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Autoencoding of long-term scalp electroencephalogram to detect epileptic seizure for diagnosis support system

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ABSTRACT

Introduction: Epileptologists could benefit from a diagnosis support system that automatically detects seizures because visual inspection of long-term electroencephalograms (EEGs) is extremely time-consuming. However, the diversity of seizures among patients makes it difficult to develop universal features that are applicable for automatic seizure detection in all cases, and the rarity of seizures results in a lack of sufficient training data for classifiers.

Methods: To overcome these problems, we utilized an autoencoder (AE), which is often used for anomaly detection in the field of machine learning, to perform seizure detection. We hypothesized that multichannel EEG signals are compressible by AE owing to their spatio-temporal coupling and that the AE should be able to detect seizures as anomalous events from an interictal EEG.

Results: Through experiments, we found that the AE error was able to classify seizure and nonseizure states with a sensitivity of 100% in 22 out of 24 available test subjects and that the AE was better than the commercially available software BESA and Persyst for half of the test subjects.

Conclusions: These results suggest that the AE error is a feasible candidate for a universal seizure detection feature.

1. Introduction

According to the definitions by the International League Against Epilepsy and the International Bureau for Epilepsy [1], “An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.” Typically, to confirm epilepsy, epileptologists have to visually inspect long-term scalp electroencephalograms (EEGs) and find the occurrence of at least one epileptic seizure, which is a time-consuming task [2]. Thus, a diagnosis support system that automatically detects seizures could significantly reduce diagnosis time.

Various features have been considered for automatic seizure detection [3,4]. They include autocorrelation [5], synchronization likelihood [6], nearest neighbor phase synchronization [7], network properties of functional connectivity [8], and morphology of EEG [9]. The rhythmic activities that are frequently observed in seizures can be detected via frequency-domain features [10–12]. Furthermore, seizures may be detectable from time-domain features such as statistical features [13], principal components [14,15], spectral features [16], and nonlinear features [17]. However, despite a number of successful reports, these handmade features are usually effective only for a particular type of seizure; the diversity of seizures makes it difficult to develop a universal feature for automatic seizure detection.

In addition, because seizures are rare events, there is only a relatively small amount of data available, which makes appropriate training difficult for supervised learning of seizure detection with linear classifiers [18], artificial neural networks [19], and support vector machines [20–22], resulting in poor seizure detection. Recently, studies conducted using big data have demonstrated that deep learning can open a new avenue for seizure detection [23–26]. However, manual

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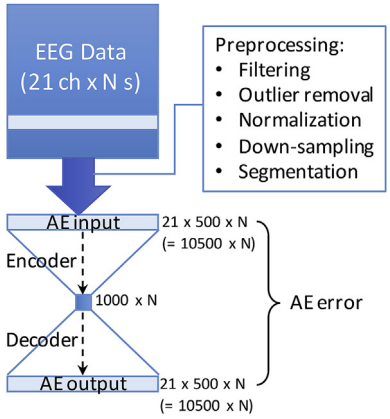

Fig. 1. Seizure detection with autoencoding. Raw EEG was preprocessed, segmented with 1-s time windows and converted to a time series of vectors, by which the AE was trained. The AE errors were used to classify a given segment into "seizure" or "nonseizure.".

preparation of labeled training data is both labor-intensive and time-consuming, and these problems increase with the amount of data.

With the objective of overcoming the above problems, in this study, we investigated whether an autoencoder (AE) can be applied for seizure detection. An AE is trained to reduce the dimensionality of data by encoding the input to a certain representation, from which the input data are reconstructed. The goal of the training is to determine the best parameters to minimize the difference between the original and reconstructed inputs [27], and AEs have been successfully applied to speech recognition [28], natural language processing [29], and anomaly detection [30]. We hypothesized that multichannel EEG signals are compressible by AE because they are spatio-temporally coupled, and that AE is able to detect a seizure as an anomalous event from interictal EEG. Consequently, AE should have significant advantages over conventional methods as it should function for any patient as a universal seizure detection feature without requiring seizure data.

2. Material and method

For seizure detection, patient-specific autoencoders (AEs) were constructed using long-term EEG that included epileptic seizures (Fig. 1). After preprocessing, the EEG signal was segmented using a 1-s window and each segmented dataset was converted to a vector, which was then used to train the AE. The AE error of each segment was then used to detect seizures.

2.1. Data

In this study, the investigation was conducted using the same data as that used in our previous study [23]. Long-term video-EEG monitoring was performed as a part of phase one of the evaluation of patients with epilepsy in the NTT Medical Center Tokyo (eight subjects) and The University of Tokyo Hospital (16 subjects). Written informed consent was obtained from all patients to use their EEG data for research. Further, use of these EEG data for this study was approved by the local ethical committee.

EEGs were obtained using 19 channels based on the 10–20 system, with two additional zygomatic electrodes [31] (Rzyg and Lzyg) (except for subject #14) and one channel for electrocardiography (ECG). The sampling rate was 1000 Hz for the patients from NTT Medical Center Tokyo and 500 Hz for patients from The University of Tokyo Hospital. The information relevant to the subjects enrolled in this study is summarized in Table 1(a). Patients diagnosed as having focal seizures based on long-term video-EEG with acceptable recording quality were included in this study. For six patients, long-term video-EEG failed to localize seizure focus owing to multiregional or widespread abnormalities on the EEGs. The total recording time of the EEGs analyzed in this study was 1124.3 h, during which 97 seizures were recorded. The total seizure duration length was 6950 s.

2.2. Preprocessing

The EEG data were first preprocessed in the following five steps: (1) 0.3-Hz high-pass, 60-Hz low-pass, and 50-Hz notch filtering to avoid unrelated information. (2) Replacement of outliers, defined as having amplitude greater than ± 100 μV, by signals with amplitudes of 100 μV or −100 μV. (3) Normalization such that the EEG signal ranged between zero and one, i.e., −100 μV corresponding to zero and 100 μV corresponding to one, to make input data for AE. Outliers were replaced to avoid losing useful information after normalization. (4) Down-sampling of the data to 500 Hz (only for subjects from NTT Medical Center Tokyo with a 1000 Hz sampling rate) to reduce the dimension of AE input and calculation cost. (5) Division of the data into 1-s data segments without overlap.

Following preprocessing, each segmented dataset had 21 channels and each channel had 500 samples; hence, they were considered as vector arrays, each with a length of 10,500 (i.e., 21 × 500).

2.3. Autoencoder

The AE was trained and optimized using the preprocessed data with a matrix size of N × 10,500, where N is the total length of the data in seconds. The purpose of the AE was to reduce the data dimension as much as possible without losing information. In this study, a one-layer AE consisting of an encoder and a decoder was used. The encoder mapped the input x ($\in R^{10,500}$) to the code z ($\in R^{1,000}$) as follows:

$$\boldsymbol{z} = \boldsymbol{S}(\boldsymbol{W}\boldsymbol{x} + \boldsymbol{b}), \quad (1)$$

where W is a 10,500 × 1,000 wt matrix, b is a 1 × 1,000 bias matrix, and S is the sigmoid function. The decoder mapped the code z to x' ($\in R^{10,500}$):

$$\boldsymbol{x}' = \boldsymbol{S}(\boldsymbol{W}'\boldsymbol{z} + \boldsymbol{b}'), \quad (2)$$

where W' is a 1,000 × 10,500 wt matrix, b' is a 1 × 10,500 bias matrix, and S is the sigmoid function.

The AE needs to optimize the weights and biases such that the difference between x' and x is minimized in terms of the L2 Loss function ($\{\sum (x - x')^2\}/2$). The AE was constructed and trained for each subject dataset with TensorFlow [32]. The Adam algorithm was used with alpha (step size) of 10^{-4}, beta1 (exponential decay rate of the first order moment) of 0.9, and beta2 (exponential decay rate of the second order moment) of 0.999, because this algorithm was computationally efficient and was able to handle nonstationary objectives [33]. The mini-batch size was set to 45,000 and the AE was trained for 25,000 epochs. The required time to train the AE with 1 h of EEG data was approximately 2.7 h using an Nvidia Tesla M60 GPU (Nvidia Corp., Santa Clara, CA).

2.4. Seizure detection based on AE error

We quantified the performance of AE in terms of the absolute difference between the AE input and output, and used the AE error to detect seizures:

$$\boldsymbol{e} = |\boldsymbol{x}' - \boldsymbol{x}|, \quad (3)$$

where x is the AE input, x' is the AE output, and e is the AE error. Because the distribution of the AE error differed among subjects, the Z score of the AE error was derived for seizure detection.

Considering that the state of a seizure differs from the interictal state and that the seizure EEG is an abnormality in the training data, i.e., only 6950 s out of 1124.3 h, the AE error should be higher in the

Table 1
Summary of data.
(a)Subject information. (b)Seizure detection performance.

(a)									(b)						
Sb#	Age	Sex	Mean Sz time, s	# of Sz	Total Sz time, s	Total rec time, h	Epileptic Focus	Sz type	SZ detection rate			False alarm rate			The best method
									B	P	AE	B	P	AE	
1	8	F	93	1	94	88.2	OLE	FBTCS	1	1	1	1.06	0.07	0	AE
2	18	F	103	6	624	47.7	TLE	FIAS	1	0.83	1	0	0.04	0.11	B
3	34	F	376	5	1889	39.9	TLE	FIAS	0.8	1	1	0.03	0.05	2.9	P
4	39	M	12	11	153	20.9	PLE	FIAS	0	0.09	1	0	0.05	4.45	AE
5	19	M	53	3	163	113.6	OLE	FIAS	0.67	1	1	0	0.19	9.43	P
6	62	F	172	5	866	66.8	MF	FAS	0.8	0.8	0.8	0	0.09	16.05	B
7	34	M	94	3	287	90	MF	FIAS	1	1	1	0.02	0.03	2.44	B
8	37	M	12	4	52	71.3	TLE	FIAS	0	0.25	0	0	0.04	0.13	P
9	20	M	120	1	121	94.8	TLE	FIAS	1	1	1	0.04	0.19	0.03	AE
10	30	M	50	1	51	19.6	TLE	FIAS	0	1	1	0	0.21	1.37	P
11	24	F	42	15	656	60.1	MF	FIAS	0	0	1	0.1	0.07	5.43	AE
12	44	F	51	2	105	59.4	TLE	FIAS	1	1	1	0.05	0.41	0.39	B
13	20	M	29	12	371	38.2	MF	FIAS	0	0	1	0	0.18	12.18	AE
14	43	F	188	2	378	27.8	TLE	FBTCS	1	1	1	0.07	0.41	0.11	B
15	17	M	40	3	125	16.8	OLE	FIAS	1	1	1	0	0.25	6.81	B
16	32	F	41	4	168	20.5	TLE	FIAS	0	0.5	1	0.05	0.15	11.5	AE
17	11	M	27	2	57	21.4	TLE	FIAS	0.5	0	1	1.05	0.05	3.1	AE
18	19	F	48	1	49	41.9	TLE	FIAS	1	1	1	0	0.34	0.1	B
19	39	M	69	1	70	5	TLE	FBTCS	0	0	1	0	0	6.5	AE
20	30	M	120	2	243	43.4	TLE	FIAS	0	0.5	1	0.02	0.47	0	AE
21	18	M	14	3	47	20.9	DMF	TS	0.33	0.67	1	4.3	2.8	1.3	AE
22	37	M	16	6	106	22	FLE	FAS	0	0.17	1	0	0.71	0.1	AE
23	49	F	115	1	116	24.5	PLE	FIAS	1	1	1	0.46	2.08	0	AE
24	34	M	52	3	159	69.8	MF	FIAS	1	0	1	0.04	0.23	0.2	B

Abbreviations: Sb, subject; Sz, seizure; rec, recording; OLE, occipital lobe epilepsy; TLE, temporal lobe epilepsy; PLE, parietal lobe epilepsy; MF, multifocal; DMF, diffuse multifocal; FLE, frontal lobe epilepsy; FBTCS, Focal to bilateral tonic-clonic seizure; FIAS, Focal impaired awareness seizure; FAS, Focal aware seizure; TS, Tonic seizure; AE, autoencoder (proposed method); B, BESA; P, Persyst.

seizure state than in interictal states. To test whether and how the AE error could discriminate between seizure and nonseizure EEGs, the seizure/nonseizure labels were made based on consensus among at least two expert epileptologists, and the following sensitivity index derived based on the labels:

$$d' = \frac{\mu_S - \mu_N}{\sqrt{\frac{1}{2}(\sigma_S^2 + \sigma_N^2)}}, \quad (4)$$

where μ_S and μ_N are the means of the Z score of the AE error, and σ_S and σ_N are the standard deviations of the Z score of the AE error in seizure and nonseizure phases, respectively. In addition, the Z score of the AE error was evaluated based on a receiver operating characteristic (ROC) curve, defined as the cumulative distribution function of the true positive rate vs. the false negative rate at a given threshold of the Z score, ranging from 0.02 to 10 with increments of 0.02.

The interictal state is expected to have small AE errors; on the other hand, higher AE errors may be observed instantaneously owing to any artifact, and continuously during the seizure state. Therefore, for practical use, we issued a seizure alarm when the AE error exceeded a given discrimination threshold for 10 consecutive seconds or longer. The discrimination threshold of the Z score of the AE error served as a parameter to determine the sensitivity of the seizure alarm. The best discrimination threshold was identified based on the ROC curve and is defined as the cumulative distribution function of the false alarm rate vs. the detected seizure rate at a given threshold, ranging from 0.02 to 10 at intervals of 0.02. The accuracy of the seizure alarm was then evaluated in minutes: When a given time window of 1 min contained a seizure period with alarms, this window was labeled as having a true positive alarm. A window with neither seizures nor alarms was labeled as a true negative. Windows containing either only seizures or alarms were labeled as false negatives or false positives, respectively. We used retrospective validation with the best threshold for each subject, by which the seizure detection rate becomes highest at the expense of the false alarm rate. For comparison, we also used the commercially available software packages BESA [34] and Persyst [35], and evaluated the accuracy of the seizure alarms in the same manner as the seizure alarm for our system. BESA is based on short time Fourier transform to quantify integrated power in the frequency band of 2.5–12 Hz for a multichannel seizure detection montage referenced against the average of Fz-Cz-Pz [34]. Persyst evaluates the scalp EEG signal for changes in background activity exhibiting rhythmicity, evolution in amplitude and/or frequency, and asymmetry [36].

3. Results

Fig. 2 shows the autoencoding of the representative EEG segments in the nonseizure (a) and seizure states (b). For the nonseizure EEG, the AE input (Fig. 2 (a) (i)) was successfully replicated by the AE output (Fig. 2 (a) (ii)) with small errors in both EEG traces in each channel (Fig. 2 (a) (iii)) or the average across channels (Fig. 2 (a) (iv)). During seizure, on the other hand, increased AE errors indicate that the autoencoding was not very successful (Fig. 2 (b)). In this specific example, oscillatory components during seizure could not be replicated, causing significant errors during a period of seizure (Fig. 2 (b) (iii) and (iv)).

Fig. 3 shows long-term monitoring of the Z score of the AE errors in a representative subject. The AE error varied widely over time, irrespective of seizure occurrence. However, high AE errors in the interictal state usually declined to the baseline level rapidly (upper left inset in Fig. 3), while high AE errors were maintained during the seizure state (upper right inset). For seizures that lasted 30 s or more, Fig. 4 shows the transient Z score of the AE error before 1 min and after 30 s of seizure onsets, demonstrating that the AE error increased successively following the seizure onsets.

Fig. 5 (a) shows the histograms of the Z score of the AE error in the seizure and nonseizure states from all of the test subjects. The AE error tended to be larger in the seizure than in the nonseizure states, and Z

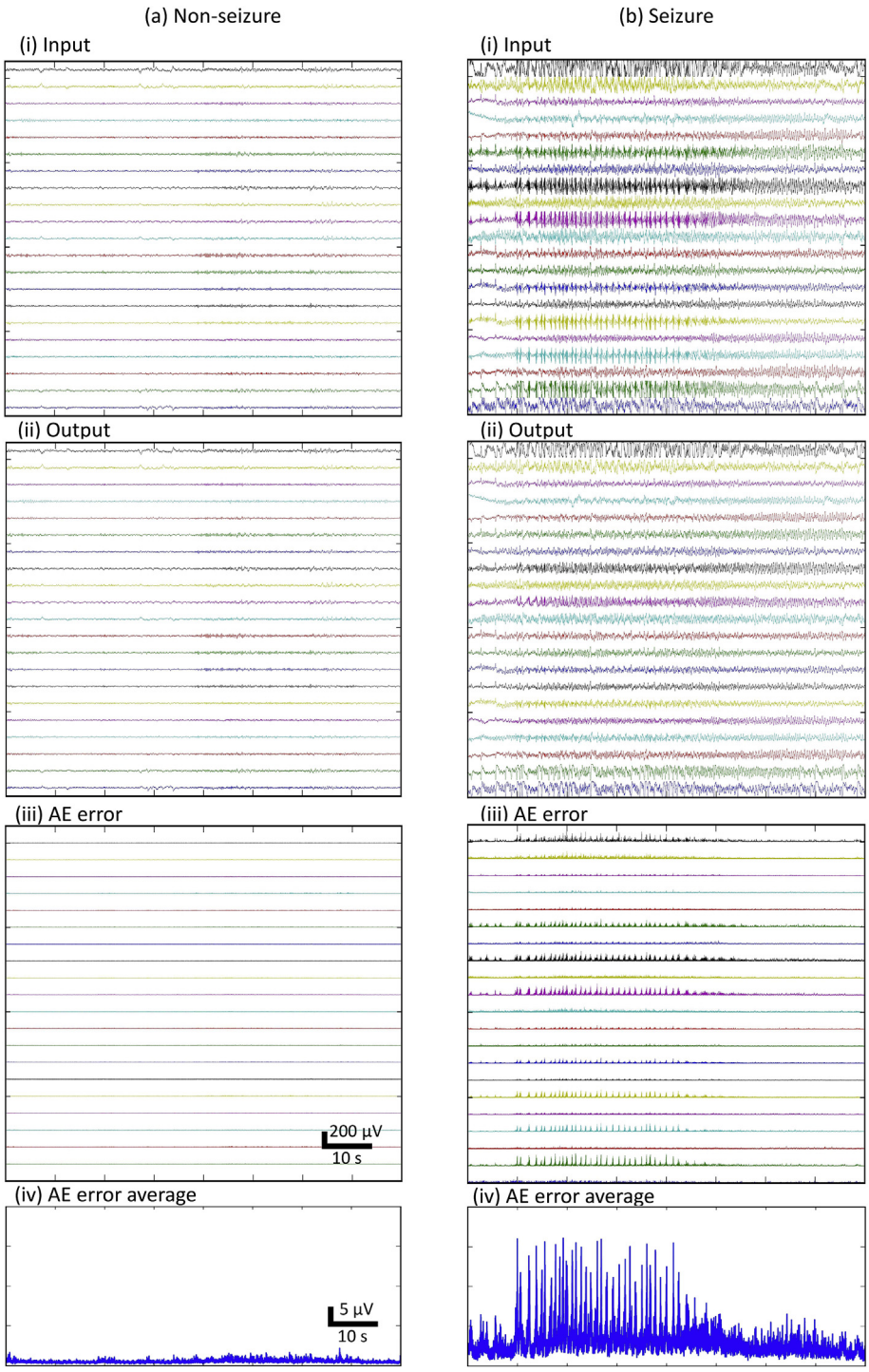

Fig. 2. Autoencoding of EEG. (a) Representative data in the seizure states. (b) Representative data in nonseizure states. (i) Input. data. (ii) AE output (reconstructed input). (iii) AE error, i.e., difference between input and output. (iv) AE error average across recording channels.

scores greater than five were only observed in the seizure state. However, the seizure state still had small AE errors with a Z score of less than one, which overlapped with those in the nonseizure states. Consequently, the sensitivity index *d'* between the seizure and nonseizure states of all of the EEG data in our dataset was 1.03, indicating that the AE errors in general had a limited ability for seizure detection. For each subject, the ROCs in Fig. 5 (b) quantified how the Z score of the AE error separated the seizure state from the nonseizure state as a function of the discrimination threshold, ranging between 0.02 and 10 in 0.02 increments. A low threshold, i.e., close to 0.02, resulted in a high true positive rate of almost 100% and a low true negative rate, while a high threshold, i.e., close to 10, led to low true positive and high true negative rates. The ROCs in some subjects suggest that the AE errors could serve as a relatively reliable indicator of a seizure with an optimal discrimination threshold, but not in others.

For practical use, we issued a seizure alarm when the Z score of the AE error exceeded a given discrimination threshold for 10 s consecutively or longer. From these seizure alarms, the seizure detection rate and false alarm rate were then quantified by 1-min windows as a function of the discrimination threshold, and the ROC curves of the

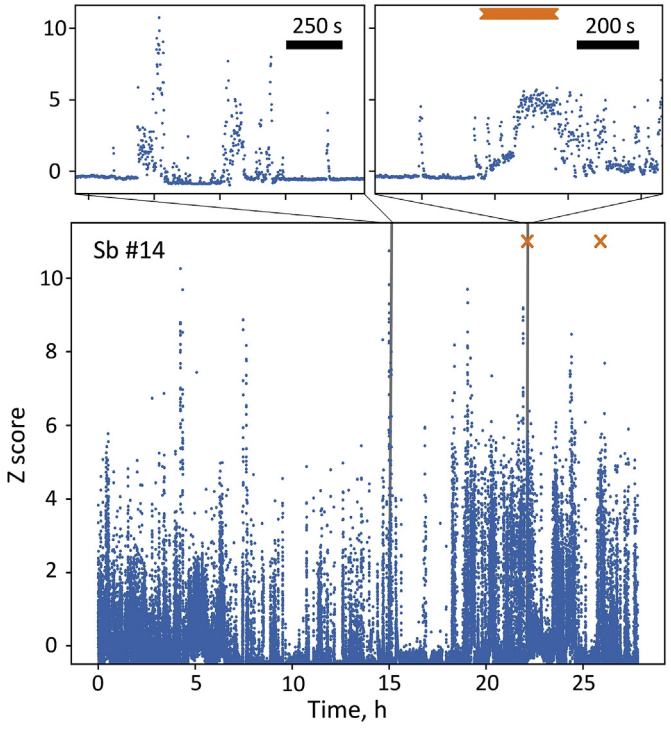

Fig. 3. Representative long-term monitoring of AE errors. Cross marks show seizures diagnosed by epileptologists. Upper insets are magnification around the seizure onsets.

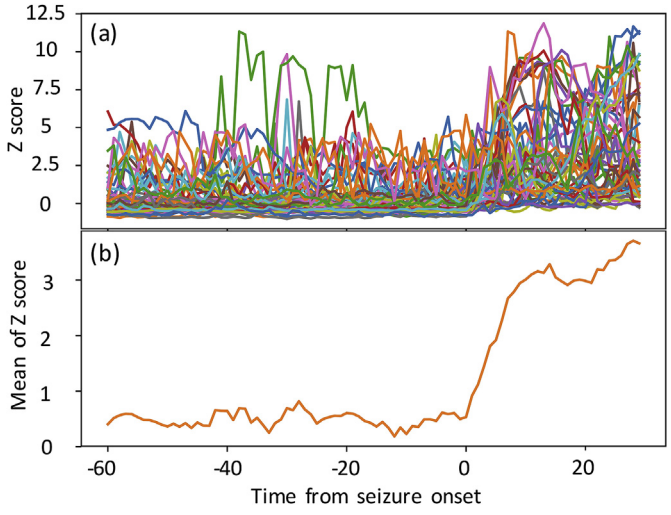

Fig. 4. AE error around the onset of the seizures. (a) Peri-seizure transients of the Z score of the AE error. Fifty-three seizures with a duration of 30 s or longer are shown. (b) Mean of the Z score of the AE error.

seizure detection rate vs. the false alarm rate were derived in each subject as shown in Fig. 5 (c). The best threshold was determined with the seizure detection rate taking priority over the false alarm rate, i.e., the lowest false alarm gave the highest seizure detection rate. Consequently, in 22 out of 24 subjects, our proposed method achieved 100% seizure detection at the best threshold with a false alarm rate ranging from 0 to 16/h (mean ± s.d. = 3.53 ± 4.64; median = 1.34) (Table 1 (b)). We similarly evaluated the commercially available software packages BESA and Persyst for seizure detection, in terms of seizure detection rate and false alarm rate, and found that our method gave the best performance in 12 out of the 24 subjects.

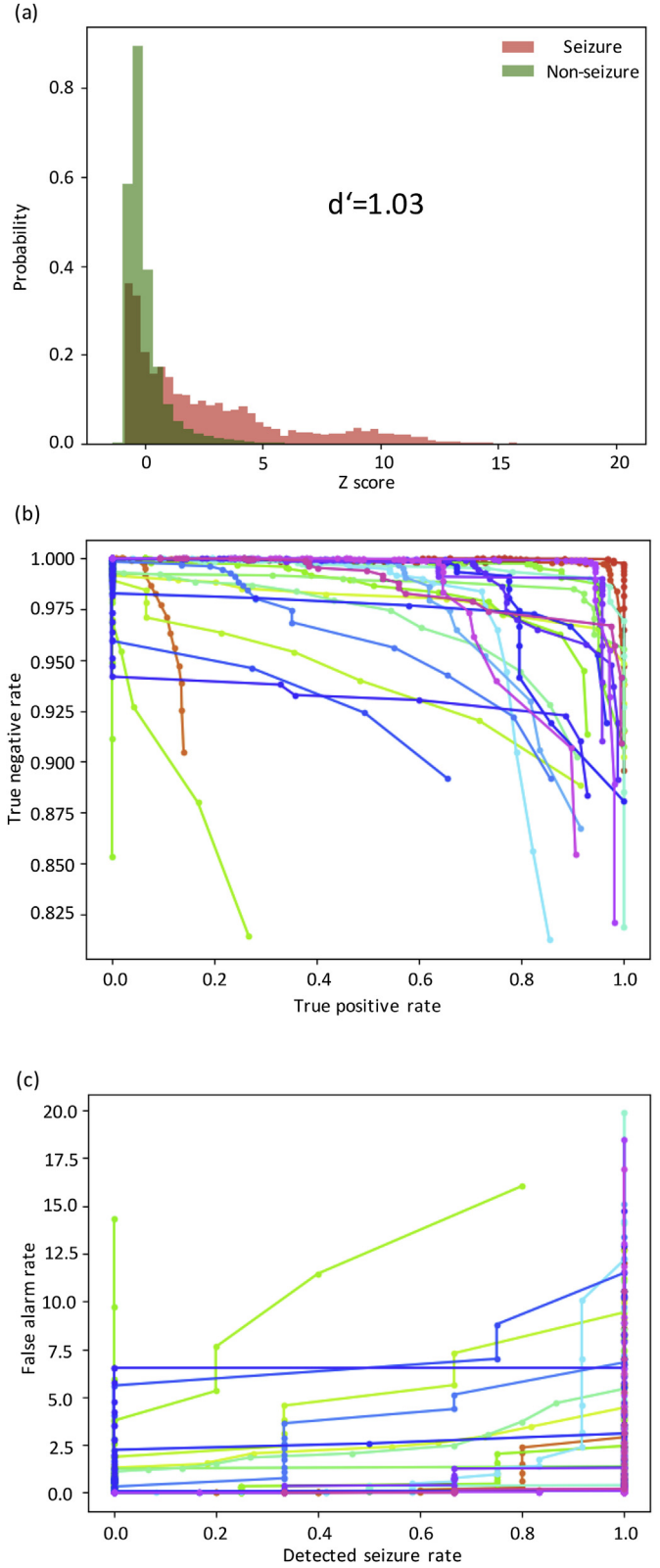

Fig. 5. Seizure detection performance. (a) Histogram of the Z score of the AE error in seizure and nonseizure. The sensitivity index of seizure and nonseizure was 1.03. (b) True positive vs. true negative rates as a function of the discrimination threshold of the Z score ranging from 0.02 to 10 in 0.02 increments. (c) Seizure detection rate vs. false alarms based on the seizure alarm for practical use (see text).

4. Discussion

In this study, we demonstrated that AE can automatically detect seizure in a patient-specific manner that does not require seizure data in training. Our system detected all the seizures in 22 out of 24 test subjects. Moreover, the AE error proved to be the best for half of the subjects when compared to BESA and Persyst (Table 1 (b)).

Various backgrounds across subjects made automatic seizure detection challenging in our dataset. The subjects ranged from 8 to 62 years old, and they all had focal epilepsy with different epileptic foci and EEG patterns. For a wide data range such as this, handmade numerical features may not always perform at a satisfactory level [37]. The two unsuccessful cases out of 24 in the present study were likely caused by poor modeling of AE with a given dimension. Otherwise, the ictal and interictal EEG may have been mutually too similar for AE to classify them as a different class. The latter is more likely because neither BESA nor Persyst was able to correctly classify them.

To date, several researchers have attempted seizure detection from EEG data. For example, Saab et al. (2005) used Bayesian formulation, with 77.9% of the seizures being detected and 0.86 false alarms per hour [38]. Wilson et al. (2004) used the reveal algorithm with matching Pursuit, small neural network rules, and a new connected-object hierarchical clustering algorithm at the same time, resulting in a 76% seizure detection rate with 0.11 false alarms per hour [39]. Shoeb et al. (2004) made a feature vector from wavelet decomposition, and demonstrated that their algorithm could detect 94% of seizures at 0.25 false alarms per hour [40]. Khan et al. (2012) used normalized coefficient of variation, kurtosis, and skewness, which was classified by a linear classifier, and demonstrated detection of all seizures at 1.1 false alarms per hour [41]. Lack of a standardized EEG dataset for seizure detection [42], and no common standard for manually labeling the seizures in the datasets [43] hamper direct comparison among these methods. Nevertheless, the large amount of data (1124.3-h continuous multichannel EEG data from 24 subjects) differentiates our work from previous studies, and provides compelling evidence that the AE-based seizure detection is effective for a significant proportion of epileptic patients. In terms of classification accuracy alone, the AE was not always better than other methods (Table 1(b)). Our recent study also demonstrated that the convolutional neural network based on supervised learning exhibited better performance than the AE with the same dataset [23]. Nevertheless, from the clinical viewpoint, an unsupervised form of learning of a universal feature in the AE has practical advantages over other methods because the AE does not need handmade features of EEG or handmade labels of seizure in the training.

Because pathologies differ among epileptic seizures, most of the existing algorithms attempt to manually create features that can only work on some patients or some seizures. No algorithm that could be considered satisfactory as a universal algorithm for seizure detection has emerged [44]. In the method proposed in this study, we expect that the AE error should be effective for all patients because the AE learns how the EEG behaves from long-term data, mostly of interictal states, instead of seizure states—which usually constitute less than 1% of the total data. On the other hand, the AE has an obvious drawback in that the AE error increases in the presence of artifacts. To counter this problem, we showed that an increase in AE error at an artifact is only momentary, whereas it increases continuously during the seizure state, i.e., for at least 10 s.

The proposed method offers the advantage of not requiring seizure data for training; the AE can be trained using only the interictal data, and seizure data are not essentially needed in training. For existing algorithms, the limitation of the seizure data in epileptic patients has often caused poor seizure detection performance owing to insufficient training. Furthermore, skill, time, and patience are required to make seizure logs in lengthy EEG data. Thus, no need for a seizure log is a significant advantage of the AE-based seizure detection method. However, poor modeling of AE results in poor performance. One of the most important challenges in the future is optimizing the AE structure to make it universally applicable to every patient. In addition, we have constructed an AE model from the entire data and evaluated the performance retrospectively, because such a retrospective application works for a diagnosis support system of long-term EEG to save the efforts of neurologists reading the EEG. The performance of online seizure detection remains to be seen because testing data should be different from training data to evaluate the method as online seizure detection.

EEG patterns commonly exhibit significant correlation and mutual information between channels [45], i.e., signs of functional networks in the brain, which are the rationale that the AE could compress EEG data by a factor of 10, as shown in the present study. Such functional networks in the brain, however, differ among subjects [46]; therefore, it is likely impossible to construct a universal AE model that is effective for every subject. Alternatively, AE-based seizure detection still leaves room for improvement, because additional multimodal data may contribute to appropriate modeling of AE in a patient-specific manner.

Conflicts of interest

There are no conflicts of interest to declare.

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