differed from step 2 in three cases (6%). In one patient the report changed from aspecific focal dysfunction to probable focal epilepsy, the second changed from normal to possible focal epilepsy, and the third changed from possible to definite focal epilepsy, because a seizure was detected by P13 outside

Table 1
Diagnostic significance.

		Step 1	Step 2	Step 3
Normal		9	8*	8
No definite abnormality		6	6	6
Focal dysfunction		5	4*	4
Diffuse dysfunction		0	0	0
Focal epilepsy	*Possible*	1	1*	1
	Probable	10	11*	11
	Definite	4	5*	5
Multifocal epilepsy	*Possible*	2	2	2
	Probable	1	1	1
	Definite	0	0	0
Generalized epilepsy	*Possible*	0	0	0
	Probable	5	5	5
	Definite	1	1	1
Epilepsy no classification		1	1	1
PNES		5	5	5
Non epileptic otherwise		0	0	0

Normal = Normal interictal EEG and no events recorded, PNES = psychogenic non epileptic seizures, * = in one record the electro-clinical diagnosis changed.

the sampled EEG.

3.2. Interictal epileptiform abnormalities

Interictal epileptiform abnormalities were present in 29 records (58 %) according to the HEs (step 3). P13 detected all records containing epileptiform activity. One record also contained TIRDA (Temporal Intermittent Rhythmic Delta Activity), which was not detected by the P13 software and also not seen in step 1. No other important interictal findings were missed by P13. There was no difference in localization and frequency of interictal (epileptiform) activity between step 2 and step 3.

3.3. Seizures

In 16 records (32 %) at least one clinical event occurred (range 1–58). In 6 of these records the events were classified as epileptic seizures (5 with focal seizures and 1 with generalized seizures; Table 2). In 5 of these 16 records the events were classified as PNES and in the remaining 5 records as subjective events with uncertain etiology.

P13 alone, detected all records containing seizures. Although in 3 records a part of the seizures were missed. In the record containing 58 absences, P13 missed five of them. Of those five, three absences were shorter than 11 s and two were longer than 11 s. The other two records contained nocturnal frontal seizures with no or subtle EEG changes (only muscle and movement artefacts).

In 27 records (54 %) false seizure detections by P13 occurred, with a total of 81 false detections with a median of two per record (range 1–19). Most of these false detections occurred during chewing or rhythmic eye blinking and were easily recognised.

One focal seizure with impaired awareness was missed by the technician in step 3. This seizure was detected by P13 in step 2.

4. Discussion

In this study we showed that the electro-clinical diagnosis after sampled visual EEG review in combination with automated detection software (P13) did not change after successive complete visual review. The advantage of this reviewing approach is that it may substantially save overall reviewing time, especially in our setting with many prolonged EEG recordings.

We also showed that our approach of sampled visual review alone is insufficient, both with respect to interictal findings as for missing seizures.

Relying on automated detection software alone is also not possible. First, sampled visual review remains necessary to get an impression of the background activity and potential (focal or diffuse) dysfunctions or rhythmic delta activity (e.g. TIRDA). We showed that reviewing an hour when awake, an hour when asleep and an hour after wakefulness is enough for this purpose. Second, automated software packages are likely to miss seizures with no or just subtle EEG correlate. This makes the software less suitable for diagnosis or monitoring very short seizures (i.e. myoclonia) and focal aware seizures, which was also shown by previous literature [9]. Therefor additional observations of nurses and markings of patients experiencing clinical events will stay required.

The aim of the study was to show non-inferiority to the human observer. An interesting observation is the seizure missed by the technician, but detected by the P13 software, showing the potential superiority of software above the human observer. This is probably not exceptional, where technicians are requested to review prolonged records at a much faster speed than real-time risking missing relevant events [15]. Studies should be designed not only to show non-inferiority of detection software, but also to enable the software to "beat" the human observer as gold standard.

Our proposed approach can be used for review of prolonged records at the EMU, since we showed non-inferiority. And although we did not investigated it formally, this approach is very likely to result in time gain, provided that the elaboration of the detection software results does not require extra time. A disadvantage of the P13 is that it has false detections, interictal as well as ictal. Reviewers must be able to filter these out. It would be very helpful if all detected findings are merged in clusters based on similar properties like morphology and localization, that reliably reflect the same functional EEG abnormality. Then groups of artefacts or nonspecific abnormalities could be disregarded, without the need to check all the individual detections. In the P13 software this is currently not possible.

Our study has some limitations. We tried to include a heterogenic group with focal epilepsies, generalized epilepsies and PNES but our sample size was too small to include all different types of epilepsies and seizures. In the 3-step-process the HEs were not blinded to their

Table 2
Detected seizures from the 6 records containing definite epileptic events.

Case	Total number of seizure(s)	Seizure type	Number occurred in sampled part	Step 1 Number detected by PB	Number detected by nurse	Step 2 Number detected by P13	Step 3 Number detected only by technician
1	58	Absence	13	5	16*	53	1
2	14	FAS	0	1	12	6	1
3	1	FIAS	0	0	1	1	0
4	1	FIAS	0	0	1	1	0
5	5	FAS	2	1	4	1	0
6	1	FIAS	0	0	0	1	0

Part 1 = first hour wakefulness, first hour sleep and first half hour after sleep (in morning), PB = push button, FAS = focal aware seizure, FIAS = focal seizure with impaired awareness * common practice for the nurse is to stop responding to absences after > 10 seizures.

previous reports. Although this is suboptimal, it prevents the known problems of interrater disagreement [16]. Finally this single centre bias also limits overall generalizability, as monitoring methods, staff expertise, and training vary widely among epilepsy centres. What may be a good set-up in our centre may not be useful or feasible for others. This especially applies for settings with no or minimal nurse observation, such as ambulatory settings.

Further validation of the software is warranted in larger cohorts, multiple centres and by multiple human experts. A progressive approach would be a design combining further validation during implementing of supporting automated software, stepwise reducing the required EEG review time. We think it's feasible to make a step toward using more medical technology in EEG reviewing.

5. Conclusions

Sampled visual review in combination with automated detection software is a promising time gaining tool in reviewing prolonged video-EEGs of adults at the EMU. It thereby remains warranted that clinical events are continuously observed by trained nurses and patients have the possibility to use a push button when experiencing seizure-like symptoms.

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Declaration of competing interest

None of the authors has any conflict of interest to disclose.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.seizure.2020.06.002.

References

[1] Wirrell ED. Prognostic significance of interictal epileptiform discharges in newly diagnosed seizure disorders. J Clin Neurophysiol. 2010;27:239–48. https://doi.org/10.1097/WNP.0b013e3181ea4288.
[2] Shin HW, Pennell PB, Lee JW, et al. Efficacy of safety signals in the epilepsy monitoring unit (EMU): should we worry? Epilepsy & Behavior. 2012;23:458–61. https://doi.org/10.1016/j.yebeh.2012.01.018.
[3] Liu X, Issab NP, Roseb S, et al. The first-hour-of-the-day sleep EEG reliably identifies interictal epileptiform discharges during long-term video-EEG monitoring. Seizure 2018;63:48–51. https://doi.org/10.1016/j.seizure.2018.10.015.
[4] Badawy RAB, Pillay N, Jetté N, Wiebe S, Federico P. A blinded comparison of continuous versus sampled review of video-EEG monitoring data. Clin Neurophysiol 2011;122:1086–90. https://doi.org/10.1016/j.clinph.2010.10.048.
[5] Halford JJ. Computerized epileptiform transient detection in the scalp electroencephalogram: obstacles to progress and the example of computerized ECG interpretation. Clin Neurophysiol 2009;120:1909–15. https://doi.org/10.1016/j.clinph.2009.08.007.
[6] Scheuer ML, Bagic A, Wilson SB. Spike detection: inter-reader agreement and a statistical turing test on a large data set. Clin Neurophysiol. 2016;128:243–50. https://doi.org/10.1016/j.clinph.2016.11.005.
[7] Halford JJ, Westover MB, LaRoche SM, et al. Interictal epileptiform discharge detection in EEG in different practice settings. J Clin Neurophysiol. 2018;35:375–80. https://doi.org/10.1097/WNP.0000000000000492.
[8] González Otárula KA, Milhaeil-Demo Y, et al. Automated seizure detection accuracy for ambulatory EEG recordings. Neurology 2019;92:e1–7. https://doi.org/10.1212/WNL.0000000000007237.
[9] Kamitakia BK, Yumb A, Leea J, et al. Yield of conventional and automated seizure detection methods in the epilepsy monitoring unit. Seizure 2019;2019(69):290–5. https://doi.org/10.1016/j.seizure.2019.05.019.
[10] Cox FME, Reus EEM, Widman G, Zwemmer JNP, Visser GH. Epilepsy monitoring units can be safe places; A prospective study in A large cohort. Epilepsy Behav. 2020;120:102–6. https://doi.org/10.1016/j.yebeh.2019.106718.
[11] Rommens N, Geertsema E, Jansen Holleboom L, et al. Improving staff response to seizures on the epilepsy monitoring unit with online EEG seizure detection algorithms. Epilepsy Behav. 2018;84:99–104. https://doi.org/10.1016/j.yebeh.2018.04.026.
[12] Wilson SB, Turner CA, Emerson RG, et al. Spike detection II: automatic, perception-based detection and clustering. Clinical Neurophysiology. 1999;110:404–11. https://doi.org/10.1016/S1388-2457(98)00023-6.
[13] Reus EEM, Visser GH, Cox FME. Determining the Spike–Wave index using automated detection software. Clin Neurophysiol 2019. https://doi.org/10.1097/WNP.0000000000000672. in press.
[14] Beniczky S, Aurlien H, Brøgger JC, et al. Standardized computer-based organized reporting of EEG: SCORE - second version. Clin Neurophysiol. 2017;128:2334–46. https://doi.org/10.1016/j.clinph.2017.07.418.
[15] Halford JJ, Shiau D, Kern RT, et al. Seizure detection software used to complement the visual screening process for long-term EEG monitoring. Am J Electroneurodiagnostic Technol. 2010;50:133–47.
[16] Bagheri E, Dauwels J, Dean BC, et al. Interictal epileptiform discharge characteristics underlying expert interrater agreement. Clin Neurophysiol. 2017;128:1994–2005. https://doi.org/10.1016/j.clinph.2017.06.252.