

# Automatic Detection of Epileptic Seizures from EEG Signals using Artificial Intelligence Methods

Ali ÖTER<sup>1\*</sup> 

<sup>1</sup>Kahramanmaraş Sütçü İmam University, Vocational School of Technical Sciences Department of Electronics and Automation, Kahramanmaraş, Türkiye

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## Anahtar Kelimeler

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YSA

## Graphical/Tabular Abstract (Grafik Özet)

In this study, epileptic seizures were determined from EEG signals using Python programming and three different machine-learning methods from artificial intelligence techniques. ANN has been determined as the most successful method. / Bu çalışmada Python programlama ile yapay zeka tekniklerinden üç farklı Makine öğrenmesi yöntemi kullanılarak EEG sinyallerinden epileptik nöbetler belirlenmiştir. En başarılı yöntem olarak YSA tespit edilmiştir.

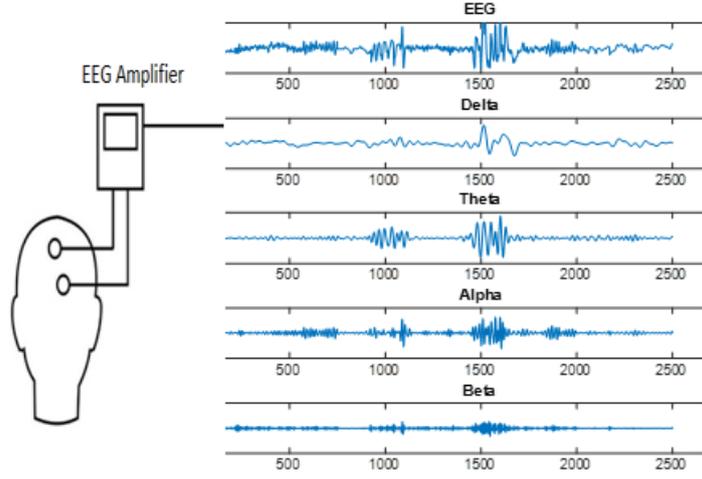


Figure A: Detection of epileptic seizures from EEG signals /Şekil A: EEG sinyallerinden epileptik nöbetlerin tespiti

## Highlights (Önemli noktalar)

- Energy and normalization processes of EEG signals were performed./ EEG sinyallerinin enerjileri ve normalizasyon işlemleri gerçekleştirildi.
- Epileptic seizures were detected from EEG data with three different machine-learning methods. / Üç farklı Makine öğrenme yöntemi ile EEG verilerinden epileptik nöbetler tespit edildi.
- It was determined that ANN was the most effective method for automatically detecting epileptic seizures. / Epileptik nöbetlerin otomatik olarak tespit edilmesinde en etkili yöntemin YSA olduğu belirlendi.

**Aim (Amaç):** This study aims to use different machine-learning algorithms to diagnose epileptic seizures. / Bu çalışma epileptik nöbetleri teşhis etmek için farklı makine öğrenme algoritmalarını kullanmayı amaçlamaktadır.

**Originality (Özgünlük):** Detection of epileptic seizures using different ML methods. / Farklı ML yöntemleri kullanılarak epileptik nöbet tespit edilmesi.

**Results (Bulgular):** An accuracy rate of almost 97% was found for the ANN classifier's performance in identifying epileptic seizures by the extraction of features from the EEG data. / EEG verilerinin özellikleri çıkarılarak YSA sınıflandırıcısının, epileptik nöbetleri tanımda başarı oranı yaklaşık %97 doğruluk oranı ile tespit edilmiştir.

**Conclusion (Sonuç):** Epileptic seizures were automatically detected using ML methods by calculating the average, normalization and energy values of EEG signals. In the performance analysis, it was observed that the results obtained by normalizing the signals and calculating the energy values were more successful. / EEG sinyallerinin ortalama, normalizasyon ve enerji değerleri hesaplanarak ML yöntemleri ile otomatik olarak epileptik nöbet tespitleri gerçekleştirildi. Yapılan performans analizlerinde sinyallere normalleştirme yöntemi ve enerji değerleri hesaplanarak elde edilen sonuçların daha başarılı olduğu gözlemlenmiştir.



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### Abstract

Epilepsy is a neurological disorder in which involuntary contractions, sensory abnormalities, and changes occur as a result of abrupt and uncontrolled discharges in the neurons in the brain, which disrupt the systems regulated by the brain. The detection of abnormal electrical impulses from cells across different regions of the brain enables the identification of epilepsy. The accurate interpretation of these electrical impulses is critical in the illness diagnosis. This study aims to use different machine-learning algorithms to diagnose epileptic seizures. The frequency components of EEG data were extracted using parametric approaches. This approach to feature extraction was utilized in training machine learning classification algorithms, encompassing Artificial Neural Network (ANN), Gradient Boosting (GB), and Random Forest (RF). The ANN classifier was shown to have the most significant test performance in this investigation, with roughly 97% accuracy and a 91% F1 score in recognizing epileptic episodes. The Gradient Boosting classifier, on the other hand, performed similarly to the ANN, with 96% accuracy and a 93% F1 score.

## Yapay Zeka Yöntemleri kullanılarak EEG Sinyallerinden Epileptik Nöbetlerin Otomatik Tespiti

### Makale Bilgisi

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### Öz

Epilepsi, beyindeki nöronlarda ani ve kontrolsüz boşalmalar sonucunda beyin düzenlediği sistemleri bozan istemsiz kasılmalar, duyu anormallikleri ve değişikliklerinin ortaya çıktığı nörolojik bir hastalıktır. Beynin farklı bölgelerindeki hücrelerden gelen anormal elektriksel uyarıların tespiti, epilepsinin tanımlanmasını sağlar. Bu elektriksel uyarıların doğru yorumlanması hastalık teşhisinde kritik öneme sahiptir. Bu çalışma, epileptik nöbetleri teşhis etmek için farklı makine öğrenme algoritmalarını kullanmayı amaçlamaktadır. EEG verilerinin frekans bileşenleri parametrik yaklaşımlar kullanılarak çıkarılmıştır. Bu özellik çıkarma yaklaşımı, Yapay Sinir Ağı (YSA), Gradient Boosting(GB) ve Rastgele Orman (RF) dahil olmak üzere makine öğrenimi sınıflandırma algoritmaları eğitildi. YSA sınıflandırıcının, epileptik nöbetleri tanımda kabaca %97 doğruluk ve %91 F1 skoru ile bu çalışmada en önemli test performansına sahip olduğu gösterildi. Gradient Boosting sınıflandırıcısı ise %96 doğruluk ve %93 F1 skoru ile YSA'ya benzer performans göstermiştir.

## 1. INTRODUCTION (GİRİŞ)

Electroencephalogram (EEG) signals are a method by which brain activity is measured and recorded. The interpretation of these signals is critical for learning about brain function. EEG signals aid in understanding the brain's physiological and functional features and activities [1]. Expert doctors usually examine interpretations of EEG signals. However, Artificial Intelligence (AI) algorithms

can also help interpret EEG signals. Many methods have been developed using different AI methods to analyze EEG signals. These methods primarily study the frequency, amplitude, phase, and wave patterns, which are the essential characteristics of EEG signals. By examining these qualities using AI, it is possible to uncover the circumstances under which the signals occur and their relevance to specific brain activity. EEG data may be analyzed

rapidly and precisely, providing more comprehensive and complete insights into brain function. Recently, interest in EEG-based signal processing and analysis has risen, and various techniques for processing EEG data have been developed. Furthermore, EEG signal databases may be created, and learning can be accomplished using these data utilizing AI algorithms. AI algorithm, for example, can evaluate a patient's EEG data to aid clinicians in detecting certain disorders or monitoring the success of a medication.

As of the 21st century, information technology is widely used in many industries, including the healthcare sector, such as the war industry, space technologies, and industrial automation technologies. While the use and effectiveness of information systems in healthcare delivery continue to increase, AI methods continue to be widely used in developing medical devices and diagnosing diseases [2]. These methods include Decision Trees (DT), Random Forest (RF), Support Vector Machines (SVM), Logistic Regression (LR), K-Nearest Neighbours- (KNN), Gradient Boosting (GB), Artificial Neural Networks (YSA), Deep Learning (DL), Fuzzy Logic, and Genetic algorithms. Early illness detection improves treatment outcomes. Machine learning approaches give valuable and successful outcomes in the early detection phase in this direction.

Epilepsy is a severe brain disease that is endemic to neurological disorders worldwide. Epilepsy is a chronic, non-communicable brain disease that affects approximately 50 million people worldwide. It is one of the earliest known diseases in human history, recorded in written records dating back to approximately 4000 BC [3]. It is a severe health problem that involves abnormal neurological electrical discharge of the brain and is seen in the patient as changes in consciousness, unwanted contractions, and sensory changes. Epilepsy is one of the most common brain diseases, representing the most frequent positive signs and symptoms of brain disorder during seizures [1]. The leading causes of this disease can include traumatic causes, infections, brain abscesses, brain tumors, malnutrition, pyridoxine deficiency, and calcium metabolism disorders. EEG is used to assess neurophysiological problems in the diagnosis of Epilepsy illness. EEG is critical in correctly classifying different types of epilepsy [4].

Many recent studies have been published using ML methods with EEG signals. The relevant studies are as follows: In the study by Iasemidis, a continuous and long-term adaptable procedure was identified to

analyze EEG records only when the first seizure occurred [5]. EEG signals are processed using AR analysis methods and applied to the ANN [6]. For the diagnosis of epileptic seizures in EEG recordings, classification experiments using ANN employing wavelet transform are carried out [7]. The diagnosis of epilepsy was provided in the works of Yücel and Özgüler by using the modeling of complicated measurements of EEG signals with varying resolutions [8]. The applicability of time-frequency analysis for classifying epileptic episodes in EEG data segments is proved, and several approaches are evaluated [9]. In 2010, researchers examined a machine-learning technique to generate particular classifiers for patients who detected the onset of acute seizures using EEG data. In the studies, epileptic seizures in EEG signals were predicted by focusing on aggregate features from a series of proposed wavelet analysis features such as cross-correlation, non-linear interdependence, difference of Lyapunov exponents, and phase locking using modern machine learning techniques [10]. They also examined the prediction of epileptic seizures using online EEG data analysis [11]. An epileptic seizure prediction system has been developed based on cloud-based deep learning of big EEG data [12]. A deep convolutional neural network was used on EEG signals to eliminate the need to subject the data to any preprocessing or size reduction algorithms for epileptic seizure detection [13]. The characteristics derived from multi-channel EEG data using various approaches were projected onto multi-spectral picture series based on electrode location [14]. Karakaya et al. performed an embedded system design of ANN to detect epilepsy in EEG signals [15]. Daoud et al. suggested a new prediction approach for patient-specific epilepsy based on deep learning and applied it to long-term EEG recordings in their study [16]. Savadkoohi et al. used a machine-learning technique to identify epileptic seizures by analyzing psychological states and electrical activity features in different brain areas [17]. Wang et al. used an RF model in conjunction with grid search optimization to detect epileptic EEG.

The suggested method performed well in the study, with an accuracy rate of 96% [18]. Chen et al. suggested a novel and valuable classifier for epilepsy diagnosis based on SVMs. To validate the proposed classifier's efficacy, its performance on the publicly accessible Bern-Barcelona and CHB-MIT EEG databases yielded classification accuracy of 93% and 94%, respectively [19]. Extensive experimental findings that outperform current technology demonstrate their high potential in real-world applications. Another study employed

patient-independent predictors of epilepsy using different learning algorithms capable of learning a global function utilizing data from more than one person with EEG signals [20]. According to Sethy et al., the performance of ML-based classifiers is assessed categorically and overall by gender in 2021. The study revealed that KNN was the best classifier for males, women, and all individuals [21]. In another study, frequency-based features were extracted from EEG signals, and it was proposed that classifiers based on collective learning be used [22]. In the study by Caglayan et al., EEG signals from epileptic patients were utilized as time series data encompassing 500 distinct person information, and the categorized data set was segmented using the k-fold cross-validation approach [23]. Manzouri et al. used time and frequency domain characteristics to evaluate the performance of two machine learning methods. They calculated the performance of their suggested algorithms in their study, with an average accuracy of 86% for RF and 84% for SVM [24].

Automatic epileptic seizure detection may be achieved using a variety of techniques. The most popular techniques, though, include ANN. By utilizing machine learning techniques and algorithms, this study aims to aid in identifying epileptic seizures. It has been done to diagnose epileptic seizures from EEG data using classifiers for ANN, GB, and RF algorithms. Classification success rates are shown using several assessment criteria. This article is structured as follows for the remaining portions. The rest of this article is divided into the following sections: The second section describes how to obtain and process the EEG signal, the methodologies employed, and the assessment standards. The third section of the study contains the suggested method, the fourth section contains the results and findings of the suggested approach, and the fifth section contains the discussion.

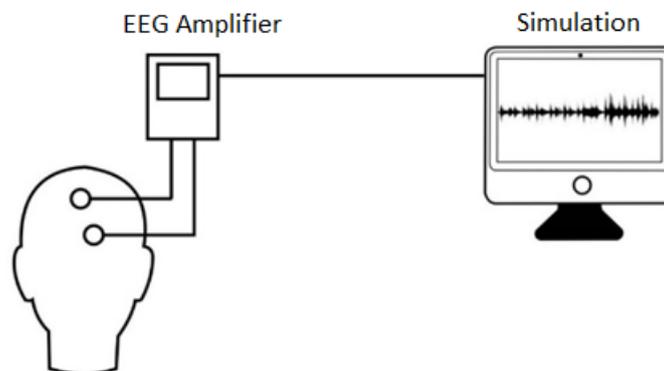
## 2. MATERIALS AND METHODS (MATERYAL VE METOD)

### 2.1. Materials (Materyal)

The datasets used to assess the effectiveness of the suggested models are crucial for data scientists and academics. The benefit of publicly accessible datasets is that they act as a standard against which outcomes may be evaluated and contrasted. The "Children's Hospital Boston, Massachusetts Institute of Technology," "Epilepsy Centre, University of California," "The Freiburg," "Bern-Barcelona" and "Bonn University" datasets are frequently used datasets for the identification of epileptic seizures. The data set from Bonn University was used in this study.

#### 2.2.1. Data acquisition (Veri toplama)

The EEG signal recordings utilized for the study were obtained from the "Kaggle" website's open-access database (web address: <https://www.kaggle.com/harunshimanto/machine-learning-algorithms-for-epileptic-seizures/>). The dataset displays the signals of both healthy and epileptic patients in various age ranges. 500 participants' EEG signals were split into 23 sections for each participant in the data set, and marks were placed on each segment. In this study, 2,300 EEG signals demonstrating epileptic seizures and 9,200 EEG signals demonstrating normal circumstances were combined to generate 11,500 data. The EEG signals, the data path of the real-time processing system to the computer, the signal processor, and the personal computer, and how to record an EEG signal from a person are symbolically shown in Figure 1.



**Figure 1.** Recording of EEG signals (EEG sinyallerinin kaydedilmesi)

### 2.1.3. Data processing (Veri işleme)

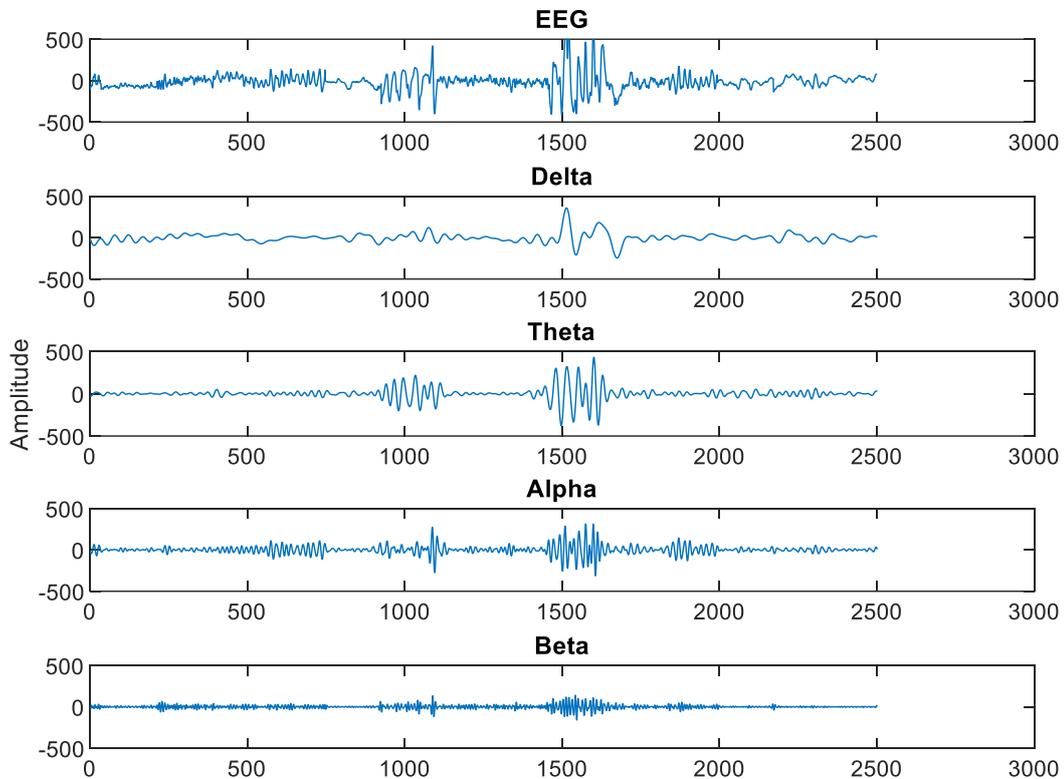
Preprocessing the data gathered throughout the research allows the network to learn faster and more precisely. It may remove noise or unnecessary data, especially in big datasets.

When working with large datasets, it is crucial to choose a suitable model. More extensive and deeper models usually provide higher accuracy but require

more extended training and higher computational power. As a result, ML algorithms are a very effective method for processing big data. However, data size, training time, scalability, data preprocessing, and model selection should be considered. Table 1 below shows the distribution of the EEG signal and frequency bands and information about the behavior of the human brain.

**Table 1.** Frequency bands of EEG signals (EEG sinyallerinin frekans bandları)

Bands	Frequency (Hz)	Meaning
Delta	< 4	Deep sleep
Theta	4-7	When adults are emotionally stressed, especially in frustration
Alpha	8-15	Loose, Calm, Awake, but eyes closed
Beta (Low)	12.5-16	Relaxed but concentrated
Beta (Mid)	16.5-20	Thinking and listening
Beta (High)	20.5-28	Excitement and anxiety
Gamma	25-100	When awareness, happiness, stress, and meditation are increased



**Figure 2.** Different frequencies bands of EEG Signal (EEG sinyalinin farklı frekans bandları)

The amplitude of EEG waves varies significantly across frequency bands. Figure 2 shows a person's 23-second EEG signal and the amplitude change in

the lower frequency regions. While the Delta frequency band has the lowest intensity frequency

distribution, the Beta frequency band has the most significant intensity frequency distribution.

The change in an average EEG signal is shown in Figure 3, and the changes seen during an epileptic seizure are shown in Figure 4. In general, epileptic seizures appear suddenly, with spikes in the EEG signals, persist for a few seconds, and disappear.

#### 2.1.4. Normalization (Normalizasyon)

Normalization is the process of rearranging numerical values in a data collection by a standard scale without disrupting the disparities in the value range. The primary goal of the normalization process is to minimize data quantity and provide more straightforward, more understandable findings that can be evaluated quickly [25, 26].

Several methods for normalizing data in the literature include decimal scaling, z-score, sigmoid, and minimum-maximum (Min-Max) [27]. In the study, Min-Max data normalization was applied. Values for artificial neural networks must be normalized or transformed to values between 0 and 1. Numbers are normalized so that the highest consumption value is 1 and the lowest is 0. The normalized formula appears as follows:

$$X_{norm} = \frac{x - X_{min}}{X_{max} - X_{min}} \quad (1)$$

$X_{norm}$  is the normalized value,  $x$  is the actual consumption number,  $X_{min}$  is the lowest of the normalized values, and  $X_{max}$  is the greatest.

All values in the EEG data set were normalized using Equation 1 and utilized in the suggested approach.

#### 2.1.5. Signal energy (Sinyal Enerjisi)

The physical quantities are directly connected to the energy change of a continuous time  $x(t)$  signal. The spectral energy density of a signal or time series explains how the energy of the signal or time series is distributed with frequency. As a result, the energy of the signal in the discrete-time plane is determined by the following equation.

$$W_i = X_i^2 \quad (2)$$

The goal of adopting this feature extraction approach is to apply it to machine learning inputs like Gradient Boosting, Random Forest, and classification algorithms like ANN.

## 2.2. Methods (Yöntemler)

Traditional ML algorithms based on various AI approaches and ANN algorithms are commonly employed in EEG signal categorization investigations. This section provides some background on the ANN, RF, and GB techniques employed in the study.

### 2.2.1. Artificial neural network (Yapay sinir ağıları)

ANN is a modeling tool that has recently received a lot of research interest. ANN in complicated data classification is widely utilized in applications such as chaotic time series estimates, image recognition, classification, system modeling, and function approximation [27-29]. It is one of the backpropagation network ANN models established initially by Werbos and afterward by Parker, Rummelhart, and McClelland [30]. The activation function employed in ANN structures must be carefully chosen to ensure the modeling's success. An important aspect to consider when selecting an activation function is that its derivative is simple to compute. The number of hidden layers and neurons in the hidden layer in an ANN network might vary depending on the issue to be solved by the network. The hidden and output layers both conduct the weighted sum operation. In recent years, the most often employed activation functions have been the sigmoid, hyperbolic tangent, and ReLU functions [4, 6]. The increased number of neurons in the hidden layer increases computational complexity and lengthens calculation time, allowing ANN to be utilized to solve more complicated problems. The output layer is the layer that produces network outputs by processing the information applied to the input layer from the intermediate levels. These outputs are provided to the outside world as network output information.

### 2.2.2. Random forest (Rastgele Orman)

It is an ML approach that uses multiple decision tree algorithms to handle classification and regression problems. It operates like a forest of many individual trees, training each tree independently and aggregating the findings to achieve the best accurate estimate. These qualities may differ amongst trees. This technique excels at high-dimensional datasets and noisy data. Furthermore, because this approach uses several trees rather than a single tree, it may be utilized to find relevant characteristics in a dataset and enhance

classification accuracy. As a result, it is well suited for usage in massive datasets and real-time applications [31, 32].

### 2.2.3. Gradient boosting (Gradyan artırma)

It is a machine-learning algorithm that is used to solve categorization classification. One of the tree-based learning approaches, this algorithm successively combines a sequence of weak estimators to reduce residual errors compared to past estimations of the anticipated target variable. It is generally used to create robust tree connections. It begins with a tree model and then guarantees that the following tree model is appropriately created depending on the prior tree model's mistakes. The procedure is repeated, with factors such as the number of trees and feature selection being optimized. It is a highly successful classification technique that may be used for massive and complicated datasets. However, this algorithm may perform poorly if the dataset is minimal or has little correlation between data [33].

### 2.3. Evaluation criteria (Değerlendirme kriterleri)

Simple diagnostic tools are required to detect studies. Each data point, including standard and epileptic seizures, was additionally indicated in the utilized dataset. Because it presents the findings graphically, ROC analysis is commonly used to assess system performance [34, 35]. This approach determines classifier performance from 0 to 1. The system determines if the signal reflects any epileptic seizures based on the rate of epileptic seizures. When the ratio exceeds 0.50, the decision is positive. When the ratio is less than 0.50, the decision is adverse. The following are some abbreviations.

- TP (True Positive): Epilepsy is present, and the classifier identified the condition as epileptic.
- TN (True Negative): No epilepsy recognized by the classifier as such.
- FP (False Positive): No epilepsy exists, but the classifier detects an epileptic episode.
- FN (False Negative): The classifier indicated an epileptic condition but found no epilepsy.

In an ideal classification system, FP and FN would be zero. The operation of the classifier is interpreted

by using performance criteria such as Accuracy, Sensitivity, Recall, Precision, and F1 Score. The performance criteria used in the study are formulated and explained below.

$$Accuracy = \frac{TP+TN}{TP+TN+FP+FN} \quad (3)$$

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

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

$$F1\ Score = \frac{2*Hassasiyet*Duyarlılık}{Hassasiyet + Duyarlılık} \quad (6)$$

## 3. EXPERIMENTAL STUDY (DENEYSEL ÇALIŞMA)

Within the study, 11.500 data from a data set of 2.300 epileptic seizures EEG signals and 9.200 normal state EEG signals were employed. A multilayer feed-forward ANN model is employed in this investigation. In the constructed model, the sigmoid function is employed as the activation function in the input and hidden layers and the relu function in the output layer. In classification investigations, using the sigmoid activation function to split the dataset into two groups is a valuable choice. All records in the data set were used to calculate ANN output values. The dataset was divided into 70% training and 30% testing for the first application and 80% training and 20% testing for the second. The training and test set data were randomly chosen based on the class distribution. The data were normalized using Equation 1 from Section 2, and their energies were determined using Equation 2. 80% training and 20% test set splitting were repeated. The assessment criteria provided are in Section 2. The findings in Tables 2 and 3 were achieved.

The success rates of classifiers created using models in which raw EEG data is utilized as input by normalizing the EEG data and computing the energies have grown dramatically. The ANN was analyzed using the "optimizer," Adam optimization technique, and the Mean Squared Error (MSE) loss model, using the "Relu" activation function in the first two layers and the sigmoid activation function in the final layer. Furthermore, Tables 2 and 3 compare the performance of six algorithms in terms of "Accuracy," "Sensitivity," "Recall," and "F1 Score" based on the test rate employed.

**Table 2.** The classification performance for ANN with 70% Train and 30% (%70 Eğitim ve %30 ile YSA için sınıflandırma performansı)

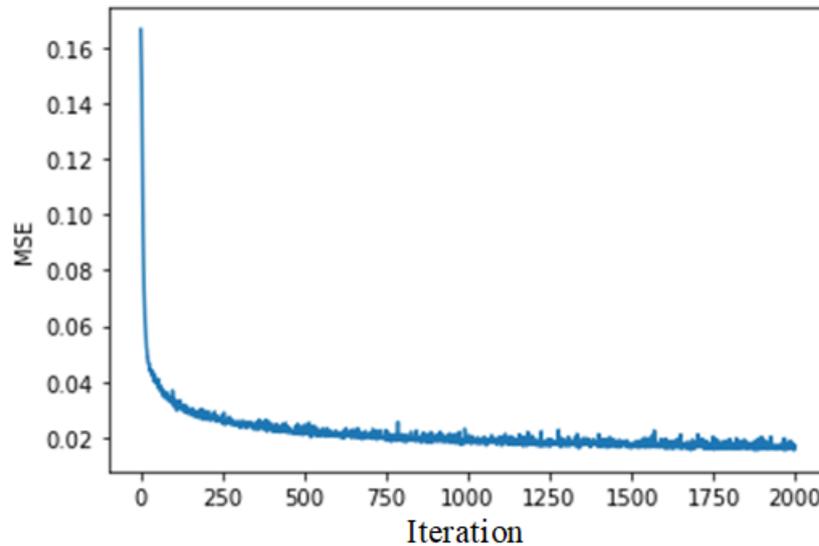
Models	Accuracy	Sensitivity	Recall	F1 Score
ANN11 (EEG)	80.12	0.44	50.00	0.87
ANN12 (Normalized EEG)	92.20	65.90	93.47	77.30
ANN13 (Normalized + Energy + EEG)	93.77	81.79	85.96	83.82

**Table 3.** The classification performance for ANN with 80% Train and 20% (%80 Eğitim ve %20 ile YSA için sınıflandırma performansı)

Models	Accuracy	Sensitivity	Recall	F1 Score
ANN21 (EEG)	80.61	6.36	60.42	11.51
ANN22 (Normalized EEG)	92.83	67.40	94.74	78.76
ANN23 (Normalized + Energy + EEG)	96.56	87.40	93.07	90.15

Evaluations of the success and mistake rates are crucial for assessing how well-implemented classifier algorithms are working. The MSE function, sometimes referred to as the mean of the square of the metrics errors, is one of the

representations of mistakes that are frequently employed. Figure 5 shows the change in the MSE ratio of the suggested strategy employing this function after 2000 iterations.



**Figure 5.** MSE curve of the ANN23 classifier (ANN23 sınıflandırıcının MSE eğrisi)

The classifier's average accuracy, sensitivity, recall, and F1 score values were determined and shown in Table 4. As a result, the ANN23 technique had the highest performance, with a 91% F1 score and around 97% accuracy. The second-most effective algorithm in the classifier is GB, one of the ML methods.

Three separate characteristics were employed in the study's ANN algorithm to identify epilepsy. Findings from ANN were used to compare the classifier performances of ML techniques like gradient boosting and multiple decision trees.

**Table 4.** Comparison of Classifier Performances (Sınıflandırıcı Performanslarının Karşılaştırılması)

Model	Accuracy	Sensitivity	Recall	F1 Score
Gradient Boosting	95.60	90.00	96.00	93.00
Random Forest	95.00	83.00	95.00	88.00
ANN	96.56	88.62	92.47	90.50

#### 4. RESULTS (BULGULAR)

EEG datasets from the past and present have been used to apply various models and approaches. Which method to be used varies depending on the data's format. The study used ANN, Gradient Boosting, Random Forest, and AI algorithms to assess EEG data. They calculated the EEG data's average, normalization, and energies, allowing for three independent performance analyses of each program. The EEG signal normalization method was followed by applying features based on computed signal energies for the classifiers to achieve optimal performance.

The ANN algorithm is predicted to be used and required, as the success rate is 96.56 to detect epileptic seizures using three different attributes. The success rate in the second application was higher than in the first. However, the Gradient Boosting algorithm was the second recommended model, with a success rate of 95.60%. According to many studies on the same data set, the suggested ANN algorithm was a few points more successful. When the proposed ANN method is considered slightly more successful than current studies, it appears suitable for detecting Epileptic seizures.

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#### 5. DISCUSSION (TARTIŞMA)

Although YSA and machine learning algorithms are popular in prediction and modeling today, deep learning approaches yield better results with more data. In future studies, the use of deep learning algorithms such as Convolution Neural Networks (CNN), Recurrent Neural Networks (RNN), Limited Boltzman ANN Machines (RBM), and Deep Belief Networks (DBN) may be suggested to generate more outstanding data from the epileptic seizure attack. However, in forming deep learning models called black boxes, the reliability of the decisions made by the algorithms is questioned. Decisions made by models can be analyzed using algorithms such as LIME, SHAP, LSTM, and SVM.

#### DECLARATION OF ETHICAL STANDARDS (ETİK STANDARTLARIN BEYANI)

The author of this paper declares that the materials and methods they use in their work do not require ethical committee approval or legal-specific permission.

#### CONFLICT OF INTEREST (ÇIKAR ÇATIŞMASI)

The authors declare that they have no competing interests.

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