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HIGHLIGHTS

- We present cross-database evaluation for classification of epileptic seizures using 5 EEG databases.
- We studied the effect of adaptive median feature baseline correction (AM-FBC), smoothing of train and test data and post-processing of classifier output.
- AM-FBC plays a significant role to overcome inter-database variation of feature distribution.

ABSTRACT

Objective: In long-term electroencephalogram (EEG) signals, automated classification of epileptic seizures is desirable in diagnosing epilepsy patients, as it otherwise depends on visual inspection. To the best of the author's knowledge, existing studies have validated their algorithms using cross-validation on the same database and less number of attempts have been made to extend their work on other databases to test the generalization capability of the developed algorithms. In this study, we present the algorithm for cross-database evaluation for classification of epileptic seizures using five EEG databases collected from different centers. The cross-database framework helps when sufficient epileptic seizures EEG data are not available to build automated seizure detection model.
Methods: Two features, namely successive decomposition index and matrix determinant were extracted at a segmentation length of 4 s (50% overlap). Then, adaptive median feature baseline correction (AM-FBC) was applied to overcome the inter-patient and inter-database variation in the feature distribution. The classification was performed using a support vector machine classifier with leave-one-database-out cross-validation. Different classification scenarios were considered using AM-FBC, smoothing of the train and test data, and post-processing of the classifier output.
Results: Simulation results revealed the highest area under the curve-sensitivity-specificity-false detections (per hour) of 1–1–1–0.15, 0.89–0.99–0.82–2.5, 0.99–0.73–1–1, 0.95–0.97–0.85–1.7, 0.99–0.99–0.92–1.1 using the Ramaiah Medical College and Hospitals, Children's Hospital Boston-Massachusetts Institute of Technology, Temple University Hospital, Maastricht University Medical Centre, and University of Bonn databases respectively.
Conclusions: We observe that the AM-FBC plays a significant role in improving seizure detection results by overcoming inter-database variation of feature distribution.
Significance: To the best of the author's knowledge, this is the first study reporting on the cross-database evaluation of classification of epileptic seizures and proven to be better generalization capability when evaluated using five databases and can contribute to accurate and robust detection of epileptic seizures in real-time.

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1. Introduction

Epilepsy is the fourth most common neurological disorder, which affects 65 million people of all ages around the world (Adeli et al., 2003; Gotman, 1982; Sirven, 2017). A sudden discharge of electrical activity in the brain causes temporary brain dysfunction, which is referred to as a seizure and recurrent seizures lead to epilepsy (Gotman, 1982; Nordqvist, 2017). The electroencephalogram (EEG) signal contains clinically related information on neural, physiological and pathological conditions of brain disorders. For epilepsy patients, long-term monitoring of EEG signals is essential for pre-surgical evaluation, which is found to be a challenging task as it requires manual intervention (Adeli et al., 2003; Acharya et al., 2012; Andrzejak et al., 2001; Blumenfeld, 2012; Hopfengaertner et al., 2014). Automated seizure detection is desirable in long-term EEG because that surrogate the manual intervention and saves experts time, improves pre-surgical evaluation and speeds up the diagnosis process. Existing studies have validated their algorithm on the same database but not on other databases to prove the generalization capability of the algorithm. Seizure detection algorithm would be more benefited when it is validated on multiple EEG databases with a good number of seizures events. Therefore, to overcome this gap, we present an algorithm for cross-database evaluation for classification of epileptic seizures using five EEG databases. Such cross-database approach also helps when insufficient epileptic seizures EEG data is available to build a seizure detection model.

1.1. Related background

Several studies have been proposed in the past for classification of epileptic seizures (Acharya et al., 2012; Aydın et al., 2009; Bogaarts et al., 2014; Gotman, 1982; Logesparan et al., 2015; Raghu et al., 2019a, 2016). The EEG signals from neonatal and adult patients were considered to develop a patient-independent seizure detection model which belongs to the same database. It was reported in Bogaarts et al. (2016b) and Logesparan et al. (2015), feature normalization procedure based on the median decaying memory (MDM) method increases the seizure detection performance. Another feature baseline correction (FBC) method called average non-seizure feature values (ANSFV) uses the first 3 min of the seizure and artifact-free EEG to correct the feature baseline (Bogaarts et al., 2014, 2016a). A patient-specific seizure onset detection model was proposed using wavelet decomposition based morphology and spatial features using Children's Hospital Boston-Massachusetts Institute of Technology (CHB-MIT) database (Shoeb et al., 2004).

Optimized deep neural network architecture was applied on EEG signals to perform binary, three-class, and five class classification of epileptic seizures (Hussein et al., 2019). Frequency–moment signatures based showed better seizure detection results using 12 patients EEG (Khamis et al., 2013). Spectral and temporal features extracted in five frequency bands classified using support vector machines (SVM) classifier (Chan et al., 2008). Zheng et al. (2014) proposed seizure prediction model using phase synchronization information of intrinsic mode functions extracted by bivariate empirical mode decomposition. A prospective multicenter study was performed in three epilepsy monitoring units including 205 patients (Fürbass et al., 2015). Further, the study was extended on retrospective EEG data of 310 patients and the publicly available CHB–MIT dataset. A multimodal automatic seizure detection algorithm showed the high sensitivity with full and reduced electrode montages (Fürbass et al., 2017). Integrated power in the frequency band 2.5–12 Hz calculated from the short-time Fourier transform (STFT) approach using adaptive thresholding was applied on 194 temporal-lobe epilepsy patients (Hopfengaertner et al., 2014).

Wavelet packet transforms (WPT) based combined seizure index (CSI) (Zandi et al., 2010) and harmonic WPT (Vidyaratne and Khan, 2017) features based models were proposed for seizure classification. Discrete wavelet transforms (DWT) based statistical features model was introduced using the classifier using Bern-Barcelona dataset and the University of Bonn (UBonn) databases (Chen et al., 2017). Rational STFT (DSTFT) based approach yielded good classification results using multi-layer perceptron (MLP) classifier. Matrix determinant feature using the SVM classifier was proposed using the Ramaiah Medical College and Hospitals (RMCH) and UBonn databases (Raghu et al., 2019a). A threshold-based seizure detection method was proposed using the minimum variance modified fuzzy entropy (Raghu et al., 2018). Recently, deep learning algorithms have been used for classification of normal, preictal, and seizure activities (Acharya et al., 2018; Ullah et al., 2018; Zhou et al., 2018). Further, promising results were obtained using entropies like approximate entropy (Srinivasan et al., 2007; Kumar et al., 2014), weighted permutation entropy (Tawfik et al., 2016), log energy and norm entropy (Raghu et al., 2016), sigmoid entropy (Raghu et al., 2019c), Renyi, spectral, Shannon and wavelet entropies (Pravin Kumar et al., 2010; Srinivasan et al., 2005; Wang et al., 2011; Raghu and Sriraam, 2017) for seizure detection. Acharya et al. (2013) have reviewed articles related to computer-aided diagnostic systems to automatically classify normal and abnormal activities using less number of features. A review on wavelet-based EEG processing for automated detection of epileptic seizures was reported in Faust et al. (2015). A systematic review on autonomic symptoms and signs during epileptic seizures which includes cardiovascular changes, respiratory manifestations, gastrointestinal symptoms, cutaneous manifestations, sexual and genital manifestations, and urinary symptoms was performed (Baumgartner et al., 2019).

The post-processing of the classifier output has gained attention using a Kalman filter (Bogaarts et al., 2014), a central linear moving average filter (MAF) (Temko et al., 2011), and MAX operator with a MAF (Ahmed et al., 2017) for seizure detection with improved performance. It was evident from the literature that the SVM classifier has been promising classification tool for epileptic seizure detection (Shoeb et al., 2004; Subasi and Gursoy, 2010; Temko et al., 2011; Bogaarts et al., 2014, 2016a,b; Ahmed et al., 2017; Sriraam and Raghu, 2017; Raghu and Sriraam, 2018).

The proposed study used two features called successive decomposition index (SDI) and matrix determinant (MD), which were proposed by our group in Raghu et al. (2019b,a). The SDI was evaluated on the RMCH, CHB-MIT and the Temple University Hospitals (TUH) databases in Raghu et al. (2019b) and MD was tested on UBonn and RMCH databases in Raghu et al. (2019a). Further, adaptive median feature baseline correction (AM-FBC) was proposed in (Raghu et al., Unpublished results) to correct inter-subject variation in feature distribution for intensive care unit (ICU) EEG recordings that were collected from Maastricht University Medical Centre (MUMC). In the same study, post-processing of classifier output proven to be ideal to improve the classification results. Above-mentioned methods were used in the present study to propose a cross-database framework for seizure detection.

Even though multiple databases were used in Vidyaratne and Khan (2017), Raghu et al. (2019a), Chen et al. (2017), Bogaarts et al. (2016b), and Fürbass et al. (2015) for epileptic seizure classification, the cross-database framework was missing for the generalization ability of the algorithm. Therefore, the present study proposes cross-database evaluation using five EEG databases for classification of epileptic seizures driven by AM-FBC, smoothing of the train and test data and post-processing of the SVM classifier output.

1.2. Importance and contributions of proposed study

Importance of cross-database validation are: (1) Cross-database algorithm can be used when sufficient epileptic seizures EEG data is not available to build a seizure detection model on new EEG recordings, (2) Cross-database evaluation confirms the generalization capability of the developed algorithm.

The followings are the contributions of our study: (1) AM-FBC was used to reduce the inter-subject and inter-database variation in the feature distribution, (2) Studied the effect of smoothing of the train and test data, (3) Post-processing of the SVM classifier output, and (4) Most importantly, cross-database evaluation was proposed using five EEG databases.

2. Materials and methods

2.1. Proposed method

Fig. 1 depicts the flow of the cross-database evaluation for classification of the epileptic seizure using five ($N = 5$) databases. Initially, the EEG recordings were pre-processed and two features (SDI and MD) were extracted. First, FBC was applied to the subjects level and then to the database level. Smoothing of the train and test data was applied before the SVM classifier was trained with leave-one-database-out cross-validation approach. The trained SVM classifier was tested on the left out database and post-processing was applied using a MAF. The same procedure was repeated five times until all the databases were used both training ($(N-1)$ times) and testing (1 time).

2.2. Clinical EEG recordings

The cross-database evaluation was performed using five databases obtained from the RMCH, CHB-MIT, TUH, MUMC, and UBonn EEG recordings.

2.2.1. RMCH

The first EEG database used for the cross-database framework was from the RMCH, Bengaluru, India after ethical approval was obtained from the RMCH ethics committee to use these EEG recordings for research purpose. The RMCH database was recorded using the International 10–20 system configuration at a sampling rate of 128 Hz using Galileo Suite NB Neuro digital EEG system. This unipolar EEG was recorded using the following 19 scalp electrodes: Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2. Reference electrode placed at the ear was used as reference for unipolar EEG. Only EEG recordings from epileptic patients were used for this study, which consists of 115 subjects (67 male and 48 female) ranging between 2.5 to 75 years. Two experts at the RMCH visually marked EEG as non-seizure and seizure segments. The RMCH database consists of 162 seizures (approximately 4.36 h of seizure data) from 115 subjects with the recording duration of each patient varied from 20 min to 3 h.

2.2.2. CHB-MIT

The second database used for the cross-database framework was obtained from the CHB-MIT[1] EEG database which is available in Physionet repository (Shoeb et al., 2004; Shoeb and Guttag, 2010). The CHB-MIT database is one of the largest open source EEG databases with 844 h of data from the 23 patients recorded at a sampling rate of 256 Hz. The CHB-MIT database was recorded using the International 10–20 system bipolar montage electrode placement with the following 23 channels: FP1-F7, F7-T7, T7-P7, P7-O1, FP1-F3, F3-C3, C3-P3, P3-O1, FZ-CZ, CZ-PZ, FP2-F4, F4-C4, C4-P4, P4-O2, FP2-F8, F8-T8, T8-P8, P8-O2, P7-T7, T7-FT9, FT9-FT10, FT10-T8, and T8-P8.

2.2.3. TUH

The third database was obtained from the TUH[2] EEG resource (Database, 2016; Obeid and Picone, 2016), which includes EEG from focal non-specific, generalized non-specific, simple partial, complex partial, absence, tonic, tonic-clonic, and myoclonic seizure. This unipolar EEG signal was recorded using the International 10–20 system electrode configuration at a sampling rate of 250 Hz. For the study, 222 seizures from 316 subjects were considered from massive EEG recordings. The electrode placement in the TUH database was the same as in the RMCH database.

2.2.4. MUMC

The fourth database was obtained from the Department of Clinical Neurophysiology, MUMC, Maastricht, The Netherlands. The MUMC EEG database was used for research purpose after approved by the hospital ethics committee. This database consists of 40 routine EEG registrations recorded at the intensive care unit. The MUMC scalp EEG recordings were recorded using BrainLab EEG recording system at a sampling rate of 250 Hz using a common average montage using 19 unipolar electrodes. This database consists of 21 h of EEG including 1273 seizure epochs with a minimum duration of 12 s and a maximum duration of 1949 s. Technician at the MUMC hospital annotated the seizure and non-seizure epochs and checked by a clinical neurophysiologist. The electrode placement in the MUMC database was the same as in the RMCH database.

2.2.5. UBonn

The fifth database used for the cross-database framework was a publicly available database from the UBonn [3](Andrzejak et al., 2001). The UBonn EEG was recorded from five different subjects under-going pre-surgical evaluations. UBonn EEG recordings were divided into five subsets (set A, set B, set C, set D, and set E), each subset consists of 100 single-channel EEG segments of 23.6 s duration recorded at a sampling rate of 173.61 Hz. Each subset EEG in UBonn belongs to normal with eyes open (set A), normal with eyes closed (set B), pre-ictal (set C), post-ictal (set D) and ictal state (set E) conditions. Sets A and B contain recordings obtained through external surface electrodes and sets C–E were recorded using intracranial electrodes. In our study, set A to set D considered as non-seizure and set E considered as seizure activity (Acharya et al., 2012; Kamath, 2013).

Table 1 provide detailed information on all the five databases used for cross-database evaluation. All the five EEG databases used in the study are belongs to retrospective data.

2.3. Pre-processing

Among the five databases, the three open source databases (CHB-MIT, TUH, and UBonn) were already pre-processed for artifacts. Initially, a 50 Hz IIR notch filter was applied to eliminate the power line noise and a bandpass filter was applied with a lower and higher cut-off frequency of 0.5 and 32 Hz respectively. In order to eliminate the artifacts like eye blinks, muscle artifacts, and electrode movements, independent component analysis (ICA) was applied to the filtered EEG (only on RMCH and MUMC databases) (Cichocki and Vorobyov, 2000; Winkler et al., 2011) using the ICA toolbox available in the EEGlab (Delorme and Makeig, 2004).

[1] http://www.physionet.org/pn6/chbmit.

[2] https://www.isip.piconepress.com/projects/tuh_eeg/index.shtml.

[3] http://epileptologie-bonn.de/cms/front_content.php?idcat=193&lang=3&changelang=3.

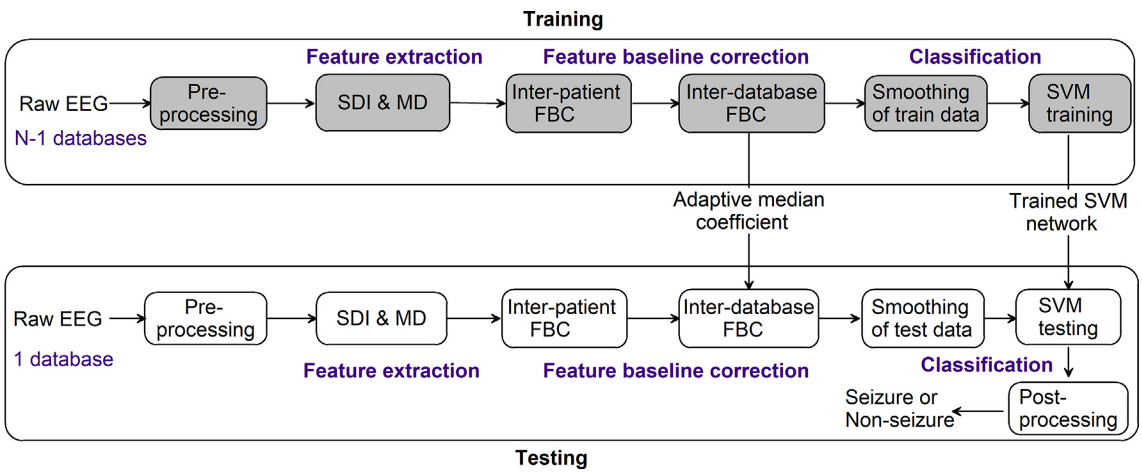

Fig. 1. The flow of the cross-database framework evaluation for seizure detection using five ($N = 5$) databases. The support vector machine (SVM) classifier was trained with ($N - 1$) databases and tested on the left out database. First, the feature baseline correction (FBC) was applied separately on each database to correct the inter-patient variation. The adaptive median coefficient estimated from trained inter-database FBC was used to correct the feature baseline of the test database. EEG: Electroencephalogram, MD: matrix determinant, SDI: successive decomposition index. .

Table 1
Details of different EEG databases used for cross-database evaluation.

	RMCH	CHB-MIT	TUH	MUMC	UBonn
Open source database	No	Yes	Yes	No	Yes
Type of EEG	Scalp	Scalp	Scalp	Scalp	Scalp and Intracranial
Type of recording	Unipolar	Bipolar	Unipolar	Unipolar	Unipolar
Sampling frequency (Hz)	128	256	250	250	173.73
Electrode position	10–20	10–20	10–20	10–20	10–20
Number of subjects	115	23	316	40	5
Age range (years)	3–60	3–22	2–90	22–89	–
Total duration (hours)	58	884	408	21	3.24
Number of channels	19	23	19	19	1 **
Number of seizures	162	182	222	1273*	100***

RMCH: Ramaiah Medical College and Hospitals, TUH: Temple University Hospitals,
CHB-MIT: Children's Hospital Boston-Massachusetts Institute of Technology,
MUMC: Maastricht University Medical Centre, UBonn: University of Bonn.
* 1273 seizure events
** Multichannel data was converted to a single channel
*** 100 seizures file each of 23.36 s duration

2.4. Feature extraction

In this study, we have used two features, namely SDI and MD that were recently proposed by our group in Raghu et al. (2019b, a). These were validated using RMCH, CHB-MIT, TUH, and MUMC databases in our previous studies (Raghu et al., 2019b,a) (Raghu et al., Unpublished results) and were extracted at a segmentation length of 4 s with 50% overlap in this study.

The procedure to estimate SDI and MD is given in Supplementary Appendix A and Supplementary Appendix B respectively.

2.5. Adaptive median feature baseline correction

Considering the fact that features have variations in the distribution in patient level and database level, FBC was applied in two stages. First, AM-FBC was applied to update the feature distribution among the patients (scenario was dominant in MUMC database). Next, feature baseline was applied on five databases to correct the inter-database feature distribution variation. The AM-FBC was successfully implemented to update the feature baseline for inter-patient variation in our previous study (Raghu et al., Unpublished results) and better classification results were obtained.

2.5.1. Inter-patient FBC

The procedure to correct the feature baseline among patients is given here.

1. Let a typical feature of all the subjects be represented as $f(sub_1, sub_2, \ldots, sub_n)$.
2. Calculate the $f(Median_{seizure})$ and $f(Median_{non-seizure})$ of all the training subjects using seizure and non-seizure feature respectively. The length of the $f(Median_{seizure})$ and $f(Median_{non-seizure})$ equals the number of subjects.
3. Estimate global median ($f(Median_{global})$) using median values of seizure and non-seizure.

$$f(Median_{global}) = Median\{f(Median_{seizure})f(Median_{non-seizure})\} \quad (1)$$

4. Now estimate the median of a single subject $f(Median_{subi})$, where $i = 1, 2, 3, \ldots, n$ subjects.

5. Now calculate the adaptive median coefficient (λ) using $f(Median_{global})$ and $f(Median_{subi})$.

$$\lambda = f(Median_{global}) - f(Median_{subi}) \quad (2)$$

6. Now correct the feature baseline of *subi* using λ as follows:

$$f_{new_i} = \lambda + f_{subi} \quad (3)$$

7. Repeat the step 4 to step 6 for all the subjects (n) using the $f(Median_{global})$.

The above procedure was applied to both SDI and MD features separately.

2.5.2. Inter-database FBC

The procedure to correct the feature baseline among databases is given in Supplementary Appendix C.

2.6. Smoothing train and test data

Smoothing of the train and test data for classification purpose reported improved results in Bogaarts et al. (2014, 2016a,b). Therefore, in this study, we have applied a 5-tap MAF to the train and test data which reduces the random noise and improves the classification results (Ahmed et al., 2017).

2.7. Classification

The cross-database framework was evaluated using the SVM classifier due to its better performance reported in previous studies (Lima et al., 2009; Liu et al., 2012; Kumar et al., 2014; Chen et al., 2017; Sriraam and Raghu, 2017; Raghu and Sriraam, 2018; Raghu et al., 2019a). During the preliminary study, the radial basis kernel function showed better performance in terms of classification results. The proposed method was evaluated using leave-one-database-out cross-validation in which, the SVM classifier was trained using four databases and tested on the left out database. The procedure was repeated five times until all the databases were used for the testing phase. The SVM classifier was tuned as follows: Kernel function = radial basis function, Kernel Scale = 1 and Box Constraint = 1.

The experiment was performed in MATLAB 2018b using 8 GB RAM, CPU 2 GHz with an Intel i3 processor.

The cross-database framework was assessed using performance parameters, namely sensitivity, specificity, and the area under the curve (AUC).

$$Sensitivity(S^{+}) = \frac{TP}{TP + FN} \quad (4)$$

$$Specificity(S^{-}) = \frac{TN}{TN + FP} \quad (5)$$

where, *TP*is seizure detected as seizure, *TN*is non-seizure detected as non-seizure, *FN*is seizure detected as non-seizure, and *FP*is non-seizure detected as seizure. The area under the receiver operating characteristic (ROC) curve was estimated using sensitivity and 1-specificity.

2.8. Post-processing

The post-processing of the classifier output has proven to be a better choice to reduce false detections and improve the classification results (Temko et al., 2011; Ahmed et al., 2017)(Raghu et al., Unpublished results). In our study, different tap lengths (2 to 10) of MAF were applied to the SVM classifier output to perform the post-processing as reported in Temko et al. (2011) and Ahmed et al. (2017) Raghu et al., Unpublished results. The post-processing output [0, 1] was assigned depending on a predefined threshold of 0.5 to classify as a seizure and non-seizure. The given EEG segment was classified as a seizure and non-seizure if the value was greater than or equal to and less than 0.5 respectively.

2.9. Classification scenarios

The proposed cross-database framework was evaluated using different classification scenarios (CS) in terms of AM-FBC, smoothing of the train and test data, and post-processing of the SVM classifier output. Table 2 depicts the 7 different CS used to evaluate the cross-database framework.

3. Results

3.1. Analysis of AM-FBC

After pre-processing, both SDI and MD features were extracted and AM-FBC was applied individually to correct the inter-patient variation in the distribution of the feature. Most inter-patient variation was seen in the MUMC database. Figs. 2a & b shows the SDI and MD feature distribution for all the five databases. We observe more variation in features distribution between databases. In the RMCH database, SDI feature values for seizure are below the SDI values of non-seizure from the other four databases. This is also the case for the MD feature values in the RMCH and MUMC databases which is referred to as inter-database feature distribution variation. Further, features from the MUMC database had more outliers due to noisy EEG recordings. In the next step, AM-FBC was applied to correct the feature baseline in inter-database. The inter-database AM-FBC results are depicted in Figs. 2c & d for SDI and MD features respectively. The Figs. 2c & d show that the features baseline has been brought to a uniform level after applying AM-FBC. A Wilcoxon rank sum test showed significance difference ($p < 0.05$) for each database between seizure and non-seizures activities. The median values of both the features before and after AM-FBC are depicted in Fig. 3. The high variation among the databases is reflected for both SDI and MD features. The median values after AM-FBC show less variation between the databases.

3.2. Cross-database results

Fig. 4 shows the ROC curve obtained from all the five databases under different CS. The ROC was grouped database wise, with and without post-processing of the classifier output. The area under the ROC curve obtained for the proposed study is reported in Fig. 5. The ROC curve obtained for the RMCH database was below the threshold line due to the effect of inter-database feature distribution variation. Overall, the best ROC curve was achieved when AM-FBC and smoothing of the test data were applied.

Table 2
Different classification scenarios used to evaluate cross-database framework.

Classification scenario	FBC	Smoothing of train data	Smoothing of test data
1	No	No	No
2	No	Yes	No
3	No	Yes	Yes
4	Yes	No	No
5	Yes	Yes	No
6	Yes	No	Yes
7	Yes	Yes	Yes

Note: All the classification scenarios were evaluated with and without post-processing. FBC: Feature baseline correction.

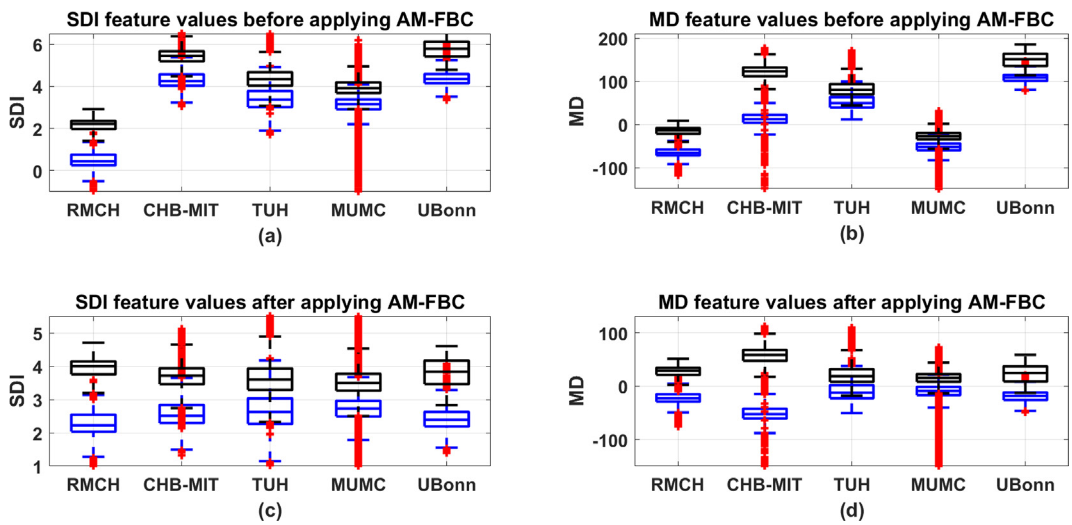

Fig. 2. The boxplot of successive decomposition index (SDI) and matrix determinant (MD) features for each database before and after applying Adaptive median feature baseline correction (AM-FBC). (a) SDI feature before applying AM-FBC. (b) MD feature before applying AM-FBC. (c) SDI feature after applying AM-FBC. (d) MD feature after applying AM-FBC. The boxplot with black boxes and blue boxes indicates seizure and non-seizure activities respectively. The red + indicates the outliers which are beyond the whiskers. RMCH: Ramaiah Medical College and Hospitals, TUH: Temple University Hospitals, CHB-MIT: Children's Hospital Boston- Massachusetts Institute of Technology, MUMC: Maastricht University Medical Centre, UBonn: University of Bonn. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

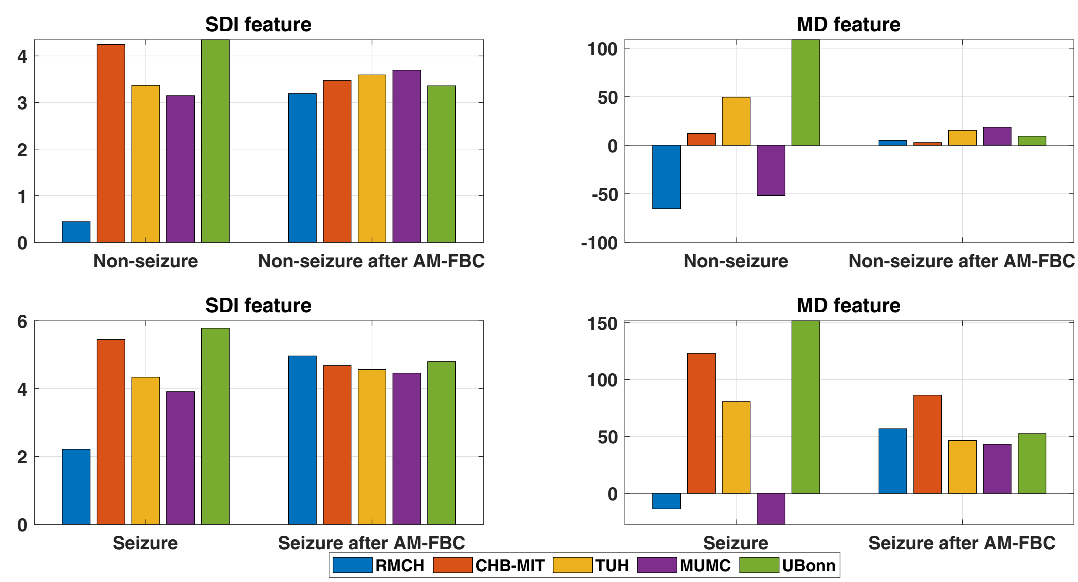

Fig. 3. The median values of successive decomposition index (SDI) and matrix determinant (MD) feature for each database before and after Adaptive median feature baseline correction (AM-FBC). Seizure and non-seizure features are plotted individually and grouped database. RMCH: Ramaiah Medical College and Hospitals, TUH: Temple University Hospitals, CHB-MIT: Children's Hospital Boston- Massachusetts Institute of Technology, MUMC: Maastricht University Medical Centre, UBonn: University of Bonn.

Fig. 5 shows the S^+, S^-, and AUC obtained for cross-database evaluation. First, we discuss CS1, where AM-FBC, smoothing of train and test data and post-processing was not applied. The AUC of 0.08 ($S^+ = 0$, $S^- = 0.90$), 0.99 ($S^+ = 0.99$, $S^- = 0.99$), 0.97 ($S^+ = 0.98$, $S^- = 0.94$), 0.83 ($S^+ = 0.41$, $S^- = 0.98$), and 0.87 ($S^+ = 1$, $S^- = 0$) was obtained for the RMCH, CHB-MIT, TUH, MUMC, and UBonn databases respectively without post-processing. The AUC performance of 0.01, 1, 0.99, 0.93, and 0.91 was obtained using the RMCH, CHB-MIT, TUH, MUMC, and UBonn databases respectively when post-processing was applied. Further, similar results were seen in case of CS2 and CS3 for all the databases leading to the worse performance for the RMCH database. The S^+ closes to zero was obtained for the RMCH database due to reason that the seizure EEG feature values of RMCH database are below the non-seizure EEG feature values in the training databases (refer to Figs. 2a & b). This was the clear indication of effect of inter-database feature distribution variation.

Now, we have applied AM-FBC to correct the feature distribution variation in inter-database. The effect of AM-FBC is already shown in Figs. 2 & 3. The AUC of 0.99 ($S^+ = 0.98$, $S^- = 0.98$), 0.81 ($S^+ = 0.99$, $S^- = 0.75$), 0.88 ($S^+ = 0.65$, $S^- = 0.96$), 0.93 ($S^+ = 0.92$, $S^- = 0.84$), 0.97 ($S^+ = 0.98$, $S^- = 0.90$) was achieved for the RMCH, CHB-MIT, TUH, MUMC, and UBonn databases respectively in CS4 without post-processing. Similarly, the AUC was increased to 1, 0.91, 0.91, 0.95, 0.99 for the RMCH, CHB-MIT, TUH, MUMC, and UBonn databases respectively when post-

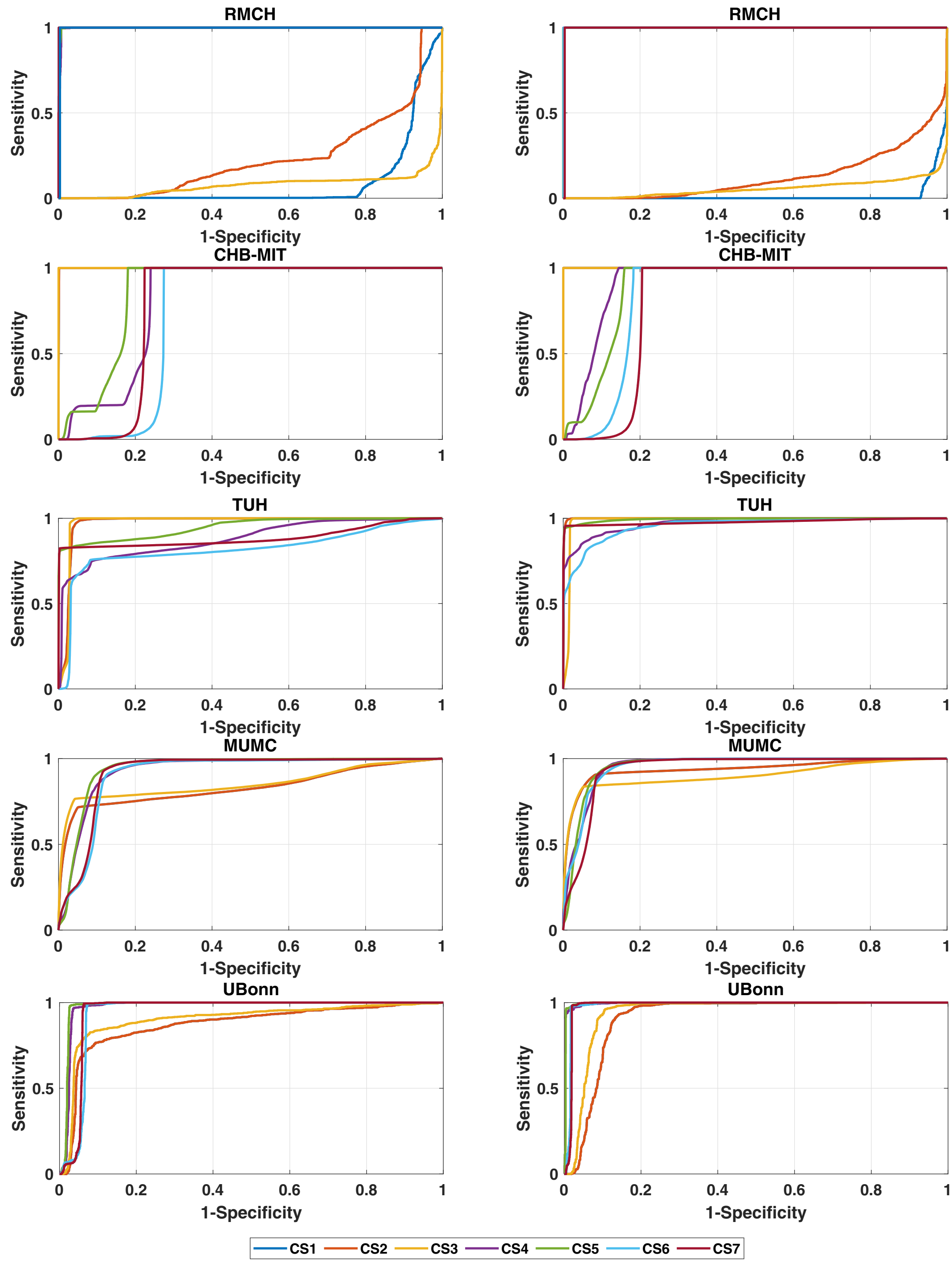

Fig. 4. The Receiver operating characteristic (ROC) curve for cross-database evaluation under different classification scenario (CS) for (a) Ramaiah Medical College and Hospitals (RMCH), (b) Children's Hospital Boston- Massachusetts Institute of Technology (CHB-MIT), (c) Temple University Hospitals (TUH), (d) Maastricht University Medical Centre (MUMC), and (e) University of Bonn (UBonn) databases. **Left column:** ROC curve without post-processing, **Right column:** ROC curve with post-processing. In legend, CS indicates classification scenario (refer to Table 2 for details).

processing was applied. The influence of AM-FBC improved the S^+ and S^- for the RMCH, MUMC and UBonn databases respectively, which was worse in CS1 to CS3.

In CS4 to CS7, we have studied the effect of smoothing of the train and test data for the SVM classifier. The AUC of 1, 0.84, 0.95, 0.95, 0.98 was obtained for the RMCH, CHB-MIT, TUH, MUMC, and UBonn databases respectively when post-processing was applied in CS5. Overall, the highest classification results were obtained in CS6 when AM-FBC applied along with smoothing of test data. The highest AUC of 1 ($S^+ = 1$, $S^- = 1$), 0.89 ($S^+ = 0.99$, $S^- = 0.82$), 0.99 ($S^+ = 0.73$, $S^- = 1$), 0.95 ($S^+ = 0.97$, $S^- = 0.85$), 0.99 ($S^+ = 0.99$, $S^- = 0.92$) was achieved for the RMCH, CHB-MIT, TUH, MUMC, and UBonn databases respectively in CS6 with post-processing. Finally, we have taken an average of all the databases classification results to assess the performance of different CS (refer to Fig. 5f). The results showed that the AUC of 0.77, 0.79, 0.77, 0.93, 0.94, 0.96, and 0.94 for CS1 to CS7 respectively with post-processing which is being high for CS6.

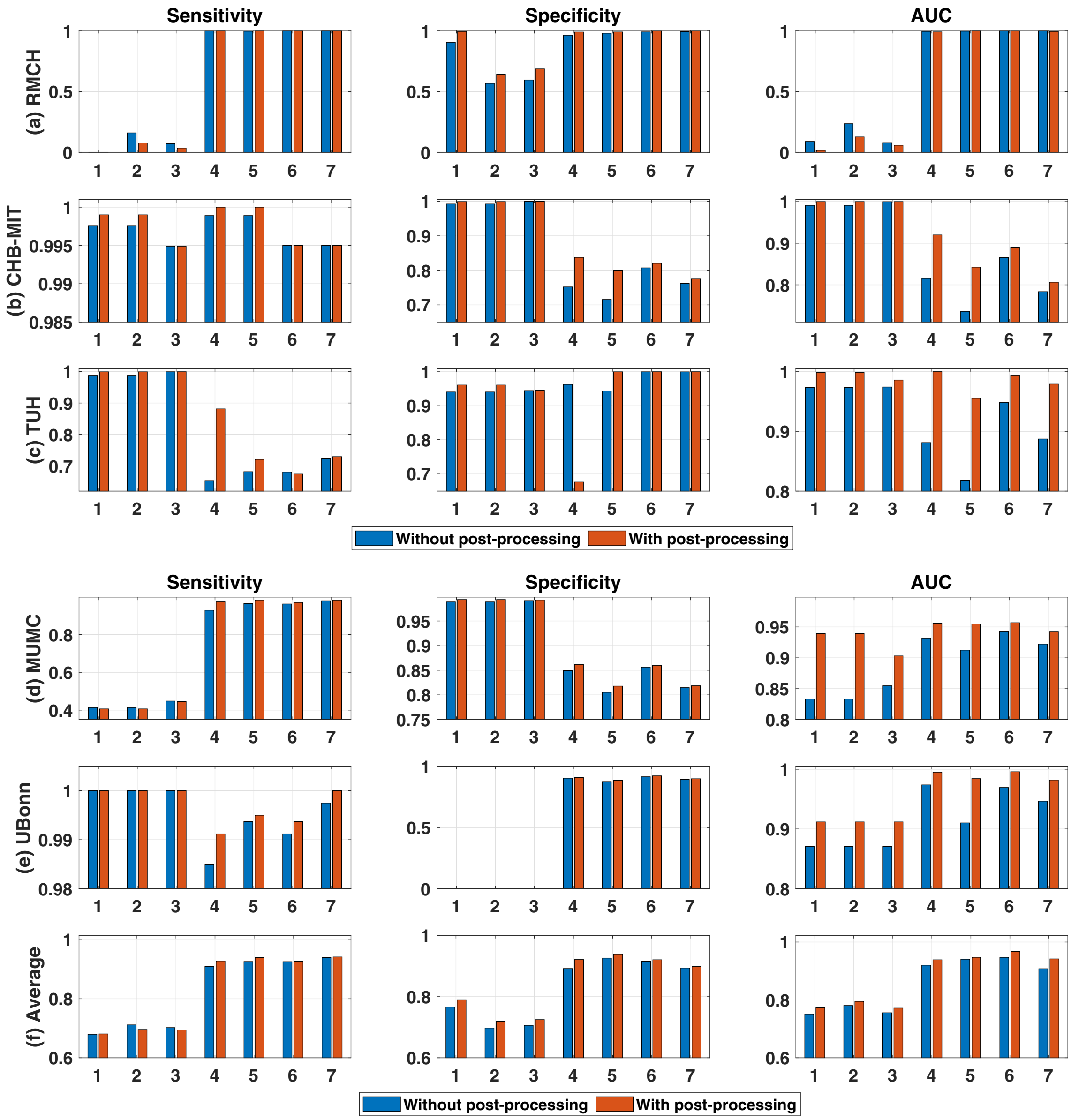

Fig. 5. Cross-database evaluation results using different classification scenario (CS) for (a) Ramaiah Medical College and Hospitals (RMCH), (b) Children's Hospital Boston-Massachusetts Institute of Technology (CHB-MIT), (c) Temple University Hospitals (TUH), (d) Maastricht University Medical Centre (MUMC), and (e) University of Bonn (UBonn) databases, (f) Average of all the five databases results. **First column:** Sensitivity (S^{+}), **Second column:** Specificity (S^{-}), **Third column:** Area under the curve (AUC). The x-tick labels indicate different classification scenarios.

The MAF length was varied between 2 to 10 to identify the optimal MAF length to reduce the false detections. It was observed that false detection rate decreases as the MAF length increases. For the optimal CS6 at the highest sensitivity, the average false detection rate (per hour) of 0.15, 2.5, 1, 1.7, and 1.1 was achieved for RMCH, CHB-MIT, TUH, MUMC, and UBonn databases respectively for MAF length of 10.

Overall, classification results showed that AM-FBC is essential to achieve the generalized results for all the databases. Further, the smoothing of the train and test data improved the classification results. The classification results suggest that the proposed cross-database approach has better generalization capability when evaluating using five databases.

4. Discussion

This study presents a cross-database evaluation for classification of epileptic seizures using SDI and MD features, AM-FBC, smoothing, and post-processing. The results showed that the highest AUC of 1, 0.89, 0.99, 0.95, and 0.99 using the RMCH, CHB-MIT, TUH, MUMC, and UBonn databases respectively.

4.1. Influence of FBC

The classification results obtained for CS1 to CS3 were not consistent for all the five databases. The S^{+} obtained for the RMCH and MUMC were close to 0 and 0.44 respectively due to inter-database feature distribution variation. It can be clearly understandable from Figs. 2 a & b that was due to the fact that the seizure EEG feature values of the RMCH and MUMC databases were below the non-seizure EEG feature values of other databases. Similarly, the S^{-} was 0 for the UBonn without applying AM-FBC for CS1 to CS3 because non-seizure EEG feature values of the UBonn database were above the seizure EEG feature values of other four databases. Even though good performance was achieved for the CHB-MIT and

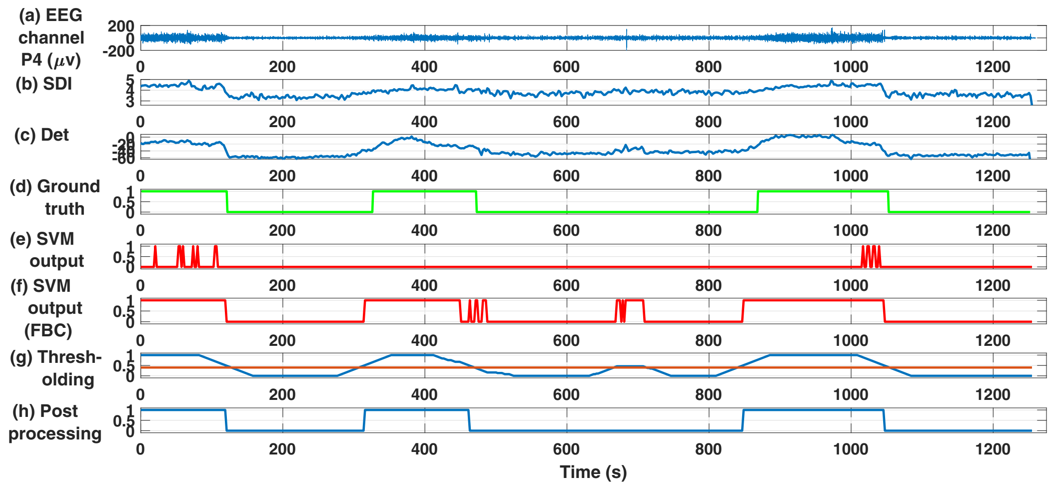

Fig. 6. Effect of post-processing for seizure detection. (a) Electroencephalogram (EEG) signal belongs to channel P4. (b) & (c) Corresponding successive decomposition index (SDI) and matrix determinant (MD) values of channel P4 respectively. (d) Ground truth, where 0 and 1 indicate non-seizure and seizure respectively. (e) Support vector machine (SVM) classifier output (without Adaptive median feature baseline correction (AM-FBC)). (f) SVM classifier output after applying AM-FBC. (g) The smoothed output after moving average filter (MAF) was applied on SVM classifier output (after AM-FBC). The threshold (red line) was set to 0.5 to make a binary decision. (h) Binary decision after applying thresholding to smoothed output.

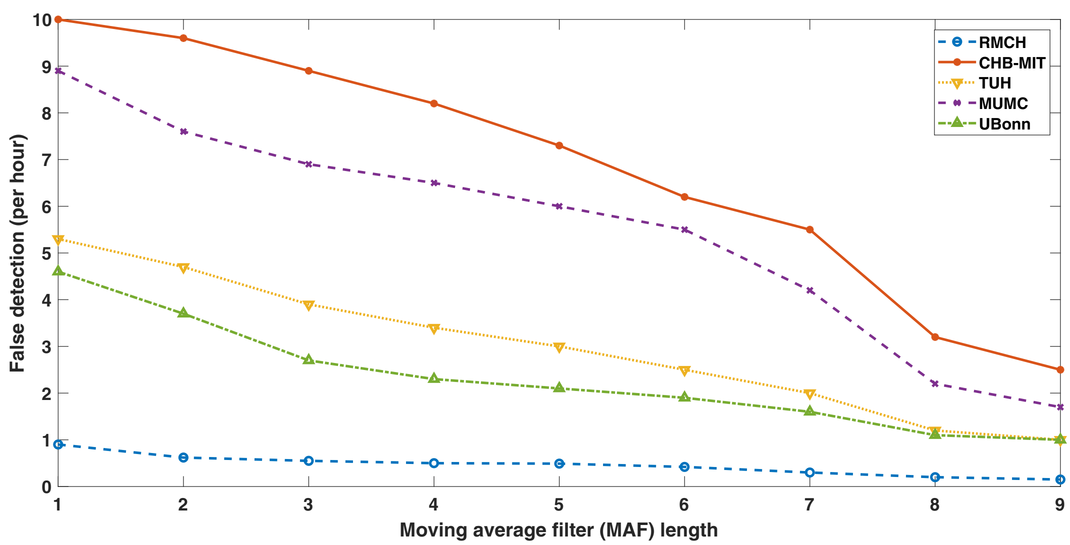

Fig. 7. Effect of moving average filter (MAF) length on false detections in post processing. RMCH: Ramaiah Medical College and Hospitals, TUH: Temple University Hospitals, CHB-MIT: Children's Hospital Boston- Massachusetts Institute of Technology, MUMC: Maastricht University Medical Centre, UBonn: University of Bonn.

TUH database in CS1 to CS3 (without FBC), the worse performance in terms of S^+ and S^- cannot be acceptable in real-time scenario. The influence of AM-FBC (refer to Figs. 2 c & d) improved the classification results in case of CS4 to CS7 (refer to Fig. 5) proving that cross-database evaluation requires FBC.

The influence of AM-FBC on cross-database evaluation is depicted in Fig. 6 when tested on MUMC database and trained using the left out databases with CS6. Figs. 6b & c shows the SDI and MD features respectively for the EEG shown in Fig. 6a. As one can observe that the misclassification in Fig. 6e are high as compared to the ground truth results in Fig. 6d when AM-FBC was not applied. As a result of AM-FBC and smoothing (refer to CS6), proper classification was seen (refer to Fig. 6f) with few false alarms and it was corrected using post-processing (refer to Fig. 6h) that the output was closely matched with ground truth labels (refer to Fig. 6d).

4.2. Influence of MAF on false detection

In our study, the MAF length was varied between 2 to 10 to identify the optimal MAF length which influences to reduce the false detections. Fig. 7 shows the effect of MAF length on false detections for all the five databases. As it can be seen from Fig. 7 that the false detection rate decreases as the MAF length increases. The best results were achieved when MAF length was 10 for CS6. The MAF length beyond 10 was not tested as it results in higher delay in detecting seizure epochs.

4.3. Comparison with other studies

It is worth noting that the exact comparison cannot be made as no studies have reported cross-database evaluation for classification of epileptic seizures. The results presented in Table 3 shows

Table 3
Comparison between the state of the art seizure detection algorithms and cross-database approach.

EEG database	Number of subjects	Duration of EEG (h)	Number of seizures	Author	Feature extraction	FBC	Classifier	Post-processing	Results
CHB-MIT	23	884	182	Vidyaratne and Khan (2017)	Harmonic wavelet packet transform fractal dimension, spatial and temporal features	No	RVM	No	S^+ = 96.0%
				Minasyan et al. (2010)	Line length	MDM	Threshold	No	AUC = 0.93
				Xiang et al. (2015)	Fuzzy entropy	No	SVM	No	S^+=98.27% A = 98.31%
				Shoeb et al. (2004)	Wavelet based features	No	SVM	No	S^+=94.24%
				Raghu et al. (2019b)	SDI	No	SVM	No	S^+=97.28%
				Raghu et al. (2019b)	SDI	No	SVM	No	S^+=95.80%
UBonn	5	3.24	100	Acharya et al. (2012)	Entropies	No	Fuzzy classifier	No	A = 99.00%
				Sharma et al. (2017)	Optimal orthogonal wavelet based features	No	LS-SVM	No	A = 100%
				Diykh et al. (2017)	Weighted complex networks	No	SVM	No	A = 100%
				Raghu et al. (2016)	Wavelet packet transform based log energy entropy	No	REN	No	A = 99.70%
				Samiee et al. (2017)	DSTFT	No	MLP	No	A = 99.80%
RMCH	115	58	162	Raghu et al. (2019a)	MD	No	SVM	No	A = 97.56%
				Raghu et al. (2019b)	SDI	No	SVM	No	S^+=97.53%
				Raghu et al. (2019c)	DWT based sigmoid entropy	No	SVM	No	S^+=96.34%
MUMC	39 term and pre-term new born	25	360	Bogaarts et al. (2014)	103 features	ANSFV	SVM	Kalman filter	AUC = 0.90
MUMC	17 ICU patients	4018	1362	Bogaarts et al. (2016b)	103 features	MDM	SVM	Kalman filter	AUC = 0.96
MUMC	39 neonatal 39 adults	613	34898[1]	Bogaarts et al. (2016a)	103 features	ANSFV	SVM	Kalman filter	AUC = 0.93
Neonatal Intensive Care Unit (NICU) of Cork University Maternity Hospital, Cork, Ireland	17 new borns	267	705	Ahmed et al. (2017)	55 features	No	SVM	Central linear MAF	S^+=89%
				Temko et al. (2011)	55 features	No	SVM	MAF	AUC = 0.71
National Society of Epilepsy (UK), Katholieke Universiteit Leuven (Belgium), and Freiburg University Hospital (Germany).	24 adults	172	47	Logesparan et al. (2015)	DWT based Relative power	Normalization	Threshold	Bitwise logical OR operator	AUC = 0.83
					Proposed				
RMCH	115	58	162		SDI and MD	AM-FBC	SVM	MAF	AUC = 1
CHB-MIT	23	884	182						AUC = 0.89
TUH	316	408	222						AUC = 0.99
MUMC	40 ICU patients	21	1273[3]						AUC = 0.95
UBonn	5	3.24	100[4]						AUC = 0.99

[1]34898 Feature vectors derived from 10s epoch, [2]1373 seizure epochs of 10 s duration, [3]1273 seizure events, [4]100 seizures file each of 23.36 s duration, A = Accuracy
RMCH: Ramaiah Medical College and Hospitals, TUH: Temple University Hospitals, CHB-MIT: Children's Hospital Boston- Massachusetts Institute of Technology, MUMC: Maastricht University Medical Centre, UBonn: University of Bonn, EEG: Electroencephalogram, RVM: Relevance vector machine, FBC: Feature baseline correction.
SVM: Support vector machine, MDM: Median decaying memory, MD: Matrix determinant, SDI: Successive decomposition index, MAF: Moving average filter, AM-FBC: Adaptive median feature baseline correction, ANSFV: Average non-seizure feature values, S^+: Sensitivity, S^-: Specificity

the comparison results of previously proposed methods with the proposed cross-database evaluation results and comparison was performed database wise. WPT based CSI showed the highest sensitivity of 90.5% from 14 patients (Zandi et al., 2010). Statistical features extracted from DWT coefficients have achieved an accuracy of 83.07% and 88.00% using the Bern-Barcelona dataset and UBonn databases respectively using the SVM classifier (Chen et al., 2017). The fractal dimension and harmonic WPT feature-based model using the RVM classifier showed a sensitivity of 96.0% and 99.8% using the CHB-MIT and UBonn EEG databases respectively (Vidyaratne and Khan, 2017). DSTFT based approach yielded a classification accuracy of 98.1% using MLP classifier.

The MDM FBC method showed an AUC of 0.93 using the CHB-MIT database (Minasyan et al., 2010) and 0.96 using the MUMC database (Bogaarts et al., 2016b). The AUC of 0.92, 0.93, and 0.93 was achieved for neonatal, adult and combined dataset respectively (Bogaarts et al., 2016a). Further, the ANFSV FBC method was implemented on 103 features using the MUMC database which showed the AUC of 0.92 (Bogaarts et al., 2014). Similarly, our previous study on the MUMC database using SDI feature showed the highest AUC of 0.98 with the help of the AM-FBC method (Raghu et al., Unpublished results). However, in our present cross-database study using MUMC database, the highest AUC of 0.95 only achieved due to the different training data. A Kalman filter was applied to the SVM classifier output for post-processing, which improved the classification results in Bogaarts et al. (2014, 2016a,b). In Temko et al. (2011) and Ahmed et al. (2017) (Raghu et al., Unpublished results), improved performance was observed when a MAF was used for post-processing. The SDI and MD features have shown better performance using the RMCH, CHB-MIT, MUMC databases with leave-one-subject-out cross-validation when the algorithm was trained and tested on same database (Raghu et al., 2019b,a) (Raghu et al., Unpublished results). One can observe that the larger feature set have been used for classification of epileptic seizures in Shoeb et al. (2004), Temko et al. (2011), Bogaarts et al. (2014, 2016a,b), Samiee et al. (2015), Sharma et al. (2017), Ahmed et al. (2017), which could result in computational complexity.

4.4. Clinical significance

One of the challenges in designing the automated seizure detection algorithms is lack of annotated seizures EEG data. The algorithm proposed in our study combines EEG from five different databases and compensates for the feature distribution variation. Our results demonstrate that the new EEG recordings from same and/or different database can be validated without spending much time on designing a new algorithm. Hence, it is cost effective in terms of designing the new algorithm and speed up the treatment procedure.

4.5. Significant findings of the study

The significant findings and contributions of cross-database evaluation are summarized as follows:

1. This is the first of its kind study reporting cross-database evaluation for automated classification of epileptic seizures using five different databases.
2. The S^{+} and S^{-} of 0 was obtained for the RMCH and UBonn databases respectively without the application of AM-FBC.
3. AM-FBC on inter-patient and inter-database level proved its need to perform the cross-database evaluation.
4. AM-FBC along with smoothing of the test data outperformed other CS on all the five databases.
5. The false detection rate decreases as the MAF length increases.

4.6. Future direction

As a future study, a deep learning technique will be implemented on these five databases to perform the cross-database evaluation. The classification results could be further improved by adding a few significant features and optimizing the algorithm. The proposed study will be validated on new EEG databases to improve the algorithm performance. Mixing the whole data could be an interesting future task to improve the generalization of the algorithm. Further, a mobile-based seizure alert system will be introduced using the proposed cross-database evaluation algorithm.

5. Conclusion

To the best of authors knowledge, we are the first to present a cross-database evaluation for automated classification of epileptic seizures using five different databases. Inter-subject and inter-database variation in the feature distribution was corrected using AM-FBC. With the application of AM-FBC, smoothing, and post-processing, the highest AUC of 1, 0.89, 0.99, 0.95, and 0.99 was achieved using the RMCH, CHB-MIT, TUH, MUMC, and UBonn databases respectively. AM-FBC along with smoothing of the test data outperformed other CS. It can be concluded that the cross-database approach has better generalization capability when evaluated using five databases. Finally, cross-database framework helps when sufficient epileptic seizures EEG data is not available to build a seizure detection model.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.clinph.2020.03.033.

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