



Detecting epileptic seizures using machine learning and interpretable features of human EEG

Oleg E. Karpov^{1,a}, Sergey Afinogenov^{2,b}, Vadim V. Grubov^{3,c}, Vladimir Maksimenko^{3,4,d}, Sergey Korchagin^{2,e}, Nikita Utyashev^{1,f}, and Alexander E. Hramov^{3,g} 

¹ National Medical and Surgical Center named after N. I. Pirogov, Ministry of Healthcare of the Russian Federation, Nizhnaya Pervomaiskaya Str. 70, Moscow 105203, Russia

² Faculty of Information Technology and Big Data Analysis, Financial University under the Government of the Russian Federation, Leningradskii Pr. 49, Moscow 125167, Russia

³ Baltic Center for Artificial Intelligence and Neurotechnology, Immanuel Kant Baltic Federal University, Nevskogo Str. 14, Kaliningrad 236041, Russia

⁴ Neuroscience and Cognitive Technology Laboratory, Center for Technologies in Robotics and Mechatronics Components, Innopolis University, Universitetskaya Str. 1, Innopolis 420500, Russia

Received 31 August 2022 / Accepted 26 October 2022

© The Author(s), under exclusive licence to EDP Sciences, Springer-Verlag GmbH Germany, part of Springer Nature 2022

Abstract Epilepsy is a neurological disorder distinguished by sudden and unexpected seizures. To diagnose epilepsy, clinicians register the signals of brain electric activity (electroencephalograms, EEG) and extract segments with seizures. It enables characterizing their type and finding an onset zone, a brain area where they originate. This procedure requires manual EEG deciphering, which is slow and necessitates the assistance of machine learning (ML) algorithms. Traditionally, ML handles this issue in a supervised fashion, i.e., after the training on the representative data, it constructs a boundary in the feature space that separates classes. As the number of features grows, this boundary becomes complex and less generalized. The feature space of brain data is high dimensional. The standard recording includes 30 signals and 50 frequencies resulting in 1500 features. Using additional time-domain features may further enlarge the feature space. Thus, selecting appropriate features is a big part of the successful classification. The selection procedure relies on either a data-based mathematical approach (e.g., principal components, PCs) or the expert domain knowledge of data (explainable features, EFs). Here, we demonstrate the benefits of using EFs. For the EEG data of 30 epileptic patients, we trained a RandomForest algorithm using PCs and EFs. The feature importance analysis revealed that explainable features outperform principal components.

1 Introduction

Epilepsy is a chronic neurological disorder manifesting in a form of recurrent seizures accompanied by abnormal brain activity [1]. According to global statistics, epilepsy is one of the most common neurological diseases [2]. Epileptic seizures vary from brief and nearly undetectable episodes to long periods of vigorous shaking [3, 4]. Seizures are often marked by involuntary movement and corresponding state of incapacity, that

lead to dangerous situations for both patient and surrounding people. Additionally, patients with epilepsy are more prone to cognitive and behavioral deficits [5]. Thus, epilepsy affects many aspects of patient's life, and antiepileptic treatment is crucial. Seizures are controllable with medications—up to 70% of patients could become seizure-free with the appropriate use of anti-seizure medicines [6, 7]. For those whose seizures do not respond to medication, surgery or neurostimulation can be used to certain degree [8, 9]. Not all cases of epilepsy are lifelong, and many people improve to the point that treatment is no longer needed [10]. However, to start antiepileptic treatment a proper diagnosis is required, the earlier the better, which leads to necessity of practical and accessible methods for epilepsy diagnostics.

Epilepsy diagnostics is commonly associated with objective seizure identification and quantification [11]. Most treatment strategies start with analyzing brain activity during seizures revealing their features. One

^a e-mail: karpovoe@pirogov-center.ru

^b e-mail: 181422@edu.fa.ru

^c e-mail: vvgrubov@gmail.com

^d e-mail: v.maksimenko@innopolis.ru

^e e-mail: korchaginser@gmail.com

^f e-mail: utyashevnp@pirogov-center.ru

^g e-mail: hramovae@gmail.com (corresponding author)

of the most common approaches to obtain this information is the electroencephalogram (EEG) study: the patients are monitored for a period of time with occasional functional trials to stimulate the arousal of epileptiform activity [12]. While this method is fairly reliable, there are certain issues. Firstly, proper epilepsy diagnostics requires collecting data for a representative number of events which is only possible during the prolonged continuous EEG monitoring. The studies show that it is common to require more than three days of EEG recording to diagnose the nature of paroxysmal episodes [12]. This issue occurs partly due to high variability of epileptic activity—exact underlying cause for epilepsy is usually unknown and can include brain injury, stroke, tumor, congenital disabilities, etc. [13–15]. Secondly, EEG approach relies heavily on data deciphering, which is commonly done manually in clinical practice [16]. Visual analysis requires much effort—an experienced specialist can spend hours reviewing the data of a single patient. Additionally, the human factor is involved, which can lead to increased error rate under conditions of high workload and fatigue. Misdiagnosis can have a heavy impact on the patient’s physical and mental health and require its own treatment and rehabilitation. Thus, an expert requires assistance from automated systems for seizure detection [17]. While fully automated detection of epileptic seizures seems very attractive, even the modern methods in this field still possess a high chance of misdiagnosis. The working solution here is partial automation, well-known as the Clinical Decision Support System (CDSS) [18]. In CDSS, the computer analyzes data and provides recommendations, and the medical expert makes the final decision.

An optimistic approach to automated epileptic seizure detection is machine learning (ML) [19, 20]. In case of ML, seizure detection comes in a form of classifier that commonly detects two classes in EEG data: “seizures” and “non-seizures” [21, 22]. A wide variety of ML techniques have been applied to this task, including support vector machine (SVM) [23–26], random forest [27–29], artificial neural network (ANN) [30, 31], k-nearest neighbors (kNN) [32, 33], deep learning [34].

As we mentioned above, epileptic activity can be highly variable which leads to under-representation and non-robust EEG footprint of an epileptic pattern. This issue leads to situation where direct application of ML classifier to raw EEG dataset may not produce enough sensible patterns. Thus, in most cases ML approach requires use of informative input features, that are commonly derived from time and frequency domains of EEG data [35]. Vast research on time-frequency structure of epileptic EEG [14, 15] reveals some major time-domain features, for example, repeatability, regularity (periodicity), synchronicity and amplitude variation of EEG, that are considered to be able to differentiate epileptic seizure from normal activity [36]. Various transformation techniques including Fourier transformation (FT), discrete wavelet transformation (DWT), continuous wavelet transformation (CWT) [37, 38] are

applied to EEG data to provide time-domain based features—for example, line length, frequency and energy [39, 40]. However, this approach often leads to great increase in number of features, which, in its turn, negatively affects computational costs, response time and performance.

ML commonly addresses classification in supervised fashion—an algorithm is trained on a set of previously labeled data to estimate outputs for unlabeled data [41, 42]. In this form, machine learning is often used to diagnose neural activity in the brain [43, 44]. Review shows that the majority of existing seizure detection methods rely on supervised ML algorithms [45]. While this approach demonstrates generally higher performance, it can suffer from the class imbalance and overfitting.

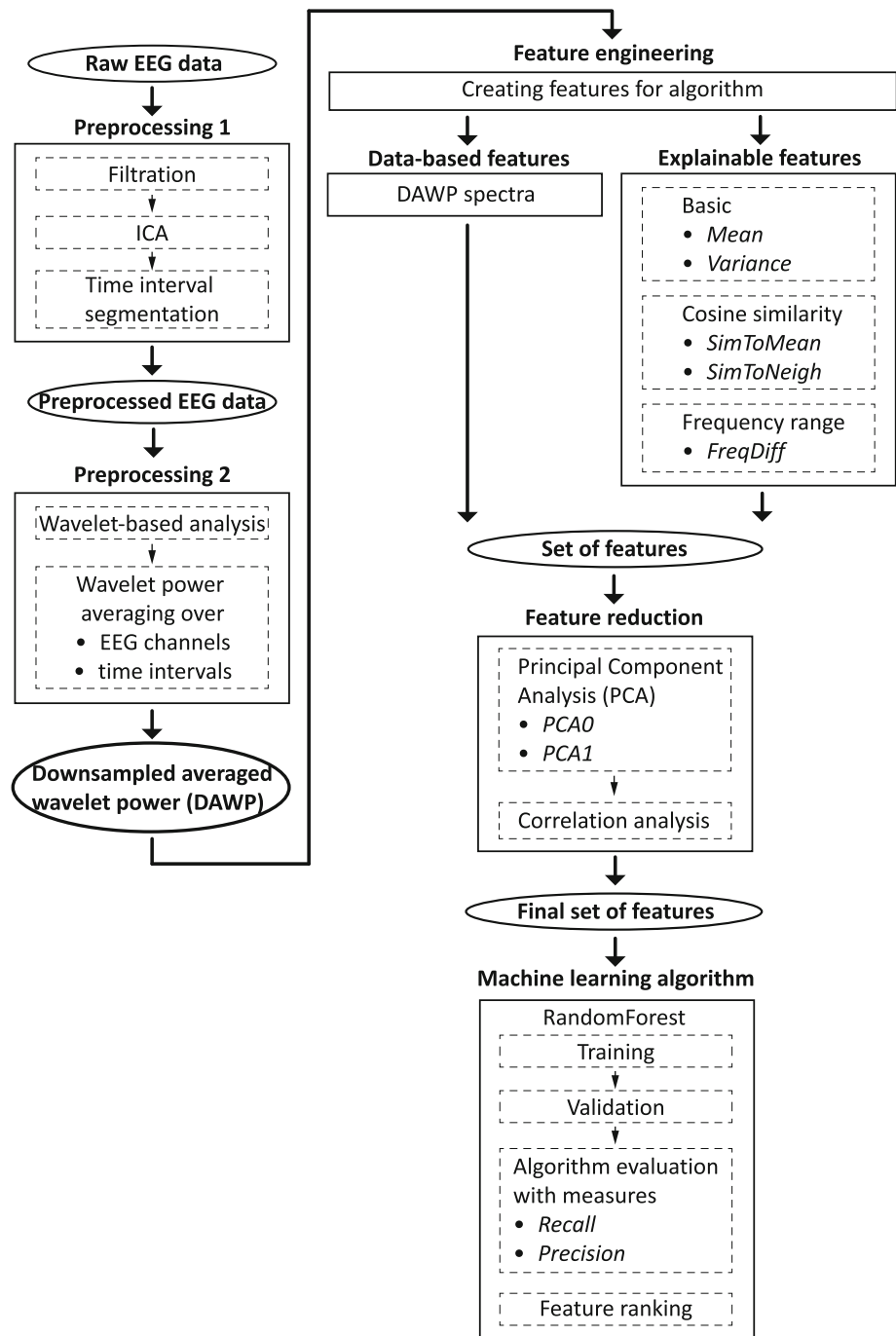
The class imbalance originates from the rare nature of seizures and requires artificial balancing for “seizure” and “non-seizure” examples in the training set. One way to manage the imbalance is constructing feature space resulting in the long distance between classes. However, stretching this concept too far often leads to overfitting. The overfitting implies that the algorithm performs satisfactorily on the training data but fails to properly classify test data. Addressing this issue relies on constructing a feature subspace with the biomarkers of seizures common for the most patients. These reasonings lead us to the problem of the feature selection and interpretability which often occurs in ML. It is crucial to analyze obtained feature space to find the most important features and perform feature reduction procedure. In this work, we aimed to propose ML-based approach to epileptic EEG marking that uses specific set of features and can possibly be applied in CDSS.

2 Methods

Figure 1 illustrates the whole pipeline of the research. Each separate step is explained in detail further in the paper.

2.1 Participants

In the study, we used anonymized long-term EEG and video-monitoring data of 30 adult subjects (15 males and 15 females, age 33.4 ± 9.4) with confirmed diagnosis “focal epilepsy”. The experimental dataset was provided by National Medical and Surgical Center named after N. I. Pirogov of Russian Healthcare Ministry (Moscow, Russia). All subjects were patients of the Department of Neurology and Clinical Neurophysiology in 2017–2019. Medical procedures were held in the Center following the Helsinki Declaration and the Center’s medical regulations, and were approved by the local ethics committee. All patients provided written informed consent before the treatment. The data was collected during patients’ regular daily routine and occasional standard physiological trials such as photic stimulation and hyperventilation [46]. Length of the

Fig. 1 Diagram with pipeline of the study

monitoring varied from 8 to 57 h and depended on the personal patient's condition [12]. Each patient had from one to five epileptic seizures during the time of the monitoring. While all the patients were subjected to physiological trials, none of the seizures was triggered by this stimulation; i.e., all epileptic seizures were spontaneous. Recorded EEG and video-monitoring data of the patients were retrospectively analyzed by the experts from the Center, and all epileptic seizures were marked.

2.2 Data acquisition and preprocessing

EEG signals were recorded with “Micromed” encephalograph (Micromed S.p.A., Italy). Dataset for each patient included 25 channels arranged in accordance with the international “10–20” system. Ground electrode was placed on the forehead and reference electrodes were placed at the ears. Sampling rate of EEG data was 128 Hz. The video monitoring system was used to track patients' states for easier data marking.

EEG signals are known to be highly susceptible to the influence of various external and internal noises, especially during prolonged recording [47]. In clinical monitoring, external noises usually emerge through poor contact of EEG electrodes, powergrid and cell-phone interference, etc. Internal noises (physiological artifacts) originate from physiological processes such as heartbeat, blinking, or breathing [48]. To deal with low- and high-frequency noises we applied band-pass filter with cutoff frequencies of 1 Hz and 60 Hz. Additionally, we used 50-Hz notch filter to diminish powergrid interference. We considered the frequency band 2–30 Hz, which includes all commonly studied waveforms (delta, theta, alpha, beta), and is often regarded as an effective frequency range of EEG [16]. To remove some undesired activity that can interfere in this frequency range (e.g., blinking artifacts) we used standard procedure based on an independent component analysis (ICA) [49].

Studies on epileptic EEG show that seizures manifest as “outliers” in EEG data [26, 50, 51]. However, outliers in data can also be caused by some external interference such as mechanical impact on EEG electrodes, which is quite common in prolonged EEG recordings [52]. The existence of two types of outliers in data can negatively affect training of ML classifier and its ability to distinct two classes. In our work we removed outliers in normal but not in epileptic EEG activity. Such preprocessing requires preliminary data labeling and analysis, which contradicts the purpose of classifier. So we removed outliers only for the training dataset, but validation and testing were performed on unaltered data.

To construct feature space from EEG data, we performed time–frequency analysis of EEG signals using CWT with Morlet mother wavelet function [53, 54]. We considered wavelet power (WP) as it is common CWT-based characteristic to describe the time–frequency structure of the epileptic EEG [55, 56]:

$$W_n(f, t) = |w_n(f, t)|, \quad (1)$$

where $n = 1, 2 \dots N$ is the number of EEG channel ($N = 25$ for the used dataset), f and t are the frequency and time point, $w_n(f, t)$ are the coefficients of CWT.

To reduce obtained feature space we considered two additional steps. The first step included averaging WP over the EEG channels. This approach is inspired by the features of spatial distribution of EEG activity during epileptic seizures. In generalized seizures, activity arises suddenly all over the brain, and all EEG signals are highly correlated [57]. In focal seizures, activity is localized in a few EEG channels near the focus, however, these channels stand out in terms of time–frequency structure of EEG signal, so even after averaging over the channels WPs for normal and pathological activity differ significantly. While this approach eliminates spatial distribution of EEG activity, it can help to differentiate normal and epileptic activity without knowledge on focus location. We calculated averaged

WP (AWP) by averaging WP values over $N = 25$ EEG channels:

$$E(t) = \frac{1}{N} \sum_{n=1}^N W_n(f, t) \quad (2)$$

The second step included further decrease of the complexity of the data via “downsampling” of AWP. We divided each EEG recording into 60-second intervals T_m , where $m = 1, 2 \dots M$, $M = L/60$, L —the length of EEG recording in seconds, “/” stands for integer division. The choice of such interval length is justified by the average duration of an epileptic seizure—from 30 to 120 s [58]. AWP values were calculated for each time interval T_m and averaged over the whole length of the interval to obtain “downsampled” AWP (DAWP):

$$e_m = \frac{1}{\Delta T} \int_{t \in T_m} E(t) dt, \quad (3)$$

where ΔT is the length of each interval T_m ($\Delta T = 60$ s).

3 Machine learning

3.1 Feature engineering

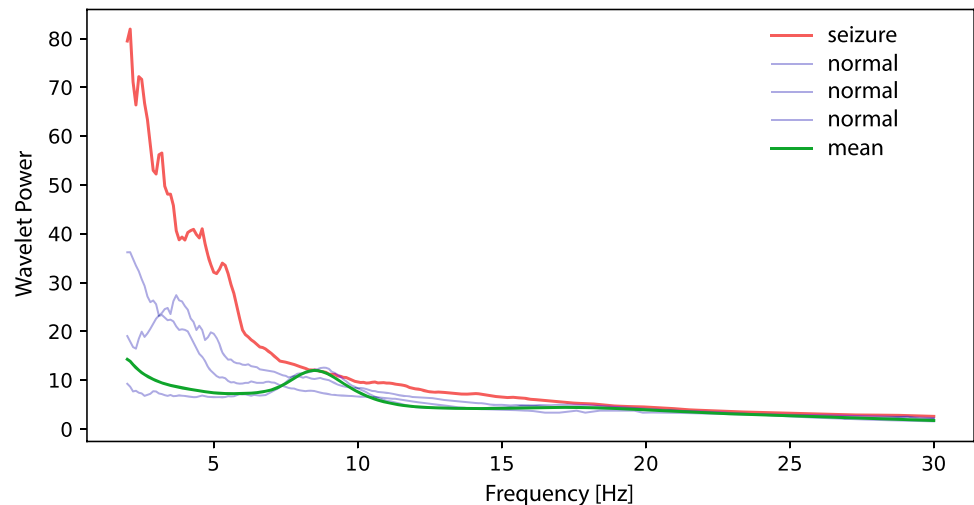
The initial feature space consisted of DAWP spectra, but we aimed to introduce several additional features. Figure 2 illustrates typical DAWP spectra of a single patient. The red curve corresponds to the epileptic seizure, blue curves are the spectra obtained in the neighbouring time-points before and after the seizure. Green curve reflects the spectrum averaged across the whole recording of this patient. Extended research on epileptic EEG reveals certain peculiarities of seizures in comparison to normal EEG [4, 14, 15, 59, 60], so introduction of new features that would capitalize on this difference can help in seizure detection greatly.

It is well-known that epileptic seizures occur due to abnormal excessive or synchronous neuronal activity in the brain [61]. The statement of abnormality suggests that EEG activity in seizure is generally different. This means that basic properties of EEG spectrum—DAWP spectrum in our case—such as dominant frequencies, peak energy, energy distribution across frequencies should also differ between epileptic and normal activity [4].

According to the explanatory Fig. 2, the DAWP spectrum has much higher power during seizure. Moreover, it demonstrates large deviation of the power between low and high frequencies. Therefore, we introduce two features capturing these properties:

- *Mean* mean DAWP across 2–30 Hz range
- *Variance* variance of DAWP in spectrum

Fig. 2 Typical DAWP spectra of a single explanatory patient. The red curve corresponds to the epileptic seizure, blue curves are the spectra obtained in the neighbouring time-points before and after the seizure. Green curve reflects the spectrum averaged across the whole recording of this patient



Additional features to assess normal and epileptic data similarity can be introduced using cosine similarity. This approach suggests considering DAWP spectrum in each time interval T_m as a vector, and it is especially popular in ML methods [62, 63]. We introduced feature *SimToMean* as cosine similarity between DAWP spectrum at given time interval T_m and mean DAWP spectrum for the patient (green curve in the Fig. 2). We suppose that this feature in addition to *Mean* and *Variance* can capitalize on the contrast between seizure and normal EEG.

Epileptic seizures in addition to being abnormal and excessive activity also occur spontaneously [64]. This fact suggests that EEG activity during the seizure differs greatly from the activity before and after the seizure. To assess this difference we introduced another cosine similarity-based feature—*SimToNeigh*. We calculated *SimToNeigh* as mean cosine similarity between DAWP spectrum at given time interval T_m and each of DAWP spectra from neighboring intervals (T_{m-3} , T_{m-2} , T_{m-1} , T_{m+1} , T_{m+2} , T_{m+3}) (these spectra are marked in blue color in the Fig. 2).

Deep understanding of the spectrum structure can also improve seizure detection. Our recent research demonstrated that some parts of the spectrum are more prone to reflect epileptic activity. In the paper [50], we reported that the absence seizures in WAG/Rij rats induced a drastic increase of WP in the frequency range of 6–8 Hz, while there were no manifestations of such behavior for other frequencies. In the follow-up research [26, 51], we showed that epileptic seizures in human patients demonstrate similar behavior in the frequency range of 2–5 Hz and not in the rest of the spectrum (5–30 Hz). Figure 2 clearly illustrates this statement. During the seizure, wavelet power (red curve) reaches the highest values at the low frequency and rapidly decreases within the 2–5 Hz frequency range. For normal activity, the difference in wavelet power between the 2–5 Hz and 5–30 Hz is much smaller (blue curves). Thus, the pronounced difference between low- and high-frequency EEG activity can be considered as a

marker of epileptic seizure. According to this conclusion we introduced another feature—*FreqDiff* as difference between DAWPs averaged over low (2–5 Hz) and high (5–30 Hz) frequencies.

Thus, we derived five new features from the data: *Mean*, *Variance*, *SimToMean*, *SimToNeigh*, *FreqDiff*. We aimed to use them along with original DAWP spectra to construct ML model. However, each DAWP spectrum contains many features—spectrum was calculated in 2–30 Hz range with 0.1 Hz step.

Large number of features negatively affects time for ML model training. Moreover, DAWP on neighboring frequencies, such as 2.1 and 2.2 Hz, are highly correlated, which leads to data redundancy. To lower the dimensionality of feature set we used principal component analysis (PCA) [65]. The analysis showed that first two components (*PCA0* and *PCA1*) contain 97.18% of all information from the initial data. These principal components, PCs are show in Fig. 3. Red dots correspond to the epileptic seizures, blue dots—to the segments of normal activity. Although these PCs explain 97.18% of data, projecting the data onto the reconstructed feature space barely allows separating seizures and normal EEG.

Finally, correlation analysis showed high correlation between *Mean* and *PCA0*, so we decided to remove *Mean* from the feature set. In the end, for constructing ML model we used six features: *PCA0*, *PCA1*, *Variance*, *SimToMean*, *SimToNeigh*, *FreqDiff*.

3.2 Algorithm

We used RandomForest, a popular supervised learning algorithm, which builds a forest with an ensemble of decision trees and averages their outputs [66]. We chose RandomForest for the following advantages: (i) due to binning the variables, RandomForest is not influenced by outliers; (ii) it handles both linear and non-linear

Table 1 Results for RandomForest Classifier

Patient	TP	TN	FP	FN	Recall, %	Precision, %
1	3	2388	129	0	100	2.27
2	1	447	32	0	100	3.03
3	2	4120	155	0	100	1.27
4	1	406	73	0	100	2.67
5	1	414	65	0	100	1.52
6	2	432	46	0	100	4.17
7	1	467	12	0	100	7.69
8	1	469	10	0	100	9.09
9	2	466	12	0	100	14.29
10	1	66	400	0	100	0.25
11	1	471	8	0	100	11.11
12	5	4409	635	0	100	0.78
13	0	440	39	1	0	0
14	1	1234	11	0	100	8.33
15	2	3746	158	3	40	1.25
16	1	407	32	0	100	3.03
17	1	422	57	0	100	1.72
18	1	465	10	4	20	9.09
19	1	472	7	0	100	12.5
20	1	420	59	0	100	1.67
21	0	449	30	1	0	0
22	0	450	27	3	0	0
23	2	1905	122	0	100	1.61
24	3	2191	43	0	100	6.52
25	1	434	45	0	100	2.17
26	4	453	23	0	100	14.82
27	0	465	14	1	0	0
28	1	468	11	0	100	8.33
29	0	457	22	1	0	0
30	4	392	9	0	100	30.77
Mean					78.67	5.33
SE					1.33	0.22

relationships; (iii) it balances the bias-variance trade-off, hence preventing overfitting; (iv) it can automatically balance data sets when one class is more infrequent than another; (v) it provides feature importance, hence allowing the interpretation.

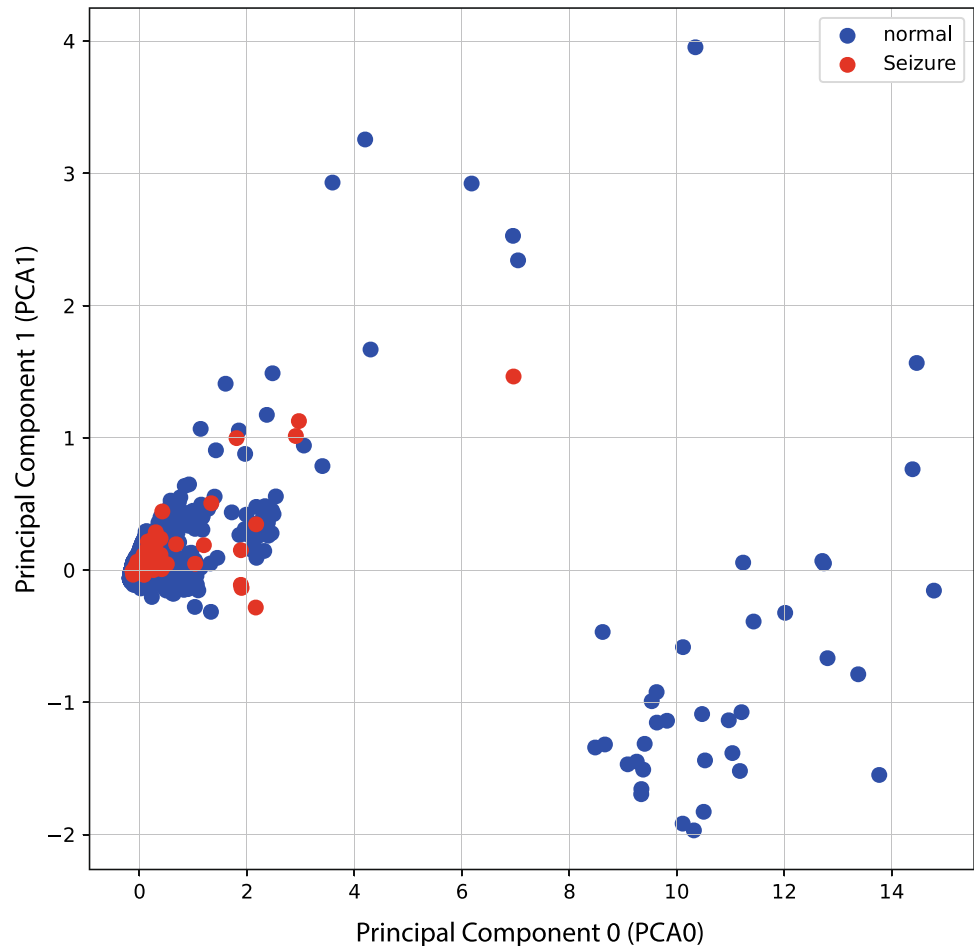
In usual tree construction (Classification and Regression Tree, CART) each node corresponds to a subset of data. Initially the root node contains all data, and at each node, the algorithm searches through all variables to find best split into two children nodes. The algorithm splits all the way down and then prunes the tree up to get minimal test set error.

In RandomForest the root node contains a bootstrap sample of data of same size as original data. A different bootstrap sample for each tree is grown. If training set

consists of N samples and M is feature space dimension, then integer m is a fixed parameter ($m \ll M$, commonly $m \approx \sqrt{M}$). At each node, m of the variables are selected at random. Only these variables are searched through for the best split. The largest tree possible is grown and is not pruned. The forest consists of K trees. To classify a new object having coordinates x , x is put down each of the K trees. Each tree gives a classification for x . The forest chooses that classification having the most out of K votes [67].

In our work we built a forest of 500 trees using the “sklearn” library in python. To control overfitting, we set restrictions on the growth of the tree. The minimum number of samples required to be at a leaf node was set to 3. Therefore, a split point at any depth was

Fig. 3 The DAWP projection on the two principal components (PCA0 and PCA1) explaining 97.18% of data. Red dots correspond to the epileptic seizures, blue dots—to the segments of normal activity



considered if it leaves at least 3 training samples in each of the left and right branches. Finally, the max depth was equal to 5; therefore, only five splits were available for each tree. Other parameters were set by default.

In training ML model we used custom cross-validation function. In our case this function is close to “leave-one-out” cross-validation, but among the patients. The model is trained on 29 patients out of total 30 and tested on the one remained patient. This approach imitates situation in medical practice when we have ML algorithm trained on K patients and we need to diagnose a new, $(K + 1)$ -th, patient, after that we can retrain the algorithm on $(K + 1)$ patients and prepare it for $(K + 2)$ -th patient, etc.

In our work we considered “seizure” to be a “positive” class, so our two-class classifier has 4 possible outcomes with corresponding meanings:

- *True Positive (TP)* correctly identified seizure;
- *True Negative (TN)* correctly identified normal activity;
- *False Positive (FP)* incorrectly identified epileptic seizure, i.e. episode of normal activity identified as seizure;

- *False Negative (FN)* missed epileptic seizure, i.e. seizure identified as episode of normal activity.

In clinical practice it is commonly important to not miss any seizures, since each episode of epileptic activity can be crucial for diagnostics. With this in mind, we have chosen Recall (Eq. (4)) as a main metrics to evaluate the efficiency of the classifier, since Recall reflects the percentage of detected seizures, and classifier with higher Recall can be considered as more prominent for clinical purpose. However, a possible application for epileptic activity classifier includes preliminary EEG marking and reducing working load on human expert. This suggests that the classifier marks some segments of EEG recording as epileptic activity, and these segments are then examined by the expert. It is important that classifier-marked segments would include as much true seizures as possible, so Precision (Eq. (5)) is another important metrics.

$$\text{Recall} = \frac{TP}{TP + FN} \quad (4)$$

$$\text{Precision} = \frac{TP}{TP + FP} \quad (5)$$

Table 2 Feature ranking

Feature	%
<i>Variance</i>	31.68
<i>SimToNeigh</i>	26.93
<i>FreqDiff</i>	24.65
<i>PCA0</i>	7.97
<i>PCA1</i>	7.04
<i>SimToMean</i>	1.73

4 Results

We used the developed classifier based on RandomForest algorithm to classify all data in the used EEG dataset. Results are presented in Table 1.

The classifier provides Recall = 78.67 ± 1.33 (mean $\pm$ standard error (SE)) and Precision = 5.33 ± 0.22 . These results are comparable to our previous work [26]. In the paper [26] we proposed unsupervised classifier for epileptic activity, which was able to achieve Recall = 76.97 ± 4.4 and Precision = 12.7 ± 1.47 on a similar epileptic EEG dataset. From Table 1 one can see, that Recall commonly has one of the two opposite values: 100% (23 subjects) or 0% (5 subjects), which was also the case in the previous work [26]. We theorize that small number of seizures in data (usually only one) can result in Recall = 100%/0%, if this only seizure is detected/missed. However, there are some occasions where multiple seizures were all detected (patients 24 and 30) or all missed (patient 22). The fact that we obtained such similar results with drastically different approaches—supervised RandomForest in this work and unsupervised SVM in [26]—may suggest that there are some peculiarities in the data itself, and the used explainable features reflect them well.

These results bring up again the importance of data analysis and feature selection. In our work we performed analysis of feature significance and ranked the features. Results are presented in Table 2.

From Table 2 one can see, that the three most significant features—*Variance*, *SimToNeigh* and *FreqDiff*—together contribute 83.26 % to classification. At the same time, features *PCA0* and *PCA1*, that contain 97.18% of all information from the “raw” data, contribute only ~ 15 %. This is an important result: most significant features are based on the knowledge of EEG data and peculiarities of seizure activity, while the features derived mathematically have low significance for classification.

5 Conclusion

In this paper, we demonstrated the importance of using explainable features for ML. For the EEG data of 30 patients, we trained a RandomForest classifier to distinguish between epileptic seizures and normal activity.

The RandomForest provides estimates for the feature importance, hence enabling interpretation of the classification rule. We designed a set of features for the classifier, some of which were derived from the raw EEG data with a mathematical approach based on the principal component analysis (PCA), while others were based on the known peculiarities of epileptic activity. As the result, the classifier demonstrated the recall of 77% which is comparable with other models trained on these data. Finally, the RandomForest algorithm assigned the importance of 31, 26, and 24% to the interpretable features, while the most informative principal components had the importance of 8 and 7%, respectively. We believe that this result emphasizes the importance of using explainable ML features, and these features are the first step to a fully explainable ML algorithm.

Acknowledgements The study was supported by the Project 36-L-22 of the Priority 2030 program of Immanuel Kant Baltic Federal University. VM thanks The President Grant (MD-2824.2022.1.2) in part of formulating research hypothesis. VG thanks The President Grant (MK-2603.2022.1.6 and MD-590.2022.1.2) in part of data analysis.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by OEK, SA, VVG, VM, SK, NU, and AEH. The first draft of the manuscript was written by VVG, VM, and AEH and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data availability The data that support the findings of this study are available from National Medical and Surgical Center named after N. I. Pirogov of Russian Healthcare Ministry but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of National Medical and Surgical Center named after N. I. Pirogov of Russian Healthcare Ministry.

Declarations

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

References

1. W.H. Organization, G.C. against Epilepsy, P. for Neurological Diseases, N.W.H. Organization), I.B. for Epilepsy, W.H.O.D. of Mental Health, S. Abuse, I.B. of Epilepsy, I.L. against Epilepsy, Atlas: epilepsy care in the world (World Health Organization, 2005)

2. E. Beghi, The epidemiology of epilepsy. *Neuroepidemiology* **54**(2), 185–191 (2020)
3. R.S. Fisher, C. Acevedo, A. Arzimanoglou, A. Bogacz, J.H. Cross, C.E. Elger, J. Engel Jr., L. Forsgren, J.A. French, M. Glynn et al., Ilae official report: a practical clinical definition of epilepsy. *Epilepsia* **55**(4), 475–482 (2014)
4. R.D. Thijs, R. Surges, T.J. O'Brien, J.W. Sander, Epilepsy in adults. *Lancet* **393**(10172), 689–701 (2019)
5. G. Motamedi, K. Meador, Epilepsy and cognition. *Epilepsy Behav.* **4**, 25–38 (2003)
6. J.W. Sander, The use of antiepileptic drugs-principles and practice. *Epilepsia* **45**, 28–34 (2004)
7. S. Ghosh, J.K. Sinha, T. Khan, K.S. Devaraju, P. Singh, K. Vaibhav, P. Gaur, Pharmacological and therapeutic approaches in the treatment of epilepsy. *Biomedicines* **9**(5), 470 (2021)
8. P. Ryvlin, J.H. Cross, S. Rheims, Epilepsy surgery in children and adults. *Lancet Neurol.* **13**(11), 1114–1126 (2014)
9. G.K. Bergey, Neurostimulation in the treatment of epilepsy. *Exp. Neurol.* **244**, 87–95 (2013)
10. World Health Organization, *Epilepsy: a public health imperative* (World Health Organization, 2019)
11. C.E. Elger, C. Hoppe, Diagnostic challenges in epilepsy: seizure under-reporting and seizure detection. *Lancet Neurol.* **17**(3), 279–288 (2018)
12. D.E. Friedman, L.J. Hirsch, How long does it take to make an accurate diagnosis in an epilepsy monitoring unit? *J. Clin. Neurophysiol.* **26**(4), 213–217 (2009)
13. S.D. Shorvon, The etiologic classification of epilepsy. *Epilepsia* **52**(6), 1052–1057 (2011)
14. E.M. Goldberg, D.A. Coulter, Mechanisms of epileptogenesis: a convergence on neural circuit dysfunction. *Nat. Rev. Neurosci.* **14**(5), 337–349 (2013)
15. G.D. Hammer, S.J. McPhee, M.H. Education, *Pathophysiology of Disease: An Introduction to Clinical Medicine* (McGraw-Hill Education Medical, New York, 2014)
16. W.O. Tatum IV., *Handbook of EEG Interpretation* (Springer Publishing Company, New York, 2021)
17. S. Beniczky, S. Wiebe, J. Jeppesen, W.O. Tatum, M. Brazdil, Y. Wang, S.T. Herman, P. Ryvlin, Automated seizure detection using wearable devices: a clinical practice guideline of the international league against epilepsy and the international federation of clinical neurophysiology. *Clin. Neurophysiol.* **132**(5), 1173–1184 (2021)
18. E.S. Berner, *Clinical Decision Support Systems*, vol. 233 (Springer, Berlin, 2007)
19. M. Mohri, A. Rostamizadeh, A. Talwalkar, *Foundations of Machine Learning* (MIT Press, Cambridge, 2018)
20. M.K. Siddiqui, R. Morales-Menendez, X. Huang, N. Hussain, A review of epileptic seizure detection using machine learning classifiers. *Brain Inform.* **7**, 1–18 (2020)
21. A.T. Tzallas, M.G. Tsipouras, D.I. Fotiadis, Automatic seizure detection based on time-frequency analysis and artificial neural networks. *Comput. Intell. Neurosci.* **2007**, 80510 (2007)
22. J. Birjandtalab, M.B. Pouyan, M. Nourani, in *First International Workshop on Pattern Recognition*, vol. 10011 (International Society for Optics and Photonics, 2016), p. 100110M
23. V. Chavakula, I.S. Fernández, J.M. Peters, G. Popli, W. Bosl, S. Rakhade, A. Rotenberg, T. Loddenkemper, Automated quantification of spikes. *Epilepsy Behav.* **26**(2), 143–152 (2013)
24. M. Zabihi, Patient-specific epileptic seizure detection in long-term EEG recording in paediatric patients with intractable seizures. Master's Thesis, Tampere University of Technology (2013)
25. O. Fasil, R. Rajesh, Time-domain exponential energy for epileptic EEG signal classification. *Neurosci. Lett.* **694**, 1–8 (2019)
26. O.E. Karpov, V.V. Grubov, V.A. Maksimenko, S.A. Kurkin, N.M. Smirnov, N.P. Utyashev, D.A. Andrikov, N.N. Shusharina, A.E. Hramov, Extreme value theory inspires explainable machine learning approach for seizure detection. *Sci. Rep.* **12**(1), 1–14 (2022)
27. C. Donos, M. Dümpelmann, A. Schulze-Bonhage, Early seizure detection algorithm based on intracranial EEG and random forest classification. *Int. J. Neural Syst.* **25**(05), 1550,023 (2015)
28. N.D. Truong, L. Kuhlmann, M.R. Bonyadi, J. Yang, A. Faulks, O. Kavehei, Supervised learning in automatic channel selection for epileptic seizure detection. *Expert Syst. Appl.* **86**, 199–207 (2017)
29. K.D. Tzimourta, A.T. Tzallas, N. Giannakeas, L.G. Astrakas, D.G. Tsalikakis, P. Angelidis, M.G. Tsipouras, A robust methodology for classification of epileptic seizures in EEG signals. *Heal. Technol.* **9**(2), 135–142 (2019)
30. L. Guo, D. Rivero, J. Dorado, J.R. Rabunal, A. Pazos, Automatic epileptic seizure detection in EEGs based on line length feature and artificial neural networks. *J. Neurosci. Methods* **191**(1), 101–109 (2010)
31. J. Birjandtalab, V.N. Jarmale, M. Nourani, J. Harvey, in *2018 IEEE Biomedical Circuits and Systems Conference (BioCAS)* (IEEE, 2018), pp. 1–4
32. S. Siuly, E. Kabir, H. Wang, Y. Zhang, Exploring sampling in the detection of multicategory EEG signals. *Comput. Math. Methods Med.* **2015**, (2015)
33. S. Lahmiri, A. Shmuel, Accurate classification of seizure and seizure-free intervals of intracranial EEG signals from epileptic patients. *IEEE Trans. Instrum. Meas.* **68**(3), 791–796 (2018)
34. J.H. Kang, Y.G. Chung, S.P. Kim, An efficient detection of epileptic seizure by differentiation and spectral analysis of electroencephalograms. *Comput. Biol. Med.* **66**, 352–356 (2015)
35. B. Direito, J. Duarte, C. Teixeira, B. Schelter, M. Le Van Quyen, A. Schulze-Bonhage, F. Sales, A. Dourado, Feature selection in high dimensional EEG features spaces for epileptic seizure prediction. *IFAC Proc. Vol.* **44**(1), 6206–6211 (2011)
36. V. Harpale, V. Bairagi, An adaptive method for feature selection and extraction for classification of epileptic EEG signal in significant states. *J. King Saud Univ. Comput. Inf. Sci.* **33**(6), 668–676 (2021)
37. H.U. Amin, A.S. Malik, R.F. Ahmad, N. Badruddin, N. Kamel, M. Hussain, W.T. Chooi, Feature extraction and classification for EEG signals using wavelet transform and machine learning techniques. *Australas. Phys. Eng. Sci. Med.* **38**(1), 139–149 (2015)
38. R. Esteller, J. Echaz, T. Tchong, B. Litt, B. Pless, in *2001 Conference Proceedings of the 23rd Annual*

- International Conference of the IEEE Engineering in Medicine and Biology Society, vol. 2 (IEEE, 2001), pp. 1707–1710
39. C. Guerrero-Mosquera, A.M. Trigueros, J.I. Franco, A. Navia-Vazquez, New feature extraction approach for epileptic EEG signal detection using time-frequency distributions. *Med. Biol. Eng. Comput.* **48**(4), 321–330 (2010)
 40. L. Logesparan, A.J. Casson, E. Rodriguez-Villegas, Optimal features for online seizure detection. *Med. Biol. Eng. Comput.* **50**(7), 659–669 (2012)
 41. G. Koller, E. Schürholz, T. Ziebart, R. Frankenberger, A. Neff, J.W. Bartsch, Clinical evaluation of pathognomonic salivary protease fingerprinting for oral disease diagnosis. *J. Personal. Med.* **1**(9), 866 (2021)
 42. S.P.K. Shiao, J. Grayson, C.H. Yu, Gene-metabolite interaction in the one carbon metabolism pathway: predictors of colorectal cancer in multi-ethnic families. *J. Personal. Med.* **8**(3), 26 (2018)
 43. A. Batmanova, A. Kuc, V. Maksimenko, A. Savosenkov, N. Grigorev, S. Gordileeva, V. Kazantsev, S. Korchagin, A.E. Hramov, Predicting perceptual decision-making errors using EEG and machine learning. *Mathematics* **10**(17), 3153 (2022)
 44. R. Islam, A.V. Andreev, N.N. Shusharina, A.E. Hramov, Explainable machine learning methods for classification of brain states during visual perception. *Mathematics* **10**(15), 2819 (2022)
 45. B. Abbasi, D.M. Goldenholz, Machine learning applications in epilepsy. *Epilepsia* **60**(10), 2037–2047 (2019)
 46. D. Kasteleijn-Nolst Trenité, G. Rubboli, E. Hirsch, A. Martins da Silva, S. Seri, A. Wilkins, J. Parra, A. Covanis, M. Elia, G. Capovilla et al., Methodology of photic stimulation revisited: updated European algorithm for visual stimulation in the EEG laboratory. *Epilepsia* **53**(1), 16–24 (2012)
 47. D.M. White, C.A. Van Cott, EEG artifacts in the intensive care unit setting. *Am. J. Electroneurodiagn. Technol.* **50**(1), 8–25 (2010)
 48. J.S. Ebersole, T.A. Pedley, *Current Practice of Clinical Electroencephalography* (Lippincott Williams & Wilkins, Philadelphia, 2003)
 49. A. Hyvärinen, E. Oja, Independent component analysis: algorithms and applications. *Neural Netw.* **13**(4–5), 411–430 (2000)
 50. N.S. Frolov, V.V. Grubov, V.A. Maksimenko, A. Lüttjohann, V.V. Makarov, A.N. Pavlov, E. Sitnikova, A.N. Pisarchik, J. Kurths, A.E. Hramov, Statistical properties and predictability of extreme epileptic events. *Sci. Rep.* **9**(1), 1–8 (2019)
 51. O.E. Karpov, V.V. Grubov, V.A. Maksimenko, N. Utashev, V.E. Semerikov, D.A. Andrikov, A.E. Hramov, Noise amplification precedes extreme epileptic events on human EEG. *Phys. Rev. E* **103**(2), 022,310 (2021)
 52. M. Krauledat, G. Dornhege, B. Blankertz, K.R. Müller et al., Robustifying EEG data analysis by removing outliers. *Chaos Complex. Lett.* **2**(3), 259–274 (2007)
 53. A.E. Hramov, A.A. Koronovskii, V.A. Makarov, V.A. Maximenko, A.N. Pavlov, E. Sitnikova, *Wavelets in Neuroscience* (Springer, Berlin, 2021)
 54. A. Aldroubi, M. Unser, *Wavelets in Medicine and Biology* (Routledge, London, 2017)
 55. E. Sitnikova, A.E. Hramov, A.A. Koronovsky, G. van Luijtelaar, Sleep spindles and spike-wave discharges in EEG: their generic features, similarities and distinctions disclosed with fourier transform and continuous wavelet analysis. *J. Neurosci. Methods* **180**(2), 304–316 (2009)
 56. A.N. Pavlov, A.E. Hramov, A.A. Koronovskii, E.Y. Sitnikova, V.A. Makarov, A.A. Ovchinnikov, Wavelet analysis in neurodynamics. *Phys. Usp.* **55**(9), 845 (2012)
 57. P. Gloor, R. Fariello, Generalized epilepsy: some of its cellular mechanisms differ from those of focal epilepsy. *Trends Neurosci.* **11**(2), 63–68 (1988)
 58. E. Trinka, J. Höfler, A. Zerbs, Causes of status epilepticus. *Epilepsia* **53**, 127–138 (2012)
 59. H. Adeli, Z. Zhou, N. Dadmehr, Analysis of EEG records in an epileptic patient using wavelet transform. *J. Neurosci. Methods* **123**(1), 69–87 (2003)
 60. E. Sitnikova, A.E. Hramov, V.V. Grubov, A.A. Ovchinnikov, A.A. Koronovsky, On-off intermittency of thalamo-cortical oscillations in the electroencephalogram of rats with genetic predisposition to absence epilepsy. *Brain Res.* **1436**, 147–156 (2012)
 61. R.S. Fisher, W.V.E. Boas, W. Blume, C. Elger, P. Genton, P. Lee, J. Engel Jr., Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia* **46**(4), 470–472 (2005)
 62. C. Luo, J. Zhan, X. Xue, L. Wang, R. Ren, Q. Yang, in *International Conference on Artificial Neural Networks* (Springer, 2018), pp. 382–391
 63. K. Park, J.S. Hong, W. Kim, A methodology combining cosine similarity with classifier for text classification. *Appl. Artif. Intell.* **34**(5), 396–411 (2020)
 64. B. Schelter, J. Timmer, A. Schulze-Bonhage, *Seizure Prediction in Epilepsy: From Basic Mechanisms to Clinical Applications* (Wiley, New York, 2008)
 65. H. Abdi, L.J. Williams, Principal component analysis. *Wiley Interdiscipl. Rev. Comput. Stat.* **2**(4), 433–459 (2010)
 66. G. Biau, E. Scornet, A random forest guided tour. *TEST* **25**(2), 197–227 (2016)
 67. L. Breiman, Manual on setting up, using, and understanding random forests v3. 1. Statistics Department, University of California, Berkeley, CA, USA, vol. 1, no. 58, pp. 3–42 (2002)

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.