Diagnostic yield of high-density versus low-density EEG: The effect of spatial sampling, timing and duration of recording

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HIGHLIGHTS

- We evaluated the effect of EEG spatial sampling and of recording duration on the diagnostic yield.
- High-density recordings did not increase the diagnostic yield significantly.
- Long-term recordings had significantly higher diagnostic yield than short-term recordings.

ABSTRACT

Objective: To investigate the effect of spatial sampling and of recording duration on the diagnostic yield of EEG for identification of interictal epileptiform discharges (IEDs). Previous studies demonstrated that high-density (HD) recordings increased accuracy of localization compared to low-density (LD) recordings.
Methods: We have prospectively evaluated the effect of spatial sampling and of recording duration in patients who had short-term (ST) recordings with a HD array of 256 electrodes following long-term (LT) recordings with a LD array consisting of the standard IFCN array of 25 electrodes. IED clusters were identified in four datasets: LT-LD, ST-LD (spatially down-sampled to the standard IFCN array), ST-HD and a shortened (90 minutes) epoch of LT-LD.
Results: Sixty consecutive patients were recruited. We identified 89 IED clusters totally. Two clusters were found by increasing spatial sampling from 25 to 256 electrodes. This modest increase was not statistically significant. Eight clusters were missed by reducing the recording duration to 90 minutes, as compared with the LT recordings (p = 0.003).
Conclusions: Recording duration is more important for the diagnostic yield of EEGs than increasing spatial sampling beyond the standard IFCN electrode array.
Significance: The standard IFCN electrode array provides sufficient spatial sampling for identification of the IEDs.

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1. Introduction

EEG is one of the most important diagnostic tools in evaluation of patients with epilepsy (Tatum et al., 2018). Recording interictal epileptiform discharges (IEDs) confirms the diagnosis in patients with first seizure and aids in classification of the epilepsy type, a prerequisite for optimal therapeutic choice (Tatum et al., 2018). However, the sensitivity of a single, routine EEG recording with

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the standard, low-density (LD) electrode array is only 50% (Salinsky et al., 1987).

IEDs show marked fluctuation in time (Scherg et al., 2012), and the short 20–30 minutes recordings do not provide sufficient sampling in half of the cases (Salinsky et al., 1987). Multiple short recordings or extended duration recordings, such as ambulatory EEG recordings or long-term video EEG recordings, increase significantly the chance of recording IEDs and hence the diagnostic yield of EEG recordings (Salinsky et al., 1987; Meritam et al., 2018; Tatum et al., 2018).

Recent technological advances made it possible to increase significantly the spatial sampling of EEG recordings (Seeck et al., 2017). High-density (HD) electrode arrays, with 256 electrodes, evenly covering the scalp, can be rapidly applied, and due to the high input impedance amplifiers, EEG signals of high quality are recorded. Increasing the spatial sampling improved significantly the accuracy of IED source localization (Brodbeck et al., 2011). Anecdotal data suggested that HD recordings were able to identify IEDs even when they were not visible in LD recordings (Seeck et al., 2017). This raises the possibility that further diagnostic gain in identifying IEDs could be achieved by significantly increasing the spatial sampling beyond the standard electrode array. However, HD arrays are less feasible for long-term (LT) recordings (Nemtsas et al., 2017) and typically, short-term (ST) 30–90 minutes recordings are done with the HD arrays (Brodbeck et al., 2011). Hence, the increase in spatial sampling practically leads to a decrease in the recording duration, compared to the LD recordings. Nevertheless, this duration corresponds to the routine EEG recordings.

In this prospective study, we have evaluated the diagnostic yield of increasing spatial sampling by comparing HD with LD arrays, and evaluated the effect of the timing and duration of the recording by comparing LT with ST recordings.

2. Methods

2.1. Patients and recordings

We recruited consecutive patients with epilepsy, admitted to the epilepsy monitoring unit (Craciun et al., 2017) for presurgical evaluation at Copenhagen University Hospital, Rigshospitalet and at the Danish Epilepsy Centre, Dianalund, Denmark. The patients gave their informed consent, and the regional ethics committee approved the study (H-2-2013-038). Exclusion criterion: patients aged six years or younger.

LT video EEG recordings (1–6 days) were done using NicoletOne system (Natus Neuro, Middleton, WI 53562 USA). For LT recordings we used the standard 25 electrode array of the International Federation of Clinical Neurophysiology (IFCN) that included the inferior temporal chain on both sides (Seeck et al., 2017). Patients were typically tapered of antiepileptic medication before the start of the monitoring.

Immediately after the end of the LT monitoring we recorded ST EEG (30–150 min, depending on the cooperation of the patients) using a HD array. The ST-HD recordings were done using the EGI-net with 256-electrodes (Philips Neuro, Amsterdam, The Netherlands).

2.2. Data analysis and evaluation

For each patient, initially we analyzed three EEG datasets: LT-LD, ST-LD and ST-HD. The ST recordings were analyzed first in a spatially down-sampled array displaying only the 25-electrodes of the IFCN. Subsequently, ST recordings were analyzed in the full HD array. Since it is impossible to analyze recordings with all 256

channels displayed on the computer screen, HD channels were divided into four channel-groups, and the recordings were browsed four times. ST and LT recordings differed not only in their duration (how long they were recorded) but also in their timing (when they were recorded), since ST recordings were done after the LT recordings. To compensate for this, we did a temporal down-sampling of the LT recordings (similar to the spatial down-sampling of the ST recordings) and analyzed the first 90 minutes of the last night of sleep, from the LT recordings (shortened-LT recordings). Hence, four different datasets were analyzed.

Two experts in reading EEGs visually analyzed each dataset. They were allowed to switch between montages, to change gain and resolution in time, as well as digital filters. For LD recordings, longitudinal and transversal bipolar montages as well as common average montage were available. For HD recordings, the array was divided into four sub-groups, with 64 channels each, displayed in common average montage. In our centers, recordings are most often browsed in common average montage, since there is published evidence that this is more sensitive than bipolar montages (Rosenzweig et al., 2014). Any discordance was resolved by consensus discussions.

The experts identified IEDs using the operational definition of the recent edition of the IFCN glossary (Kane et al., 2017). Within each dataset, IEDs with peak negativity at the same electrode and with similar voltage topographies were grouped into IED clusters, at sub-lobar resolution, and these were logged for further analysis and comparison with the IED clusters from the other datasets of the same patient.

We evaluated the effect of spatial sampling on the diagnostic yield by comparing the number of IED-clusters identified in the HD array with the number of IED clusters identified in the LD array of the same ST recordings. Since the HD and LD recordings were simultaneous, this comparison was not affected by the timing and duration of the recordings.

We evaluated the effect of timing and duration of the recordings on the diagnostic yield by comparing the LT recordings with the ST recordings analyzed in LD array. This comparison was not affected by the spatial sampling, since both recordings were analyzed in LD array.

We compared the number of identified IED clusters in the different datasets using McNemar test with random permutation of the measurement within patient, to provide control of the type 1 error in presence of correlated observations (Eliasziw and Donner, 1991). The level of significance was set to 0.05.

3. Results

Sixty patients (32 women) aged between 7 and 61 years (mean: 32.5, median 30 years) were recruited to the study. The duration of the LT recordings was between 1 and 6 days (mean: 3.98; median: 4 days). The duration of the ST recordings was between 30 and 139 minutes (mean: 77.96, median: 73 minutes).

Totally, 89 IED clusters were identified in 57 patients. Three patients did not have IEDs in any of the recordings. Table 1 shows the number and localization of the IED clusters identified in the four datasets.

The effect of spatial sampling on the diagnostic yield: HD arrays identified two IED clusters in the ST recordings (one parietal and one frontal) that were missed in the LD arrays. This modest increase in diagnostic yield (2.63%) was not statistically significant (p = 0.5). Figs. 1 and 2 show the IEDs that were missed in the LD array. Although the sharp-transients are visible in the LD array too, they are less well-defined and they were originally interpreted as fluctuations of the background activity (Benbadis and Lin, 2008).

Table 1
Number and localization of the IED clusters identified in the four datasets. LT: long-term, ST: short-term, LD: low-density, HD: high-density recordings. Shortened-LT: 90 minutes epoch from the LT recording.

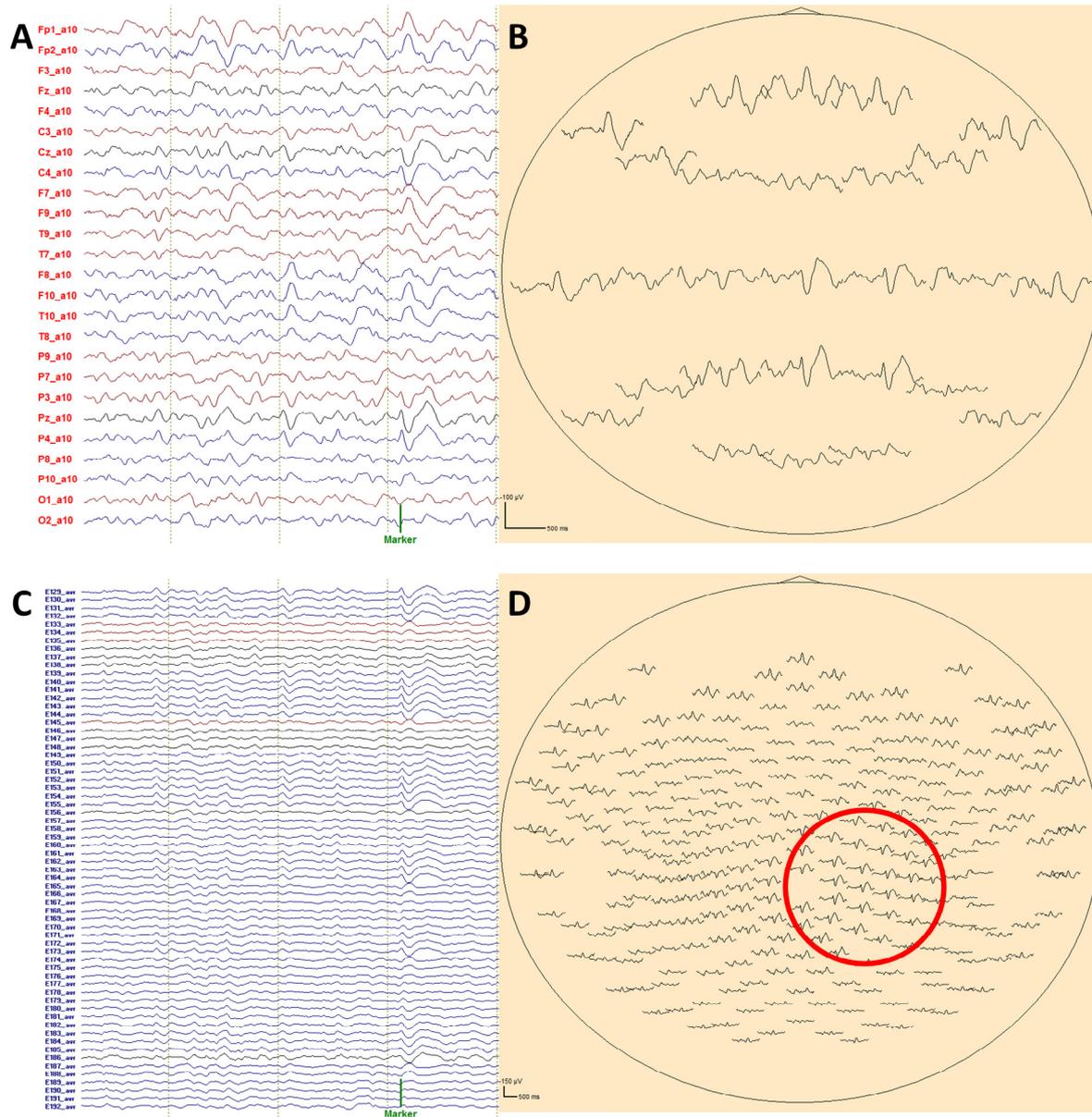| Type of recording	Frontal	Temporal	Central	Parietal	Occipital	Total
LT-LD	23	50	5	4	2	84
Shortened-LT-LD	21	45	5	3	2	76
ST-LD	20	45	5	4	2	76
ST-HD	21	45	5	5	2	78

Fig. 1. LD and HD EEG arrays in a patient with right parietal focus. A and B: LD array. C and D: HD array. Spikes are at the green vertical marker in A and C, and highlighted by the red circle in D.

In the HD array, due to the higher spatial sampling, the IED became obvious and were identified during the data analysis.

The effect of recording duration: the shortened, 90-minutes epochs of the LT recording (down-sampling in time of the LT recordings) missed eight clusters (p = 0.003) that were identified by analyzing the whole duration of the LT recordings. In this analysis both evaluations were using LD arrays.

The effect of timing of recording: LT recordings identified 11 IED clusters that were missed by the ST recordings. In this analysis, both evaluations were using LD array. On the other hand, ST recordings done following the LT recordings identified three IED clusters that were missed by the LT recordings. The diagnostic yield of LT recordings was significantly higher compared with the ST recordings (p = 0.048).
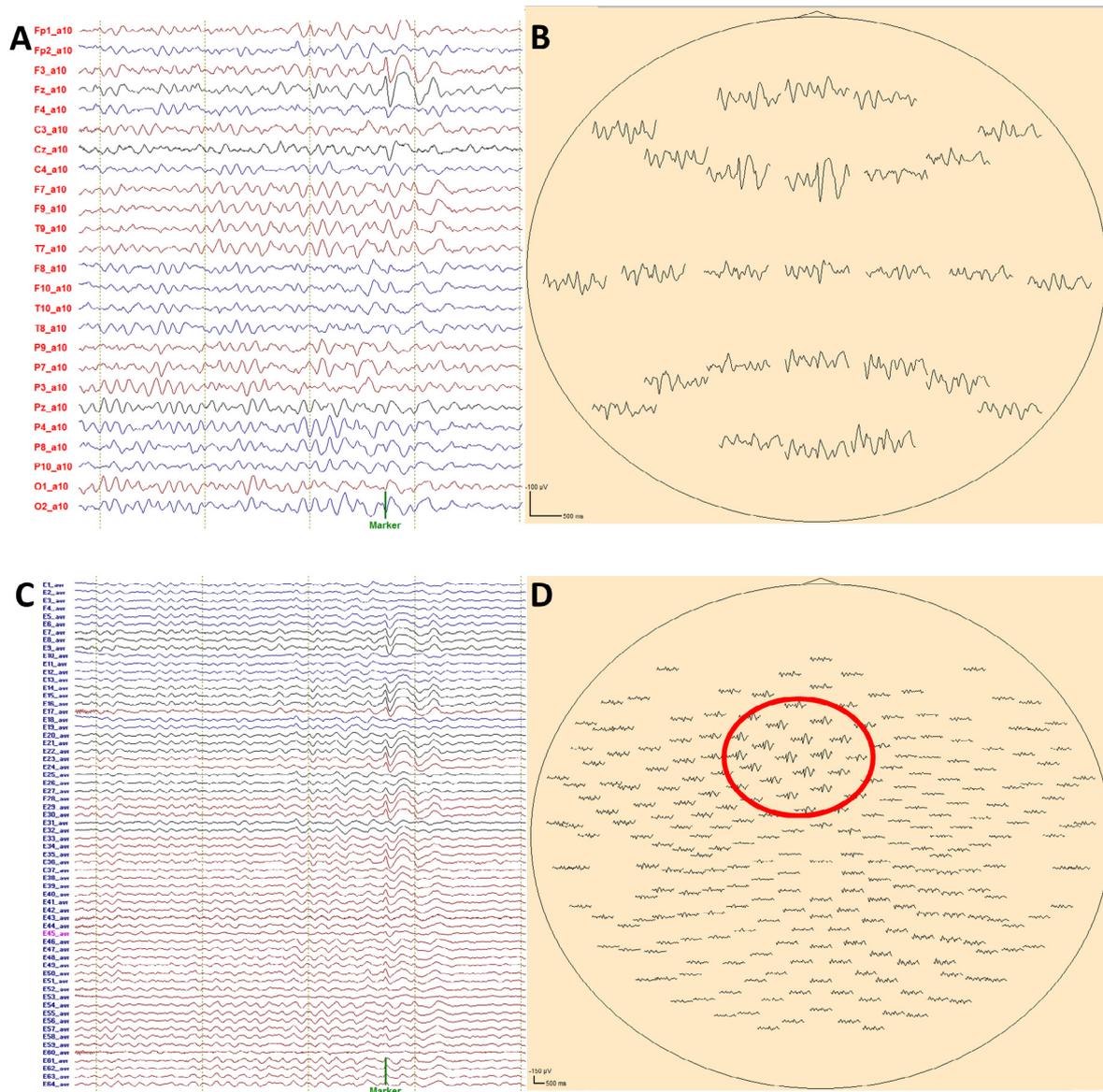
Fig. 2. LD and HD EEG arrays in a patient with left frontal parasagittal focus. A and B: LD array. C and D: HD array. Spikes are at the green vertical marker in A and C, and highlighted by the red circle in D.

4. Discussion

In this prospective study, spatial sampling beyond the standard IFCN array did not significantly increase the diagnostic yield. Only two additional IED clusters were identified in the HD array (2.6%). On the contrary, extended duration of the recording (median 4 days) led to a significant increase in the diagnostic yield, which is in accordance with previous studies (Tatum et al., 2018).

Simultaneous recordings with scalp and intracranial electrodes showed that in order to pass the skull at least 10 cm^2 of cortex had to be involved in the generation of the IEDs (Tao et al., 2005). The smearing effect of the skull leads to a wide distribution of the signals on the scalp, which can be detected by the lower density electrode array too. This explains why we failed to find a significant difference between the yield of the HD and the LD arrays. It is important to emphasize that our LD array was set up according to the IFCN standard (Seeck et al., 2017) and it included the inferior temporal chain, hence being able to record IEDs originating in the inferior-basal part of the temporal lobe (Bach Justesen et al., 2018). Previous studies demonstrated that localization of IEDs (Brodbeck et al., 2011) and of ictal EEG activity (Nemtsas et al., 2017, Rosenzweig et al., 2014) was more accurate when increasing the spatial sampling and HD arrays provided better information for mapping the propagation of epileptiform activity. However, this was not the case for identification of IEDs (diagnostic yield). Only two clusters (2.6%) labeled as non-epileptiform sharp transients in LD recordings were re-classified as epileptiform, in HD recordings. None of the clusters labeled as IED in LD array were considered non-epileptiform in HD array. There are two important explanations. First, our LD array included the six electrodes in the inferior temporal chain. This is a considerable improvement compared to the classical 10–20 array (Bach Justesen et al., 2018). Second, we identified the IEDs using the six operational criteria of the IFCN (Kane et al., 2017), which helps distinguishing between epileptiform and non-epileptiform sharp transients. One of these criteria is on the assessment of the voltage maps. These are constructed by interpolating data from the recording electrodes, so that the whole scalp surface has a voltage representation.

Several studies suggested that High Frequency Oscillations (HFOs) can be recorded with scalp electrodes (Kuhnke et al., 2019, Thomschewski et al., 2019). Since HFOs are much more focal than IEDs in scalp recordings, theoretically, a possible benefit of HD recordings could be the increased identification of HFOs. However, our study did not address this aspect.

In infants, the smearing effect of the scalp is significantly less than in adults and older children (Seeck et al., 2017). Therefore, it is theoretically possible that HD recordings could have a higher diagnostic yield for IEDs in that age group.

We only recruited patients who had focal epilepsy and, hence our findings comprise only focal IEDs. However, generalized IEDs have wide, bilateral, and synchronous distribution. Therefore, it is unlikely that the HD array would record more generalized IEDs than the LD array. We evaluated the diagnostic yield only for identification of IEDs and in patients older than 6 years. As mentioned above, the HD array could have a higher diagnostic yield for HFOs and for IEDs in infants. This needs further investigation.

It is important to highlight that detection sensitivity was determined in patients referred for epilepsy monitoring and is not representative of the yield in screening outpatients (only three patients did not have IEDs).

5. Conclusions

Increasing the spatial sampling of EEG beyond the standard IFCN array does not increase the diagnostic yield for identifying IEDs significantly. Extended duration (LT) recordings have significantly higher diagnostic yield than routine (ST) recordings.

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Author statements

The corresponding author, Sándor Beniczky, has full access to all data and the right to publish such data. All authors participated in a meaningful way in the preparation of the manuscript.

Disclosure of Competing Interest

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

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