T.C.
INONU UNIVERSITY
GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES

EPILEPTIC ACTIVITY DETECTION USING LINEAR AND NON-LINEAR METHODS

MASTER THESIS

Ceren CANYURT

Department of Biomedical Engineering

Thesis Advisor: Assistant Prof. Dr. Reyhan ZENGIN

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ACKNOWLEDGMENTS AND FOREWORD

At every stage of this thesis work, without withholding their help, suggestions, knowledge, experience, and support, and in everything support me my advisor Assistant Prof Dr. Reyhan ZENGIN,
To my family, who supported me in every way during my studies, as well as throughout my life,

thank you.

PROMISE OF HONOR

I declare that this work titled "EPILEPTIC ACTIVITY DETECTION USING LINEAR AND NON-LINEAR METHODS", which I submitted as a master's thesis, was written by me without resorting to any help that would contradict scientific morals and traditions, and that all the sources I have used are those that are shown in accordance with the method both in the text and in the bibliography, and I confirm this with my honor.

Ceren CANYURT

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INDEX OF SYMBOLS AND ABBREVIATIONS

CT : Tomography
MRI : Magnetic Resonance Imaging
μV : Microvolt
LGS : Lennox Gastaut Syndbme
JME : Juvenile Myoclonic Epilepsy
JTKN : Generalized Tonic-Clonic Sezures
BRE : Beingn Rolondic Epilepsy
VNS : Vagal Nerve Stimulation
RMS : Root Mean Square
ELM : Neural Network Machibe
O-SampEn : Optimized Sample Entropy
MPE : Multiscale Permutation Entropy
STPE : Short-Term Permutation Entropy
GSTPE : SSTPE Gradient
STE : Short-Term Energy
STM : Short-Term Mean
RBBoost : Random Balance Boost
KNN : K-Nearest Neighbor
ApEn : Approximate Entropy
LZ : Lempel-Ziv
DWT : Discrete Wavelent Transform
CD : Correlayion Size
FSC : Fuzzy Sugeno Classifier
SVM : Support Vector Machine
PNN : Probablistic Neural Network
DT : Decision Tree
GMM : Gaussion Mixture Model
NBC : Naive Bayes Classifier
r : Threshold
N : Length Data
fApEn : Fuzzy Approximate Entropy
RBF : Radial Basis Fuction
NNge : Non-Nested Generalized Examples Classifier
BFDT : Best First Decision Tree
VMD : Variable Mode Decomposition
MMRVFLN+ : Multilayer Multicare Random Vector Functional Link Network Plus
FPR/h : Negligible False Positive Rate
KL : Kullback-Leiler
EMD : Empirical Mode Decomposition
ShEn : Shannon Entropy
SE : Spectral Entropy
RE : Renyi Entropy
IMF : Intrinsic Mode Function
BILSTM : Bidirectional Long-Term Memeor
ICA : Indepenent Component Analysis
FFT : Fast Fourier Transform
PSD : Power Spectral Density

SmpE : Sample Entropy
PE : Permutation Entropy
CHB-MIT : EEG Data from Boston Children's Hospital

ÖZET

Yüksek Lisans Tezi

DOĞRUSAL VE DOĞRUSAL OLMAYAN YÖNTEMLER İLE EPİLEPTİK AKTİVİTE TESPİTİ

Ceren CANYURT

İnönü Üniversitesi
Fen Bilimleri Enstitüsü
Biyomedikal Mühendisliği Anabilim Dalı
72+XI sayfa

2022

Danışman: Dr. Öğt. Üyesi Reyhan ZENGİN

Bu çalışmada yüksek doz ilaç kullanımına rağmen nöbeti engellenemeyen epilepsi hastalarının nöbetlerinin önceden tespit edilmesi amaçlanmıştır. Bu amaç doğrultusunda epilepsinin teşhisi ve tedavisinde de kullanılan elektroensefalografi (EEG) kayıtları analiz edilmiştir. EEG analizi için doğrusal ve doğrusal olmayan analiz yöntemleri araştırılmıştır. Bonn Üniversitesi verilerinde zaman alanında belirlenen eşik değeri geçen peak (tepe noktalarının) sayısına ve güç spektral yoğunluğuna bakılmıştır. Fakat sağlıklı ve epileptik verilerin farklı dosyalarda olmaları incelemeyi yetersiz kılmıştır. Bu nedenle, CHB-MIT verilerinde doğrusal analiz yöntemlerinden sinyalin ortalaması, sinyalin ortalama karekökü (RMS) ve doğrusal olmayan sinyal analiz yöntemlerinden Shannon entropi, sample entropi, permütasyon entropi, approximate entropi ve spectral entropi değerleri hesaplanmıştır. Bu hesaplamalarda sinyal ortalaması ve RMS özellikleri ile sırasıyla %58.4, %75 doğruluk ile nöbet dönemi belirlenmiştir. Entropi yöntemlerinde ise ayrı ayrı düşünüldüğünde sırası ile %75, %66.6, %66.6, %79.2 ve %62.5 doğruluk ile nöbet dönemi tespit edilmiştir. EEG sinyallerindeki nöbet tespitinde sample entropi değerinin yükselmesi veya permütasyon entropisi değerini azalması baz alındığında doğruluk %79.2 ye yükselmiştir. Ayrıca approximate entropi değerinin azalması veya spectral entropi değerinin azalması baz alındığında doğrulıuk değeri %83.3 değerine yükselmiştir. Bu durum nöbet başlangıcının bir entropi yöntemi ile tespit edilemediği durumda diğer entropi yöntemi ile tespit edilebileceğinin göstergesidir. Ayrıca epileptik EEG sinyallerinin analizinde nöbet öncesinde tespit edilen bazı değişiklikler bulunmaktadır. Bu değişikjliklerin incelenmesi ve farklı analiz yöntemleri ile de tespit edilmesi durumunda epilepsi nöbetlerinin önceden tespit edilebileceği öngörüsüne varılmıştır.

Anahtar Kelimeler: Epilepsi, Sinyal analizi, Sinyalin ortalama değeri, Sinyalin ortalama karekökü, Shannon entropi, Sample entropi, Permütasyon entropisi, Approximate entropi, Spectral Entropi.

ABSTRACT

Master Thesis

EPILEPTIC ACTIVITY DETECTION USING LINEAR AND NON-LINEAR METHODS

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Graduate School of Nature and Applied Sciences
Department of Biomedical Engineering

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In this study, it was aimed to detect the seizures of epileptic patients whose seizurescould not be prevented despite the use of high-dose medication. For this purpose, electroencephalography (EEG) recordings used in the diagnosis and treatment of epilepsy were analyzed. Linear and nonlinear analysis methods were investigated for EEG analysis. In the University of Bonn data for the time domain, the number of peaks crossing the threshold, and the power spectral density were investigated. However, the fact that healthy and epileptic data are in different files made the analysis insufficient. In CHB-MIT data, the mean of the signal and root mean squareof the signal (RMS) from linear analysis methods and Shannon entropy, sample entropy, permutation entropy, approximate entropy, and spectral entropy from nonlinear signal analysis methods were calculated. In these calculations, the signal mean and RMS properties through the seizure period were determined with %58.4, %75 accuracies, respectively. In entropy methods, when considered respectively, the seizureperiod was determined with %75, %66.6, %66.6, %79.2 and %62.5 accuracy. In the detection of seizures in EEG signals, the accuracy has increased to %79.2, based on the increase in the sample entropy value or the decrease in the permutation entropy value. In addition, the accuracy value increased to %83.3 based on the decrease in the approximate entropy value or the decrease in the spectral entropy value. This is an indication that when the onset of a seizure cannot be detected with one entropy method, it can be detected with another entropy method. In addition, there are some changes detected before the seizure in the EEG signal analysis. It has been predicted that epileptic seizures can be detected beforehand if these changes are examined and detected by different analysis methods.

Keywords: Epilepsy, Signal analysis, Signal mean value, Signal mean square root, Shannon entropy, Sample entropy, Permutation entropy, Approximate entropy, Spectral entropy.

1 .LITERATURE RESEARCH

1.1 What is Epilepsy?

The word epilepsy means to be caught or to have a crisis in ancient Greek. In French, epilepsy, which comes from Latin, means sara [1]. Epilepsy is the involuntary movement of body extremities (arms and feet) as a result of sudden discharges in the brain. Although the causes of epileptic seizures differ from person to person, there are cases where the exact cause cannot be determined. The factors that cause epilepsy are generally as follows: Hippocampal sclerosis, brain tumors, hypoxic (ischemic brain injuries), central nervous system infections, developmental disorders of brain tissue, developmental disorders in brain vessels, hereditary diseases, and genetic causes.

1.2 History of Epilepsy

Epilepsy was first mentioned 2000 years ago in a chapter of the Babylon textbook (in the British Museum). Babylonian physicians suggested that demons or ghosts caused epilepsy and that the treatment was a spiritual matter. Because of these thoughts of Babylonian physicians, patients were punished by excluding them from society. However, Hippocrates, unlike the Babylonian doctors, saw the disease as a brain disorder and wrote a book about epilepsy called "The Sacred Disease" [2].

In ancient Mesopotamia, epilepsy was mentioned in a part of 40 tablets, called ’Sakikku kil’, meaning ’All Diseases’ [3]. In the 19th century, epilepsy emerged as a new discipline. This concept has become common in Europe and North America. In 1857, a hospital was established for ’paralyzed and epileptic’ patients in London. In addition, benevolent and humane epilepsy colonies were established against the social problems of epileptic patients. In 1873, Hughlings Jackson laid the modern foundation for dysfunction in epilepsy by arguing that seizures are the result of sudden short electrochemical discharges. Later, the electrical excitability of the animal and human cortex of the brain was discovered

by David Ferrier, Gustav Theodor Fritsch, and Eduard Hitzig. In 1909, an organization called the International League AgainstEpilepsy was founded around the world. In 1912, the drug called phenobarbital wasused as a primary drug in the treatment of epilepsy. In the 1920s, Hans Berger developed human electroencephalography. After the 1930s, there were important developments such as EEG showing electrical discharge in the brain, different discharge patterns in different seizure types, and revealing the discharge areas of the seizures that occurred. In 1938, a drug called phenytoin was used as the primary drug in the treatment of epilepsy. A rapid drug discovery took place after the 1960s.In the following years, computerized tomography (CT), magnetic resonance imaging (MRI), MRI spectroscopy, and positron emission tomography techniques were usedto reveal sensitive brain disorders caused by epilepsy [2].

1.3 How is Epilepsy Diagnosed?

In order to diagnose epilepsy accurately, seizures must be observed and reported to the doctor. If possible, the duration of the seizure should be recorded with a videocamera and shown to the doctor. If necessary, electroencephalography (EEG) and some blood tests can also be checked. There are more than 30 types of epileptic seizures, ranging from short-term seizures to complex seizures. Therefore, video recordings are an important element in the diagnosis of epilepsy, as they provide information about the time and duration of the seizure [3].

1.4 Electroencephalography

Electroencephalography is the cerebral bioelectrical activity recorded by electrodes placed on the scalp of the human skull through a conductive gel. EEG is the most important laboratory method used in diagnosing epilepsy, classifying seizures, and following the disease. The basis of EEG activity recorded from the scalp is the postsynaptic potential of cortical pyramidal cells. Intracellular and extracellular electrical potential differences create postsynaptic potentials. This potential is collected in thecortex and spread to the scalp from the structures surrounding the brain [4]. An example of EEG signals taken from the scalp is shown in Figure 1.1.

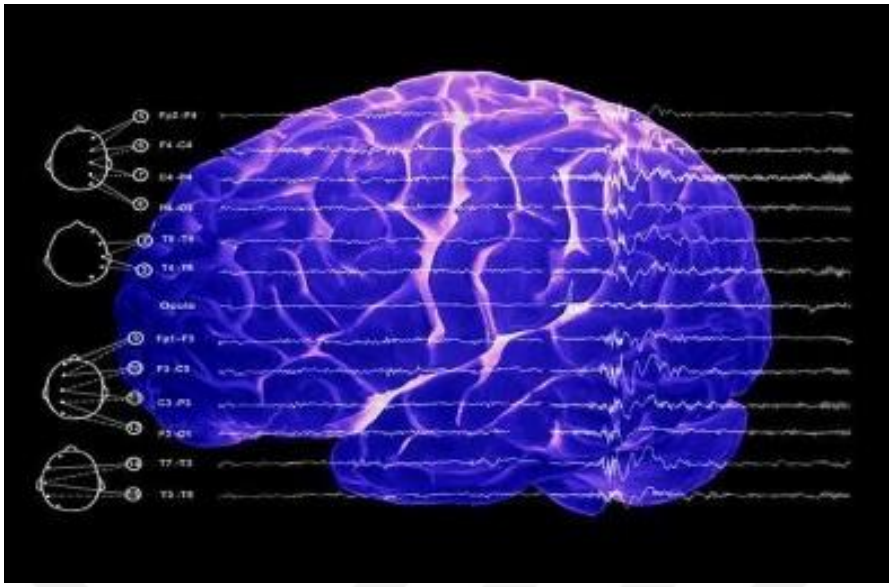


Figure 1.1 : Signals received with electrodes placed on the scalp of the skull [5].

1.4.1 EEG activity qualities

1.4.1.1 Waveform

The term waveform is used to describe the morphology or appearance of a wave. Any electrical potential change between two recording electrodes, regardless of the waveform, is called a wave. Each wave or series of waves is called an activity. It is known that there are many waveforms. Although the shapes and durations of irregular waves are not equal, there is symmetry in regular waves, that is, regular descent and rise are observed.

Waves can also be classified as monophasic, biphasic, triphasic, or polyphasic. Monophasic waves are known as waves that show a single deflection (deviation) upor down the isoelectric line. The diphasic wave has two components in opposite directions, and the triphasic wave has three components that change around the isoelectric line. A polyphasic wave appears to have two or more components in different directions [4]. Figure 1.2 shows examples of various waveforms.

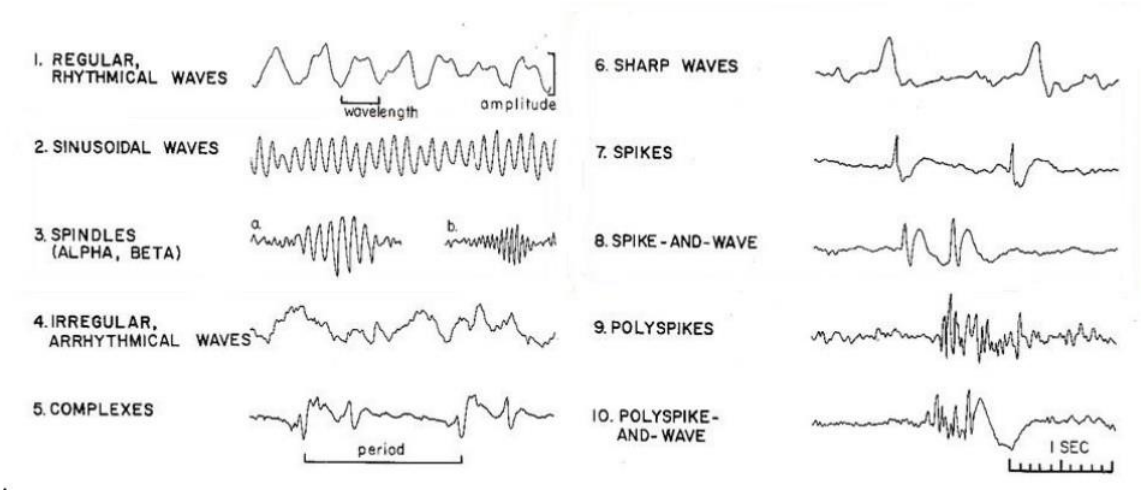


Figure 1.2 : Waveforms of EEG [6].

1.4.1.2 Repetition

The repeatability of waves is being rhythmic or arithmetic. In rhythmic repetitive waves, there are similar intervals between waves. It is usually regular and often sinusoidal. Arrhythmic repetitive waves are defined by varying and irregular intervals between waves. They usually have an irregular shape [4].

1.4.1.3 Frequency

Frequency indicates how many times a repeating wave repeats in one second. The frequency of a wave or repetitive wave is determined by measuring the duration and wavelength of a single wave and calculating its inverse. EEG waves are examined in five sub-band ranges. Table 1.1 shows the subbands of EEG waves and the frequency ranges of these bands [4]. Figure 1.3 shows the lower frequency bands of the EEG waves.

Table 1.1 : EEG waveforms chart.

Name of subband	Symbol	Range
Theta	θ	4-8 Hz
Alpha	α	8-12 Hz
Beta	β	12-22 Hz
Gamma	γ	22-40 Hz

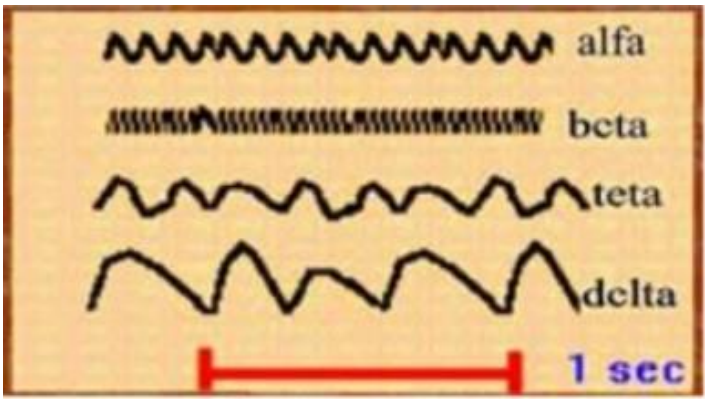


Figure 1.3 : Lower frequency bands of the EEG signal [4].

1.4.1.4 Amplitude

The amplitude of EEG waves is measured in microvolts (μV). It is measured by comparing the vertical length of a wave with the recorded calibration signal height at the same gain and filter settings [4].

1.4.1.5 Scatter

EEG signal distribution refers to the electrical activity recorded with electrodes placedon different parts of the head. Widespread, diffuse, or generalized distribution refers to simultaneous activity in all or nearly all of the head [4].

1.4.1.6 Phase relationship

The phase relationship is used to express the timing and polarity of the wave components in one or more channels. Waves of different frequencies can appear in different channels. Thus, peaks and troughs are formed at the same time. These waves are said to be in phase. If the waves at the frequency do not come togetherin this way, then it is said that there is a phase separation (out of phase). Phase differences can be expressed based on phase angles. For example, there is a 180-degree phase difference between two peaks in opposite directions. Phase shows the time relationship between different components of a rhythm in a single channel. For example, a sinusoidal wave has 90° between its peak and its zero point, and 360°with the next peak [4].

1.4.1.7 Timing

It's timing in different areas of the head may be the same or different. The terms simultaneous and synchronous mean that two events occur at the same time. These terms are often used interchangeably. However, while the term "synchronous" is sometimes used to emphasize simultaneous occurrence, "simultaneous" can be used more broadly to denote simultaneous occurrence, which can only be seen in an imprecise manner, within the relatively slower recording speed of the EEG [4].

1.4.1.8 Reactivity

Reactivity describes the changes that can occur in some normal and abnormal patterns with various maneuvers. Some patterns may be provoked or increased, decreased or inhibited by eye-opening and closing, hyperventilation, photic or sensorystimuli, changes in alertness, movement, or other maneuvers [4].

1.4.2 Age-related EEG changes

Some EEG changes occur with aging. These changes cause great variation among individuals. The most common change is a slowdown in alpha band frequency in normal elderly compared to younger adults. Although the reason for the decrease in EEG is not fully explained, it is usually caused by vascular factors [4].

1.4.3 Identification of abnormal EEG

If an EEG contains interictal paroxysmal (inter-seizure) patterns and ictal (seizure moment) patterns other than normal activity, it is called an abnormal EEG [4].

Interictal paroxysmal (intermittent) patterns: Spike, sharp, multiple thorns, fast spike currents, spike and slow wave Complex, slow spike and wave complex.

Ictal (seizure) patterns: generalized Tonic Clonic Convulsion, absence, complex partial seizures, simple partial seizures, myoclonic seizures, tonic seizures, atonic aeizures.

1.4.4 The correlation between EEG patterns and neurological diseases

The presence of epileptic waves in the EEG supports the diagnosis of epilepsy, but its absence does not exclude the diagnosis of epilepsy. EEG always remains normal in 10% to 40% of epileptic cases. Sleep, sleep deprivation, photic stimulation,

hyperventilation facilitate the emergence of discharges in epileptic patients. West syndrome, Lennox-Gastaut Syndrome, Childhood Absence Epilepsy, Benign Rolandic Epilepsy, Juvenile Myoclonic Epilepsy, Temporal lobe seizures can be easily recognized by special EEG findings [4].

1.5 Classification of Epileptic Seizures

Epileptic seizures differ according to the regions of the discharges that occur in the brain. The International Society for Combating Epilepsy classified epilepsy between 1991 and 1998. Although these classifications are still valid, a new classification was proposed in 2001 [7]: partial seizures, generalized seizures, and absence seizures.

1.5.1 Partial seizures

Partial seizures are the effects of discharge in a certain area of the brain in limited areas of it. These are studied in three different classes [3].

- In simple partial seizures, the person loses consciousness. This does not mean that it can stop or control the seizure. Seizures begin and end in a specific area of the brain. These seizures are not situations that another person might notice, such as immersion, and waking from dreaming.
- In complex partial seizures, the person experiences changes in consciousness or loss of consciousness. It starts with the electrical discharge of the brain and all parts of the brain are affected. The person may experience a dreamlike state. There may also be situations such as winks or emotional outbursts.
- In secondary partial seizures, the electrical discharge in the brain starts at one point, but affects all parts of the brain. In other words, the seizure starts as partial and continues as a generalized one. This can happen in three different ways:
  - The seizure that started as a simple partial seizure may continue as a generalized seizure.
  - The seizure that starts as a complex partial continues as a generalized seizure.
  - The seizure that starts as a simple partial seizure turns into a complex partial seizure. Complex partial seizures can evolve into generalized seizures [8].

1.5.2 Generalized seizures

If the electrical activity in the brain affects all parts of the brain simultaneously from the beginning of the discharge, or if it affects the whole brain as a secondary partial, it is called generalized seizure. Generalized tonic-clonic seizures are most common. Generalized tonic-chronic seizures are popularly known as epilepsy. During the seizure, contractions and relaxations occur in all the muscles in the body. With thedischarge of the muscles in the rib cage, the air discharged from the lungs causesbelching. This state is called the tonic period.

After a short time, the conical phase of the seizure begins. During this period, the tongue or cheeks may be bitten. After a minute or so, the body begins to relax.The patient begins to come to herself. During the tonic period, since there is a lossof consciousness in chronic seizures, the patient is not aware of what she is going through at first. Various pains may occur in the patient after the seizure. If the seizure lasted longer than five minutes or if it was the first seizure, the patient mayneed to apply to a health care provider.
Most generalized seizures are idiopathic (the cause of the seizure is unclear). There is no cure for such epileptic seizures. Because there is no tissue damage or any symptom that causes seizures [3]. Although most patients with seizures state that they feel the seizure, there is no definite information about this situation.

1.5.3 Absence seizures

Seizures that affect the whole brain, called generalized, are absence seizures. Absence seizures are mild seizures but can be life-threatening if their frequency increases. The absence seizures can be seen in children. Although the child can hear the beginning of the sentence that is said to her during the absentmindednessdue to the seizure, she may not hear the end. This suggests that children lack attention.

Since the patient breathes deeply during the seizure, the patient may be asked to take deep breaths during EEG shots.

- Myoclonic seizures or splash seizures are a type of seizure that occurs when the patient experiences a jump before falling asleep. In these seizures, contractions may occur in the whole body or arms. During the seizure, consciousness is clear but does not perceive what is happening. Seizure before falling asleep is a physiological finding, not a symptom of disease.
- In Tonic and Atonic seizures, the patient falls to the ground as a result of muscle contraction or relaxation. Muscle contraction occurs in tonic seizures and muscle

relaxation occurs in atonic seizures. As a result of contractions and relaxations in the muscles, the patient loses her balance and falls to the ground. Since patients fall forward, they can use helmets for protection [8].

Classifying epileptic seizures only by type causes the information about the patient to be ignored. Therefore, there are various syndromes of epilepsy disease.

Various symptoms are taken into account in the determination of epilepsy syndromes. These symptoms are can be listed as: Age at onset of seizures, seizure type, typical EEG patterns, genetic factors, behaviors during the seizure, triggering factors, expected disease course, response to treatment.

1.6 Types of Epilepsy Syndrome

Different epilepsy syndromes have been described. Epilepsy syndromes are generally divided into three main headings according to the cause or etiology:

- Idiopathic epilepsy: The disease does not have an obvious cause, but there may be a genetic link [8].
- Symptomatic epilepsy: Symptomatic epilepsy is defined as "epilepsies developing secondary to a known lesion or disease of the brain". In the majority of symptomatic epilepsies, seizures are focal, and mainly the first symptom of the seizure usually points to the anatomical site of origin. However, every focal seizure in childhood is not due to a known lesion, and even the group we call idiopathic partial epilepsies constitutes the most common epilepsy in childhood.
- Cryptogenic epilepsy: Cases where doctors believe the disease is due to a cause, but cannot diagnose the cause of the disease [8].

1.6.1 Common epilepsy syndromes

- **Infantile Spasms:** Infantile spasm is a syndrome that begins in infancy, in which a hypsarrhythmia (formation of abnormal waves with high voltage values) pattern is seen on EEG. It is a severe epileptic encephalopathy characterized by spasms clinically. It may cause psychomotor regression during infancy. The pathophysiology is not fully elucidated [9].
- **Lennox-gastaut Syndrome:** Lennox-gastaut syndrome (LGS) has specific EEG patterns with multiple seizure types. It is a treatment-resistant epileptic encephalopathy with a poor prognosis, including cognitive impairment [10].

- **Childhood absence epilepsy:** Childhood idiopathic generalized seizures are a common occurrence. It is a syndrome characterized by seizures recurring many times during the day, short-term, loss of consciousness in which awareness disappears, and pauses in movements are observed.
- **Juvenile myoclonic epilepsy:** In juvenile myoclonic epilepsy (JME), unilateral or bilateral recurrent irregular myochronic beats are seen mostly in the upper extremities. It is a type of epilepsy often accompanied by generalized tonic-clonic seizures (JTKN) and less frequently by absences. Myoclonic beats are triggered by awakening and sleep deprivation. Electroencephalography (EEG) shows generalized spike wave (4-6 Hz) and multiple spike wave complexes [11].
- **Benign rolandic epilepsy (BRE):** It is the most common and best-known epilepsy syndrome of childhood and accounts for 15-25 % of all childhood epilepsy. The transmission pattern and gene localization of BRE have not yet been fully determined [12].
- **Temporal lobe epilepsy:** Temporal lobe epilepsy is a heterogeneous syndrome in terms of etiology, age of onset and response to treatment. Complexpartial seizures are common in this syndrome. It is generally seen around 30- 35% [13].
- **Frontal lobe epilepsy:** Frontal lobe epilepsy exhibits a clinical picture that starts with strange, stereotypical behaviors, acts of violence that are perceived as purposeful, and ends abruptly. The clinical picture with the aforementioned symptoms often leads to confusion with pseudo-seizure and sleep disorders [14].
- **Reflex epilepsy:** Reflex seizures are seizures induced by a specific afferent stimulus or patient activity. It is classified as characterized by generalized and focal seizure findings. Reflex epilepsies are syndromes that include all epileptic seizures developed with sensory stimuli [15].

1.7 Epilepsy Treatment

Epilepsy is a treatable disease. Since the causes of epileptic seizures are not known exactly or differ from person to person, the duration of treatment also differs fromperson to person [3].

Treatment of epilepsy is first started with medication. In cases where the drug isnot effective, surgical treatment is applied if possible.

1.7.1 Medication

The drugs used in the treatment of epilepsy are the ones used to suppress seizures,not for therapeutic purposes, like drugs used in the treatment of diabetes mellitus [3]. Since the drugs are used to suppress the seizures, it is recommended to take the drugs regularly without interrupting their time. The drugs and their doses are determined by considering the seizures of the person.

Epilepsy drugs are designed to regulate electrical activity in brain cells. Drugs used in the treatment of epilepsy are given as [8]: Phenobarbitone, phenytoin, sodium valproate,carbamazepine, primidone, Vigabatrin, zonisamide,oxcarbamazepine, felbamate, gabapentin, topiramate, tiagabine, lacosamide, levetiracetam, pregabalin.

1.7.2 Surgical treatment

If the patient is resistant to epilepsy drugs, that is, if the seizures cannot be stoppedor reduced despite the drugs used, surgical treatment can be applied. For surgical treatment to be applied, the cause of the disease (a tumor in the brain, occlusion in the cerebral vessels, etc.) must be a cause that can be treated with surgical intervention. Surgical intervention can be done in two different ways: the first and most preferred is aimed at eliminating the epileptic focus (resective surgery), and the second is aimed at reducing the spread and frequency of seizures (functional surgery, palliative surgery).

Resective surgery: As the first step in resective surgery, a number of tests are applied to the patient. These tests help determine the patient's history of seizures. By looking at the findings, the focus of the disease is tried to be determined. If it isconcluded that the seizure focus will not cause any physical damage to the patient as a result of surgical intervention, surgical intervention is performed. If the focus ofthe seizure is a tumor or a lesion in the brain, the positive outcome of the surgical intervention is high. However, if the seizure focus cannot be detected, EEG data is taken as a basis for surgical intervention.

Paritive (functional) surgery: In parietive (functional) surgery, it is tried to ensure that the seizure is effective in less area by cutting the ways of spread of the seizure. It is mostly applied in generalized seizures and sudden fall seizures.

Vagal Nerve Stimulation (VNS): Another treatment method is vagal nerve stimulation, popularly known as an epilepsy battery. VNS was first applied in 1988. It is generally preferred in patients who are resistant to epilepsy drugs. In the treatmentof vagal nerve stimulation, spiral electrodes are placed on the vagal nerve in the leftregion of the

neck. These electrodes are connected subcutaneously with the pacemaker in the pocket opening to the left chest. With vagal nerve stimulation, shortterm low current values are given to the vagal nerve, which regulates heartbeat, breathing patterns, and bowel movements. The applied electrical current prevents the occurrence of seizures by regulating the uncontrolled electrical discharge that causes epileptic seizures in the brain.

If the patient's seizures decrease as a result of VNS, the dose of the drugs usedin the patient is rearranged by the neurologist. The dose setting in drugs differs from patient to patient. There are patients whose daily drug use is reduced by half a year after VNS treatment, and there are also patients for whom the treatment is notbeneficial. Reducing the use of epileptic drugs with serious side effects is of great importance, especially in pediatric patients.

In VNS, the value and duration of the electrical activity to be sent to the vagal nerve are predetermined. If these settings are not sufficient for the patient, with the approval of his/her doctor, the patient can hold a special magnet close to the pacemaker, that is, the epilepsy battery, and send a warning to the vagal nerve atany time. This is a situation that is mostly used in patients who do not see the benefit of VNS treatment [16].

Nemos T-VSN: Nemos T-VNS is a noninvasive type of VNS. In Nemos T-VSN, a special electrode is placed in the left ear. This electrode is connected to the phonesized nemos T-VSN device as shown in Figure 1.4. In the Nemos T-VSN device, the electrical currents to be sent to the vagal nerve are adjusted. In Nemos T-VSN, thevagal nerve is not stimulated directly, but through a branch that passes through the outer ear. Nemos T-VSN daily use and settings are made by the relevant neurologist.It is often used to decide whether vagal nerve stimulation therapy is appropriate forthe patient. If the patient does not respond to the treatment, the treatment can bestopped immediately [17].

Figure 1.4 : Nemos T-VSN [17].

1.8 What Should be done During an Epileptic Seizure?

We can list what we should do when faced with someone who has an epileptic seizure:

- We should avoid situations that would complicate or restrict the patient's movements.
- If the patient's environment is not safe, we should put the patient in a safeplace.
- We must isolate the patient from items that may cause injury.
- We should check their clothes, if they have tight clothes, we should loosenthem.
- We should take the patient in the most suitable position to allow her saliva toflow out.
- If she is clenching her teeth, we should never try to open it or put anything inher mouth.
- Any forceful movement of the jaw is definitely harmful.
- Medication should not be given to the patient during the seizure, unfounded techniques should not be applied for the seizure to pass. (like smelling onions, cologne-like things).
- It should be checked whether the patient has any health card showing that he/she has epilepsy.
- It should be waited for the seizure to end.
- Patients with seizures are often exhausted and do not know what to do after the seizure, so they should not leave the patient's side and gently restrain thepatient in dangerous situations such as heading for the road or facing an openwindow [7].

1.9 Literature Review of Epilepsy

Epilepsy is one of the most common brain diseases in the world, and new cases of epilepsy are seen every year. The prevalence of epilepsy has led to many studies. The first recorded work on epilepsy is Hippocrates' book, 'Holy Disease'. Contrary to what Babylonian physicians thought the disease was caused by demons or ghosts, Hippocrates argued in this book that epilepsy was a brain disease [2]. If more recentstudies are started to be examined, one can say that there are cases that showsimilar symptoms with epileptic seizures but do not have epileptic seizures. In suchcases, the seizures are called 'Pseudo-Epilepsy Seizures'.

There are some studies to distinguish pseudo-epileptic seizures from true epileptic

seizures. In 1999, Varlı stated that the distinction between false epileptic seizures and true epileptic seizures could not be made with the observations done by the clinician. It was concluded that EEG records should be examined in order to make a correct distinction [18]. In another study on epilepsy conducted by Canal and Koçerin 2011, the differences between EEG signals from healthy and epileptic individuals were analyzed using neural networks and genetic algorithms [19]. Furthermore, it is shown that it is possible to reduce or stop seizures in patients who are not candidates for surgery with VNS [16]. Parvez and Paul in 2014 classified EEG signals by frequency band analysis. As a result of that study, it has been shown that witha good combination of sensitivity and resolution, preictal (pre-seizure) and interictal(post-seizure) EEG signals can be classified [20]. In 2014, frequency analysis was performed from healthy and epileptic EEG signals. In that study, normal EEG classification with epileptic signal was performed using Fourier transform. They dividedthe epileptic EEG signals into five frequency ranges as alpha, beta, gamma, delta and theta and separated the EEG signals according to their frequencies [21]. A prototype developed that to be used in long-term EEG recordings in order to remove the limitations experienced in the patient's life in long-term EEG recordings. The developed product resembles a behind-the-ear hearing aid consisting of two electrodes [22].

Debener et al., in 2015, conducted a study to prevent the deterioration in EEG signals due to the increase in electrode impedance as a result of the evaporation of the gel used during EEG recordings over time. In their study, electrodes were placedunder the C-shaped screen film to be used around the ear. The gel is also used in the designed system, but the evaporation of the gel and the disturbances in the EEGhave minimized thanks to the design [23]. In 2016, a product stated that the best recordings for the in-ear EEG recording technique were obtained from the electrodeclose to the temporal lobe [24]. It is shown that surgical treatment for patients with refractory epilepsy was applied to only five percent of patients who were candidates for surgical treatment [25]. VNS was applied to 11 patients with refractory epilepsy in the Aegean medical faculty hospital and they observed the condition of these patients between 2010 and 2014. As a result of this four-year study, they concludedthat the effect of VNS therapy has increased over the years. They stated that studies should be done in longer times for healthy results [26]. A design has been made tostimulate the vagus nerve with a constant wave of stimulation. The stimulator can be controlled and operated by the smartphone, and also provided flexible stimulus options for various nerve stimulation experiments. The low power consumption and small volume of the designed system have proven that it can meet the needs of medical experimental research and self-

treatment of the patient [27].

In the diagnosis and treatment stages of epilepsy, it is very time-consuming to examine long-term EEG recordings by experts and to detect seizures. Therefore, EEG signals are analyzed with linear signal analysis or nonlinear signal analysis methods in order to detect the epileptic seizure in EEG automatically. Although EEG signals are not linear, in linear signal analysis they are considered as linear. In linear analysis method, EEG signals are analyzed in the time domain, frequency domain, and time-frequency domain. In the time domain analysis, energy, power, variance, standard deviation, mean, and root mean (RMS) of signals are checked. In the frequencydomain, spectral power density and subband frequency values are investigated [28]. In one study, the epileptic region in the signal was identified using the Elman neural network, a special recurrent neural network, with features extracted in the time andfrequency domain [29]. For the diagnosis of seizures in the EEG signal, the signals are separated into subbands by wavelet decomposition and classified by genetic algorithm [30]. A prediction filter has been proposed, which shows the presence of spikes and sharp waves in seizure regions in EEG signals. In another study, the seizure region was determined by the increase in the estimation error energy of thefilter in the seizure region [31]. Furthermore, epilepsy disease was defined by performing EEG signal analysis with a single hidden layer feedforward artificial neural network machine (ELM) in 2012 [32]. Seizure was detected in EEG signals applied to artificial neural network with multi-stage nonlinear filtering preprocessing [33]. In one study, classifying preictal and interictal EEG signals by using features such as frequency and amplitude in gamma band signal has been shown [34]. Singh et.al. classified the EEG signals using the difference in RMS bandwidth and average frequency seen in epileptic zone rhythms [35].

Raghu et.al. showed that the epileptic EEG signal has a larger variance, maximum value, wavelet log energy entropy, RMS, and band power properties, while the normal EEG signal has a larger minimum value, wavelet Shannon entropy, and zero-crossing characteristics [36]. Mahapatra et.al classified ictal and interictal EEG signals using the RMS frequency [37]. To distinguish the epileptic region in EEG signals, a feature has been proposed as a time-domain energy-based called exponential energy [38]. In recent studies, the features used for the diagnosis of seizures inthe EEG signal were examined. It has been shown that seizures can be determinedby using the variance, energy, nonlinear energy, and Shannon entropy calculated inthe raw EEG signal or by using the variance, energy, kurtosis, and line length calculated over the wavelet coefficients [39,40].

As it is mentioned above, EEG signals are not linear, but in linear signal analysisthey

are considered as linear. For this reason, the preference of nonlinear analysis methods may give better information than the EEG signal for the diagnosis of epilepsy. Entropy, one of the nonlinear analysis methods, is a thermodynamic concept that gives information about system disorder [28]. It is used to measure the irregularity in EEG signals during an epileptic seizure. Kannathal et al. [41] and Songet al. [42] showed the difference between seizure EEG signals and healthy EEG signals using the entropy methods as Shannon entropy, Renyi's entropy, Kolmogorov-Sinai entropy, sample entropy, and approximate entropy. When the entropy values of the epileptic and normal signals were compared, it was observed that the entropyvalues of the epileptic signal were higher than normal. This showed that there was adecrease in the flow of information during the seizure [41,42]. EEG signals were decomposed into signal subbands by applying discrete wavelet transform at different levels. The separated signals were determined the seizure by using approximate entropy and spectral entropy [43, 44]. Signals were classified with the calculated wavelet entropy, spectral entropy, and sample entropy values by repetitive Elman-based neural networks and radial-based neural networks [45]. The extreme learning machine is combined with the optimized sample entropy (O-SampEn) algorithm. With this algorithm, it was determined whether there was a seizure in the EEG signal [46].

Nicolaou et.al and Xiang et.al. classified the permutation entropy, fuzzy entropy and sample entropy values of EEG signals calculated by support vector machine [47,48]. It has been shown that fuzzy entropy has a better seizure detection index thansample entropy [48]. In another entropy method, distribution entropy, the epilepsysignal was segmented in three different ways and entropy values were calculated. Distribution entropy has been observed minimally affected in the parameter selection [49]. Raghu et. al. used Shannon spectral entropy to differentiate between two groups of patients with idiopathic epilepsy. They showed that Shannon spectral entropy measured in a specific frequency range can serve to follow the developmentof patients suffering from idiopathic epilepsy [50]. In another study, EEG signals were separated into subbands by discrete wavelet transform. Of the power spectralanalysis in the frequency domain and of the amplitude values in the time domain, the sigmoid entropy was calculated. It was concluded that sigmoid entropy, which has less computational complexity, can be used to analyze epileptic seizure behavior, which also includes brain dynamics [51]. In a recent study, it was shown that the patients can be warned before the seizure by determining the time between the preictal and ictal state by inferring the distribution entropy feature has been stated [52]. Zhang et. al. proposed multidimensional sample entropy and compared with sample entropy, and they showed

that seizure onset was more pronounced in the multidimensional sample entropy [53].

Li et. al. found that permutation entropy was more sensitive than sample entropy for recognizing nonlinear activity in EEG data and predicting the absence seizures [54]. Since permutation entropy is a fast complexity measure in time series, it has been used for seizure detection in online devices. It was observed that permutation entropy makes a reliable distinction, but the sensitivity of the study could notbe measured due to limited data [55]. Jouny et.al. proposed that the seizure detection was attempted with a combination of eighteen different feature extraction methods, including Shannon entropy, sample entropy, and permutation entropy [56]. In a study in 2012, the permutation entropy was calculated by making different synchronizations of the EEG electrodes. Within the analyzed database, the frontal-temporal scalp areas appeared to be consistently associated with higher permutation entropylevels compared to the remaining electrodes, while lower permutation entropy values were seen in the parietoccipital areas. This showed that from different parts of the brain were abnormalities leading to the onset of seizures [57]. Multiscale permutation entropy (MPE) was proposed to describe the dynamics in EEG recordings andMPE values were classified using linear discriminant analysis. It has been shown that the seizure-free state, pre-seizure and seizure moment can be differentiated by dynamic features in MPE and EEG. This result supported the view that seizures were predictable from EEG data [58].

Bhanot et. al. used four feature vectors for seizure detection: short-term permutation entropy (STPE), STPE gradient (GSTPE), short-term energy (STE), andshort-term mean subtracted from ictal and interictal (STM). With these features, RB-Boost (Random Balance Boost) algorithm with k-fold cross validation was used to classify data as ictal and interictal [59]. Peng et.al. extracted nine features for eachEEG channel, including power spectral density in six subbands, sample entropy, permutation entropy, and spectral entropy. The features of each channel were ordered according to the F-statistic value and the classification results were improvedby selecting the most informative features [60]. In a recent study, channel selectionhas been made in EEG signals to minimize the complexity and computational power of classification. The channels were selected according to their permutation entropyvalues using the K-nearest neighbor (KNN) algorithm combined with the genetic algorithm. By channel selection, accuracy, sensitivity, and specificity values in seizure detection were improved. They tried to determine which part of the brain was associated with the onset of seizures for a particular patient and determined that theP7-O1 channel was most effective in the selected patient group. They found that the seizure

predictions made by selecting the channel are more accurate and less computational burden than the seizure predictions made by using all channels [61]. Approximate entropy (ApEn) measures the predictability of the current amplitude values in the signal based on previous amplitude values. ApEn is preferred because of its reliability and computationally low density. Srinivasan V. et al. proposed a neural network-based automatic epilepsy detection system using ApEn asan input feature. Seizure detection was performed with high accuracy with the proposed system [62]. Invasive electroencephalogram (EEG) recordings of patients with medically intractable focal epilepsy with approximate entropy and Lempel-Ziv (LZ) complexity were analyzed. It was observed that ApEn and LZ values increasedduring a seizure at focal electrodes. Based on changes in seizure status, they showed that these techniques can be used to detect changes in EEG due to epileptic seizures [63]. A classification detection method is proposed to automatically detect different types of epileptic EEG (containing spike-wave, sharp-wave, spike-slow complex wave, and sharp-slow complex wave) data using ApEn coupled discrete wavelet transform (DWT). As a result of the study, a higher detection rate was achieved with a lower false detection rate [64]. In addition, EEG signals were separated into subbands for epilepsy detection. ApEn values were looked at to evaluatethe complexity of the EEG signal and each subband. T-student statistical analysis was used to evaluate the discrimination ability of this method [65]. ApEn and Correlation Size (CD) were calculated for epileptic EEG and normal EEG segments, and signals were compared. It is found that there were statistically significant differences between the nonlinear properties of epileptic EEG and normal EEG signals [66].

Guo L. et al. developed an automatic epileptic seizure detection method combined with an artificial neural network for classification related to the presence or absence of seizure in EEG signals. They used the approximate entropy property derived from the multiple wavelets transform for detection [67]. ApEn and sample entropy methods were used to extract the quantitative entropy characteristics of different EEG series. It was determined that the mean ApEn and sample entropy values for epileptic time series were less than non-epileptic time series [68]. In a study conducted in 2012, ApEn, sample entropy, phase entropy 1, and phase entropy 2 properties were obtained in the EEG signal for the separation of normal, ictal, and preictal states in EEG signals.The resultant features were classified with seven different classifiers (Fuzzy Sugeno Classifier (FSC), Support Vector Machine (SVM), K-Nearest Neighbor (KNN), Probabilistic Neural Network (PNN), Decision Tree (DT), Gaussian Mixture Model (GMM) and Naive Bayes Classifier

(NBC)). The fuzzy classifier has been shown to detect all three classes with high accuracy [69]. EEG signals are decomposed with DWT to calculate approximate entropy and detail coefficients. The ApEn values of these coefficients were calculated and the differences between normal EEG and epileptic EEG were determined. It has been shown that seizures can be detected with an artificial neural network [70]. ApEn values were used to detect seizure onset. It has been shown that the onset and end of seizures in EEG signals can be detected with ApEn [71].

Restrepo J. F. et al. proposed that the wrong parameter selection in ApEn (embedding size, threshold(r), and data length(N)) and the presence of noise in the signal weakens the discrimination capacity. In that study, $r_{max}(ApEn(m, r_{max}, N) = ApEn_{max})$ property was used to distinguish dynamics, and r_{max} provided useful additional information in classification [72]. A wavelet-based fuzzy approximate entropy (fApEn) method has been proposed for the classification of healthy, interictal, and ictal EEG signals. It was also shown that the fApEn value decreased during the ictal period and successfully differentiated all three conditions [73]. Vijith V. S. et al. extracted the ApEn, sample entropy, and Hurst exponent properties of epileptic and normal EEG signals and made a clear distinction between them [74]. A classification method using ApEn, sample entropy, and ray entropy have been proposed to classify focused and unfocused EEG. In this method, six different classification methods (Naive Bayes (NBC), Radial Basis Function (RBF), Support Vector Machines (SVM), KNN classifier, Non-Nested Generalized Examples classifier (NNge), and Best First Decision Tree (BFDT)) were used. The NNge classification was found to have the highest accuracy among them [75].

In a study conducted in 2017, EEG signals were separated into subbands with DWT.The ApEn and Shannon entropies of the signal and each subband were calculated and support vector machines were used for classification [76]. For Focus EEG and Out of Focus EEG classification, ApEn, sample entropy, and fuzzy entropy features were extracted and classification was performed with high accuracy [77]. In another study, a convolutional neural network combined method based on ApEn and repetition quantitation analysis was proposed for the detection of automated EEG recordings. The proposed method has been shown to have good performance [78].Rout S. K. et al. proposed a system in which the variable mode decomposition (VMD) and ApEn features extracted from the EEG signals and the multilayer multicore random vector functional link network plus (MMRVFLN+) are combined. The superior classification accuracy, negligible false positive rate (FPR/h), simplicity, feasibility, robustness, and applicability of the proposed method

have shown that it can automatically identify episodes of epileptic seizures [79]. A new method of varying samples difference has been proposed for the diagnosis of epilepsy in EEG signals. Five features of EEG were investigated for the proposed method. It has been shown that the shift sample difference method in seizure separation has better performance than the commonly used DWT and empirical mode decomposition methods [80]. In another study, the approximate entropy and sample entropy values of the high band frequencies extracted from the EEG signals were calculated with the Directed transfer function. Using the K nearest neighbor and support vector machine, the signals were classified as epileptic and normal. It was stated that the seizure activity contained in the EEG signal of the proposed system has the advantage of finding accuracy [81].

Another entropy method is spectral entropy, which uses frequency domain properties. With short sliding time windows for seizure detection in EEG signals, the feature extraction of the data was done with time domain, frequency domain, and nonlinear methods. They stated that the best results with discriminant analysis were obtained from a combination of linear and nonlinear features [82]. In another study, a continuous wavelet transform has been proposed to calculate the spectrum of scalp EEG data. Entropy and scale-averaged wavelet power were extracted to indicate epileptic seizures using the moving window technique. Five patients tests with different seizure types showed that wavelet spectral entropy and scale-averaged wavelet power were more efficient than renormalized entropy and KullbackLeiler (KL) relative entropy to indicate epileptic seizures [83]. EEG was decomposed by wavelet transform and coefficient sets were obtained and spectral entropy was applied to these coefficient sets for the detection of epileptic seizures. It showed a low measure of the spectral entropy value for the ictal state compared to the healthy and interictal states, and the distinction was made with high accuracy [84].

Mirzaei et al. investigated EEG and frequency subbands to detect epileptic seizures in their study. They applied a discrete wavelet transform (DWT) to decompose the EEG into its subbands. By applying histogram and spectral entropy approaches to EEG subbands, they differentiated normal and abnormal states of the brain with a high probability [85]. Blanco et al. compared the spectral entropy results calculated in different frequency bands of EEG signals to decide which bandmight be a better tool for predicting epileptic seizures. They said that entropy at high frequencies has great potential as a predictor because it reveals changes in the moments before the seizure [86]. The EEG signal is decomposed into subbands using multiple wavelet transform and spectral features

such as average spectral size, spectral entropy, and spectral square entropies are extracted. It has been shown that the classification of these features using k-NN achieves high accuracy [87].

With varying mode decomposition (VMD), a series of bands with central frequencies in the EEG signals are decomposed into limited mode. Mode spectral entropies are calculated from these mode center frequencies. To detect the presence of epileptic seizures, this mode of spectral entropies is compared and detected with high accuracy [88]. For the prediction of epileptic seizures, feature extraction was performed with spectral entropy using power spectral density as probability density in Shannon entropy. Support vector machine (SVM) and K-nearest neighbor (KNN) algorithms are used for classification. A seizure occurrence was predicted using the first 9 minutes of a 10-minute interval before the seizure. The proposed algorithm not only had acceptable accuracy, but was also the most successful in terms of computational complexity, the energy required for computations, and time delay compared to other studies in the literature [89].

Wijayanto and Rizal stated that EEG signals can be analyzed by empirical mode decomposition (EMD) methods since EEG signals are non-linear, non-Gaussian, and non-stationary. In their study, they used the entropy feature (Shannon entropy (ShEN), spectral entropy (SE), Renyi entropy (RE), and permutation entropy (PE)) to characterize each intrinsic mode function (IMF) generated from the EMD for classification of epileptic seizure EEG. They detected seizures with higher accuracy with the Renyi entropy method, which is one of the entropy methods used [90]. For the classification of EEG data, a model consisting of bidirectional long-term memory (Bi-LSTM) (RNN) architecture memory units, neural numbers, and learning algorithms, which is a kind of repetitive neural network, has been proposed. Instantaneous frequency and spectral entropy properties are used to train the proposed model. In this model, both the classification success of the optimization algorithms and the effect of changing the number of neurons on the performance were investigated. Classification has been carried out with high success [91].

1.10 Objectives of the Thesis

For the detection of epileptic seizures, EEG signals containing epileptic activity should be analyzed by signal analysis methods. Analysis methods to be used from linear and non-linear signal analysis methods should be clarified and investigated in detail. The planned targets for the detection of epileptic seizures are as follows:

- The general characteristics of EEG signals and the difference between them and epileptic EEG should be investigated.
- Linear analysis methods should be investigated because they have easier and simpler theories in terms of application. Linear analysis method(s) that give more accurate results in seizure detection should be determined.
- Since EEG signals are not linear, information may be lost during linear analysis. For this reason, nonlinear signal analysis methods should be investigated for a more accurate determination.
- Seizures in EEG signals should be tried to be detected with the investigated linear analysis methods.
- Linear and nonlinear signal analysis methods used for seizure detection in EEG signals should be compared. It should be determined which method or methods are better for detection.

1.11 Thesis Outline

In Chapter 2, preprocessing methods used in the linear signal analysis are mentioned. Normalization methods that can be used to compare signals with different criteria are specified. Linear analysis methods and non-linear analysis methods are explained.

In Chapter 3, information about the EEG data used is given. In addition, the analysis results obtained were interpreted. In Chapter 4, the results are discussed and suggestions are made for the further stages of the study.

2 .MATERIAL AND METHOD

An epileptic seizure can be defined as the involuntary movement of body parts as a result of sudden electrical discharge in the brain. There are many reasons for this sudden discharge. Apart from known causes, there are also seizures whose cause cannot be determined. Different treatment approaches are applied in the treatmentof epilepsy. First of all, drug treatment is applied, and if necessary, surgical treatment methods are also applied. However, in some patients, surgical intervention cannot be performed since the seizure cannot be determined. In these patients, the occurrence of seizures is prevented with the use of high-dose drugs. Long-term EEG data are examined very importantly to determine the treatment processes of patients before the surgical intervention or for whom the cause of seizures cannot be determined. Different signal analysis methods are used to determine the seizure onset and seizure period in EEG signals. In this thesis study, linear and non-linear signal analysis methods were used for the analysis of long EEG signals.

Prediction and diagnosis of seizures in epilepsy patients are important issues. Signal analysis should be performed to detect seizures from EEG signals. Signal analysis is used to convert features in EEG data into a numerical description. For example, information about the frequency, energy, power, or complexity of the signalis obtained by signal analysis [28]. These features are not clearly visible from the EEG signals, so they are extracted by linear or non-linear analysis methods.

2.1 Linear Signal Analysis Methods

In linear signal analysis, EEG signals are considered linear, and the characteristics of the EEG data such as the energy of the signal, the strength of the signal, the frequency content, and the complexity of the signal can be expressed numerically.

In EEG signal analysis, first, preprocessing should be applied to remove artifacts in the signal. After the preprocessing step, feature extraction should be done fromthe signals.

2.1.1 Preprocessing

EEG signals recorded in a single EEG channel can be represented as $x_c(t)$ continuous signals. Here t and c represent the time and the channel, respectively. EEG signals can also be represented as $x_c[n]$ as a discrete signal. In this step, the EEG signal is adapted as $x_c[n]$, and the noise in the signal is removed. Normalization operations are performed to make comparisons with data on different criteria [28].

That is, in preprocessing, EEG signals are prepared for feature extraction.

For better preprocessing, the signals with the sampling frequency Fs should contain frequencies up to $Fs/2$ that meet the Nyquist criterion. If there are frequencies higher than $Fs/2$, they cause the distortions known as overlap. Therefore, if the signal contains frequencies higher than $Fs/2$, these frequencies should be removed from the signal before sampling. For this process, filtering is done by passing the desired frequencies.

In addition, another operation performed in the signal processing step is normalization. This step is performed to compare the signals recorded in different criteria. The normalization can be done by several different methods [28]. Normalization methods:

- **Statistical or Z-Score Normalization**

It is preferred when there are very extreme values in the data. The equation is given as follows [92]:

$$x' = \frac{x_i - \mu_i}{\sigma_i} \quad (1)$$

In this equation x' is the normalized data, x_i is the input value, μ_i is the mean of the input set, σ_i is the standard deviation of the input set.

- **Min-Max Normalization**

It is used to reduce the data to the 0-1 value range. The equation is given as follows [92]:

$$x' = \frac{x_i - x_{min}}{x_{max} - x_{min}} \quad (2)$$

In this equation x' is the normalized data, x_i is the input value, x_{min} is the smallest number in the input set, x_{max} is the largest number in the input set.

- **Median Normalization**

This normalization method is made by taking the median of each input. The equation is given as follows [92]:

$$x' = \frac{x_i}{Median(a_i)} \quad (3)$$

In this equation $x^{'}$ is the normalized data, x_i is the input value, a_i is median ofthe input set.

- **Sigmoid Normalization**

This method classifies data in the range of 0 to 1 or -1 to 1. The equation is given as follows [92]:

$$x' = \frac{e^{x_i} - e^{x_i}}{e^{x_i} + e^{x_i}} \quad (4)$$

In this equation $x^{'}$ is the normalized data, x_i is the input value, e is natural logarithm value.

Finally, the preprocessing step should be addressed the artifacts. The artifacts are tried to be removed using following strategies: [28]:

- Ignoring: Feature extraction methods are assumed to be only minimally affected, and artifacts are treated as if they do not exist.
- Rejection: Artifact is (automatically) identified and contaminated channels or periods are excluded from the analysis.
- Removing: Artifact is re-identified and, if possible, removed from the EEG signal by separation methods such as independent component analysis (ICA) or wavelet filtering. There is less data loss compared to the rejection method.
- Training: The system is trained to identify and deal with common artifacts.

Weak artifacts, such as from cardiac activity, are ignored as their effect is assumedto be minor.

Ocular artifacts are ignored in most cases because they are assumed to have minimal impact on signal processing methods. Although this assumption is not correct, rejection results in large amounts of data loss. But because it is computationally hard, rejecting is preferred [28].

The presence of muscles close to the electrodes on a scalp EEG is the reason why muscle artifacts are common. Rejection is not an option as removing channels from the analysis may result in information loss. Lifting is a better solution, but it is a difficult task because muscle artifacts frequencies overlap with normal and seizure EEG frequencies, especially in the 15-20 Hz range. Muscle artifact separation uses wavelet filters instead of conventional filters because they avoid distortion effects. Periods of heavy muscle artifact may be completely dismissed [28]. More complex detection algorithms use strategy 4 and

selectively train the system to deal with artifacts.

2.1.2 Feature extraction

Feature extraction is the step in which statistics or features required for seizure detection is extracted from the data. The feature extraction done at this stage is important for classification. It is the key to classification performance.

2.1.2.1 Time domain analysis

Time-dependent forecasting features are known as time-domain analysis. For the classification of epileptic EEG, the time-domain analysis checks the characteristics such as an increase in amplitude, regularity, and synchronicity observed during epileptic events [28].

Amplitude (energy) and variance (strength) of the signal

The instantaneous amplitude of a signal at n instants is given as $|y[n]|$. The amplitude of the signal is also called the energy of the signal. The square of the amplitude value of signal ($|y[n]|^2$) gives the variance of the signal. The instantaneous energy of the signal does not give much information about unobservable waveforms as the entire signal cannot be observed. Therefore, it is preferable to take the average energy of the signal. The average of the signal is given as:

$$\mu_y(k) = \frac{1}{N}\sum_{n=k+1}^{k+N} y[n] \quad (5)$$

where $\mu_y[k]$ is the mean of the sequence $y[n]$ of length N starting at time k.

The variance $y[n]$ of a signal gives an idea of the spread and regularity of the signal by calculating how much it deviates from its mean. The variance of a signal is calculated as:

$$\sigma_y^2(k) = \frac{1}{N-1}\sum_{n=k+1}^{k+N}(y[n] - \mu_y[k])^2 \quad (6)$$

where $\sigma_y^2[k]$ is the variance of an N long string $y[n]$, and $\mu_y[k]$ is the mean of the signal. The square root of the variance $\sigma_y[k]$ is known as the standard deviation [28].

Periodicity (Auto Correlation)

The autocorrelation function provides information on how many times a signal repeats itself. It can often be used to describe regularity. For a real $y[n]$ signal, the autocorrelation function is defined as:

$$CORR_y[\tau, k] = \frac{1}{N}\sum_{n=k+1}^{k+N} y[n+\tau]y[n], \quad 0 < \tau < N\,, \ \tau = 0 \quad (7)$$

In autocorrelation, comparison of autocorrelations between functions of different sizes is not correct, since scaling is not performed at equal intervals. Duringa seizure, there is an increase in regularity often observed on the EEG, wherethe signal becomes more oscillating. Therefore, autocorrelation is used to detect seizures. [28].

Synchronization

Synchronization gives information about how similar the signals are to each other. It is calculated similarly to auto-correlation except that it is applied to two differentsignals (y_1 and y_2) [28].

$$CORR_{y_1,y_2}[\tau,k] = \frac{1}{N}\sum_{n=k+1}^{k+N} y_1[n+\tau]y_2[n], \quad 0 < \tau < N\,, \;\; \tau = 0 \qquad (8)$$

Root Mean Square (RMS)

The square root of the mean square (RMS) is defined as the arithmetic mean of thesquares of a set of numbers. The RMS is also known as the quadratic mean. If thesignal is periodic and sinusoidal, the RMS value is close to zero [36].

$$RMS = \sqrt{\frac{1}{N}\sum_{i=1}^{N} x_i^2} \qquad (9)$$

Mean

It is the mean of the amplitude values of the signal. If the signal is regular, valuesclose to zero are expected [93].

$$Mean = \frac{1}{N}\sum_{i=1}^{N} x_i \qquad (10)$$

2.1.2.2 Frequency domain analysis

Frequency is a measure of how often an event occurs in a unit of time. EEG signals contain events occurring at different frequencies. These differences may not bevisually obvious because they overlap in the time domain. For frequency analysis ofsignals, signals are examined in the frequency domain using the Fourier transform.

The Fast Fourier Transform (FFT) for discrete-time finite time-domain signals $y[n]$ is given as in the following equation with $k+2...k+N$ of an arbitrary windowed signal for $n = k + 1$ [28].

$$FFT[w,k] = \sum_{n=k+1}^{N} y[n+k]e^{-jwn},\; w = \frac{2\pi m}{N}\,,\;\; m = 0,1,2,\dots,N-1 \qquad (11)$$

In frequency domain transform, all information in the signal is preserved. In addition, the

signal can be converted back to the time domain using the inverse Fourier transform.

How much power each frequency contributes to the signal is calculated by its power spectral density (PSD). The PSD value of a signal is found by squaring the Fourier transform of the signal [28].

$$PSD[w,k] = |FFT[w,k]|^2 \quad (12)$$

PSD analysis is important for understanding the static and dynamic properties of EEG. Only PSD analysis is not sufficient for seizure detection. Synchronization, periodicity, the energy of the signal, and the strength of the signal should also support frequency domain analysis [28].

The time-domain and the frequency-domain analyzes contain the same information. But they differ in the features they emphasize. Therefore, it is important to obtain the same results in both analyzes.

2.1.2.3 Time-Frequency domain analysis

There are many methods such as Wigner-Ville distributions, wavelet analysis, and Gabor atoms, which are used in both time and frequency analysis for non-stationarysignals [28].
Wavelet analysis functions $\Psi[n]$;

A. Zero integrated

$$\sum_{n=-\infty}^{\infty} \Psi\,[\mathrm{n}] = 0 \quad (13)$$

B. Has limited power

$$\sum_{n=-\infty}^{\infty} |\Psi\,[\mathrm{n}]|^2 < \infty \quad (14)$$

Wavelets can be used as basis functions to provide a combination of both temporal and frequency information.

$\Psi_{ab}[n]$ is the wavelet function sampled by b in the function and scaled by a. This function is given as:

$$\Psi_{ab}[n] = \frac{1}{\sqrt{a}} \Psi\,[\frac{n-b}{a}] \quad (15)$$

When $a = 1$, $b = 0$, $\Psi_{10}[n]$ is called main wavelet. If the scaling value "a" is between 0 and 1 (0<a<1), contraction occurs over time. If a>1, extension occurs over time. Scaling values allow finding different resolutions in time and frequency ofcontent [28].

Wavelet transformation is required to perform the frequency and time domain analysis of a signal $y[n]$ with wavelet analysis. The wavelet transform $W_{ab}[n]$ can be defined as:

$$W_{ab}[n,k] = \sum_{\tau=k+1}^{k+N} y[k]\Psi_{ab}[n,\tau], \quad k+1 < n < k+N \qquad (16)$$

In the wavelet transform of the signal $y[n]$, information can be obtained only about the frequencies in the same band as $\Psi_{ab}[n]$. This operation is known as the convolution operation. The signal is filtered to obtain the information about the desired frequencies in the signal [28].

2.2 Non-Linear Signal Analysis Methods

RMS and mean values are useful for extracting information from the signal produced by a linear system. Linear signal analyzes are preferred due to the ease of application and simplicity of the theory. More information about the signal can be obtained by nonlinear signal analysis. An important problem in nonlinear analysis is the noise of the signal. For better and more accurate results, nonlinear analysis methods should be applied after the signal becomes a noise-free signal. Nonlinear analysis methods can be divided into three categories. The first one is the size property, which gives an idea of how complex a system is; the second one is the property of Lyapunov bases, which gives an idea of how predictable a system is; and the thirdone is the entropy property, which gives an idea of how random a system is [28]. Inthis study, we have chosen to analyze the entropy property of the signal to predictthe seizure some time ago using the disorderedness of the signal.

Entropy was first used in thermodynamics to provide information about the disorder of a system. It is also a measure of randomness and can be calculated based on different properties of the signal. In general, it gives information about the disorderand regularity of the entire system of entropies.

In the literature, researchers have applied different entropy methods such as Shannon entropy, distribution entropy, approximate entropy, permutation entropy, sample entropy, fuzzy entropy, sigmoid entropy, spectral entropy, and transfer entropy [43–54]. In this study, 5 different entropy methods were used. The first entropy method used is Shannon entropy, which uses the amplitude value of the signal as aprobability. The second is sample entropy, which measures the regularity of physiological signals regardless of their length. The third is permutation entropy, which is one of the embedded types of entropy that directly uses time series in entropy calculations. The fourth is approximate entropy, which uses previous amplitude valuesto measure the predictability of the current amplitude value. And finally, the fifth isspectral entropy, which measures in which bands the frequency distribution of

the signal is intense.

2.2.1 Shannon entropy

In the late 1940s, Shannon took the amplitude of the signal as a probability for the data transmission unit and applied it to the concept of entropy [94].

Let's define the Shannon entropy (ShEn) of a discrete probability distribution $p(k) \in [0, 1]$; where k is the number of different probabilities and p(k) is the probability of event K occurring [28]:

$$H_q[n, \in] = -\sum_{k=1}^{K} p(k) log_2 p(k) \quad (17)$$

To define entropy in bits, the logarithm is taken in base 2. Here, the probabilityp(k) of event K for the sequence $y[n]$ is calculated as [28]:

$$p(k) = \frac{Time\ that\ y[n] is\ in\ bin\ k}{Total\ lenght\ of\ y[n](N)} \quad (18)$$

High entropy values are observed when signals have a wide and flat probability distribution, and low entropy values are observed if they have a narrow and peaked distribution.

2.2.2 Sample entropy

Sample entropy (SmpE) is a method of measuring the regularity of physiological signals regardless of their length. The SmpE(m,r,n) value can be defined as the negative logarithm of the similarity probability of the tolerance value (r) for the points (m) in any time series of length n. The sample entropy formula is given as [95]:

$$SmpE\ (m, r, n) = -log \frac{A}{B} \quad (19)$$

where m is the length of the arrays to be compared, r is the tolerance value toaccept matches, and n is the length of the original data. A and B are defined as follows:

$$A = \frac{(n-m-1)(n-m)}{2} A^m(r),\ B = \frac{(n-m-1)(n-m)}{2} B^m(r) \quad (20)$$

where $A^m(r)$ is the probability that the two sequences will match for the $m + 1$points and $B^m(r)$ is the probability that the two sequences will match for the m point.SmpE is consistent for each (m, r) value to be selected [95]. This situation has beeneffective in the preference of sample entropy in the selection of entropy.

2.2.3 Permutation entropy

Another method for assessing complexity in time series is permutation entropy (PE), which is based on a comparison of neighboring values. In permutation entropy, low noise in the signal does not affect the complexity of the chaotic signal. In this entropy, fast and robust information can be obtained as calculations can be made on very large data sets without the need for preprocessing of parameters [96].

Calculating permutation entropy is given as follows [97]:

Step 1: The first step in calculating permutation entropy is to transform a onedimensional time series into a matrix of overlapping column vectors. Two parameters are used for this step. First, the embedding time delay τ controls the number of time periods between elements of each of the new column vectors. It is recommended to select 1. Second is the embedding dimension, which controls the length of each of the M new column vectors. It is recommended to select in the range of $3 \leq M \leq 7$. For $\tau = 1$ and M=3, the matrix created from the example array x(t) = {4,7,9,10,6,11,3}:

$$\begin{matrix} 4, & 7, & 9, & 10, & 6, \\ 7, & 9, & 10, & 6, & 11, \\ 9, & 10, & 6, & 11, & 13, \end{matrix} \tag{21}$$

The number of items to be found in the columns is determined by the embedding size M. How many columns will be in the matrix is determined by the calculation of $T - (M - 1)\tau$. T is the length of the vector $x(t)$. Also, since the time delay τ is selected as 1, there is a time interval between the elements.

Step 2: In order to calculate the similarity of the columns in the matrix created, permutation vectors of size M up to $M!$ are generated. 3! = 6 the permutation vectors generated for:

$$\begin{matrix} \pi_1 = 0, 1, 2 \\ \pi_2 = 0, 2, 1 \\ \pi_3 = 1, 0, 2 \\ \pi_4 = 1, 2, 0 \\ \pi_5 = 2, 0, 1 \\ \pi_6 = 2, 1, 0 \end{matrix} \tag{22}$$

Step 3: It is necessary to calculate the match ratios of the permutations with the columns in the matrix. For this, each value in the column is restructured according to its magnitude:

$$\begin{matrix} 0, 0, 1, 1, 1 \\ 1, 1, 2, 0, 2 \\ 2, 2, 0, 2, 0 \end{matrix} \tag{23}$$

If there are two or more elements with the same value in the column, the sorting is based on the positions of the elements in the array.

Step 4: The relative frequency of a permutation is calculated by dividing the number of columns that matches by the total number of columns.

Table 2.1: The relative frequencies of the generated permutations.

Permutation	N. of Matching Columns	p_i
π_1	2	2/5
π_2	0	0/5
π_3	1	1/5
π_4	2	2/5
π_5	0	0/5
π_6	0	0/5

Step 5: Finally, Equation (25) is used to calculate the PE of order *M* of the signals:

$$PE_M = -\sum_{i=1}^{M!} p_i log_2 p_i \quad (24)$$

$$PE_3 = -(2/5\ log_2 2/5 + 1/5\ log_2 1/5 + 2/5\ log_2 2/5) = 1.5219 \quad (25)$$

PE can be normalized and limited to the range $0 - 1$. 28 equations are used for the normalization PE value [97].

$$PE_{M,norm} = -(\frac{1}{log_2 M!}) \sum_{i=1}^{M!} p_i log_2 p_i \quad (26)$$

The embedded parameter, M , should be chosen between $3 - 7$ in order to distinguish the stochastic and deterministic features of the signal. In this study, M is chosen as 3. PE values are in the range of $0 - 1$. In a regular time series, the PE value is close to zero, whereas in an irregular and random time series, the PE value is close to 1. Since the EEG series becomes regular during the seizure, the PE value is close to zero during the seizure.

2.2.4 Approximate entropy

Another way to learn about the amount of regularity and unpredictability of the fluc tuations in the time series of data is the Approximate entropy (ApEn). ApEn was developed by Steve M. Pincus by changing the Kolmogorov-Sinai entropy. It was originally developed for the analysis of medical data such as heart rate. Moreover, it was applied in fields such as finance, physiology, human factors engineering, and climate

sciences [98].

The steps to calculate the approximate entropy are as follows [98]:

Step 1: Time series data $u(1), u(2), \ldots, u(N)$ consisting of N raw data values obtained from equally spaced measurements over time is created.

Step 2: r is the filtering level and m is the length of the data being compared.

Step 3: $x(i) = [u(i), u(i+1), \ldots, u(i+m-1)]$ defined by $x(1), x(2), \ldots, x(N-m+1)$ vector array is created.

Step 4: The set $\{x(j)\}$ represents the sequences $x(j)$, where $j = 1, .., N-m+1$. Each value of $x(j)$ in set $\{x(j)\}$ is compared with the value of $x(i)$:

$$C_i^m(r) = (number\ of\ x(j)\ such\ that\ d[x(i), x(j)] \leq r)/\ (N - m + 1) \quad (27)$$

where the d value represents the maximum distance between $x(i)$ and $x(j)$.

$$d[x, x^*] = max_a\ |u(a) - u^*(a)| \quad (28)$$

Step 5: For the calculation of ApEn, the parameters $\Phi^m(r)$ and $\Phi^{m+1}(r)$ are defined as follows:

$$\Phi^m(r) = (N - m + 1)^{-1} \sum_{i=1}^{N-m+1} log(C_i^m(r)) \quad (29)$$

$$\Phi^{m+1}(r) = (N - m + 1)^{-1} \sum_{i=1}^{N-m+1} log(C_i^{m+1}(r)) \quad (30)$$

Step 6: ApEn(m,r,N) is defined using $\Phi^m(r)$ and $\Phi^{m+1}(r)$:

$$ApEn(m, r, N) = \Phi^m(r) - \Phi^{m+1}(r) \quad (31)$$

The m value is usually chosen as 2 or 3, while the r value is application dependent [98].

2.2.5 Spectral entropy

Spectral entropy(SE) is a modified method by using power spectral energy instead of amplitude values used as a probability in Shannon entropy. It is a measure of the spectral complexity present in the signal [99]. A low spectral entropy value means that the frequency distribution is dense in some frequency bands [100]. The Fouriertransform of the signal x(i), i =1,2,..,N is X(i). In spectral entropy calculation, X(i) value is considered as probability. Spectral entropy equation (32) is defined as in [101] :

$$SE = -\sum_{i=1}^{N} p_i\ log_2 p_i \quad (32)$$

$$p_{i=\frac{x(i)}{\sum_{j=1}^{N} x(j)}} \quad (33)$$

The spectral entropy is normalized to minimize the effects of data lengths. Normalized Spectral entropy is:

$$SE = -\frac{1}{log_2 N}\sum_{i=1}^{N} p_i \, log_2 p_i \quad (34)$$

Spectral entropy gives the maximum value of 1 when the amplitude distribution of the signal is flat, especially when the amplitude values of the frequency component in each frequency band are equal. Otherwise, if the amplitude distribution is summed in only one frequency component, the spectral entropy returns the minimum value of 0, especially where only one frequency component has a nonzero amplitude value. The equation in this case 34 the spectral entropy range is definedbetween [0,1] [101].

3. FINDINGS AND DISCUSSION

In this thesis study, two different data sets are used: Bonn University EEG data and EEG data collected from Boston Children's Hospital (CHB-MIT) [102, 103]. Bonn University data belong to 5 different data sets and 5 different patients. Data were recorded using a 10-20 electrode system. Information about these sets is in Table 3.1 below:

Table 3.1: University of Bonn EEG datasets.

Set Name	Feature of the set
A set	Normal EEG data recorded from normal individuals with eyes open
B set	Normal EEG data recorded from normal individuals with eyes closed
C set	Epileptic EEG data obtained from epilepsy patients from the hippocampal region of the brain between seizures
D set	Epileptic EEG data recorded between seizures from an epileptogenic region from epilepsy patients
E set	EEG data recorded during an epileptic seizure

The raw data of the University of Bonn is shown in Figure 3.1 and the electrode design is shown in Figure 3.2.

In addition, CHB-MIT EEG data collected from the Boston children's hospital were also used. There are 23 subjects 5 men from 3-22 years old and 17 women from 1.5-19 years old. The EEG data in files 1 and 21 belong to the same person (subject) but they were recorded at different times. Case chb24 was added to this data in December 2010 and is not a currently known piece of information about the patient. Table 3.2 contains information about the gender and age of CHB-MIT patients. EEG signals of 24 patients (subjects) with a 256 Hz sampling rate of 23 channels were recorded as FP1-F7 (1), F7-T7 (2), T7-P7 (3), P7-O1 (4), FP1-F3(5), F3-C3 (6), C3-P3 (7), P3-O1 (8), FP2-F4 (9), F4-C4 (10), C4-P4 (11), P4-O2(12), FP2-F8 (13), F8-T8 (14), T8-P8 (15), P8-O2 (16), FZ-CZ (17), CZ-PZ (18),P7-T7 (19), T7-FT9 (20), FT9-FT10 (21), FT10-T8 (22) and T8-

P8 (23). The places of electrodes are labeled as FP: frontopolar, F: frontal, T: temporal, O: occipital, C: central, and P: parietal [103]. In Figure 3.3, the raw EEG data of a 19-year-old female patient, and in Figure 3.4 the electrode design used is shown.

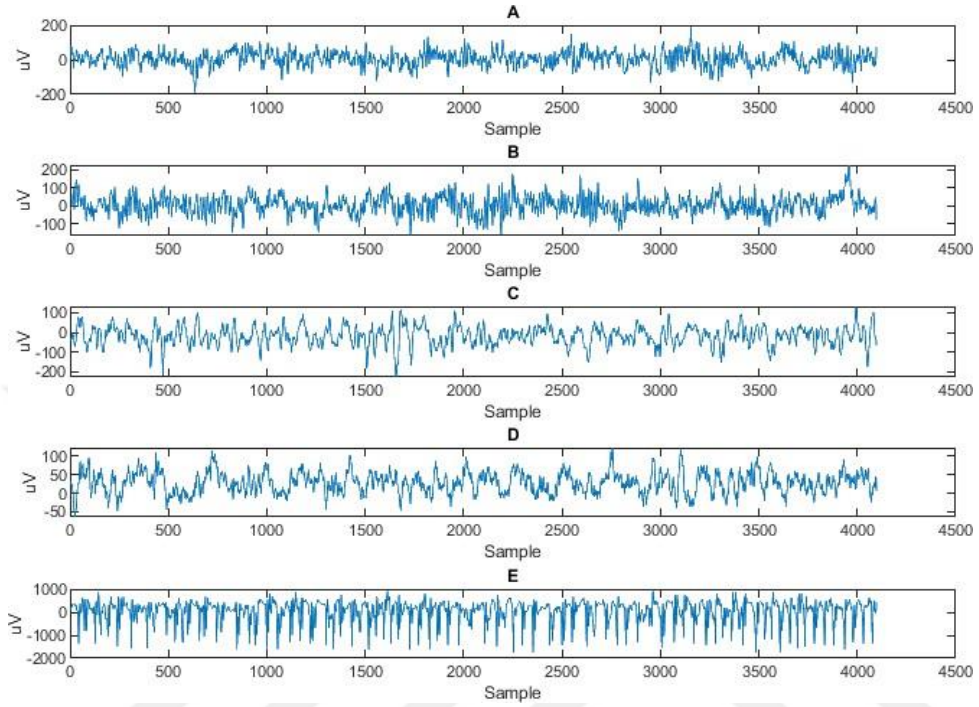


Figure 3.1: University of Bonn raw EEG data.

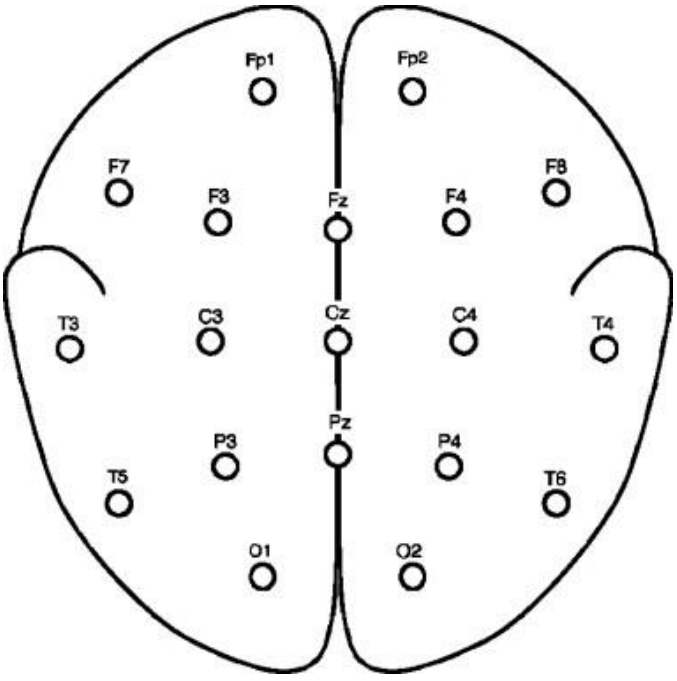


Figure 3.2: Electrode design used in University of Bonn data [102].

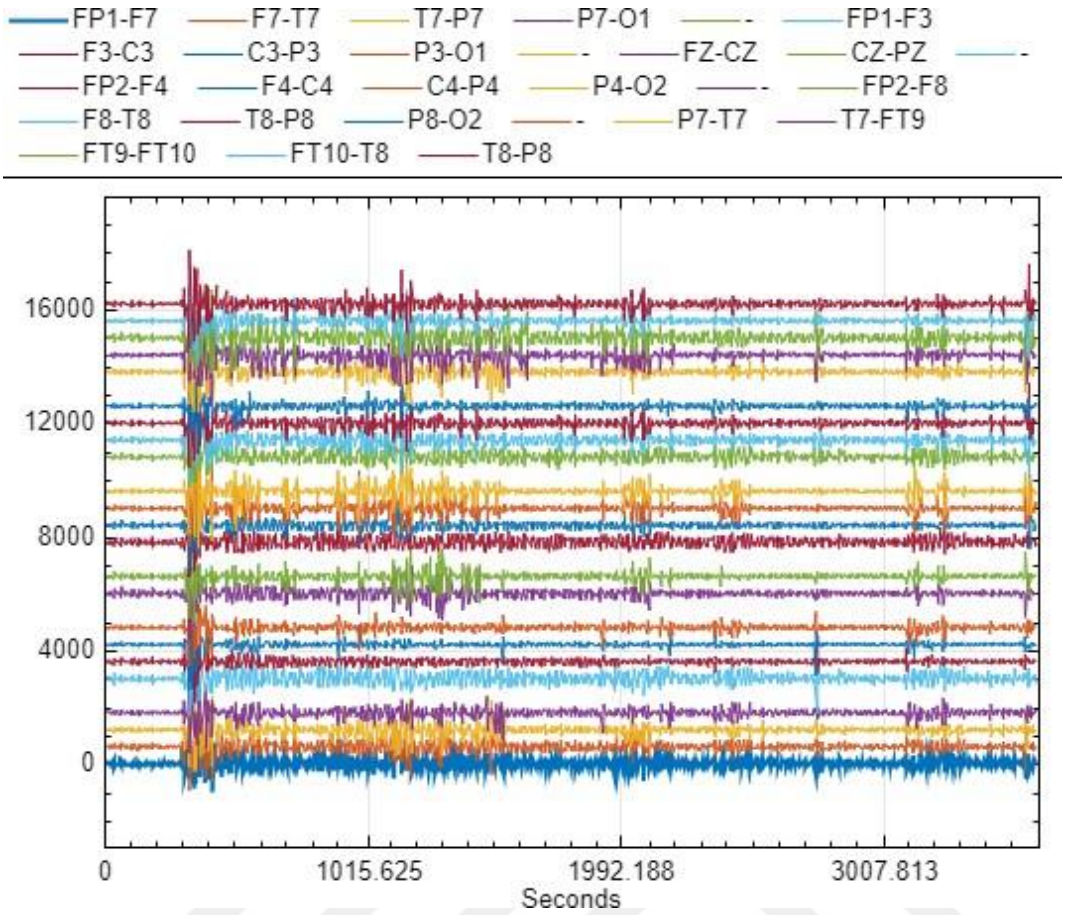


Figure 3.3: Raw EEG data of a 19-year-old female patient from the CHB-MIT database. The signals are separated at 600 uV size.

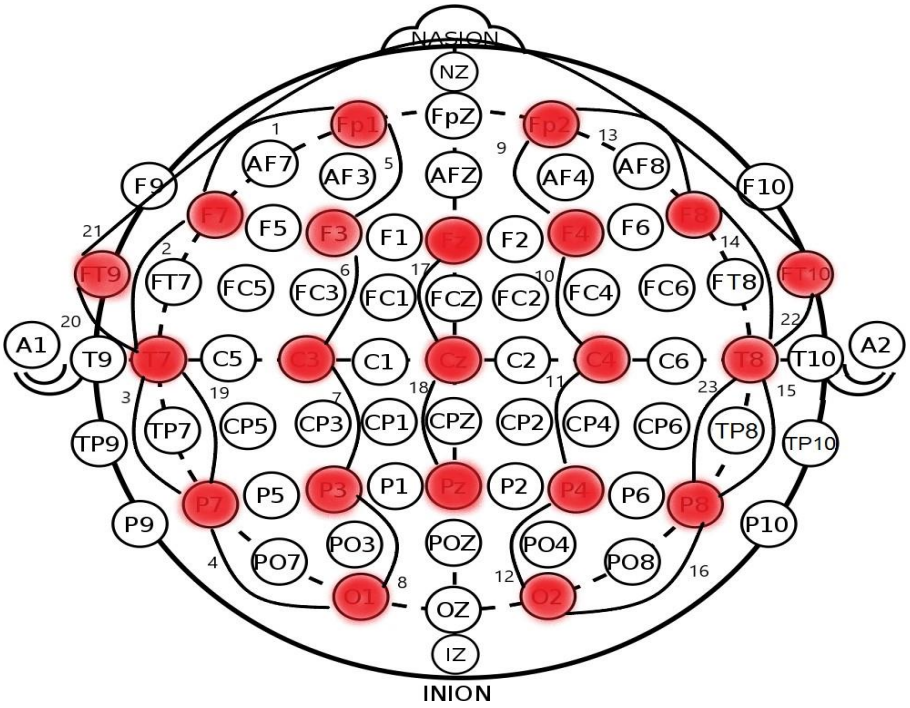


Figure 3.4: Electrode diagram of CHB-MIT data.

Table 3.2: Gender and age of CHB-MIT patients.

Patient	Gender	Age (Years)
chb01	F	11
chb02	M	11
chb03	F	14
chb04	M	22
chb05	F	7
chb06	F	1.5
chb07	F	14.5
chb08	M	3.5
chb09	F	10
chb10	M	3
chb11	F	12
chb12	F	2
chb13	F	3
chb14	F	9
chb15	M	16
chb16	F	7
chb17	F	12
chb18	F	18
chb19	F	19
chb20	F	6
chb21	F	13
chb22	F	9
chb23	F	6

Using the University of Bonn data, it was tried to distinguish between healthy EEG signals and epileptic EEG signals with linear analysis methods. In non-linear analysis methods, the data of the Boston Children's Hospital, which contains both preictal and ictal data in a file, were used to detect epileptic activity. It is aimed to determine how few electrodes can be differentiated in the University of Bonn data. To do this, the signals obtained from the electrodes around the ear were examined based on vagal nerve stimulation and in-ear EEG recordings.

In this study, EEG signals recorded from T7, T8, P7, and P8 electrodes located around the ear in the 10-20 electrode system were analyzed.

Steps of time-domain analysis are given as follows :

- A 40 Hz low-pass filter is applied.
- A median filter is applied to filter out the DC noise in the signals.
- The difference signal is created by subtracting the filtered EEG signal from thenormal EEG signal.
- The difference signal has been developed to be free of noise.
- Half of the maximum amplitude value found in the developed signal is acceptedas the threshold value. The peaks that exceed this threshold value are plottedin the signal.

The number of peaks crossing the threshold gives the spike rhythmicity and the maximum amplitude value of the spikes crossing the threshold gives the relative peak amplitude.

Healthy EEG and epileptic EEG signals from the T3 electrode are shown in Figure 3.5 and Figure 3.6, respectively. The one-second representations of these signals are given in Figure 3.7 and Figure 3.8, respectively.

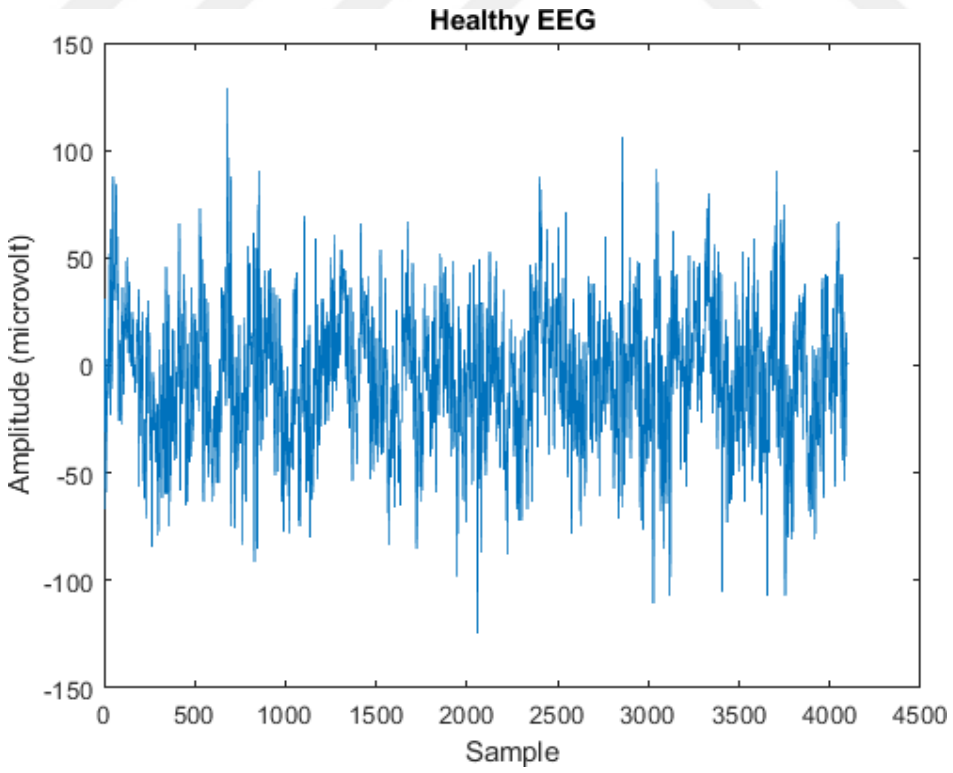


Figure 3.5: Healthy EEG signal from T3 electrode.

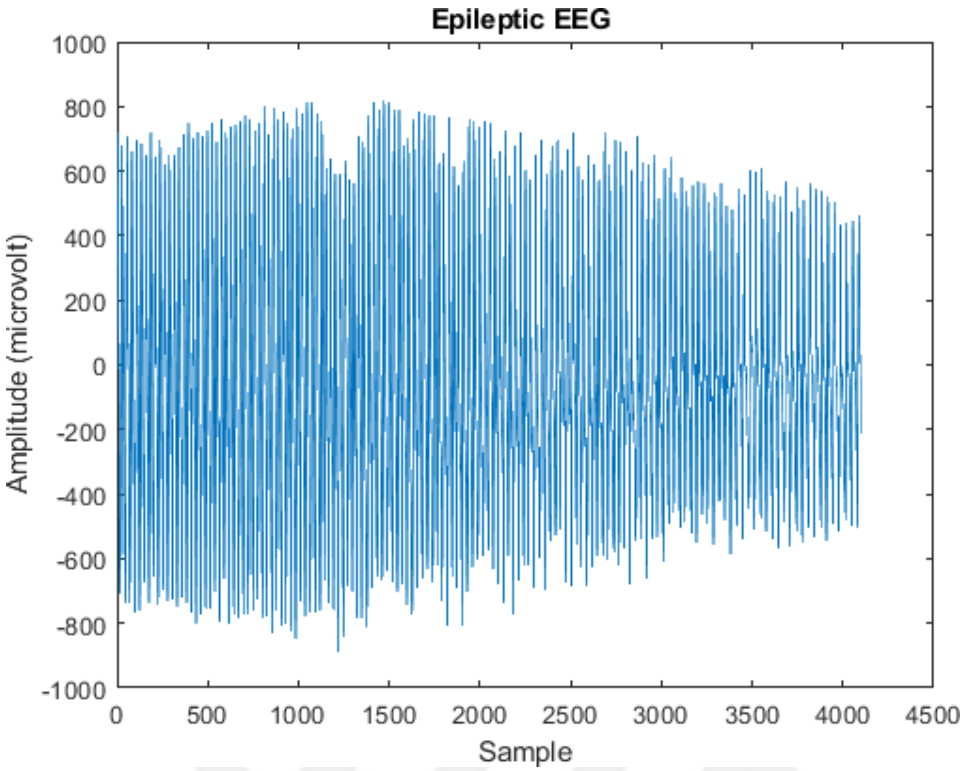


Figure 3.6: Epileptic EEG signal from T3 electrode.

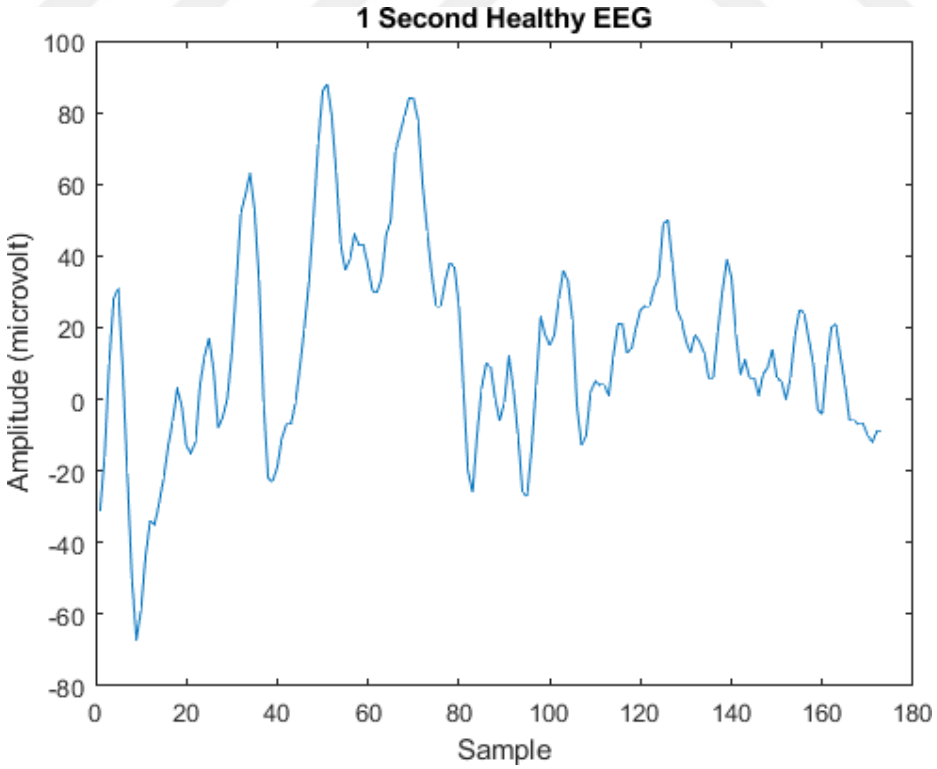


Figure 3.7: A one-second view of the healthy EEG signal received with the T3 electrode.

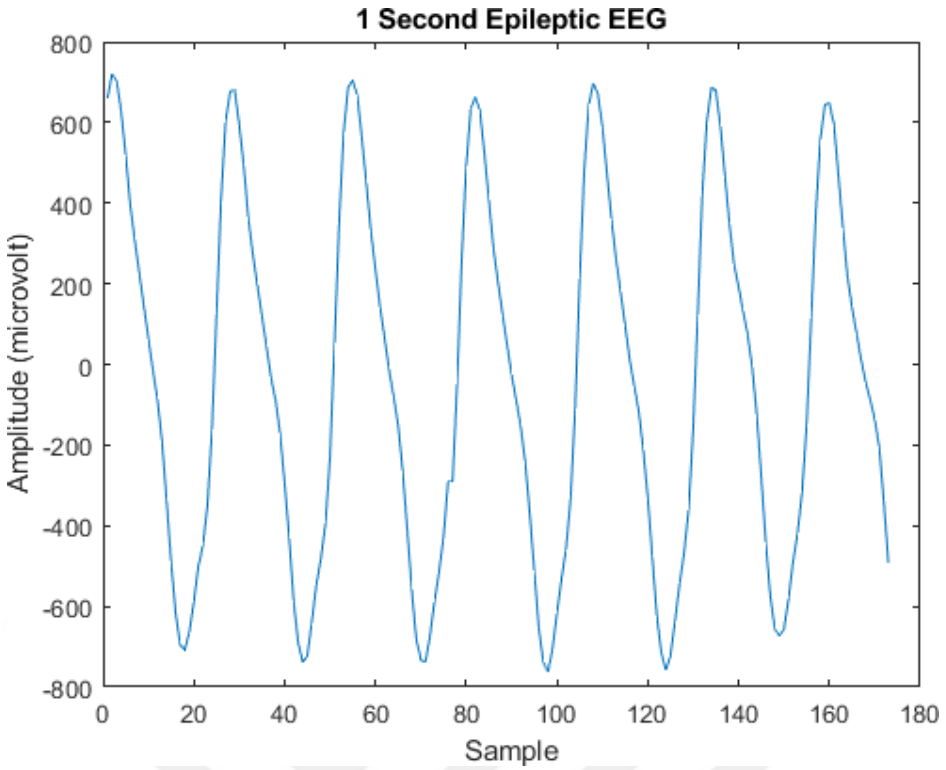


Figure 3.8: A one-second view of the epileptic EEG signal received with the T3 electrode.

With the time-domain analysis, the number of spikes that exceed the thresholdvalue in normal and epileptic EEG signals is 6 and 11, respectively. The spikes obtained by time-domain analysis are shown in Figure 3.9 and Figure 3.10, respectively.

In the epileptic signal, the number of peaks exceeding the threshold is higher. However, since healthy data and epileptic data are in different text files, the amplitude values of both signals are different. This causes a difference in threshold values. For this reason, such a comparison of the peak numbers that exceed the threshold value does not give us exact information.

In frequency domain analysis, the power spectral density (PSD) of the signals is calculated. The power spectral density of epileptic EEG signals is also much higher than that of healthy EEG signals. The power spectral density of the healthy and epileptic signals are given in Figure 3.11 and Figure 3.12, respectively.

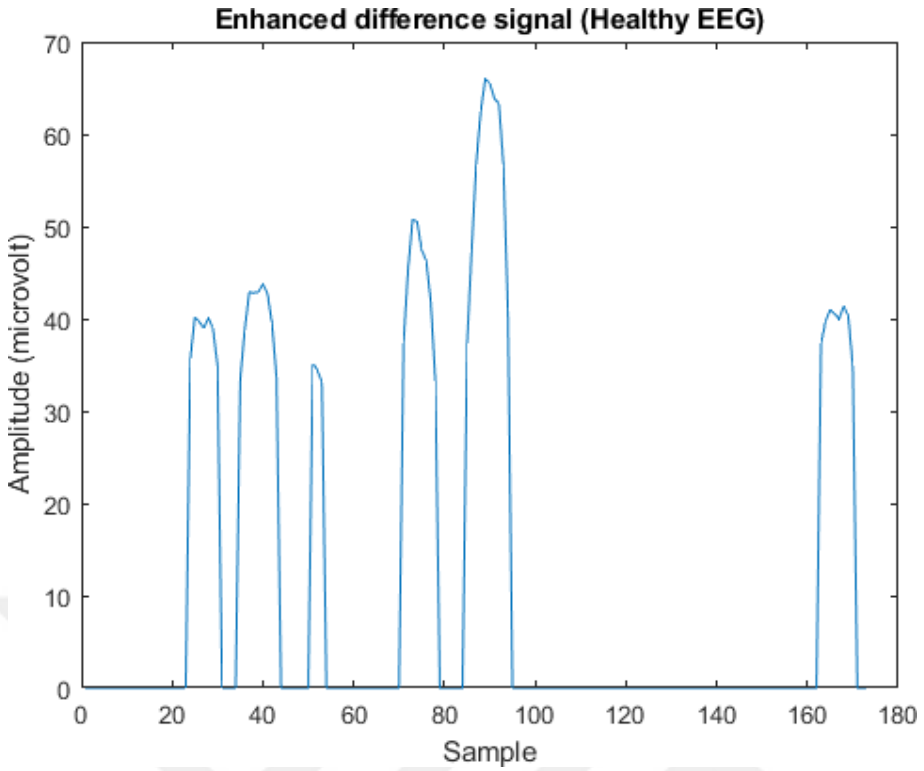


Figure 3.9: The spikes found in the healthy EEG signal received with the T3 electrode.

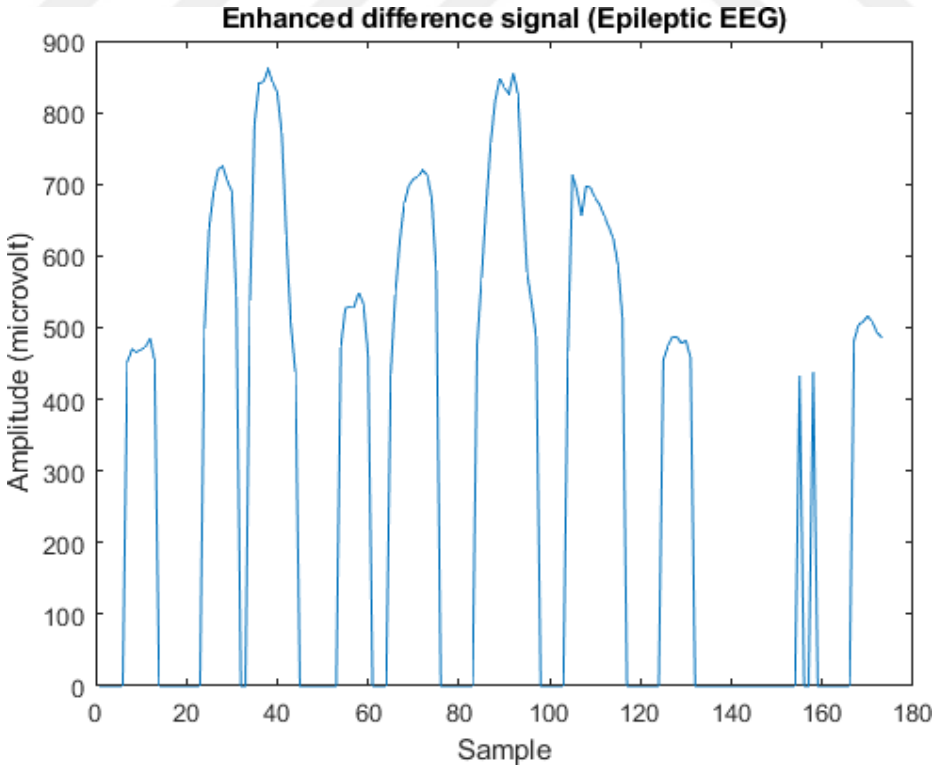


Figure 3.10: The spikes found in the epileptic EEG signal received with the T3 electrode.

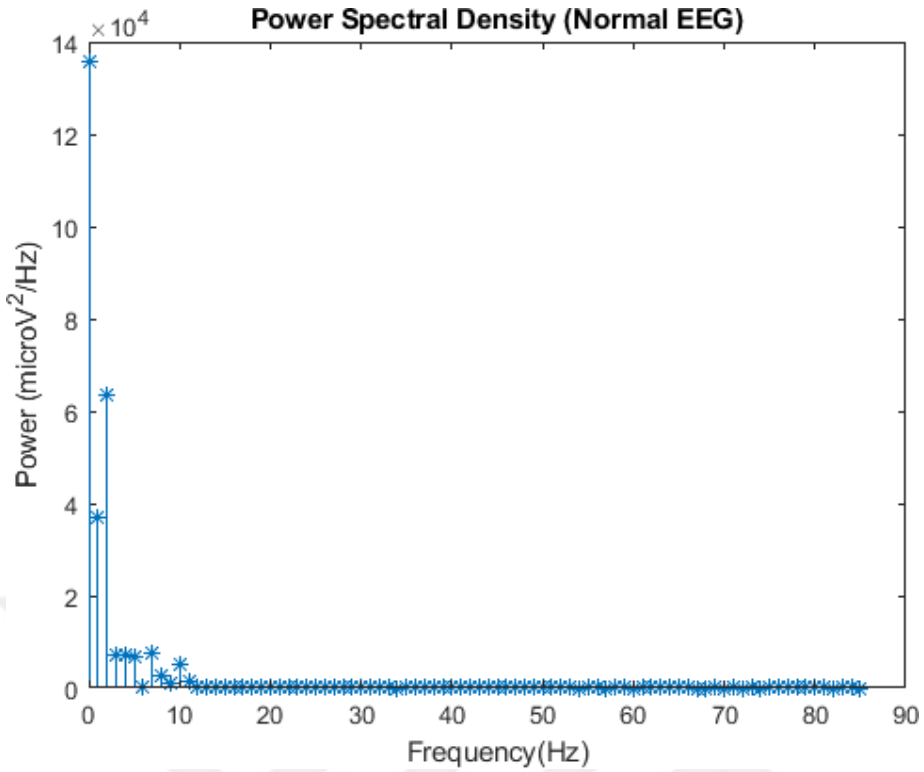


Figure 3.11: The spikes in the epileptic EEG signal received with the T3 electrode.

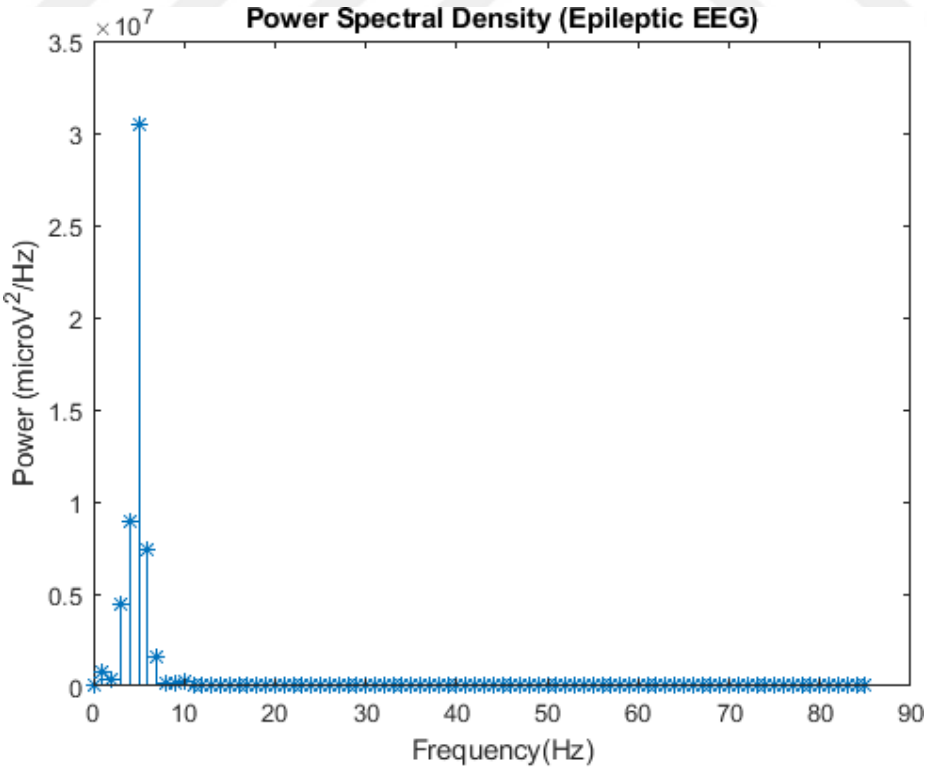


Figure 3.12: The spikes in the epileptic EEG signal received with the T3 electrode.

Linear analysis methods are generally statistical methods. The fact that the signals are in different text files in the University of Bonn data is a disadvantage in examining the differences. In the CHB-MIT data, the signals were recorded in a certain time period and the seizure deletions were marked, which makes the examinations easier. Therefore, in this study, the seizure period was tried to be determinedby the mean of the signal and the root mean square (RMS) value, which is one of the linear analysis methods in the time domain in the CHB-MIT data.

We calculated the RMS and mean values of the EEG signal of each channel of each patient (subject). It is known that statistical features are used to determine the seizure moment in the time domain from the linear analysis method. To see thechange in the seizure period more clearly, 5 minutes before and 5 minutes after the onset of the seizure EEG signals were taken from the patient.

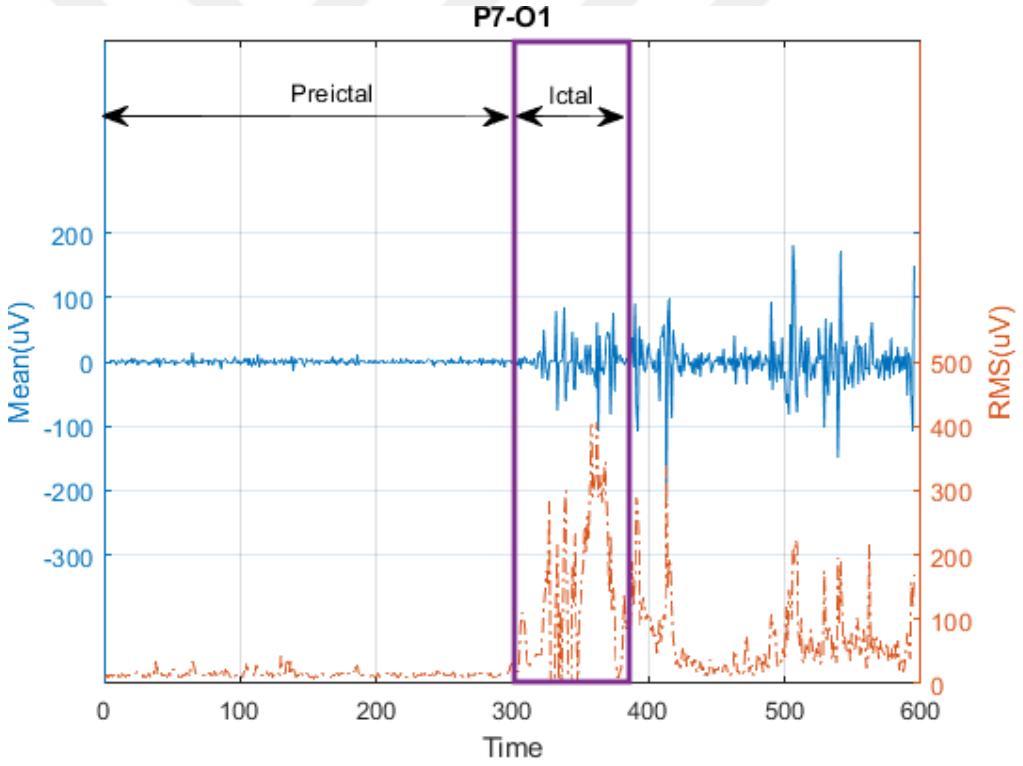


Figure 3.13: RMS and mean values of the P7-O1 channel of a 19-year-old female patient. The y-axis on the left side ofthe graph shows the mean values of the EEG signal in μV. The y-axis on the right shows the RMS value of the EEG signal in μV. The x-axis represents time. The ictal state representing the seizure is framed by purple.

As seen in Figure 3.13, the RMS value is higher in the ictal condition than in the preictal condition. In addition, the mean value, positive and negative aspects move away from zero. As seen in Figure 3.14, this situation is also seen in other channelsof the same patient.

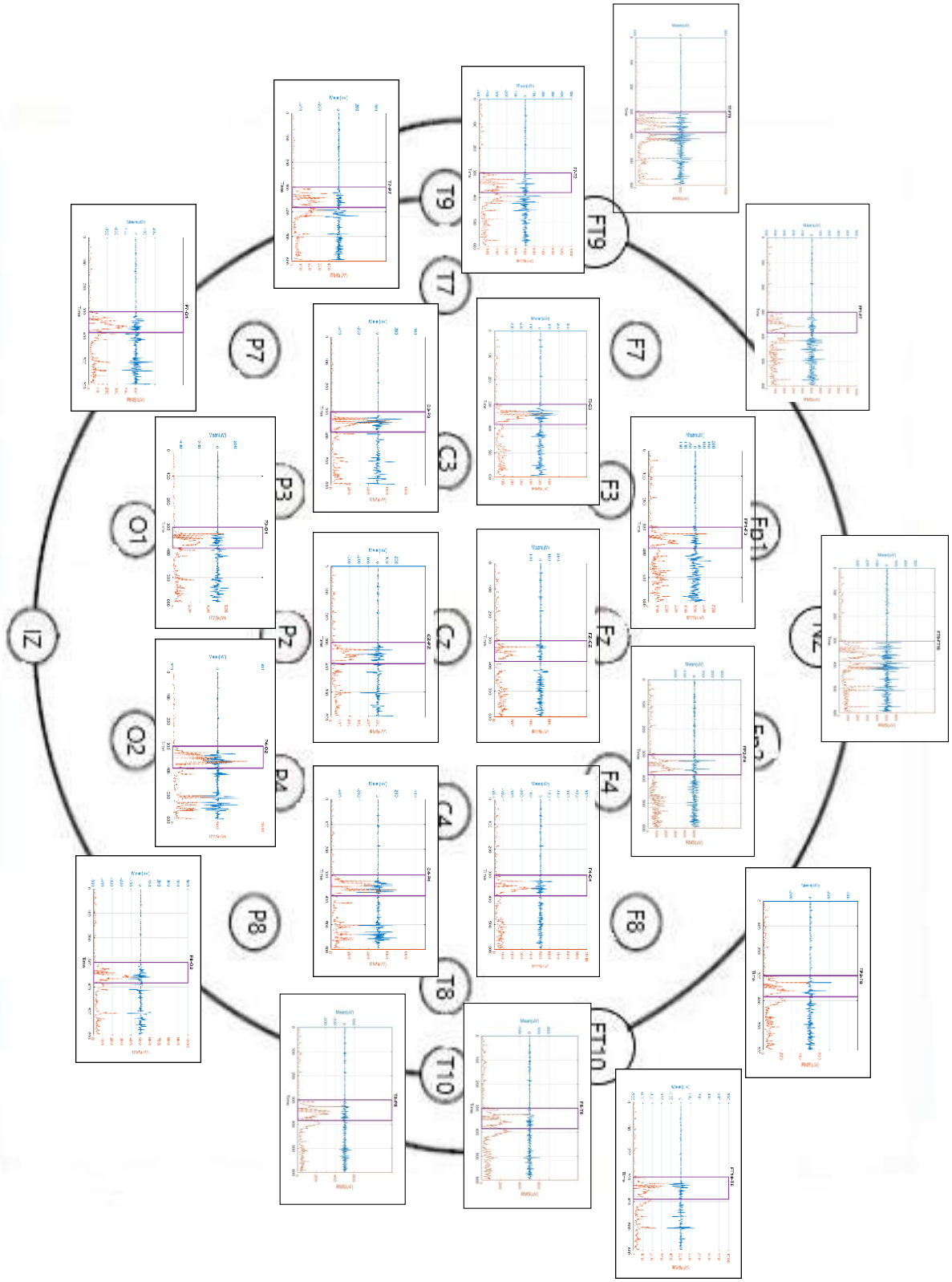
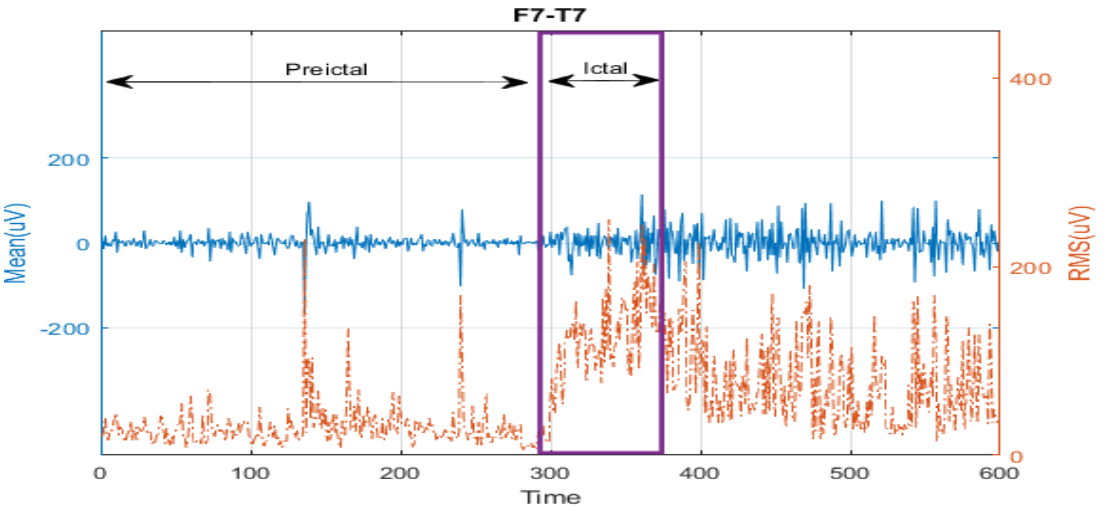
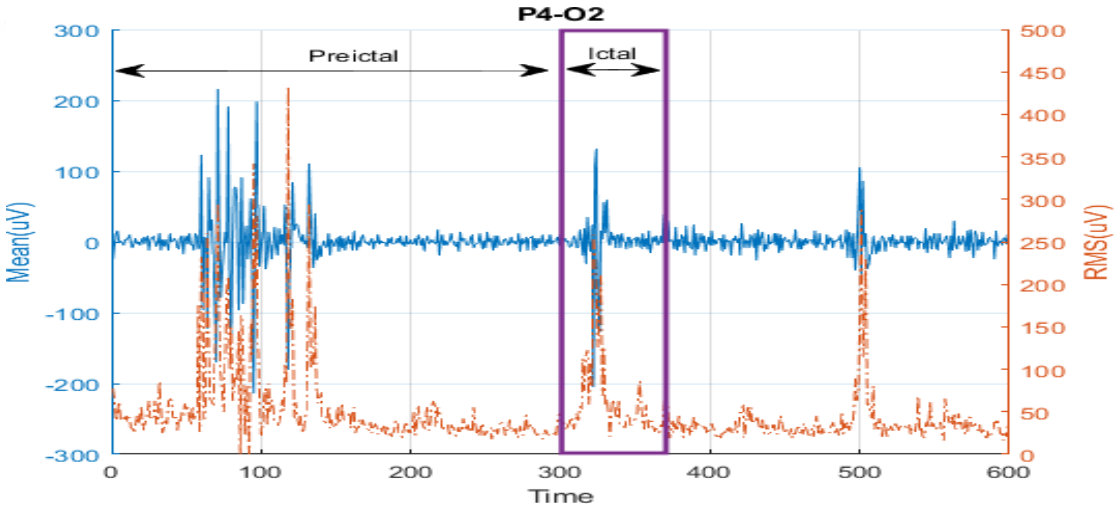


Figure 3.14: RMS and mean values of EEG data from all channels of a 19-year-old woman patient.



(a) F7-T7 channel of a 14-year-old female patient.

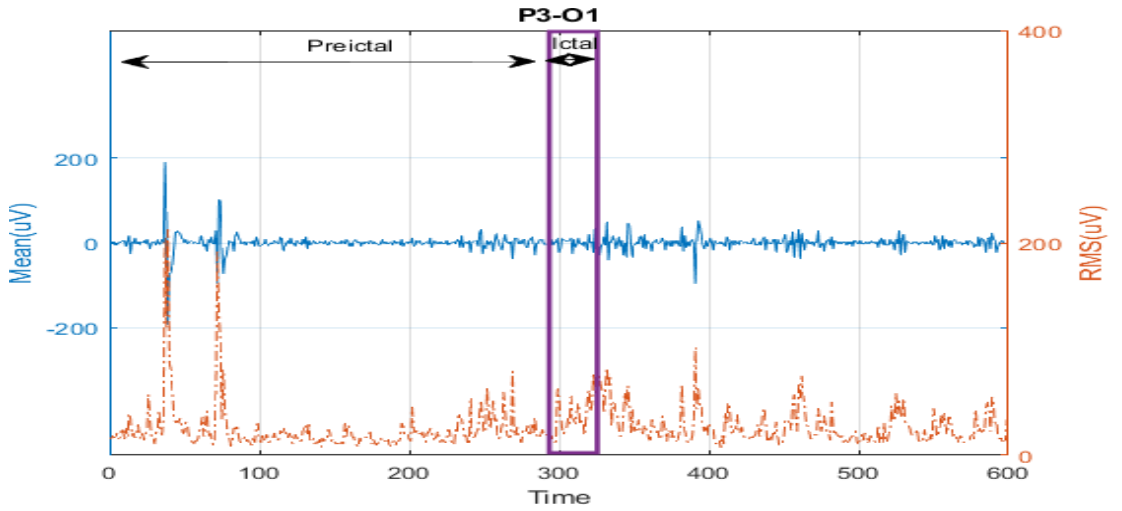


(b) P4-O2 channel of a 2-year-old female patient.

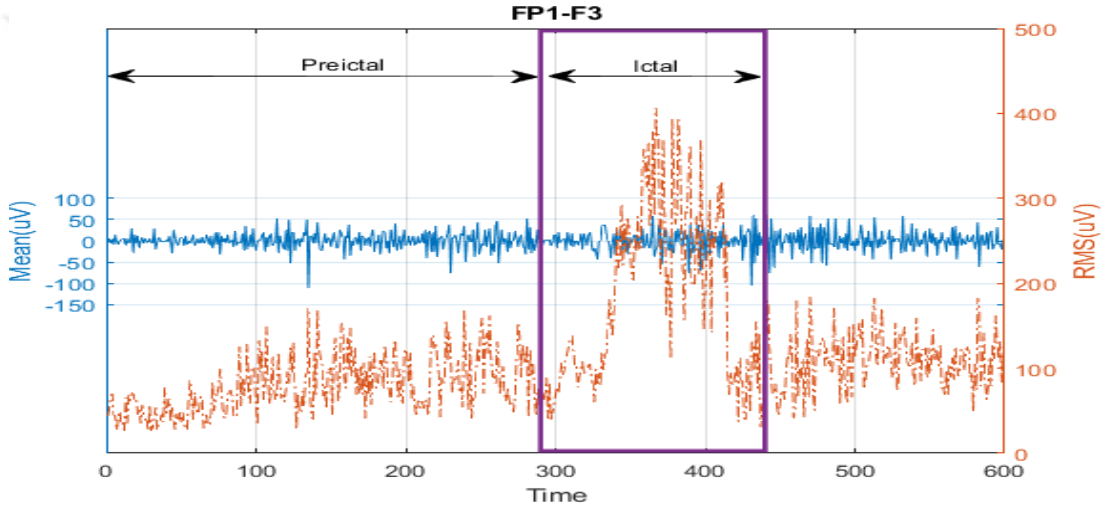
Figure 3.15: RMS and mean graphs from different channels of different patients.

Figure 3.15a shows the RMS and mean values of the F7-T7 channel of a 14- year-old female patient. In this graph, it is seen that the RMS value increases in the ictal state compared to the preictal state, and the mean value in the ictal state moves away from zero in positive and negative directions compared to the preictal state. In addition, it is observed that there is a change in the RMS value and the mean value 50 and 150 seconds before the onset of the seizure.

Figure 3.15b shows the RMS and mean values of the P4-O2 channel of a 2- year-old female patient. In this patient, an increase in RMS values and deviation from zero in the mean value are observed in the ictal state compared to the preictal state. More pronounced changes are seen up to 200 seconds before the onset of the seizure.



(a) P3-O1 channel of a 7-year-old female patient.

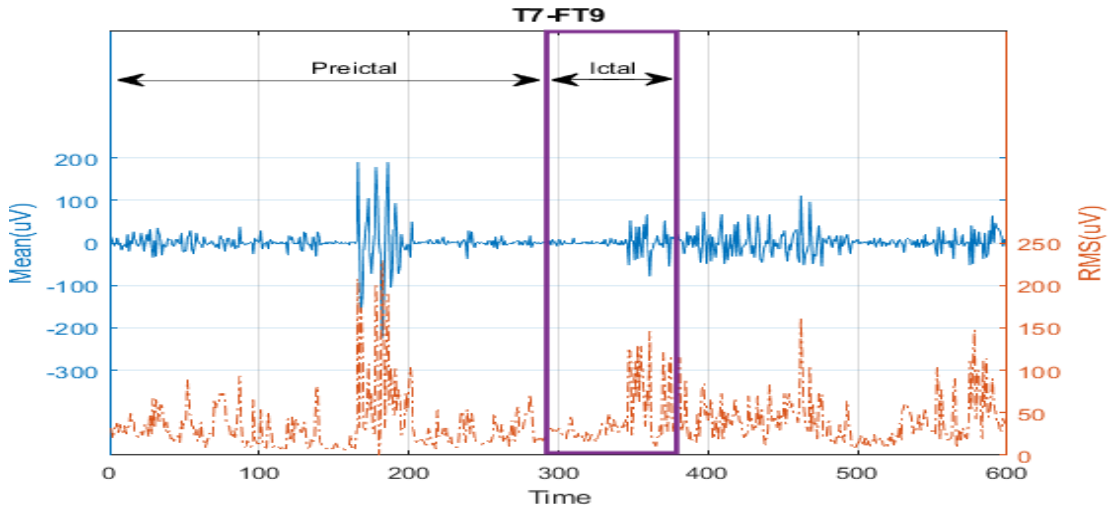


(b) FP1-F3 channel of a 7-year-old female patient.

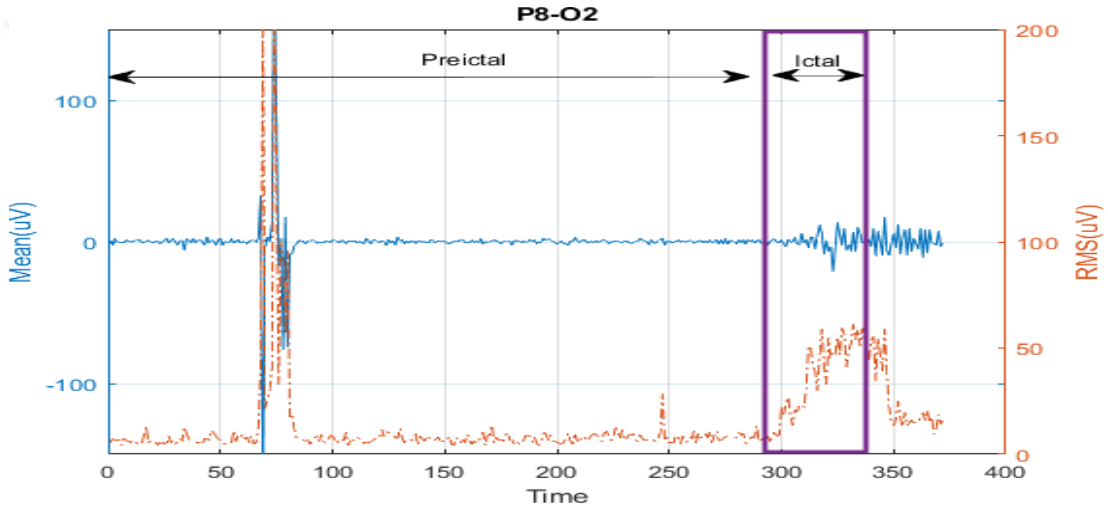
Figure 3.16: RMS and mean graphs from different channels of different patients.

Figure 3.16a shows the RMS and mean values of the P3-O1 channel of a 7- year-old female patient. This patient's RMS and means values in the ictal state are not distinguishable from the values in the preictal state. However, a change in RMS and mean values are observed approximately 250 seconds before the onset of theseizure.

Figure 3.16b shows the RMS and mean values of the FP1-F3 channel of another 7-year-old female patient. The RMS value increases in the ictal state compared to the preictal state. The difference between the mean value in the ictal state and the mean value in the preictal state is indistinguishable.



(a) T7-FT9 channel of a 22-year-old female patient.



(b) P8-O2 channel of an 18-year-old female patient.

Figure 3.17: RMS and mean graphs from different channels of different patients.

Figure 3.17a shows the RMS and mean values of the T7-FT9 channel of a 22- year-old female patient. Towards the end of the ictal region, changes in RMS and mean values are observed. In addition, changes in both RMS and mean values are observed approximately 100 seconds before the onset of the seizure.

Figure 3.17b shows the RMS and mean values of the P8-O2 channel of an 18- year-old female patient. In the ictal state, an increase in RMS values and a deviationfrom zero in mean values are observed. RMS and mean values change approximately 250 seconds before the seizure.

The patient data given in Figure 3.15, Figure 3.16, and Figure 3.17 were randomly selected to show the changes in RMS and mean values.

EEG signals are considered linear when using the RMS and mean methods. However, EEG signals are not linear. There are some information losses in the analysis of non-linear EEG signals with linear analysis methods. Nonlinear analysis methods should be used to obtain more comprehensive information about epilepticseizures from signals. In this study, nonlinear analysis methods such as Shannon entropy, permutation entropy, sample entropy, approximate entropy, and spectral entropy were preferred. Among these entropies, Shannon entropy is a type of spectralentropy that uses the amplitude value of the signal as a probability in entropy calculations. Permutation entropy is a type of embedded entropy that directly uses timeseries to estimate entropy. Sample entropy is a method that measures the regularity of physiological signals regardless of their size. The consistency property of sample entropy is another reason for preference. Approximate entropy is a method that measures the predictability of the current amplitude values of physiological signals with previous amplitude values. Spectral entropy measures the extent to which the amplitude values of EEG signals are distributed in frequency bands.

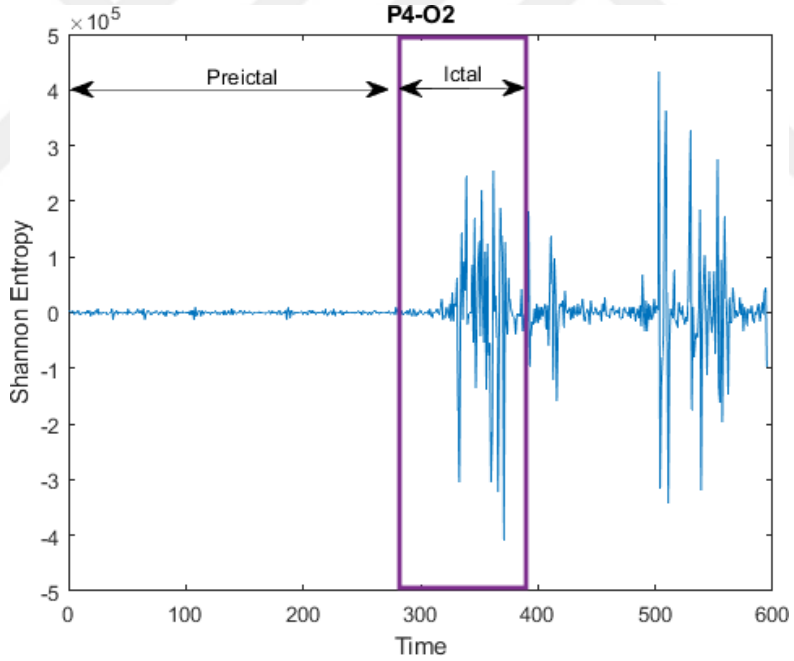


Figure 3.18: Shannon entropy values of the P4-O2 channel of an 19-year-old female patient. The y-axis of the graphshows the Shannon entropy values of the EEG signal. The x-axis represents time in *s*. The ictal state representing the seizure is framed by purple.

Figure 3.18 shows the Shannon entropy values of the P4-O2 channel of a 19- year-old female patient. It is calculated by considering the probability of amplitudevalues in the Shannon entropy data set. Shannon entropy deviates from zero due to the complexity of the amplitude values in the ictal period. Figure 3.19 shows the Shannon entropy values of all channels of the same patient.

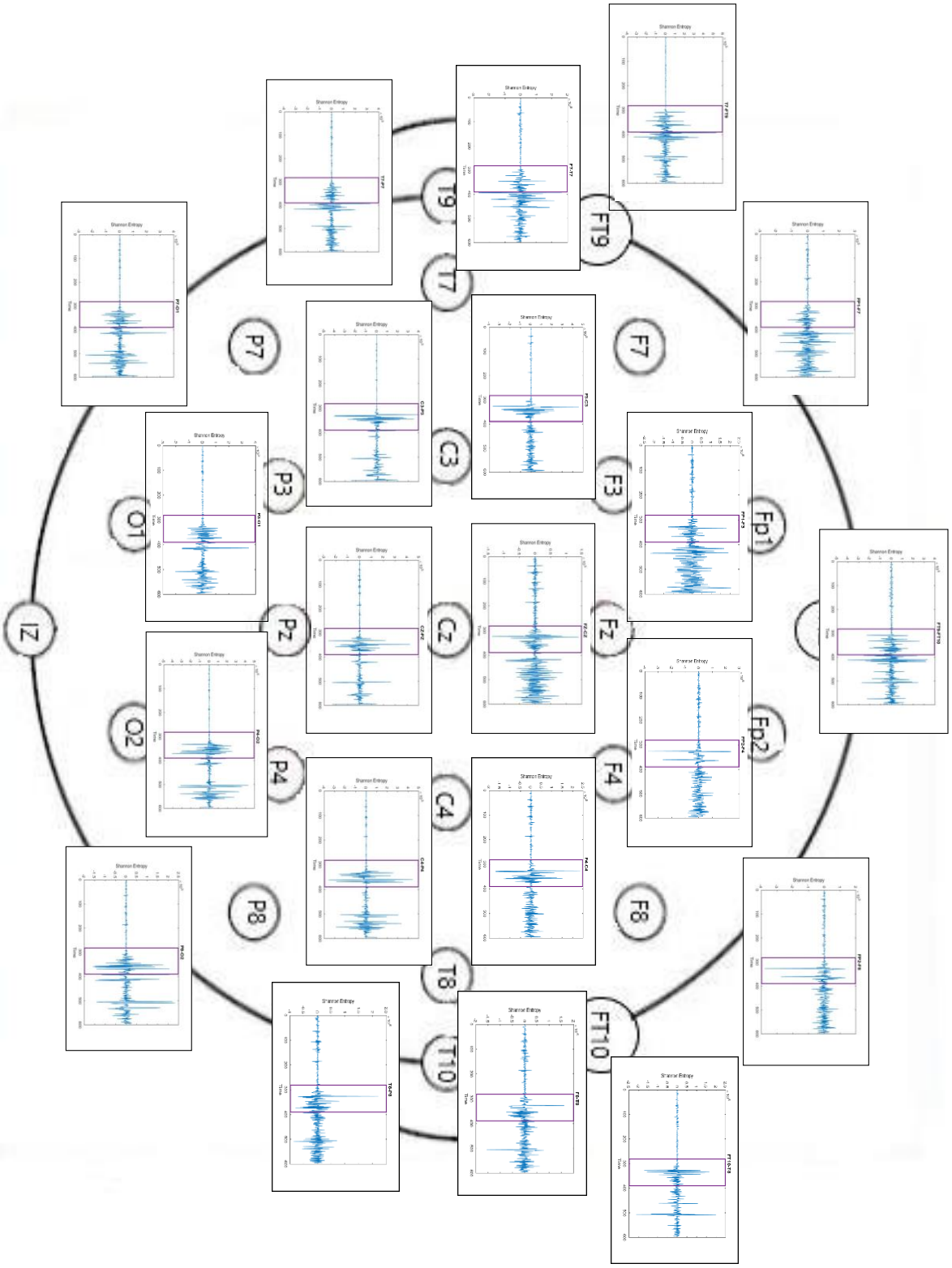
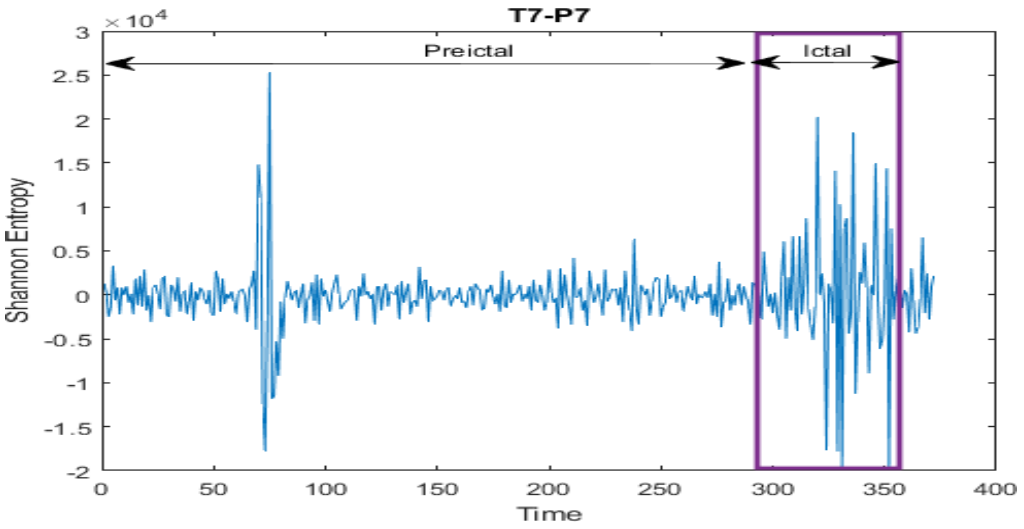
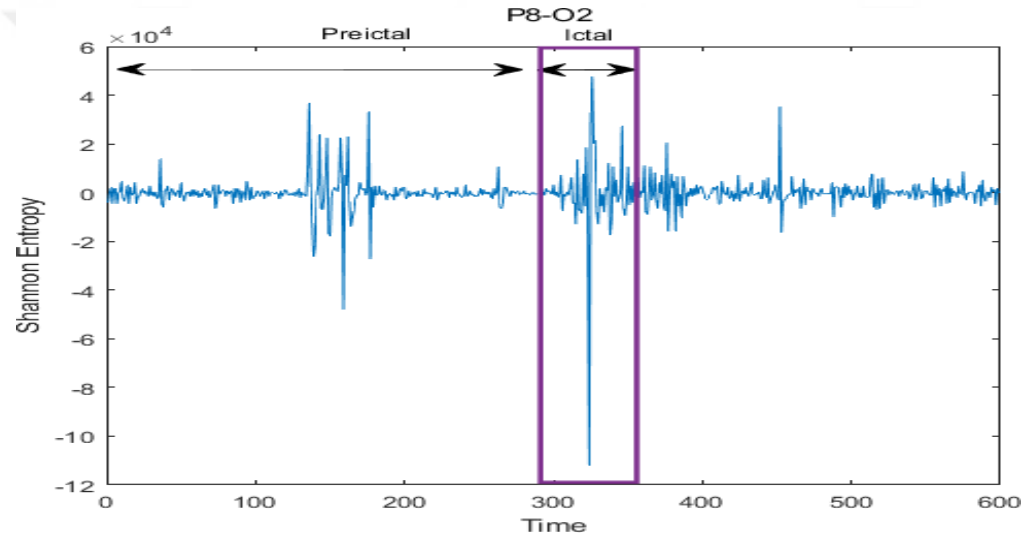


Figure 3.19: Shannon entropy values of all channels of an 19-year-old female patient.



(a) T7-P7 channel of an 18-year-old female patient.

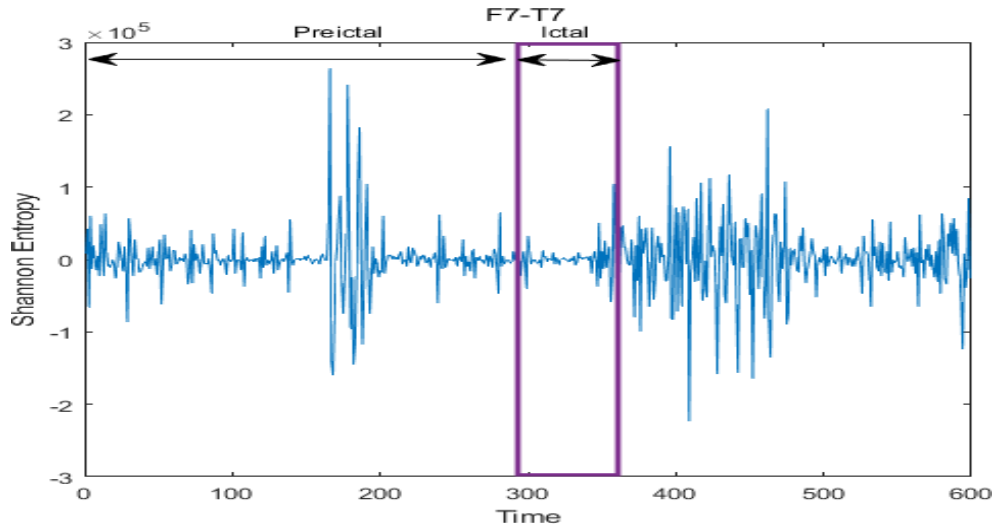


(b) P8-O2 channel of a 14-year-old female patient.

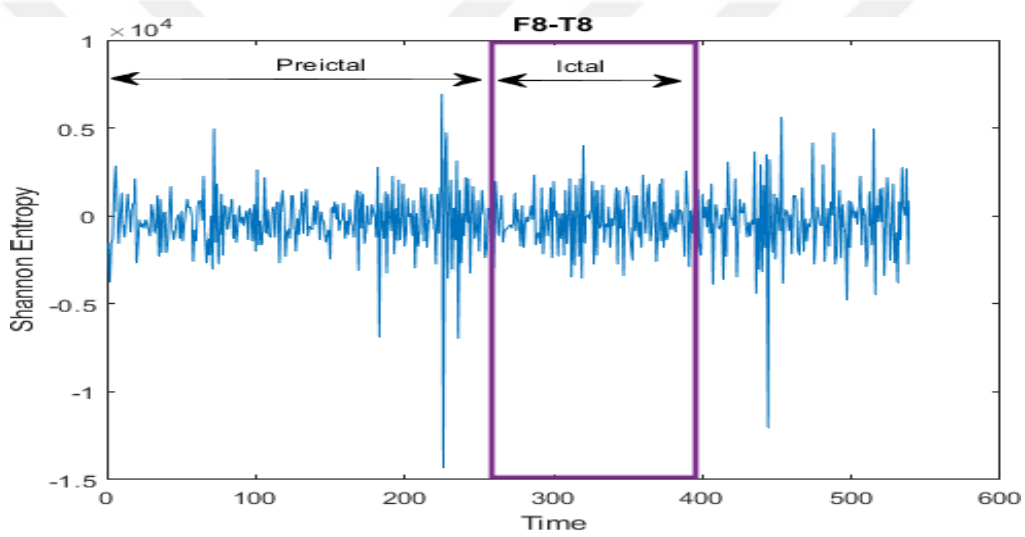
Figure 3.20: Shannon entropy values of different channels of different patients

In Figure 3.20a, Shannon entropy values of the T7-P7 channel of an 18-year-old female patient are shown. In the ictal period, Shannon entropy values moved away from zero. In addition, a sudden change in Shannon entropy values is observed about 250 seconds before the seizure.

Figure 3.20b shows the Shannon entropy values of the P8-O2 channel of a 14- year-old female patient. In the ictal period, in addition to the fact that Shannon entropy values move away from zero, a sudden change in entropy values is observed about 150 seconds before the onset of the seizure.



(a) F7-T7 channel of an 22-year-old male patient.

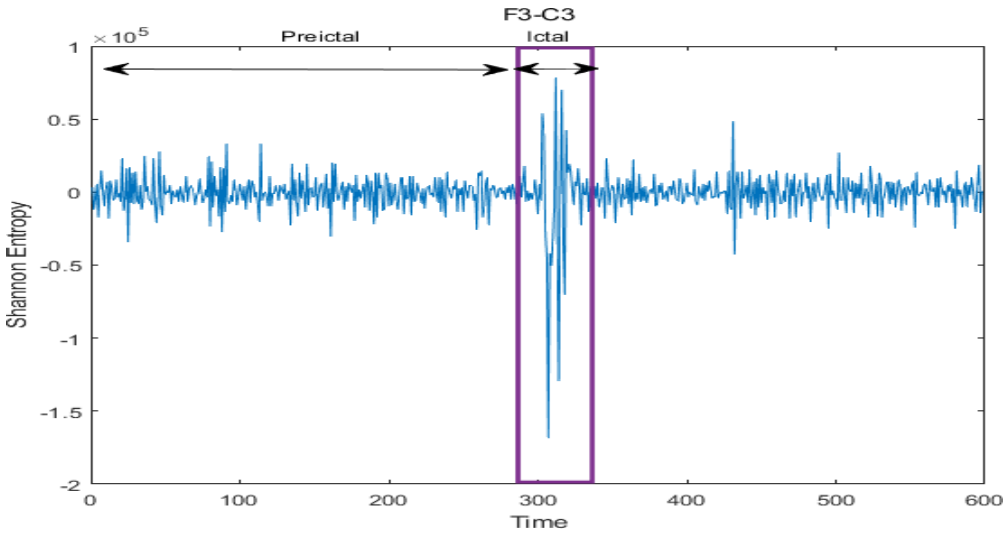


(b) T8-P8 channel of a 16-year-old male patient.

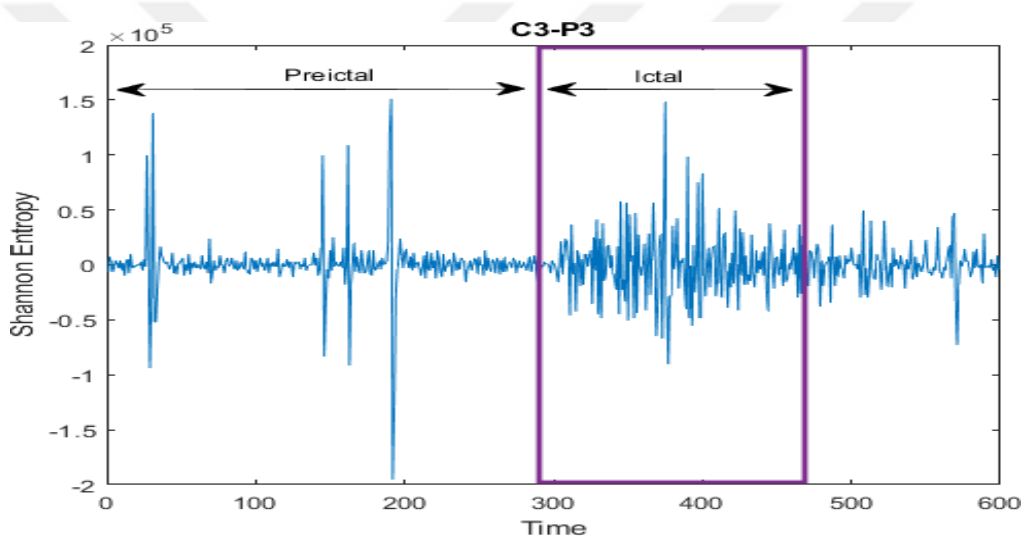
Figure 3.21: Shannon entropy values of different channels of different patients

Figure 3.21a shows the Shannon entropy values of the F7-T7 channel of a 22- year-old male patient. In the ictal period, Shannon entropy values do not move away from zero. However, a sudden change in entropy values is observed about 100 seconds before the onset of the seizure.

Figure 3.21b shows the Shannon entropy values of the T8-P8 channel of a 16- year-old male patient. The difference between the ictal period and the preictal period cannot be distinguished.



(a) F3-C3 channel of an 11-year-old female patient.



(b) C3-P3 channel of a 3.5-year-old male patient.

Figure 3.22: Shannon entropy values of different channels of different patients

Figure 3.22a shows the Shannon entropy values of the F3-C3 channel of an 11-year-old female patient. In the ictal period, the Shannon entropy moves away fromzero.

Shannon entropy values of the C3-P3 channel of a 3.5-year-old male patientare shown in Figure 3.22b. In the ictal period, besides the departure from zero in Shannon entropy, there are sudden changes at different times before the seizure.

Figure 3.20, Figure 3.21, and Figure 3.22 show Shannon entropy changes in different channels of different patients.

In epileptic seizures, the entire brain is usually affected. During the transition from the preictal state to the ictal state, complexity occurs in the signals. Because of this complexity, the sample entropy value is expected to increase at the onset ofthe seizure [53]. Permutation entropy is expected to decrease at the onset of the seizure [56]. It was observed that the permutation entropy value decreased in themajority of the patients at the onset of the seizure.

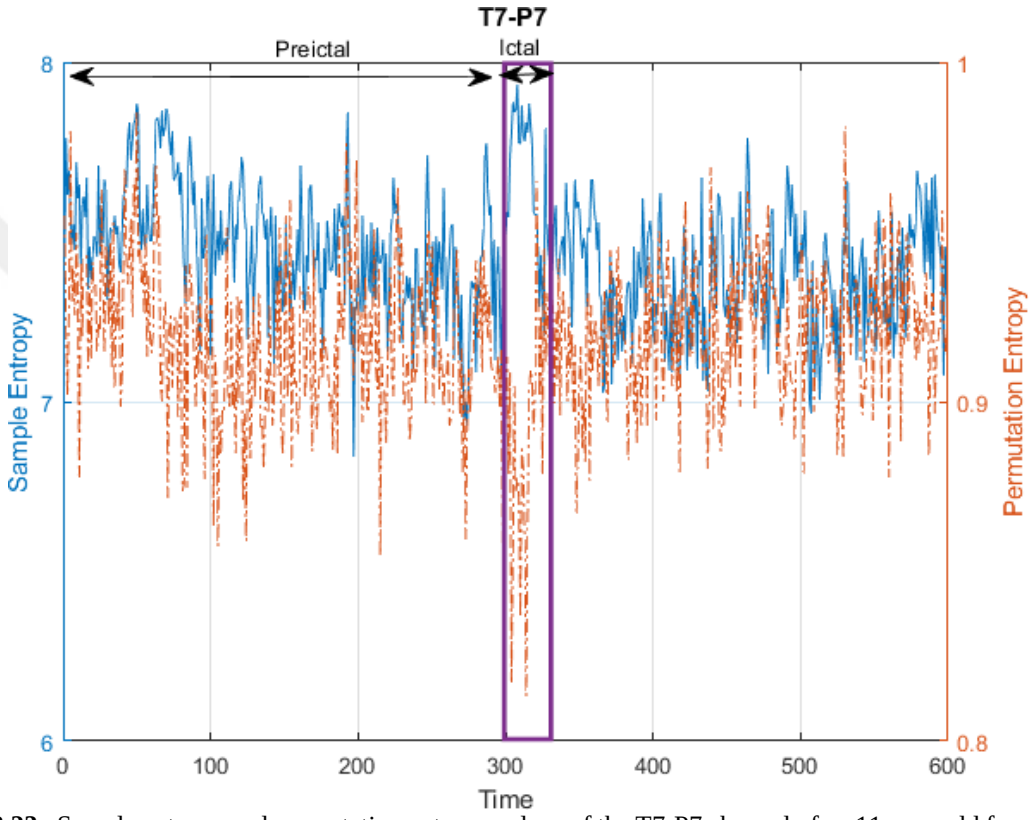


Figure 3.23: Sample entropy and permutation entropy values of the T7-P7 channel of an 11-year-old female patient. They-axis on the left side of the graph shows the sample entropy values of the EEG signal. The y-axis on the right shows the permutation entropy values of the EEG signal. The x-axis represents time in s. The ictal staterepresenting the seizure is framed by purple.

In Figure 3.23, it is seen that the sample entropy value increases at the beginningof the seizure and the permutation entropy decreases. In other words, the ictal region can be determined by considering sudden decreases and increases in entropy values. Figure 3.24 shows the sample entropy and permutation entropy values of allchannels of the same patient.

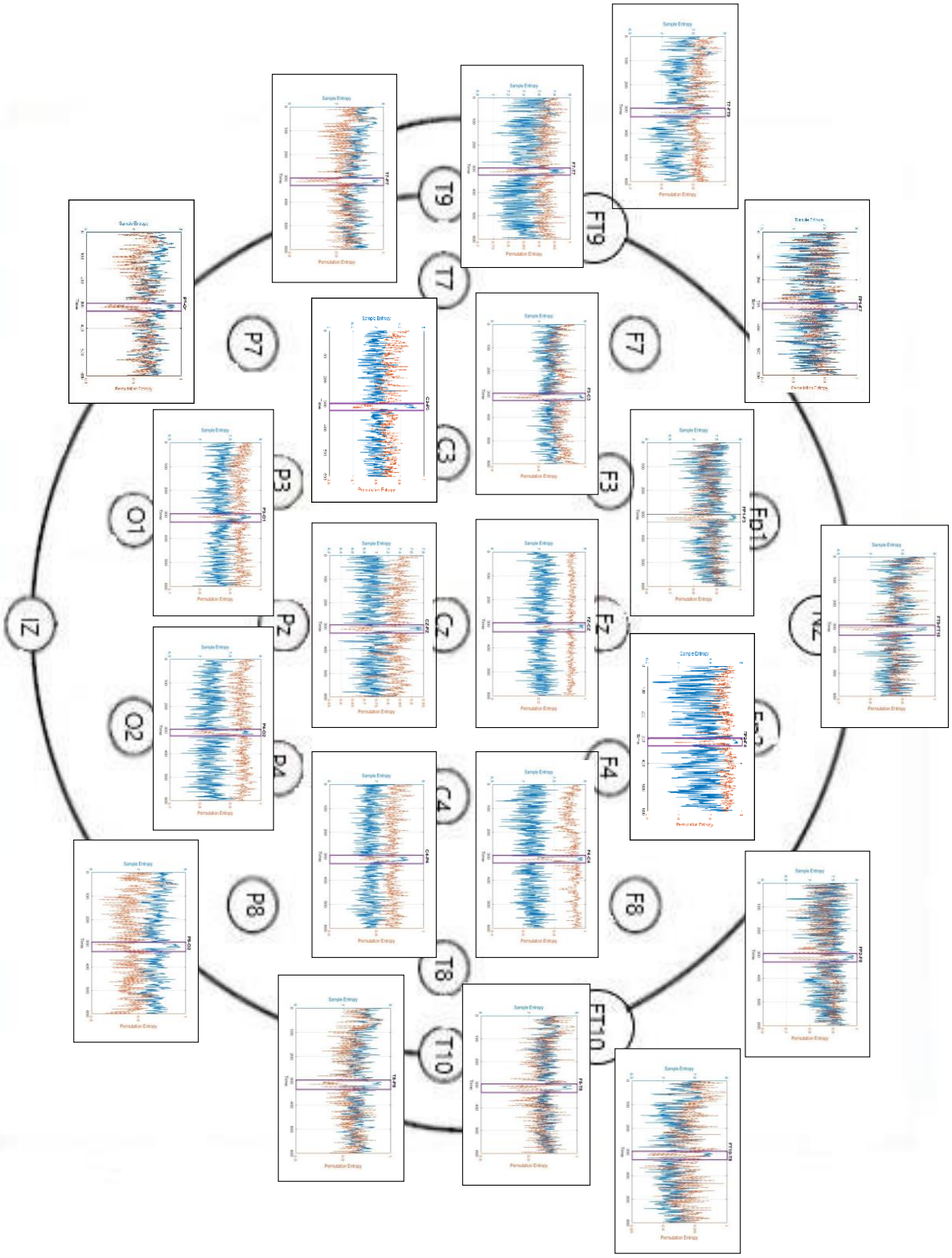
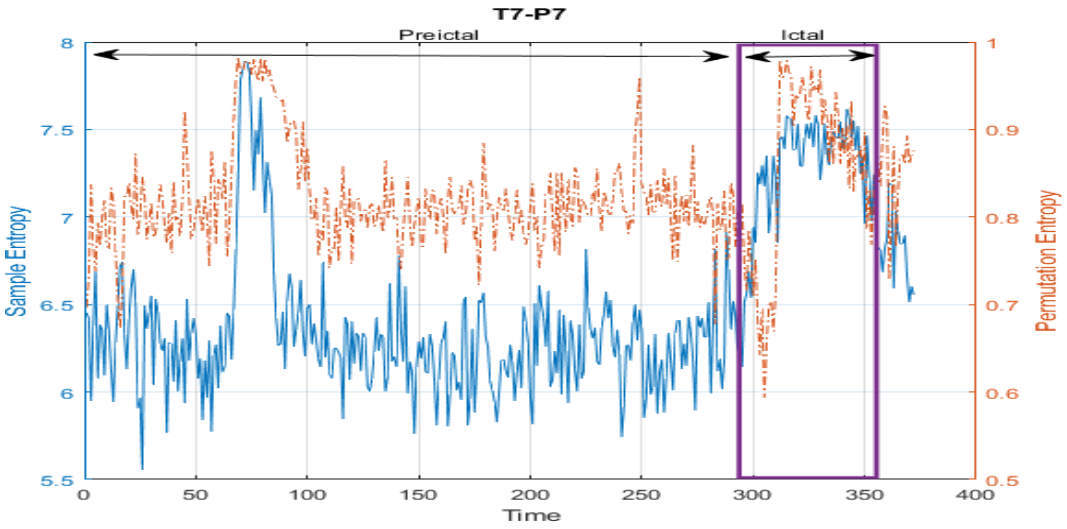
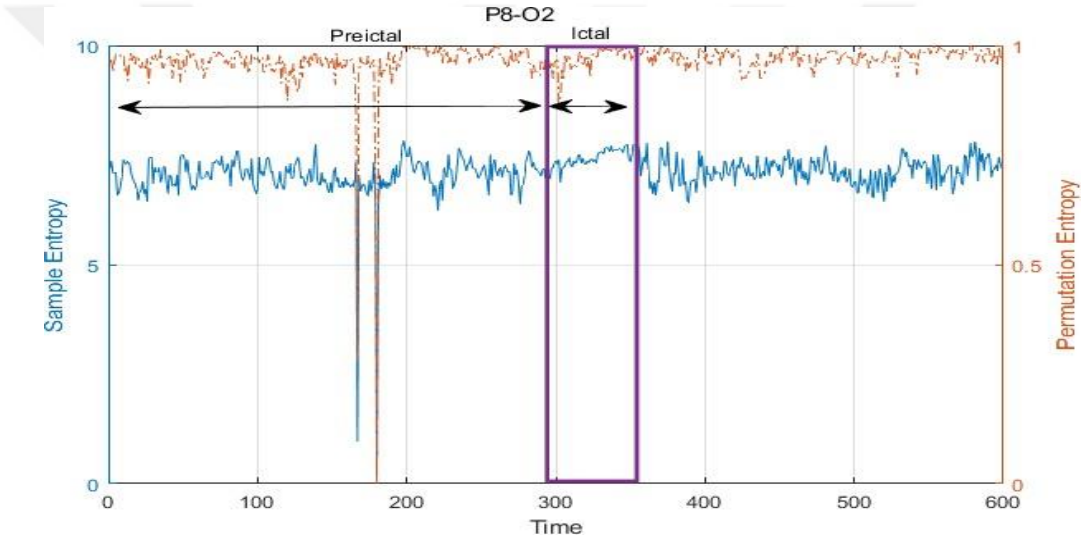


Figure 3.24 : Sample entropy and permutation entropy values of all channels of an 11-year-old female patient.



(a) T7-P7 channel of an 18-year-old female patient.

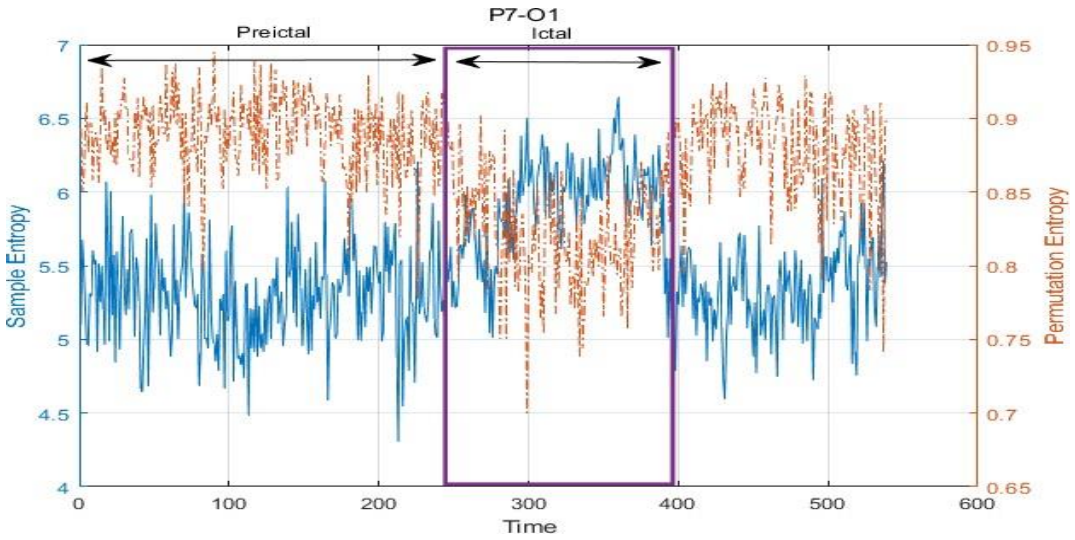


(b) P8-O2 channel of a 22-year-old male patient.

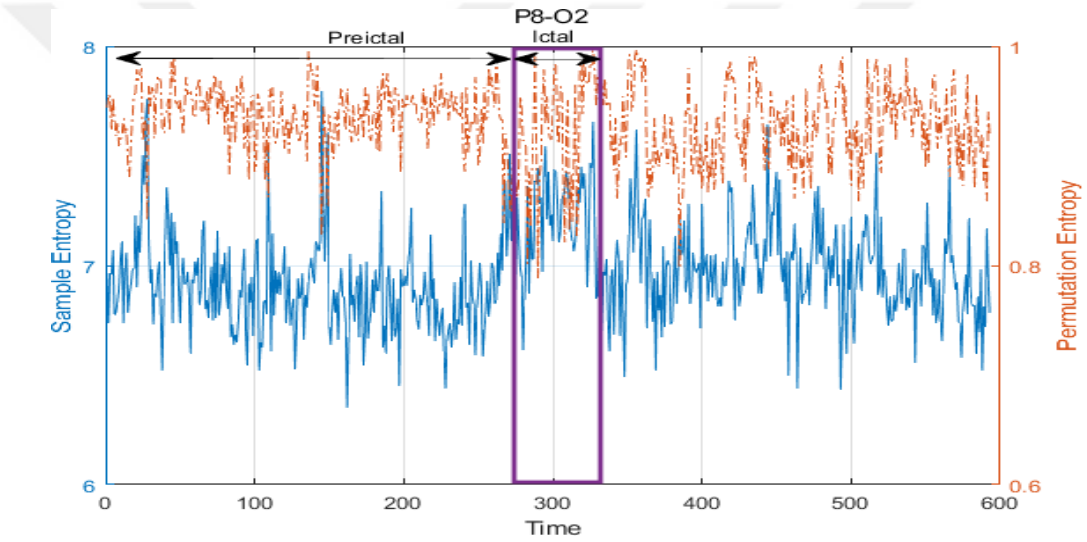
Figure 3.25 : Sample entropy and permutation entropy values of different channels of different patients

Figure 3.25a shows the entropy values of the T7-P7 channel of an 18-year-old female patient. In the ictal state, there was an increase in both entropy values compared to the preictal state. In addition, changes in entropy values are observed approximately 250 seconds before the onset of the seizure.

Figure 3.25b P8-O2 channel values of a 22-year-old male patient are shown. The distinction between the ictal state and the preictal state cannot be fully made with either entropy method. However, a sudden change in entropy values is observed until 120 seconds before the onset of the seizure.



(a) P7-O1 channel of a 16-year-old male patient.

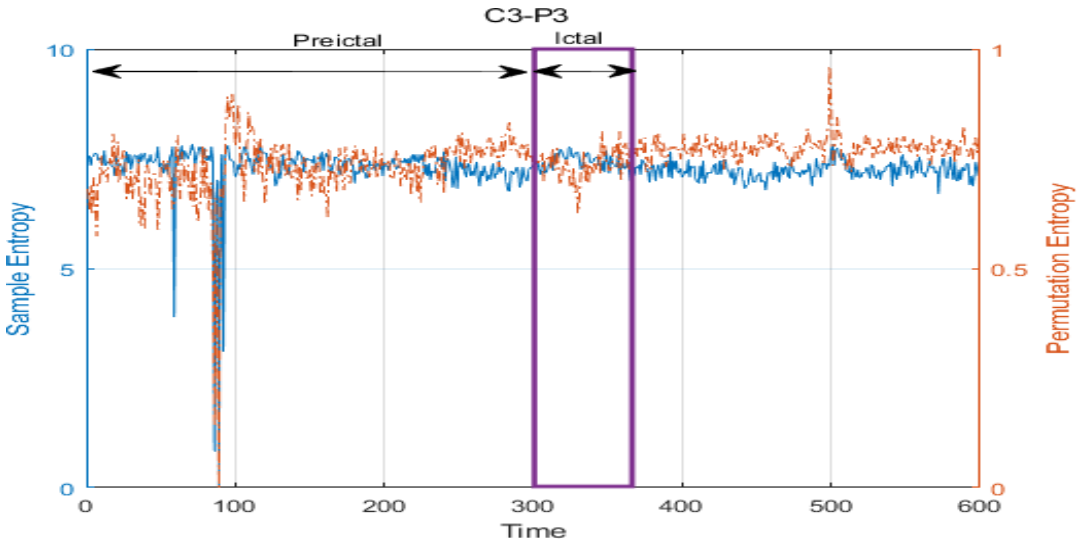


(b) P8-O2 channel of a 12-year-old female patient.

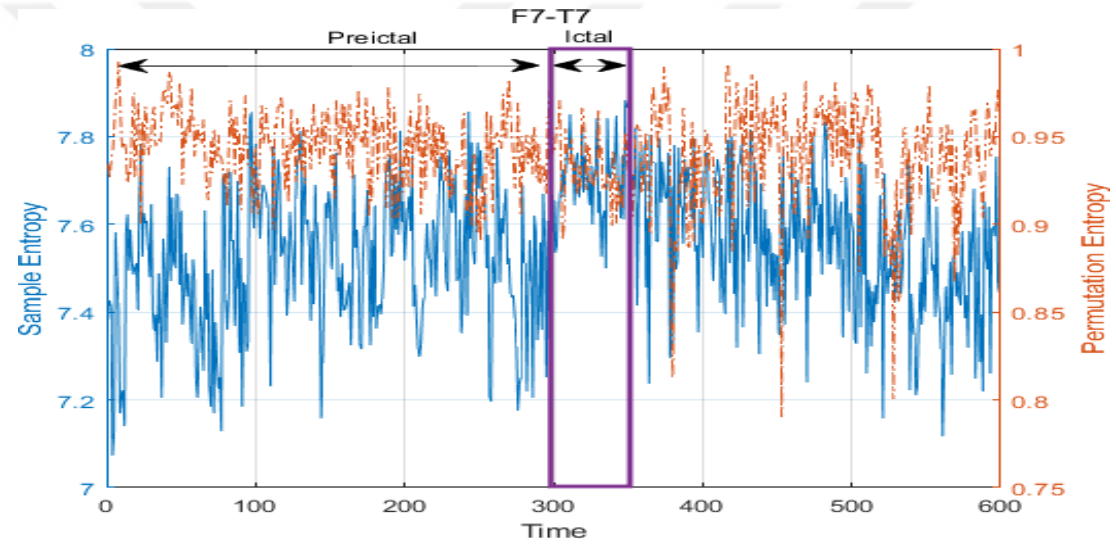
Figure 3.26 : Sample entropy and permutation entropy values of different channels of different patients

Figure 3.26a shows the entropy values of the P7-O1 channel of a 16-year-old male patient. While the sample entropy value increases in the ictal case compared to the preictal case, it decreases in the permutation entropy value.

Figure 3.26b shows the values of the P8-O2 channel of a 12-year-old female patient. In this patient, while the entropy value for example increases in the ictal state, it is not possible to distinguish between the ictal state and the preictal state inpermutation entropy.



(a) C3-P3 channel of a 2-year-old female patient.

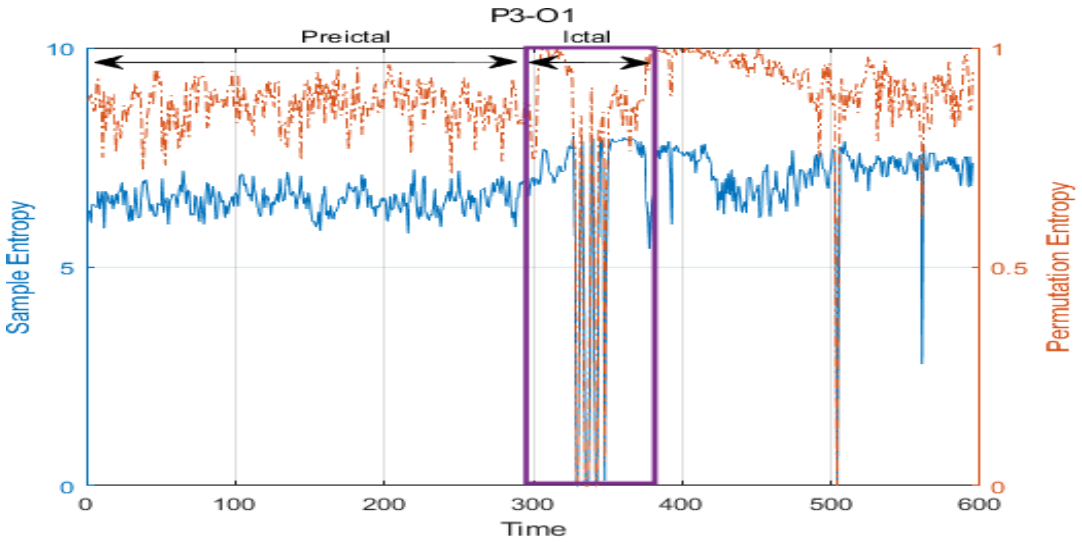


(b) F7-T7 channel of a 3-year-old female patient.

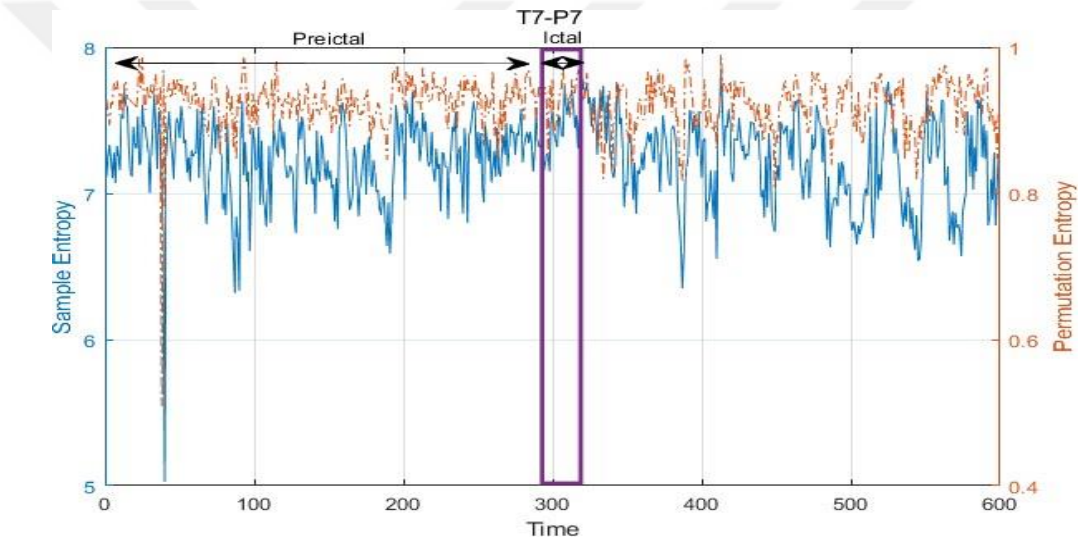
Figure 3.27 : Sample entropy and permutation entropy values of different channels of different patients

Figure 3.27a shows the values of the C3-P3 channel of a 2-year-old female patient. In the sample entropy ictal case, there is a slight increase compared to the preictal case, while there is a slight decrease in the permutation entropy. In addition, there was a sudden change in both entropy values about 210 seconds before the onset of the seizure.

Figure 3.27b shows the entropy values of the F7-T7 channel of a 3-year-old female patient. The difference between the ictal state and preictal state cannot be distinguished with either entropy method.



(a) P3-O1 channel of a 19-year-old female patient.



(b) T7-P7 channel of a 7-year-old female patient.

Figure 3.28: Sample entropy and permutation entropy values of different channels of different patients

Figure 3.28a shows the values of the P3-O1 channel of a 19-year-old female patient. While there is an increase in both entropy values at the beginning of theseizure, sudden decreases are observed in both entropy values during the seizure. Figure 3.28b shows the sample entropy and permutation entropy values of the T7-P7 channel of a 7-year-old female patient. The seizure duration was very short. With both entropy methods, the difference between ictal and preictal states could not be determined. In addition, a sudden change is observed in both entropy methods approximately 250 seconds before the onset of the seizure.

Figures 3.25, Figure 3.26, Figure 3.27, and Figure 3.28 are randomly chosen to show the different states observed in permutation entropy and sample entropy values.

The approximate entropy gives information about the disorder of the signal. Epileptic EEG signals are more regular than normal EEG signals [70, 73]. For this reason, ApEn values of epileptic EEG signals are lower than normal EEG signals [62, 66, 68, 70, 73]. Spectral entropy is a measure of the spectral distribution of EEG signals [99]. Since the frequency distribution in epileptic EEG signals is concentrated in certain frequency bands, the spectral entropy value is lower [84].

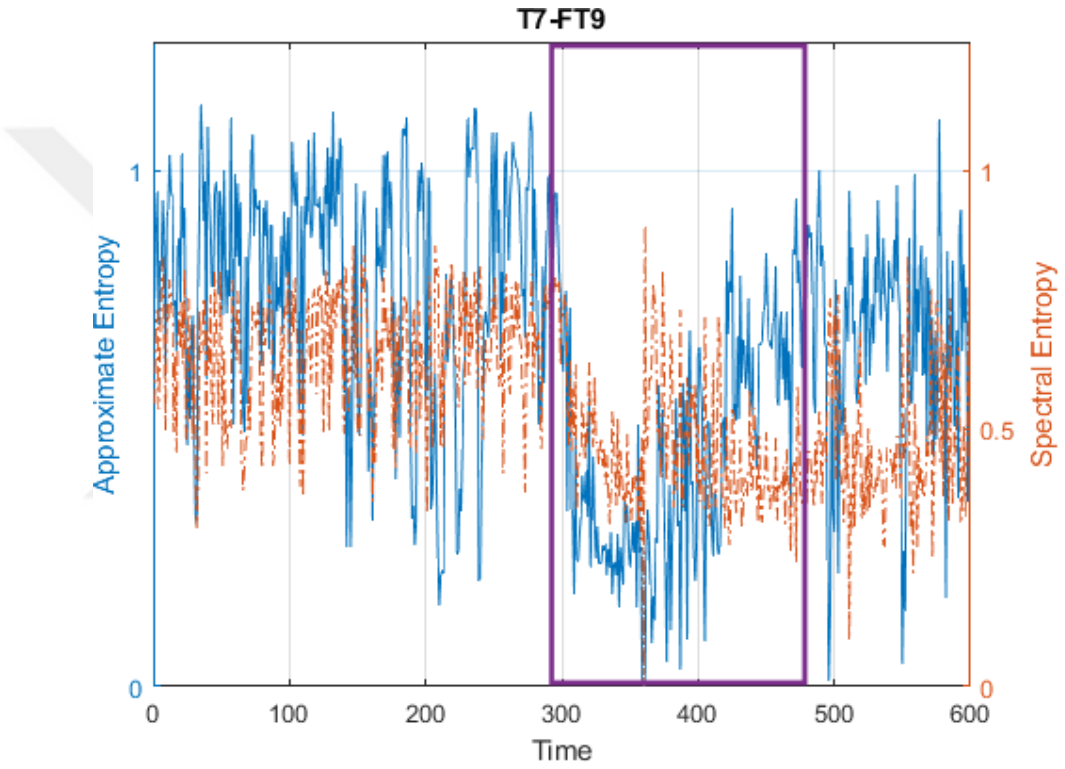


Figure 3.29: Approximate entropy and spectral entropy values of the T7-FT9 channel of a 3.5-year-old male patient. They-axis on the left side of the graph shows the approximate entropy values of the EEG signal. The y-axis on the right shows the spectral entropy values of the EEG signal. The x-axis represents time in *s*. The ictal staterepresenting the seizure is framed by purple.

Figure 3.29 shows the approximate entropy and spectral entropy values of the T7-FT9 channel of a 3.5-year-old male patient. In addition, approximate entropy and spectral entropy values of all channels of the same patient are shown in figure 3.30.

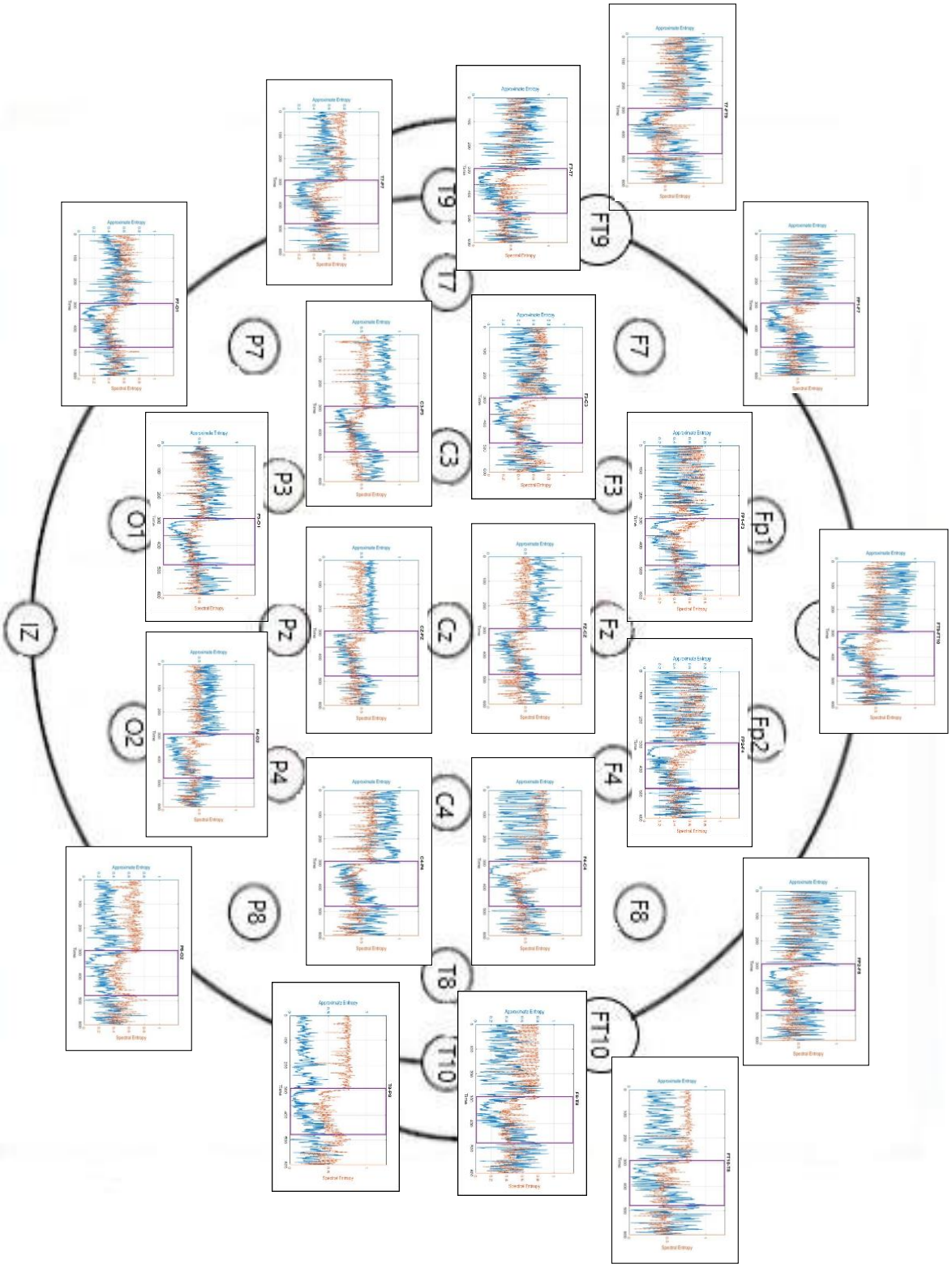
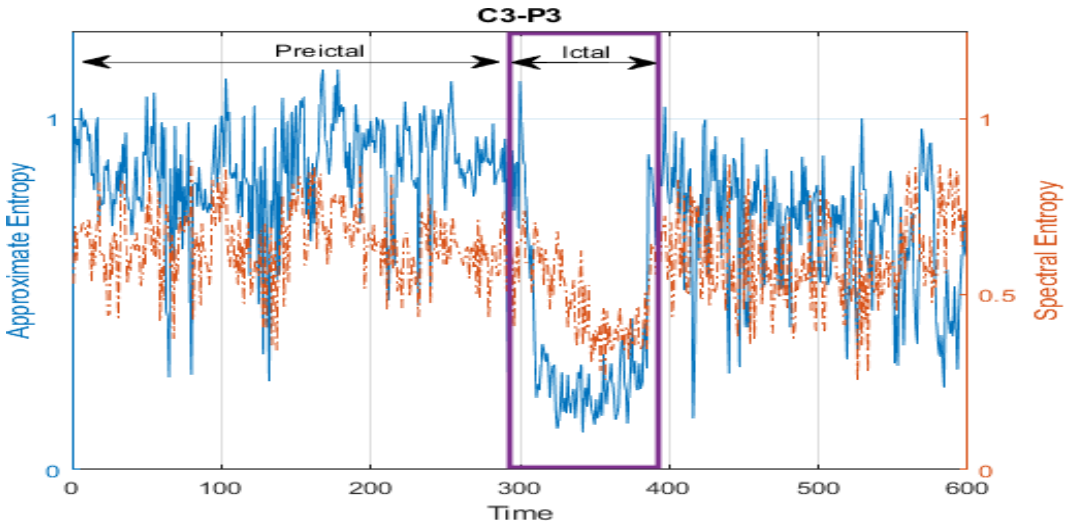
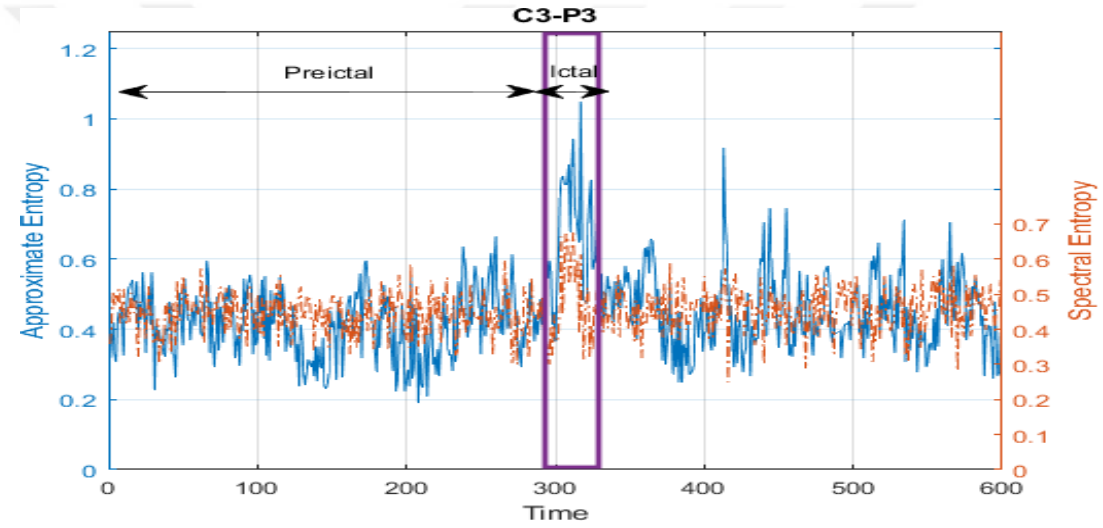


Figure 3.30 : Approximate entropy and spectral entropy values of all channels of a 3.5-year-old male patient.



(a) C3-P3 channel of a 14.5-year-old female patient.

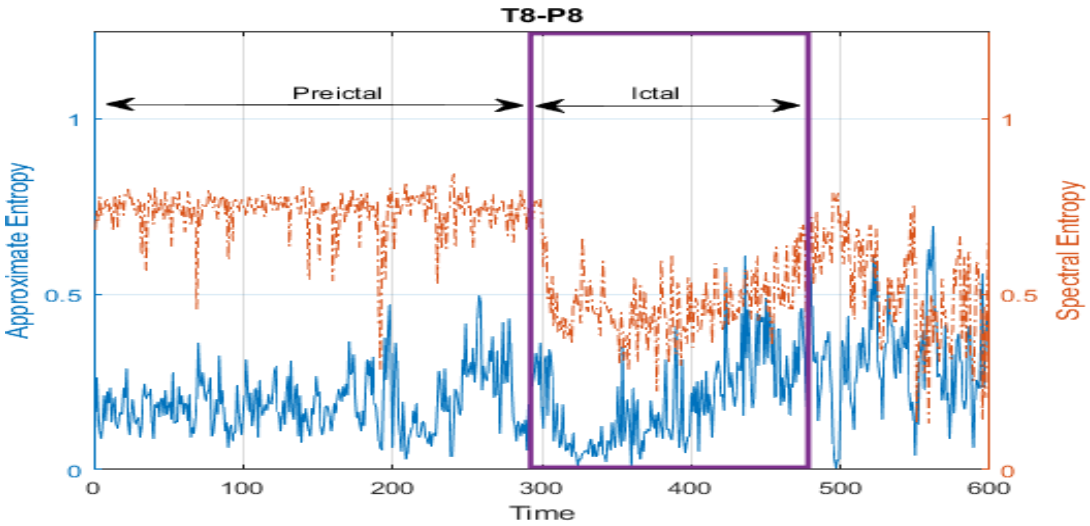


(b) C3-P3 channel of a 9-year-old female patient.

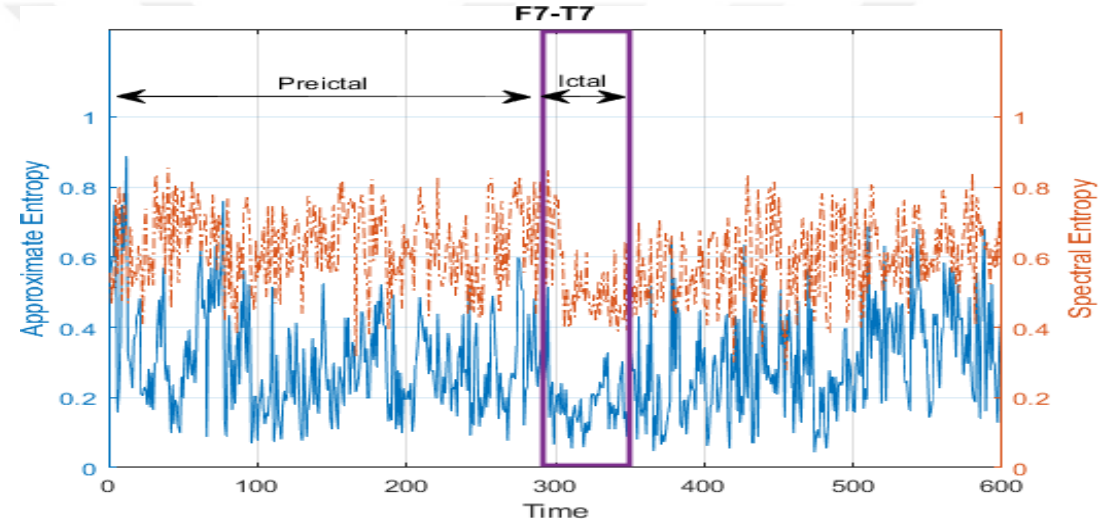
Figure 3.31: Approximate entropy values and spectral entropy values belonging to different patients.

Figure 3.31a shows the approximate entropy and spectral entropy values of the C3-P3 channel belonging to a 14.5-year-old female patient. As expected, there is adecrease in seizure duration in both entropy methods.

Figure 3.31b shows the approximate entropy and spectral entropy values of the C3-P3 channel belonging to a 9-year-old female patient. Contrary to the expected decrease, an increase in entropy values are observed in this patient during the seizure period. Figure 3.31 show the values of the same channel belonging to different patients. While the expected situation during the seizure period is observed in figure 3.31a, it is not observed in figure 3.31b. this is an indication that the samemethods are not decisive for every patient or every channel.



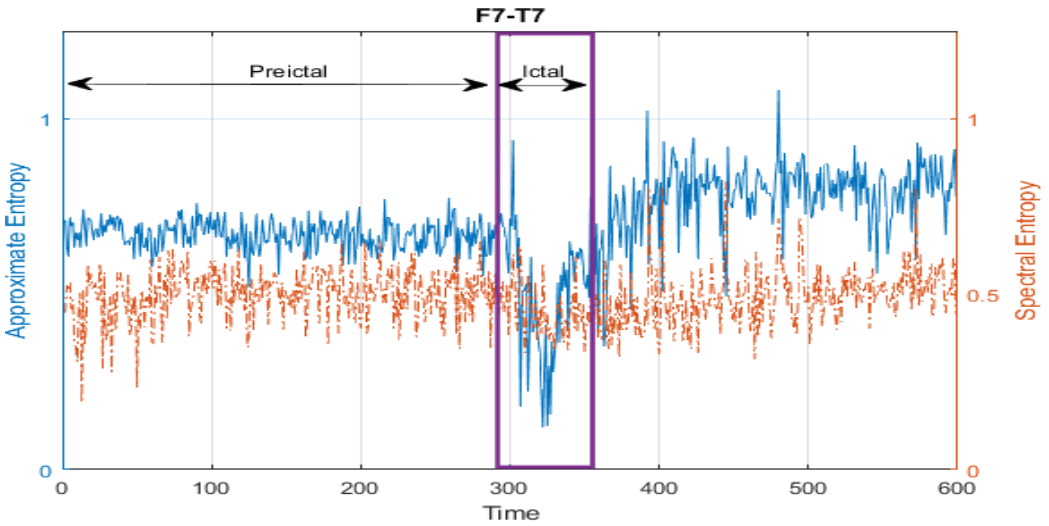
(a) T8-P8 channel of a 3.5-year-old male patient.



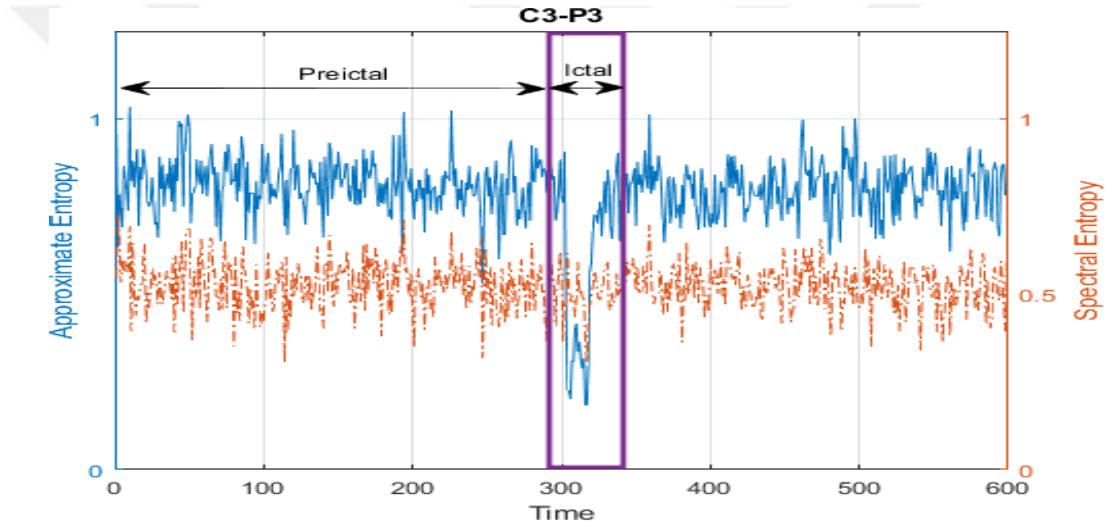
(b) F7-T7 channel of a 3-year-old female patient.

Figure 3.32: Approximate entropy values and spectral entropy values belonging to different patients.

Figure 3.32a shows the approximate entropy and spectral entropy values of theT8-P8 channel belonging to a 3.5-year-old male patient. Approximate entropy and spectral entropy values are decreased at the onset of seizure. There is also a sudden decrease in spectral entropy about 100 seconds before the onset of the seizure. Figure 3.32b shows the approximate entropy and spectral entropy values of the F7-T7 channel belonging to a 3-year-old female patient. This patient was a decrease in onset seizure both entropy methods.



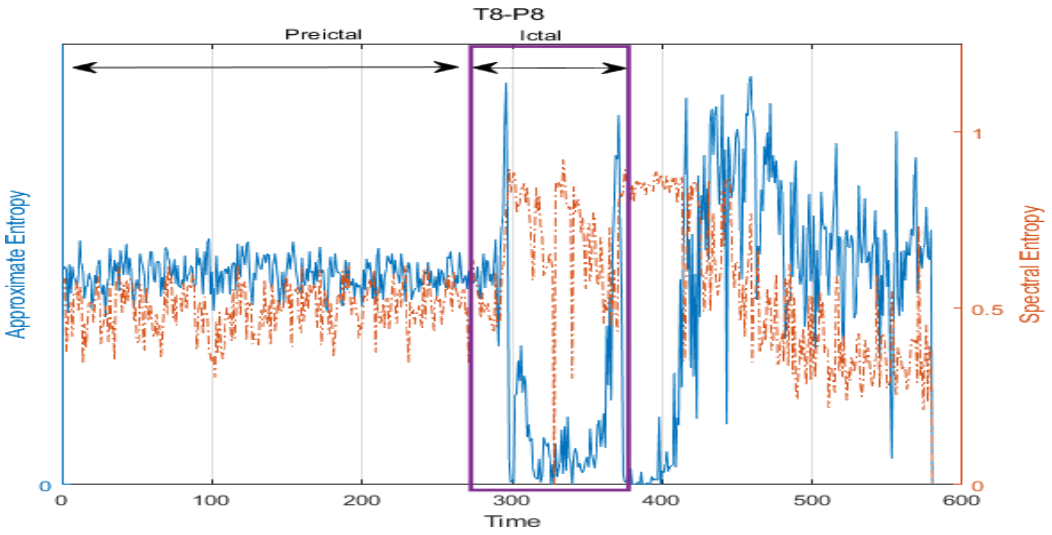
(a) F7-T7 channel of a 11-year-old female patient.



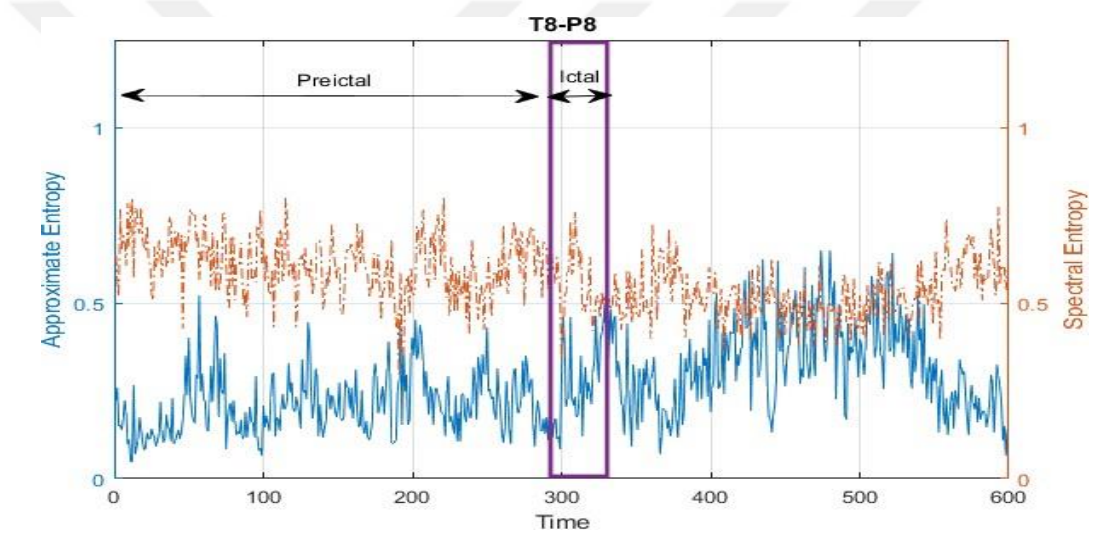
(b) C3-P3 channel of a 11-year-old female patient.

Figure 3.33: Entropy values of different channels of the same patient recorded at different times.

Figure 3.33 shows the entropy values of the EEG signals of an 11-year-old female patient recorded at different times. In figure 3.33a, the entropy values of theT7-P7 channel are lower in the ictal period than in the preictal period. Figure 3.33b shows the entropy values of the C3-P3 channel. While there is a decrease in approximate entropy in the ictal period, there is no change in spectral entropy betweenthe ictal state and the preictal state.



(a) T8-P8 channel of a 19-year-old female patient.



(b) T8-P8 channel of a 1.5-year-old female patient.

Figure 3.34: Approximate entropy values and spectral entropy values belonging to different patients.

Figure 3.34a shows the entropy values of the T8-P8 channel of a 19-year-old female patient. Approximate entropy is lower in the ictal period than in the preictal period. On the other hand, there is a sudden decrease in spectral entropy during the seizure.

Figure 3.34b shows the entropy values of the T8-P8 channel of an 11-year-old female patient. With both entropy methods, it is not possible to distinguish between the ictal state and the preictal state.

Figures 3.31, Figure 3.32, Figure 3.33, and Figure 3.34 are randomly chosen to show the different states observed in approximate entropy and spectral entropy values.

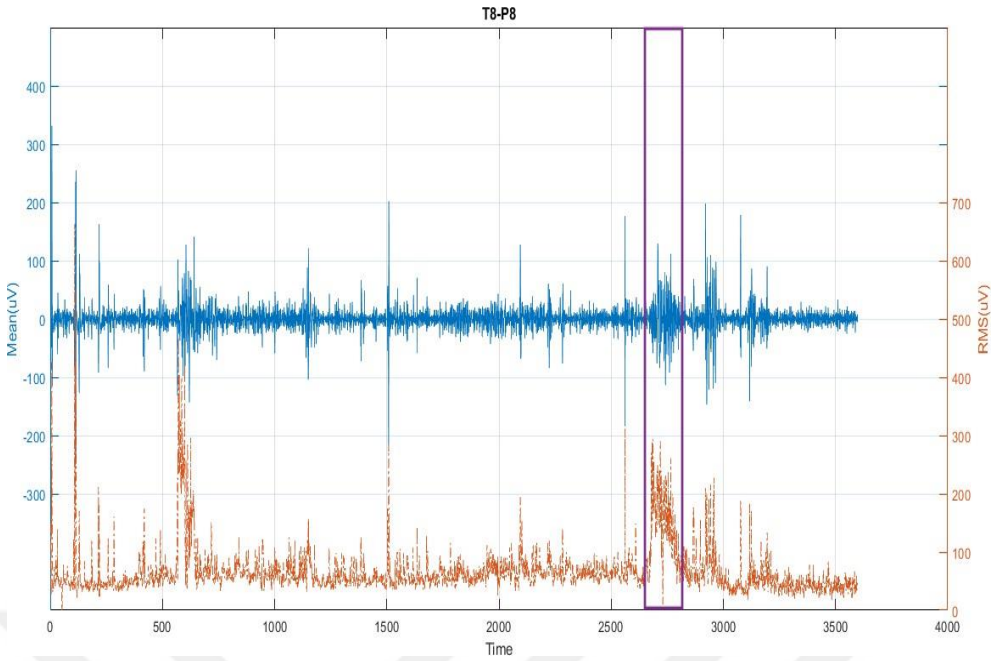


Figure 3.35: RMS and mean values belonging to the T8-P8 channel of the one-hour signal of a 3.5-year-old male patient.

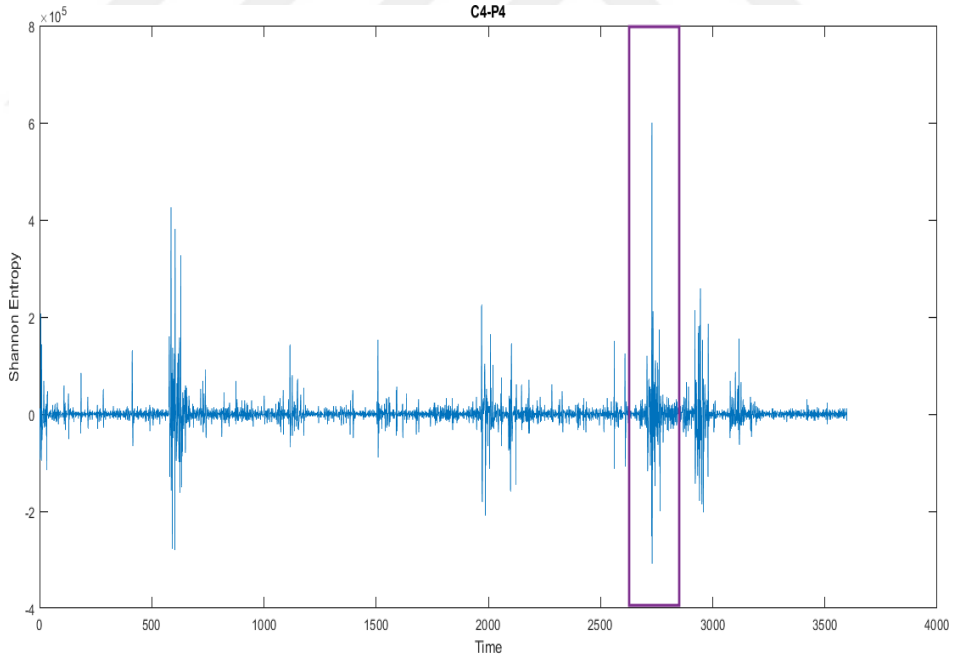


Figure 3.36: Shannon entropy values belonging to the C4-P4 channel of the one-hour signal of a 3.5-year-old male patient.

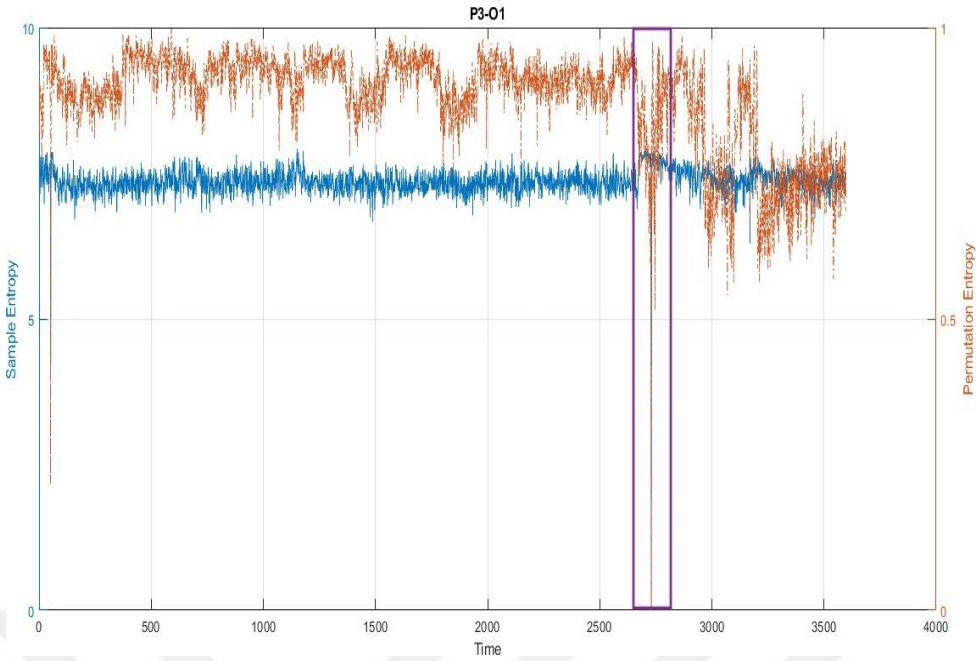


Figure 3.37: Sample entropy and permutation entropy values belonging to the P3-O1 channel of the one-hour signal of a 3.5-year-old male patient.

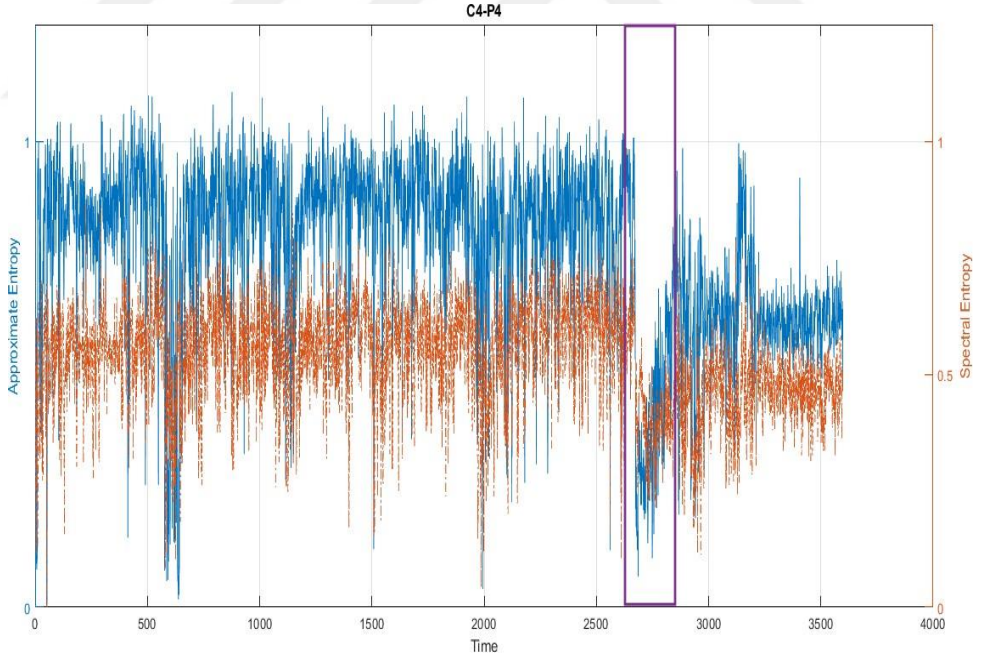


Figure 3.38: Approximate entropy and spectral entropy values belonging to the C4-P4 channel of the one-hour signal of a 3.5-year-old male patient.

The analysis of one-hour EEG recordings of a 3.5-year-old male patient with different methods are shown in Figure 3.35 , Figure 3.36, Figure 3.37, and Figure 3.38. Figure 3.35 shows the mean and RMS values of the one-hour EEG signal ofthe T8-P8 channel. At the onset of the seizure, an increase in RMS values and deviations in the mean value are observed. There are also changes before the seizure.

Figure 3.36 shows the Shannon entropy values of the one-hour EEG signal of the C4-P4 channel. It is observed that there is a deviation in the Shannon entropy values during the seizure. In addition, there are changes in entropy values before the seizure.

Figure 3.37 shows the permutation entropy and sample entropy values of the one-hour EEG signal of the P3-O1 channel. While there is an increase in sample entropy values at the beginning of the seizure, a sudden decrease is observed in the permutation entropy value during the seizure.

Figure 3.38 shows the approximate entropy and spectral entropy values of the one-hour EEG signal of the C4-P4 channel. There is a decrease in both entropy methods at the beginning of the seizure. Also, there is a change in entropy values before the seizure.

For both statistical analyzes and entropy methods, it was preferred to examine 5 minutes before and 5 minutes after the onset of the seizure to better analyze the changes occurring at the onset of the seizure.

4. CONLUSIONS AND RECOMMENDATIONS

In the University of Bonn data, healthy and seizure data can be classified by amplitude values, the number of peaks exceeding the threshold, and power spectral analysis. But the fact that the data is in separate txt files is not healthy for comparison. Therefore, one hour of data (CHB-MIT) including the seizure period was analyzed.

In 18 of the 24 patient data in the CHB-MIT dataset, it was observed that the RMS values increased in the ictal state compared to the preictal state. In addition, in 14of them, the mean value moves away from zero in the ictal state compared to the preictal state. In other words, according to the mean and RMS values of the EEG signal, the ictal region was determined at a rate of 58.4% and 75%, respectively. Linear analysis methods are preferred due to the ease of application and theory. But EEG signals are not linear. Therefore, information loss may occur in the analysis with linear analysis. It was also analyzed with entropy, one of the non-linear analysismethods, to avoid information loss.

In this study, 5 different entropy methods were used. In the first method, Shannon entropy, since the complexity of the signal increases during the seizure period, the entropy value moves away from zero in positive and negative directions during the seizure. This difference was observed in 18 of 24 patients, ie 75% of patients, in theCHB-MIT data.

When the sample entropy and permutation entropy values in the CHB-MIT dataare analyzed separately, it is seen that the sample entropy value increased in 16 (66.6%) of 24 patient data in the ictal state compared to the preictal state. A decrease in permutation entropy was observed at seizure onset in 16 of 24 patients (66.6%). When both entropy methods were examined together, two different situations emerged. In the first case, the increase in the sample entropy and the decrease in the permutation entropy were examined and this situation was found in 13 (54.2%) patients. In the latter case, the increase in the value of the sample entropy during the seizure or the decrease in the permutation entropy was examined and observedin 19 (79.2%) patients. It is also seen in cases where the sample entropy value decreases during the seizure or the permutation entropy value increases during the seizure.

When the approximate entropy and spectral entropy values in the CHB-MIT data are analyzed separately, it is seen that the approximate entropy value in 19 (79.2%)of the data of 24 patients decreases in the ictal state compared to the preictal state. Also, a decrease in spectral entropy was observed at the onset of seizure in 15 (62.5%) of 24 patients. The observed reductions in approximate entropy are more specific than in spectral entropy. When both entropy methods were examined together, two different situations emerged. In the first case, the decrease in approximate entropy and spectral entropy was examined and this situation was found in 16 (66.6%) patients. In the second case, the decrease in approximate entropy value or decrease in spectral entropy during a seizure was examined and observed in 20(83.3%) patients. It is also seen in cases where the approximate entropy or spectralentropy value increases during the seizure.

In Table 4.1, and Table 4.2 seizure detection status in patients for each analysis method in CHB-MIT data is shown. As seen in the tables, if the seizure status in patients cannot be detected with one method, it can be detected with another method[1]. This indicates that the probability of detecting seizures will increase if more methods are used for analysis.

In addition, there are some changes detected before seizures in EEG signal analysis. These changes are common to different analysis methods. These changes are thought to be a precursor to seizures. It is aimed to determine the cause of thechanges and to investigate their relationship with the seizure in future studies. It willbe examined whether the seizure can be predicted through these changes.

[1]RMS: Root Mean Square, Mean: Signals mean value, ShEn: Shannon entropy, SmpE: Sample entropy, PE: Permutation entropy, ApEn: Approximate entropy, SE: Spectral entropy.

Table 4.1 : Seizure detection status in patients with analysis methods.

Patient	Analysis Methods						
	RMS	Mean	ShEn	SmpE	PE	ApEn	SE
chb01	✓	✓	✓	✓	✓	✓	✓
chb02	✓	✓	✓	✓	✓	✓	✓
chb03	✓	✓	✓	✓	✓	✓	-
chb04	-	-	✓	-	✓	✓	✓
chb05	✓	✓	✓	✓	✓	✓	-
chb06	-	-	-	-	-	✓	-
chb07	✓	✓	✓	✓	✓	✓	✓
chb08	✓	✓	✓	✓	✓	✓	✓
chb09	✓	✓	✓	✓	✓	✓	✓
chb10	✓	-	-	✓	✓	✓	-
chb11	✓	-	-	✓	-	✓	-
chb12	✓	✓	✓	-	-	✓	✓

Table 4.2 : Seizure detection status in patients with analysis methods.

Patient	Analysis Methods						
	RMS	Mean	ShEn	SmpE	PE	ApEn	SE
chb13	-	-	-	-	-	-	✓
chb14	-	-	✓	-	-	-	-
chb15	✓	-	-	-	-	-	-
chb16	-	-	-	-	✓	-	-
chb17	✓	-	✓	✓	✓	✓	✓
chb18	✓	✓	✓	✓	✓	✓	✓
chb19	✓	✓	✓	✓	✓	✓	-
chb20	✓	✓	✓	✓	-	✓	✓
chb21	-	✓	✓	-	✓	-	✓
chb22	✓	-	✓	✓	✓	✓	✓
chb23	✓	✓	✓	✓	-	✓	✓
chb24	✓	✓	✓	✓	✓	✓	✓
Detection Rate(%)	75	58.4	75	66.6	66.6	79.2	62.5

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