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FULL-LENGTH ORIGINAL RESEARCH

Personalized seizure signature: An interpretable approach to false alarm reduction for long-term epileptic seizure detection

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Abstract

Objective: Long-term automatic detection of focal seizures remains one of the major challenges in epilepsy due to the unacceptably high number of false alarms from state-of-the-art methods. Our aim was to investigate to what extent a new patient-specific approach based on similarly occurring morphological electroencephalographic (EEG) signal patterns could be used to distinguish seizures from nonseizure events, as well as to estimate its maximum performance.

Methods: We evaluated our approach on >5500 h of long-term EEG recordings using two public datasets: the PhysioNet.org Children's Hospital Boston–Massachusetts Institute of Technology (CHB-MIT) Scalp EEG database and the EPILEPSIAE European epilepsy database. We visually identified a set of similarly occurring morphological patterns (seizure signature) seen simultaneously over two different EEG channels, and within two randomly selected seizures from each individual. The same seizure signature was then searched for in the entire recording from the same patient using dynamic time warping (DTW) as a similarity metric, with a threshold set to reflect the maximum sensitivity our algorithm could achieve without false alarm.

Results: At a DTW threshold providing no false alarm during the entire recordings, the mean seizure detection sensitivity across patients was 84%, including 96% for the CHB-MIT database and 74% for the European epilepsy database. A 100% sensitivity was reached in 50% of patients, including 79% from the CHB-MIT database and 27% from the European epilepsy database. The median latency from seizure onset to its detection was 17 ± 10 s, with 84% of seizures being detected within 40 s.

Significance: Personalized EEG signature combined with DTW appears to be a promising method to detect ictal events from a limited number of EEG channels with high sensitivity despite low rate of false alarms, high degree of

interpretability, and low computational complexity, compatible with its future use in wearable devices.

KEYWORDS
false alarms, ictal EEG, seizure detection, seizure signature

1 | INTRODUCTION

Ambulatory long-term monitoring and detection of all seizure types, using wearables compatible with a normal social life, represent both an unmet need and a significant challenge. Non-electroencephalography (EEG)-based wrist- or arm-worn solutions, using either accelerometry,[1–6] surface electromyography,[7–10] electrodermal activity, or any combination of those,[11–14] have so far only proved reliable to detect generalized tonic–clonic seizures (GTCSs) or major motor seizures.[15] EEG-based solutions might prove more effective to detect other seizure types, but face several issues, including high sensitivity to artifacts and stigma due to the appearance of currently available EEG caps.[16] However, advances in miniaturized electronics now allow recording of EEG using low-stigma electrodes placed either behind the ear (behind-the-ear EEG),[17–21] in the ear canal (ear-EEG),[22,23] hidden in the temples of glasses,[24–26] or in a smart headband.[27] Among other issues that need to be addressed to develop effective ambulatory EEG-based seizure detection, the specificity of the embedded online algorithm is a key factor. Currently available EEG-based online seizure detectors used in video-EEG monitoring units are associated with an unacceptable rate of false alarms for ambulatory patients, varying between .1 and 5 per hour.[28]

Based on the well-known observation that the EEG signature of seizures demonstrates a high level of interindividual heterogeneity and intraindividual reproducibility, we developed a novel approach to seizure detection, based on an interpretable and patient-specific EEG similarity analysis using dynamic time warping (DTW). The latter was chosen to be compatible with energy-efficient online processing, which could later be embedded in a wearable. The algorithm was evaluated on EEG data recorded during in-hospital long-term monitoring, with a threshold set at no false alarm during several days of recordings. The purpose of the study was to assess the extent to which the proposed method could be used to distinguish seizures from nonseizure events in long-term EEG recordings, and its maximum achievable sensitivity without false positive alarms.

Key Points

- We developed a method that dramatically minimizes false detection of ictal EEG by using the intraindividual stereotypy of ictal patterns
- Patients' specific signatures were visually identified across two seizures, and their reoccurrence was searched for using dynamic time warping
- The method was tested in 54 patients and >5500 h of recordings from the CHB-MIT Scalp EEG and the EPILEPSIAE European epilepsy databases
- At a preset threshold that ensured no false alarms, DTW achieved an 84% sensitivity overall, which reached 100% in half of the patients
- This novel method, based on the intraindividual stereotypy of ictal patterns, appears promising for very long-term ambulatory monitoring

2 | MATERIALS AND METHODS

2.1 | Datasets

We used the scalp EEG recordings from the PhysioNet.org Children's Hospital Boston–Massachusetts Institute of Technology (CHB-MIT) Scalp EEG database[29] and EPILEPSIAE European epilepsy database.[30] The former consists of >980 h of long-term EEG recordings obtained from 24 pediatric subjects, aged 10 ± 6 years, whereas the latter contains a total of >4600 h of continuous recordings obtained from 30 patients with epilepsy aged 41 ± 15 years. Ictal and interictal phases are clearly indicated in both databases. For ictal events, the EEG onset and offset timestamps of each seizure are specified in the provided metadata. In one of the two databases (EPILEPSIAE), 31 of the 277 seizures (11%) were annotated as clinical seizures without indication of a detectable EEG onset. Given the EEG-based nature of our method, we decided to exclude these events from our study. EEG signals in both databases were sampled at $f_s = 256$ Hz, and the placement

of scalp electrodes was based on the international 10–20 system.[31] We did not apply any additional filter for the purpose of this study.

2.2 | Personalized seizure signature

We defined a personalized seizure signature S as a set of similarly occurring morphological patterns p_i that are likely to be seen within each seizure, in which each p_i represents one unique patient's specific seizure pattern. Seizure patterns, of 1- to 10-s duration, were manually selected at the individual level by visualizing raw ictal parts of two randomly chosen seizures from the same patient, across all EEG signal channels on two different screens (see Figure 1). This procedure was performed blinded to any indication provided in the available databases regarding channels affected in each seizure. Seizures where artifacts contaminated all EEG channels were excluded from this process. Similarity between patterns was assessed by taking into consideration the duration, waveforms, and pair of channels where they were best observed. Thus, seizure patterns were all defined by their occurrence across two different EEG channels. The number of seizure patterns selected per patient could vary from one to three. Multiple patterns proved necessary in some patients, either to account for different seizure types in the same individual, or to increase sensitivity. Nonetheless, we followed a conservative approach through which we aimed to minimize the number of seizure patterns needed for a given seizure signature, as well as the number of different seizures used for their extraction. Once a first pattern had been selected, we assessed its sensitivity according to the detection method described further. In the event that sensitivity exceeded 50%, we did not search for another pattern. In contrast, if sensitivity remained <50%, we then searched for another pattern within the same seizures from which the first pattern was selected. If sensitivity remained <50%, we then selected other seizures for pattern identification.

2.3 | Epileptic seizure detection flow in long-term EEG recordings

Once a pattern p_i was selected, the corresponding EEG segment from the seizure displaying the best signal quality was used to search for similar patterns in the entire available recording. To perform this comparison, we first normalized the EEG traces by removing the average value of the channels that constitute the seizure signature. Then, the similarity was estimated by minimizing the distance between the signal segment and the selected seizure pattern. We used DTW as the underlying distance metric,[32] rather than the commonly used Euclidean distance,[33] to account for similarly occurring morphological segments being out of phase in the time axis.[34] Euclidean distance assumes a temporal alignment of the considered morphological segments and is very sensitive to small distortions in the segment shape. DTW takes these distortions into consideration by aligning the signal segments before calculating the distance measure. To detect seizures across

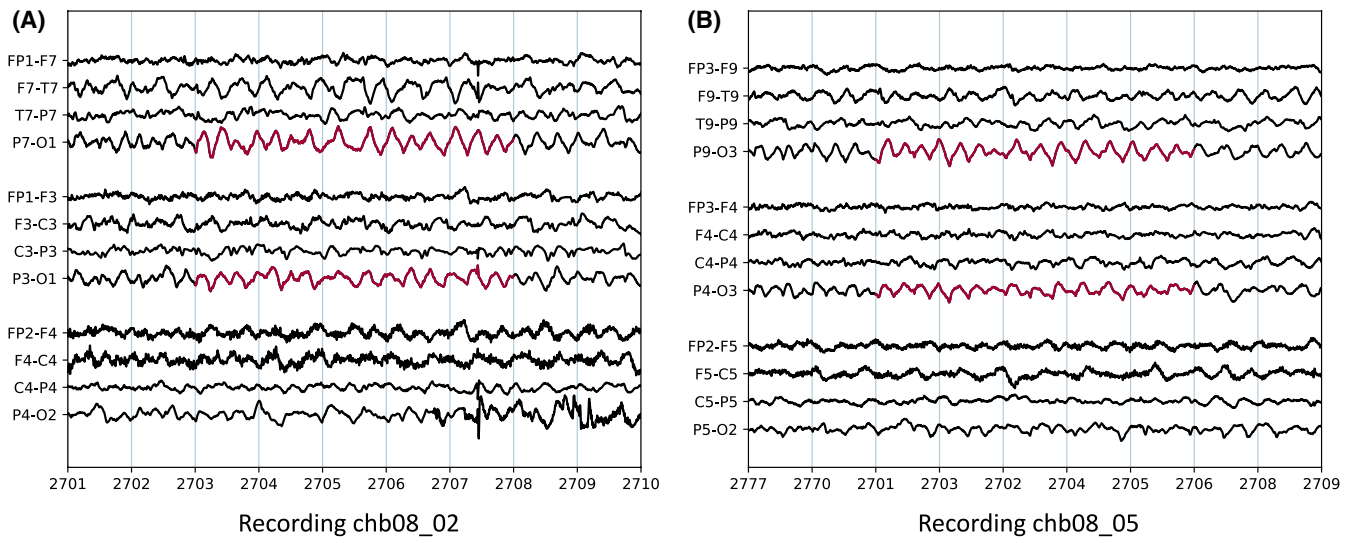

FIGURE 1 Selection of a personalized seizure signature. Two raw ictal electroencephalographic (EEG) recordings correspond to randomly chosen Seizures #2 and #5 from Patient chb08 from the CHB-MIT (Children's Hospital Boston–Massachusetts Institute of Technology) Scalp EEG database. Recordings start 14 and 13 s after seizure onset for (A and B), respectively, and are plotted using the Python Matplotlib library. Visual inspection of the two seizures delineated a comparable 5-s long seizure pattern involving channels P7-O1 and P3-O1. That observed in A was then used as a personalized seizure signature to detect other seizures from the same patient

the entire duration of available recordings, we used a sliding window, the length of which corresponded to that of the pattern p_i, with a step of 1 s. Once the DTW metric D_i had been calculated over the entire recording of a given patient, we set up an optimal threshold h_i, specific to this patient, that allowed detection of as many seizures as possible without false positives (see Figure 2). As previously described, sensitivity was then calculated for each patient and seizure signature, and the number of patterns adapted to its performance.

2.4 | Evaluation metrics

To assess the performance of our approach in terms of the maximum number of seizures that can be detected without false positive alarm over the entire duration of available recordings for each patient, we used sensitivity as the main evaluation metric $\frac{t_p}{t_p+f_n}$, where t_p and f_n represent the number of true positives and false negatives, respectively. We also calculated the detection latency as the time in seconds from the seizure onset to the detection time. Due to the difference in performance of our method on the two databases used, we performed a post hoc analysis to compare the quality of their ictal EEG signal using the state-of-the-art Score 1 metric.[35]

3 | RESULTS

The number of seizures and duration of available EEG recordings per patient used in this study are given in Table 1. Overall, the median number of seizures and mean duration of recordings across the two datasets were 7 ± 2 seizures and 103 ± 65 h of recordings (i.e., approximately 4 days) per patient.

The overall performance of our method is shown in Figure 3, where vertical bars represent the sensitivity obtained in each patient across the entire duration of available EEG recordings. A detailed list of seizures detected using the selected signature from each patient is available in Table S1, with illustrations of such signatures in Figure 1 and Figures S1–S9.

In the 24 subjects from the CHB-MIT database, the no-false-positive mean sensitivity ± SD was 96% ± 11%, reaching 100% in 19 patients (79%), with all patients benefiting from >68% sensitivity (Table 1, Figure 3A). The personalized seizure signature used to achieve this performance consisted of a single seizure pattern in 71% of patients (17 patients), two different seizure patterns in five patients (21%), and three patterns in two subjects (8%; Table 1). The performance was lower in the 30 patients from the European epilepsy database, where the no-false-positive mean sensitivity ± SD was 74% ± 30%, including 26 patients (87%) with >50% sensitivity, eight of whom (27%) showed 100% sensitivity (Table 1, Figure 3B). One patient (3%) only demonstrated 33% sensitivity, and no seizures could be detected in three patients (10%). This performance was achieved using a single pattern in 11 patients (37%), whereas two and three patterns were required in 14 (47%) and two (7%) patients, respectively (Table 1). When pooling the two databases together, the average sensitivity was 84% ± 25%.

We visually inspected all undetected seizures from both datasets and identified that 42% were not detected due to the absence of the chosen EEG seizure signature in the remaining seizures (Figures S9–S13), whereas 29% were completely obscured by artifacts, which hindered the pattern detection. In addition, 22% of seizures did not demonstrate clearcut ictal discharge on scalp EEG, even though they were annotated with an EEG onset, and 7% appeared too short to identify a reproducible pattern. To further explore the reasons underlying the differences in performance over the two databases, we calculated the Score 1 EEG quality metric. As illustrated in Figure 4, the dispersion of values proved greater in the European

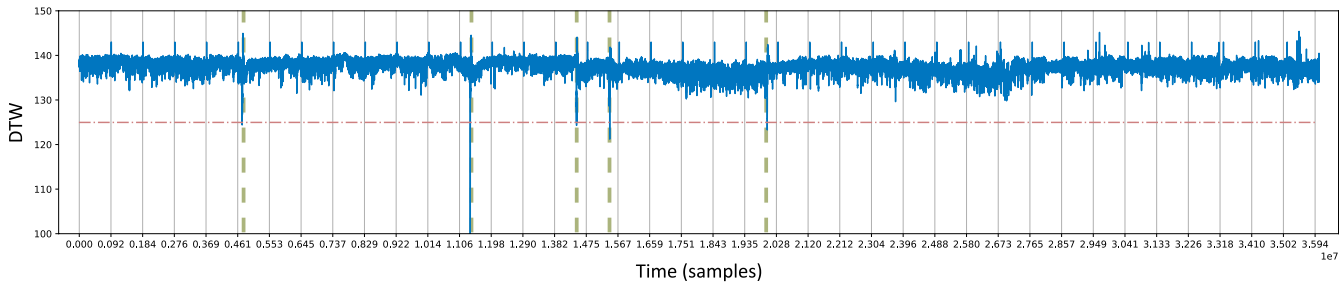

FIGURE 2 Selection of threshold *hi* for the dynamic time warping (DTW) metric *Di*. Graph displays DTW *Di* values calculated over 39 h of recording from Patient chb05 from the CHB-MIT (Children's Hospital Boston–Massachusetts Institute of Technology) Scalp EEG database using his personalized seizure signature extracted from Seizure #2. Vertical green dashed lines indicate the occurrence of five seizures during this recording, and are associated with low *Di* values. The red dash-dot horizontal line shows the applied threshold *hi* that enables detection of all seizures while ensuring lack of false positive results

TABLE 1 Number of recorded seizures, detected seizures, chosen EEG patterns, and duration of available EEG recordings per subject

CHB-MIT database																									
Patient ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Seizures, *n*	7	3	7	4	5	10	3	5	4	7	3	40	12	8	20	10	3	6	3	8	4	3	7	16
Detected seizures, *n*	7	3	7	4	5	10	3	5	4	7	3	27	12	8	19	7	3	6	3	8	3	3	6	16
Pattern number	1	1	1	1	1	3	1	1	1	1	1	3	2	1	2	2	2	2	1	1	1	1	1	1
Recording duration, h	41	36	39	157	40	67	68	21	68	51	35	24	33	26	41	19	22	36	30	28	33	32	27	22
European epilepsy database																								
Patient ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Seizures, *n*	11	7	10	6	6	11	6	7	8	5	18	6	10	9	8	6	4	6	9	4	20	4	7	7	9	10	5	6	9	9
Detected seizures, *n*	9	6	9	4	6	10	6	7	6	6	6	7	8	7	5	4	3	5	6	4	20	3		6	9	7	5		8	5
Pattern number	1	1	1	2	2	1	1	2	1	3		2	1	1	2	2	2	2	2	2	1	1		3	1	2	2		2	2
Recording duration, h	165	160	162	144	160	160	178	138	94	116	119	136	139	160	159	163	119	93	160	179	162	165	267	160	163	95	168	138	238	160

Abbreviations: CHB-MIT, Children's Hospital Boston–Massachusetts Institute of Technology; EEG, electroencephalographic.

epilepsy database, with several recordings having a particularly low EEG signal quality.

The detection latency results for both databases are shown in Figure 5, with 171 of 179 (96%) detected seizures from the CHB-MIT database and 129 of 181 (71%) from the European epilepsy database identified in <40 s following seizure onset. This latency necessarily depended of the position of the selected seizure signature within each seizure.

3.1 | Unlabeled seizures

In two subjects, the optimum threshold to detect as many seizures as possible without false positive alarms was abnormally low due to the presence of sharp declines in the DTW metric, highly suggestive of seizure occurrence, during interictal periods. After a careful review of the corresponding EEG traces by expert neurologists, we concluded that these sharp declines in DTW likely corresponded to unlabeled ictal EEG discharges. This is illustrated in Figure 6 for one of the two patients, chb24, from the CHB-MIT database. The other subject with suspected unlabeled seizures was Patient #308102 from the European epilepsy database.

4 | DISCUSSION

We found that an original algorithm, based on the identification of personalized EEG-based seizure signatures previously defined in two seizures from the same patient, appears capable of distinguishing seizures from nonseizure activities, while ensuring a high sensitivity without false alarms in the majority of patients. The video-EEG recordings available in the two tested databases amounted to an average duration of approximately 4 days, suggesting that false alarm rates (FARs) for longer periods of recordings would be lower than one every 4 days, a figure likely to be acceptable for many patients. Furthermore, the computing and energy requirements of our algorithm make it appropriate for embedding and continuous monitoring within a wearable device including behind-the-ear EEG,[17–21] ear-EEG,[22,23] smart glasses,[24–26] and smart headbands.[27] Moreover, our algorithm can be used for long-term subdermal EEG monitoring, which offers higher resolution signal with fewer artifacts.[36]

Our method does not belong to any type of previously described seizure detection algorithm. Its novelty relies on the use of morphological patterns that are likely to be seen in EEG signals at the time of seizures for the majority of epileptic patients. Other automatic seizure detection algorithms are based on a set of predefined features extracted

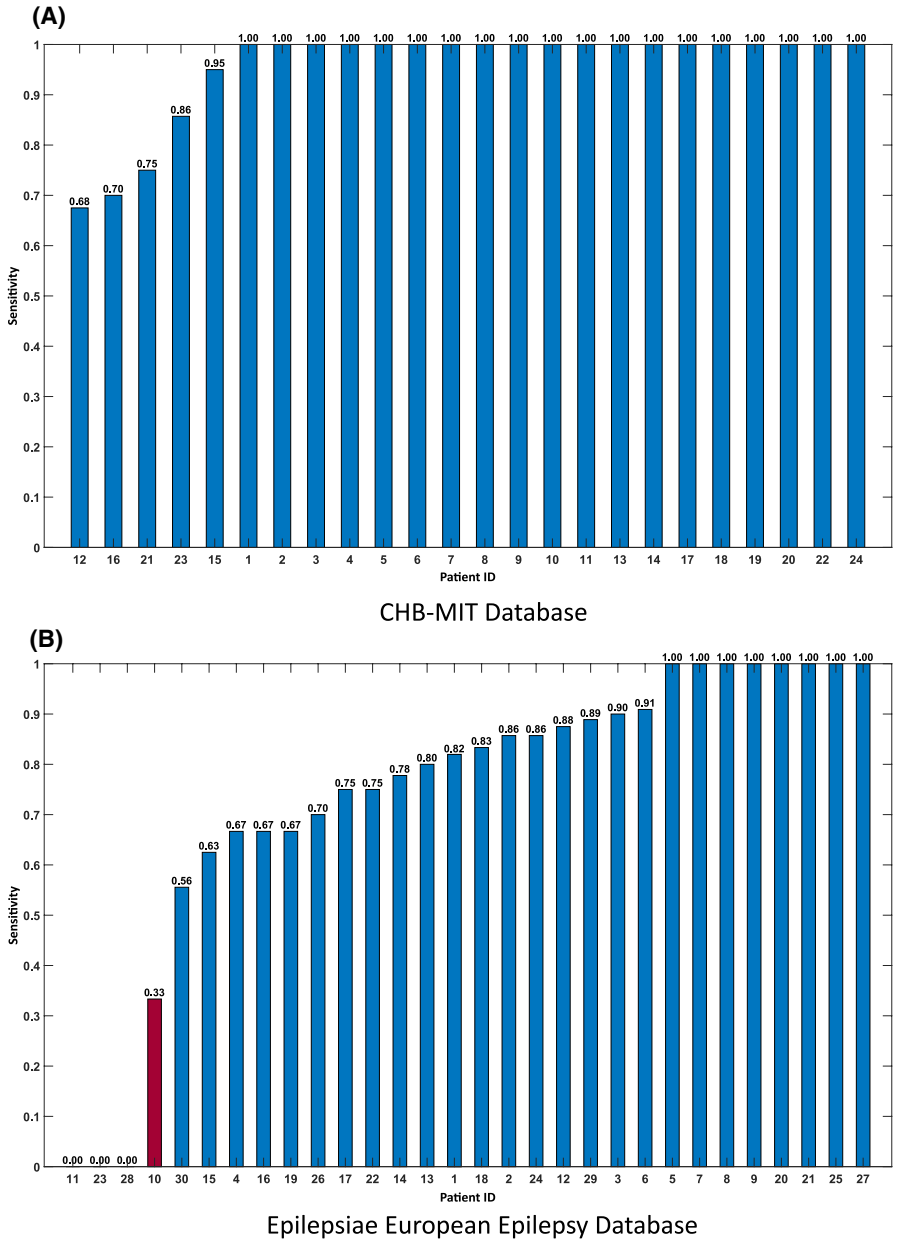

FIGURE 3 False alarm-free sensitivity of our method in each individual patient. (A) Patients from the Children's Hospital Boston–Massachusetts Institute of Technology (CHB-MIT) database: False alarm-free sensitivity was >50% in all 24 patients (blue columns), including 100% sensitivity in 19 (79%). (B) Patients from the EPILEPSIAE European epilepsy database: False alarm-free sensitivity was >50% in 87% of patients (blue columns), including 100% in eight patients (27%). One patient (3%) only demonstrated 33% sensitivity (red column), and no seizure could be detected in three patients (10%)

from EEG signals that are sent to the input of a trained classifier that distinguishes seizures from nonseizure activities. The most commonly reported features rely on the time and frequency domain EEG signal analysis.[37–40] One of the EEG-based state-of-the-art methods for epileptic seizure detection used a periodic waveform analysis to detect rhythmic EEG patterns that are likely to be found during seizures.[37] These rhythmic patterns are detected by thresholding two main features: the periodic energy index (PEI), representing the maximum harmonic EEG signal energy, and the periodic waveform index, obtained by normalizing the PEI to the total signal energy. This algorithm was evaluated on 4300 h of EEG recordings obtained from 48 patients, reaching a mean sensitivity of 83%, with an average FAR of .3/h. Another similar approach to extract relevant EEG features uses a short time Fourier transform to calculate the integrated power in the frequency band 2.5–12 Hz from a multichannel seizure detection montage referenced against the average of Fz-Cz-Pz.[38] An adaptive thresholding technique was further applied to detect seizure occurrences, resulting in a sensitivity of 87.3% and an FAR of .22/h obtained on 25 278 h of EEG recordings in 159 patients.

Similar methodology based on the calculation of different features has also been used in wearable EEGs. A behind-the-ear EEG device, using time and frequency domain features along with different entropies and a support vector machine classifier, achieved a mean sensitivity of 69% and an FAR of .49/h.[20] Time domain features such as a moving-median filtered sliding window variance estimate were also used to detect seizures from ear-EEG signals, reaching a sensitivity of 100% without false alarms.[41]

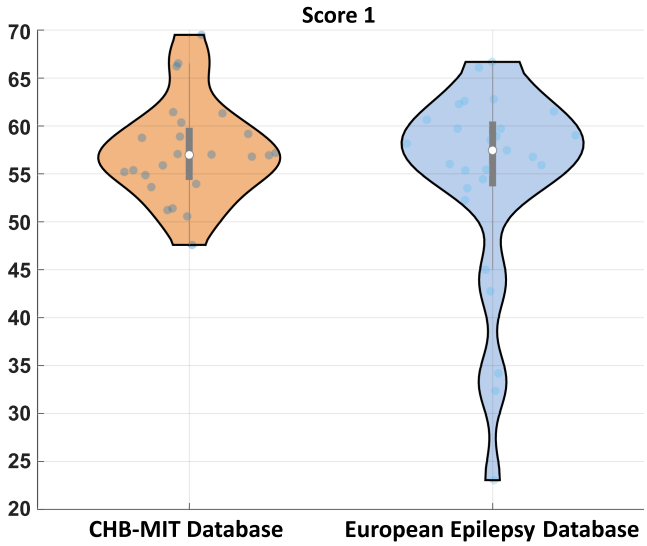

FIGURE 4 Quantitative electroencephalographic (EEG) signal quality assessment. The Score 1 values for the EEG recordings of the two databases show a number of lower quality recordings (low Score 1 values) in the European epilepsy database as compared to the Children's Hospital Boston–Massachusetts Institute of Technology (CHB-MIT) database

However, this latter method was only tested on a small dataset of three subjects, and for the detection of GTCSs specifically.

Apart from feature-based algorithms, the current trend in machine learning has used deep learning, including a convolutional neural network (CNN), to automatically learn EEG features intrinsic to seizures and nonseizure events, without any feature engineering beforehand.[42–45] Such methods have reached an average sensitivity of 94.07% with an FAR of .66/h, obtained on the CHB-MIT database.[42] Another end-to-end seizure detection algorithm, based on a deep CNN, used additional dropout layers and batch normalization after every convolutional layer, yielding an overall sensitivity of 95.8% and an FAR of .58/h obtained across 29 pediatric patients.[41] Apart from feeding a deep neural network with raw EEG signals, EEG image-based representation can be used for seizure detection.[44,46] First, EEG signals are transformed into a sequence of topology-preserving multispectral images, and then a recurrent-convolutional neural network is trained, resulting in an average sensitivity of 85% and an FAR of .8/h. A seizure detection algorithm based on a generative adversarial network using unsupervised learning was recently applied to behind-the-ear EEG, and resulted in a sensitivity of 96.3% and an FAR of .14/h.[19]

As illustrated above, currently available EEG-based algorithms suffer from false positive alarms that range between .1 and 5 per hour,[28] hindering their acceptance in ambulatory long-term patients' monitoring.[46] This issue is likely to partly reflect the level of interindividual differences in ictal scalp EEG patterns, which necessarily reduces the capacity for any given nonpersonalized algorithm to distinguish ictal from interictal EEG patterns across individuals. In contrast, one can take advantage of the well-known high level of intraindividual stereotypy of seizure patterns to achieve better performing EEG-based seizure detection, as demonstrated in this study. A first step in that direction was to take into account the six most common types of ictal EEG morphologies in an otherwise feature-based algorithm trained through a support vector machine classifier.[47] When applied on >1400 h of recordings and 57 patients, this method achieved an average correct detection rate of >96%, with a mean FAR of <.25/h as compared to <.5/h when not using specific ictal morphologies. Overall, this study demonstrated the value of a more personalized seizure detection approach without the necessity to adapt the algorithm to individual patients. Nonetheless, this interesting approach still suffers from a relatively high FAR, as compared to the lack of such false positives provided by our method over an average duration of 4.3 days of recording per patient (5580 h in total). On the other hand, our method comes with some limitations. Although we only needed a single seizure pattern to detect all ictal events without false alarms in the majority of cases, multiple patterns were required for some patients to optimally distinguish the ictal events from the interictal background. One future line of work shall be to combine these patterns in a single seizure signature to optimize the online EEG processing.[48,49] In other patients, several seizure signatures will still be required to detect truly different seizure types occurring in the same patient.

We observed a difference in the sensitivity of our method between the two datasets used in this study, with greater sensitivity for the CHB-MIT database than for the European epilepsy database. One possible explanation for this observation is the difference in the two databases' age groups and types of epilepsy. Namely, EEG signals from the CHB-MIT database were collected from pediatric patients (aged 10 ± 6 years), whereas those from the European epilepsy database were primarily collected from adults (aged 41 ± 15 years). The CHB-MIT and EPILEPSIAE databases also differ in terms of EEG montage, with the former providing bipolar montage and the latter providing common-average montage. Another possible explanation could be the difference in EEG signal quality observed between the two databases, with only patients from the European epilepsy database showing low Score 1 values, suggesting poor EEG signal quality.

Given the EEG-based nature of our seizure detection method, we excluded from this study those seizure events not associated with a detectable EEG onset, which represented 31 of 475 seizures (7%) across the two databases. It is well known that some seizures are

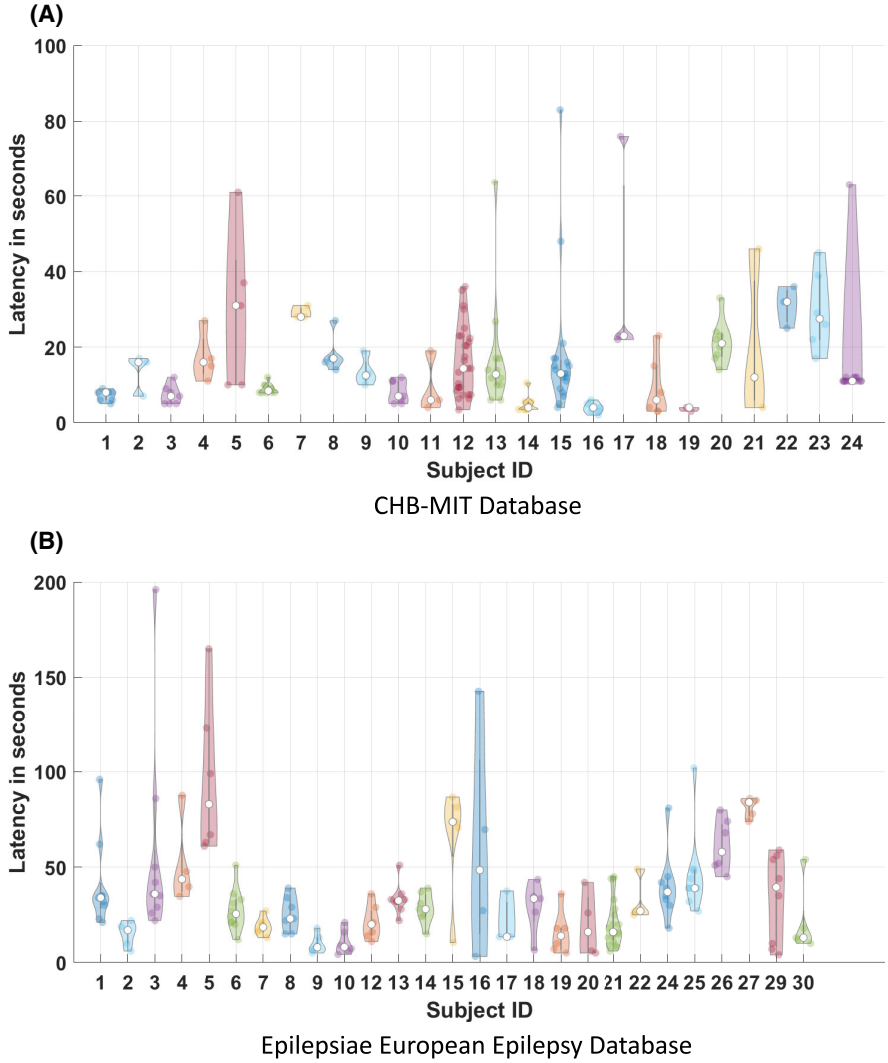

FIGURE 5 Latency of seizure detection per individual patient for the CHB-MIT Database (A) and EPILEPSIAE European Epilepsy Database (B). Violin plots with median (white dots) and interquartile (colored dots) values of the latency in seconds from seizure onset (as recorded in the database) to seizure detection, in each individual patient

not associated with detectable scalp EEG findings, a situation that cannot be tackled with our method. There were also a few cases for which our approach failed to detect a significant proportion or even all epileptic seizures. Here again, this appeared to reflect the lack of visually detectable scalp EEG ictal discharge in some patients, whereas in others, our false negative findings appeared to reflect either the presence of muscle or movement artifacts completely obscuring EEG traces, an insufficient duration of seizure, or the lack of reproducibility of the seizure signature.

Further caution needs to be considered in the interpretation of the performance of our method. First, the value of each individual threshold used to distinguish seizures from nonseizure events was selected a posteriori on the basis of the entire signal recording. A prospective assessment might provide less sensitive findings or more false alarms. An online version of the algorithm is currently being developed to test this critical issue. Our method, while relying on only two EEG leads to delineate a seizure signature, took advantage of the entire 10–20 system to select the most appropriate couple of leads. In future ambulatory solutions, a lower number of recording leads will be available, which could also reduce the performance of our method. Most importantly, the EEG recordings used for this study were obtained in patients undergoing in-hospital video-EEG monitoring, during which patients are mostly laying in their beds with limited motor activities. In a real-life setting, daily motor activities are likely to generate much more movements and muscle artifacts than those observed in-hospital. This issue might be tackled by using subcutaneous EEG recordings[36] or optimized methods to reject artifacts. Another limitation of our approach is that it first needs to identify the most typical seizure pattern(s) in each individual. Currently, this would be primarily performed during in-hospital video-EEG monitoring, an investigation increasingly undertaken in patients with drug-resistant seizures. In the future, home-based video-EEG, which is rapidly developing in several countries, will leverage the possibility to obtain ictal EEG recordings.[50] Another related limitation of our method is

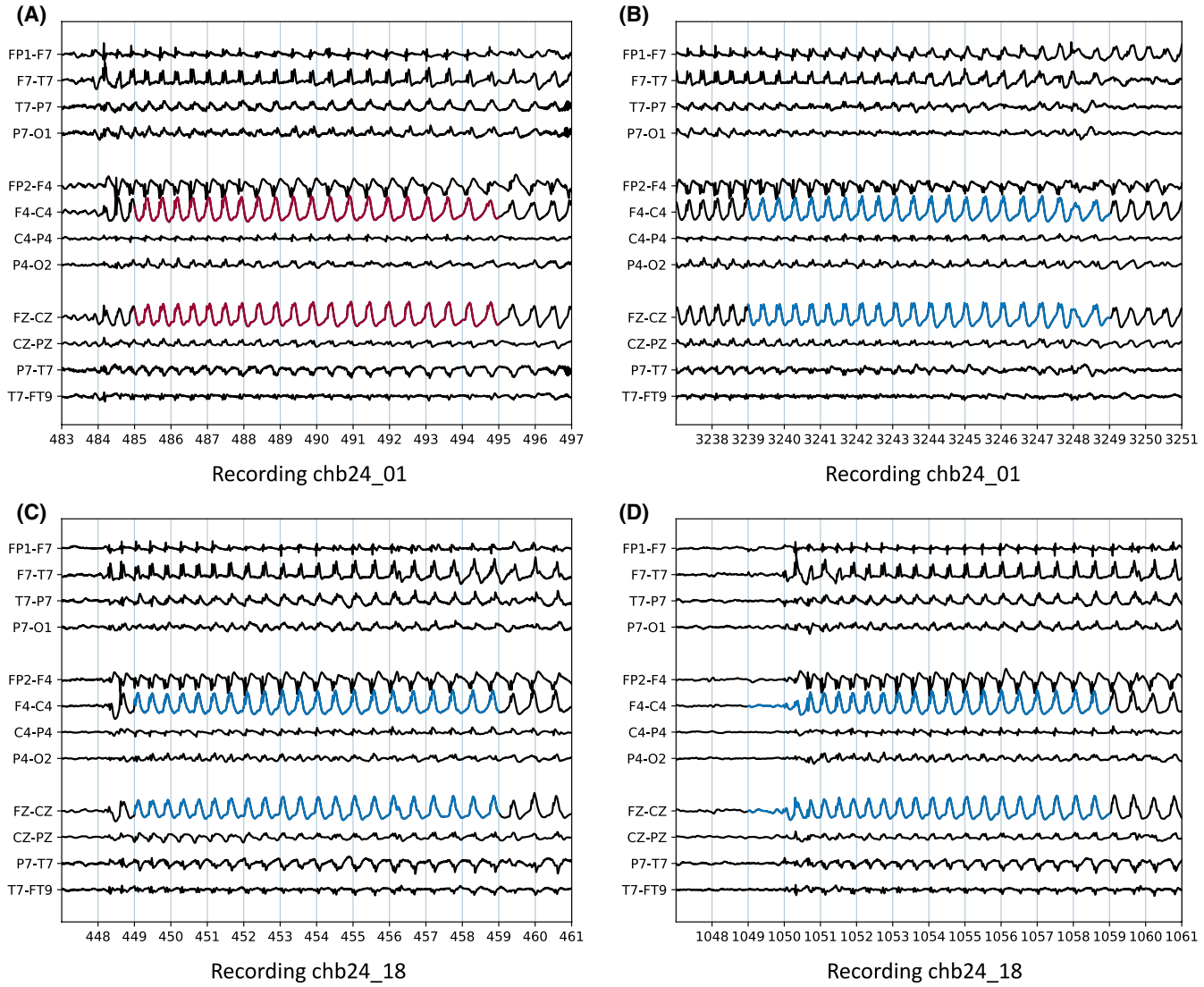

FIGURE 6 Unlabeled seizures detected by our algorithm. (A) A 10-s personalized seizure signature was selected from Seizure #1 and channels F4-C4 and FZ-CZ (red waveforms) in Patient chb24 from the CHB-MIT (Children's Hospital Boston–Massachusetts Institute of Technology) database. (B–D) Our dynamic time warping-based algorithm detected three very comparable segments (blue waveforms) in the same patient. These were not labeled as seizures in the database, but the electroencephalographic pattern is highly suggestive of an ictal event

that seizure signatures were delineated through visual inspection of EEG. This could be readily replaced by applying motif discovery algorithms,[51,52] an approach we are planning to implement in the near future.

5 | CONCLUSIONS

The main aim of this study was to present a patient-specific approach for EEG-based ambulatory long-term automatic seizure detection based on the reproducible morphological seizure segments, with the intention of removing false positive alarms. According to its performance tested over two public databases and 54 patients, our highly interpretable and energy-efficient algorithm, based on the similar morphological EEG signal patterns observed across seizures in individual patients, appears to represent a suitable tool for future wearable EEG seizure detection systems.

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CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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REFERENCES

1. Becq G, Kahane P, Minotti L, Bonnet S, Guillemaud R. Classification of epileptic motor manifestations and detection of tonic-clonic seizures with acceleration norm entropy. IEEE Trans Biomed Eng. 2013;60(8):2080–8.
2. Beniczky S, Polster T, Kjaer TW, Hjalgrim H. Detection of generalized tonic-clonic seizures by a wireless wrist accelerometer: a prospective, multicenter study. Epilepsia. 2013;54(4):e58–61.
3. Patterson AL, Mudigoudar B, Fulton S, McGregor A, Poppel KV, Wheless MC, et al. SmartWatch by SmartMonitor: assessment of seizure detection efficacy for various seizure types in children, a large prospective single-center study. Pediatr Neurol. 2015;53(4):309–11.
4. Kusmakar S, Karmakar C, Yan B, Obrien T, Muthuganapathy R, Palaniswami M. Automated detection of convulsive seizures using a wearable accelerometer device. IEEE Trans Biomed Eng. 2019;66(2):421–32.
5. Kusmakar S, Karmakar CK, Yan B, O'Brien TJ, Muthuganapathy R, Palaniswami M. Detection of generalized tonic-clonic seizures using short length accelerometry signal. Annu Int Conf IEEE Eng Med Biol Soc. 2017;2017:4566–9.
6. Johansson D, Ohlsson F, Krýsl D, Rydenhag B, Czarnecki M, Gustafsson N, et al. Tonic-clonic seizure detection using accelerometry-based wearable sensors: a prospective, video-EEG controlled study. Seizure. 2019;65:48–54.
7. Conradsen I, Beniczky S, Wolf P, Jennum P, Sorensen HB. Evaluation of novel algorithm embedded in a wearable sEMG device for seizure detection. Annu Int Conf IEEE Eng Med Biol Soc. 2012;2012:2048–51.
8. Szabó C, Morgan LC, Karkar KM, Leary LD, Lie OV, Girouard M, et al. Electromyography-based seizure detector: preliminary results comparing a generalized tonic-clonic seizure detection algorithm to video-EEG recordings. Epilepsia. 2015;56(9):1432–7.
9. Halford JJ, Sperling MR, Nair DR, Dlugos DJ, Tatum WO, Harvey J, et al. Detection of generalized tonic-clonic seizures using surface electromyographic monitoring. Epilepsia. 2017;58(11):1861–9.
10. Beniczky S, Conradsen I, Henning O, Fabricius M, Wolf P. Automated real-time detection of tonic-clonic seizures using a wearable EMG device. Neurology. 2018;90(5):e428–34.
11. Poh MZ, Loddenkemper T, Reinsberger C, Swenson NC, Goyal S, Sabtala MC, et al. Convulsive seizure detection using a wrist-worn electrodermal activity and accelerometry biosensor. Epilepsia. 2012;53(5):e93–7.
12. Milosevic M, Van de Vel A, Bonroy B, Ceulemans B, Lagae L, Vanrumste B, et al. Automated detection of tonic-clonic seizures using 3-D accelerometry and surface electromyography in pediatric patients. IEEE J Biomed Health Inform. 2016;20(5):1333–41.
13. Onorati F, Regalia G, Caborni C, Migliorini M, Bender D, Poh MZ, et al. Multicenter clinical assessment of improved wearable multimodal convulsive seizure detectors. Epilepsia. 2017;58(11):1870–9.
14. Regalia G, Onorati F, Lai M, Caborni C, Picard RW. Multimodal wrist-worn devices for seizure detection and advancing research: focus on the Empatica wristbands. Epilepsy Res. 2019;153:79–82.
15. Beniczky S, Jeppesen J. Non-electroencephalography-based seizure detection. Curr Opin Neurol. 2019;32(2):198–204.
16. Hoppe C, Feldmann M, Blachut B, Surges R, Elger CE, Helmstaedter C. Novel techniques for automated seizure registration: patients' wants and needs. Epilepsy Behav. 2015;52(Pt A):1–7.
17. Gu Y, Cleeren E, Dan J, Claes K, Van Paesschen W, Van Huffel S, et al. Comparison between scalp EEG and behind-the-ear EEG for development of a wearable seizure detection system for patients with focal epilepsy. Sensors. 2017;18(2):29.
18. Guermandi M, Benatti S, Morinigo VJK, Bertini L. A wearable device for minimally-invasive behind-the-ear EEG and evoked potentials. In: 2018 IEEE Biomedical Circuits and Systems Conference (BioCAS). Cleveland, OH: Institute of Electrical and Electronics Engineers; 2018. p. 1–4.
19. You S, Cho BH, Yook S, Kim JY, Shon YM, Seo DW, et al. Unsupervised automatic seizure detection for focal-onset seizures recorded with behind-the-ear EEG using an anomaly-detecting generative adversarial network. Comput Methods Programs Biomed. 2020;193:105472.
20. Vandecasteele K, De Cooman T, Dan J, Cleeren E, Van Huffel S, Hunyadi B, et al. Visual seizure annotation and automated seizure detection using behind-the-ear electroencephalographic channels. Epilepsia. 2020;61(4):766–75.
21. Becker T, Vandecasteele K, Chatzichristos C, Van Paesschen W, Valkenborg D, Van Huffel S, et al. Classification with a deferral option and low-trust filtering for automated seizure detection. Sensors. 2021;21(4):1046.
22. Zibrandtsen IC, Kidmose P, Christensen CB, Kjaer TW. Ear-EEG detects ictal and interictal abnormalities in focal and generalized epilepsy—a comparison with scalp EEG monitoring. Clin Neurophysiol. 2017;128(12):2454–61.
23. Jørgensen SD, Zibrandtsen IC, Kjaer TW. Ear-EEG-based sleep scoring in epilepsy: a comparison with scalp-EEG. J Sleep Res. 2020;29(6):e12921.
24. Sopic D, Aminifar A, Atienza D. e-Glass: a wearable system for real-time detection of epileptic seizures. In: 2018 IEEE International Symposium on Circuits and Systems (ISCAS). Florence, Italy: Institute of Electrical and Electronics Engineers; 2018. p. 1–5.

25. Zanetti R, Aminifar A, Atienza D. Robust epileptic seizure detection on wearable systems with reduced false-alarm rate. Annu Int Conf IEEE Eng Med Biol Soc. 2020;2020:4248–51.
26. Thomas AH, Aminifar A, Atienza D. Noise-resilient and interpretable epileptic seizure detection. In: 2020 IEEE International Symposium on Circuits and Systems (ISCAS). Seville, Spain: Institute of Electrical and Electronics Engineers; 2020. p. 1–5.
27. Lin SK, Istiqomah WLC, Lin CY, Chiueh H. An ultra-low power smart headband for real-time epileptic seizure detection. IEEE J Transl Eng Health Med. 2018;6:2700410.
28. Baumgartner C, Koren JP. Seizure detection using scalp-EEG. Epilepsia. 2018;59(Suppl 1):14–22.
29. Goldberger AL, Amaral LA, Glass L, Hausdorff JM, Ivanov PC, Mark RG, et al. PhysioBank, PhysioToolkit, and PhysioNet: components of a new research resource for complex physiologic signals. Circulation. 2000;101(23):E215–20.
30. Ihle M, Feldwisch-Drentrup H, Teixeira CA, Witon A, Schelter B, Timmer J, et al. EPILEPSIAE—a European epilepsy database. Comput Methods Programs Biomed. 2012;106(3):127–38.
31. Jurcak V, Tsuzuki D, Dan I. 10/20, 10/10, and 10/5 systems revisited: their validity as relative head-surface-based positioning systems. NeuroImage. 2007;34(4):1600–11.
32. Berndt DJ, Clifford J. Using dynamic time warping to find patterns in time series. In: AAAI Press, editor. Proceedings of the 3rd International Conference on Knowledge Discovery and Data Mining. Seattle, WA: AAAI Press; 1994. p. 359–70.
33. Mueen A, Keogh E, Zhu Q, Cash S, Westover B. Exact discovery of time series motifs. Proc SIAM Int Conf Data Min. 2009;2009:473–84.
34. Keogh E, Ratanamahatana CA. Exact indexing of dynamic time warping. Knowl Inf Syst. 2005;7(3):358–86.
35. Mohamed S, Haggag S, Nahavandi S, Haggag O. Towards automated quality assessment measure for EEG signals. Neurocomputing. 2017;237:281–90.
36. Duun-Henriksen J, Baud M, Richardson MP, Cook M, Kouvas G, Heasman JM, et al. A new era in electroencephalographic monitoring? Subscalp devices for ultra-long-term recordings. Epilepsia. 2020;61(9):1805–17.
37. Hartmann MM, Fürbass F, Perko H, Skupch A, Lackmayer K, Baumgartner C, et al. EpiScan: online seizure detection for epilepsy monitoring units. Annu Int Conf IEEE Eng Med Biol Soc. 2011;2011:6096–9.
38. Hopfengärtner R, Kasper BS, Graf W, Gollwitzer S, Kreiselmeyer G, Stefan H, et al. Automatic seizure detection in long-term scalp EEG using an adaptive thresholding technique: a validation study for clinical routine. Clin Neurophysiol. 2014;125(7):1346–52.
39. Heck CN, King-Stephens D, Massey AD, Nair DR, Jobst BC, Barkley GL, et al. Two-year seizure reduction in adults with medically intractable partial onset epilepsy treated with responsive neurostimulation: final results of the RNS System Pivotal trial. Epilepsia. 2014;55(3):432–41.
40. Wilson SB, Scheuer ML, Emerson RG, Gabor AJ. Seizure detection: evaluation of the Reveal algorithm. Clin Neurophysiol. 2004;115(10):2280–91.
41. Zibrandtsen IC, Kidmose P, Kjaer TW. Detection of generalized tonic-clonic seizures from ear-EEG based on EMG analysis. Seizure. 2018;59:54–9.
42. Li Y, Yu Z, Chen Y, Yang C, Li Y, Allen Li X, et al. Automatic seizure detection using fully convolutional nested LSTM. Int J Neural Syst. 2020;30(4):2050019.
43. Avcu M, Zhang Z, Chan D. Seizure detection using least EEG channels by deep convolutional neural network. 2019 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP). Brighton, UK: Institute of Electrical and Electronics Engineers; 2019. p. 1120–24.
44. Thodoroff P, Pineau J, Lim A. Learning robust features using deep learning for automatic seizure detection. Proceedings of the 1st Machine Learning for Healthcare Conference, Boston, MA; 2016. p. 178–90.
45. Vidyaratne L, Glandon A, Alam M, Iftekharuddin KM. Deep recurrent neural network for seizure detection. In: 2016 International Joint Conference on Neural Networks (IJCNN). Vancouver, BC: Institute of Electrical and Electronics Engineers; 2016. p. 1202–7.
46. Xu Y, Nguyen D, Mohamed A, Carcel C, Li Q, Kutlubaev MA, et al. Frequency of a false positive diagnosis of epilepsy: a systematic review of observational studies. Seizure. 2016;41:167–74.
47. Meier R, Dittrich H, Schulze-Bonhage A, Aertsen A. Detecting epileptic seizures in long-term human EEG: a new approach to automatic online and real-time detection and classification of polymorphic seizure patterns. J Clin Neurophysiol. 2008;25(3):119–31.
48. Diao C, Wang B, Cai N. A novel data fusion algorithm for multivariate time series. In: 2018 Chinese Control and Decision Conference (CCDC). Shenyang, China: Institute of Electrical and Electronics Engineers; 2018. p. 6331–3.
49. Zhu W, Xiao F. Improvement of time series data fusion based on evidence theory and DEMATEL. IEEE Access. 2019;7:81397–406.
50. Brunnhuber F, Slater J, Goyal S, Amin D, Thorvardsson G, Freestone DR, et al. Past, present and future of home video-electroencephalographic telemetry: a review of the development of in-home video-electroencephalographic recordings. Epilepsia. 2020;61(Suppl 1):S3–10.
51. Chiu B, Keogh E, Lonardi S. Probabilistic discovery of time series motifs. In: Proceedings of the ACM SIGKDD International Conference on Knowledge Discovery and Data Mining. New York, NY: Association for Computing Machinery; 2003. p. 493–498.
52. Yingchareonthawornchai S, Sivaraks H, Rakthanmanon T, Ratanamahatana CA. Efficient proper length time series motif discovery. In: 2013 IEEE 13th International Conference on Data Mining. Dallas, TX: Institute of Electrical and Electronics Engineers; 2013. p. 1265–70.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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