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A Review on Drug Addiction Diagnosis Methods Using Brain Activity and Structure Based on Electroencephalogram Signals

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Abstract

Heroin is an industrial narcotic whose use in the short and long term leads to addiction. Heroin addiction has different effects on the human body. Among the negative effects created is the effect on human brain activity. Monitoring human brain activity is done using brain signal or electroencephalogram (EEG). EEG is an efficient method to examine the functional and cognitive activity of the brain, especially with the changes made in the brain of heroin addiction. Various researches have been done to investigate the changes made on EEG. However, a review research that can summarize the researches has not been presented so far. This paper has been done for reviewing previous researches in examining the changes made on EEG. The results of the review show a decrease in the power of the alpha sub-band in the T6 channel, a significant difference between the ratio of the power in the beta sub-band and the alpha sub-band. Also, alpha sub-band neural activity in people who quit heroin addiction is in parietal (BA3 and BA7), frontal (BA4 and BA6) and limbic (BA24). Also, the results show that the duration of heroin use has an effect on the EEG.

Keywords: addiction, electroencephalogram, feature extraction, power spectrum, P300 component
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1. Introduction

Today, addiction to drugs is recognized as a complex disease. The biological, psychological, and social aspects of addiction complicate cognition and therefore its treatment. Long-term drug addiction affects the individual's body [1-9]. Consequences such as sexual and mental disorders, gastrointestinal disorders, liver and kidney dysfunction, and impairment of proper brain function can be mentioned as harmful effects of drug abuse [10-17]. Drug use impairs the nervous system, information processing by neurons, and the brain. Neural intermediaries in different brain regions, especially the reward system, are influenced by drug use and create a strong sense of pleasure in the individual. The created sense of pleasure is such that other natural pleasures will not activate the brain's reward system. Chronic drug use leads to long-term cognitive impairments and changes in the central nervous system (CNS) function. Clinical findings and imaging confirm the impact of heroin use on the prefrontal cortex, insular cortex, thalamus, amygdala nuclei, and sensory-motor structures. Magnetic resonance imaging (MRI) confirms a decrease in gravy matter density in the prefrontal and cingulate regions. Gary matter contains brain neurons, and its decrease directly affects memory, muscle control, sensory perception, emotions, speech, and decision-making abilities of the brain [18-44]. Electroencephalogram signals represent brain activity, and any changes in brain activity have a direct effect on the electroencephalogram. Since addiction affects the brain, electroencephalogram analysis can be used to diagnose addiction in individuals. The effect of addiction on brain signals has also been confirmed in [45-50].

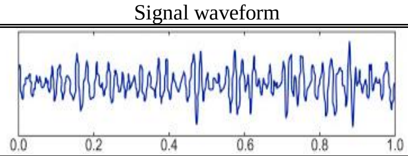
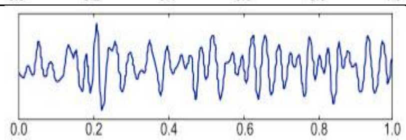
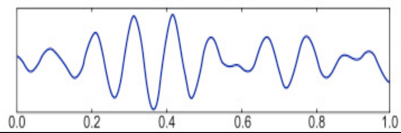
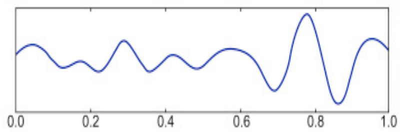
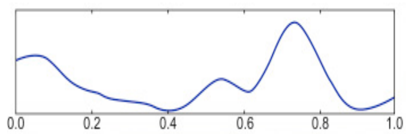
Various standards are used to record brain signals, one of which is the 10-20 standard. EEG signals of individuals in different states, such as healthy individuals or addicts, differ. To investigate these differences, EEG signal decomposition into different sub-bands can be used. Although the EEG signal can be decomposed into different frequency sub-bands, they are all part of a dynamic set that works in harmony with each other. These sub-bands include: the delta sub-band in the frequency range of 0.5 to 3 Hz, the theta sub-band in the frequency range of 4 to 7 Hz, the alpha sub-band in the frequency range of 8 to 13 Hz, and the sensory-motor rhythm sub-band in the frequency range of 12 to 15 Hz, beta sub-bands exist in frequency ranges from 14 to 50 Hz, and the gamma sub-band is above 30 Hz [51-73].

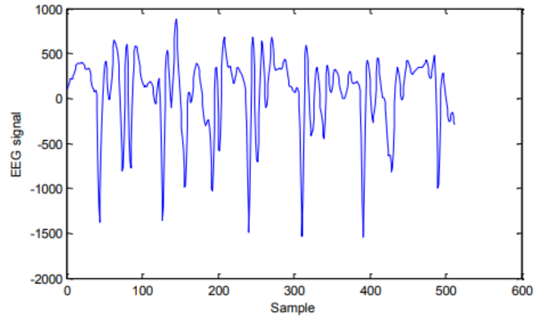
Table (1) shows the extracted sub-bands from the electroencephalogram signal of a healthy individual [74,75]. Fig. 1 shows an example of an EEG signal in a healthy individual and an addicted individual [76,77]. As can be observed, distinguishing an addicted individual from a healthy individual based on visual inspection of the EEG signal is not possible due to the similarity and complexity of the signal. The main objective of brain studies in addiction research is to assess the neurophysiological changes in addicted individuals [78-82].

Based on this, event-related potentials (ERPs), which are measured using electroencephalogram signals, provide a more reliable evaluation compared to behavioural measures for studying changes and information processing. Event-related potentials benefit from sufficient temporal accuracy for detecting rapid cognitive and perceptual processes that occur in response to stimuli. Numerous clinical experiments have been conducted to investigate neuro-electrophysiological changes in humans due to substance use [83-86].

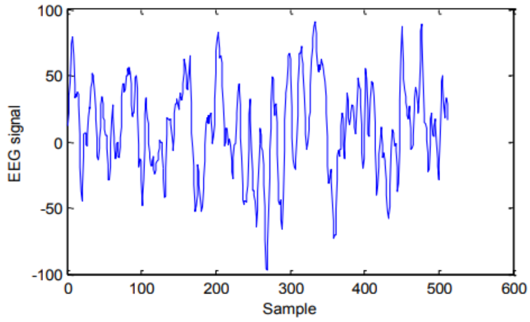
Although clinical experiments and research are helpful in creating distinctions between addicted and healthy individuals, it seems that they may not be precise enough for effective differentiation. Signal processing methods can have a significant impact in this regard. In the context of EEG signal processing, efforts have been made to extract features that differentiate healthy and addicted individuals. Various features, such as temporal, spatial, frequency-domain, and multiresolution transformations like wavelet or nonlinear transformations, have been utilized to distinguish healthy and addicted individuals. Multiple studies have been conducted on the impact of addiction on the electroencephalogram signal and feature extraction in the time, frequency, and multiresolution domains [86-92].

Table.1.
Sub-bands extracted from EEG signal from healthy person

Brainwave type	Location	Amplitude	Signal waveform
Gamma	Frontal-central areas	Smallest	
Beta	Parietal, somatosensory, frontal, and motor areas	Very low	
Alpha	Occipital and parietal regions	Low	
Theta	Hippocampus region	Low-medium	
Delta	Mostly in thalamus region	High	



(a) Electroencephalogram signal of an epileptic person



(b) Electroencephalogram signal of a healthy person

Fig. 1. An example of an electroencephalogram signal in a healthy person and an addicted person and the extracted sub-bands

Multiple methods have been proposed for feature extraction in the frequency domain from EEG signals. Frequency-domain analyses are essential, similar to time-domain analyses, because frequency representation of an EEG signal provides useful information about EEG signal patterns. Power spectral density (PSD) and normalized PSD with respect to total power are commonly used for extracting features that indicate power distribution in each frequency. Some of these features include frequency energy, intensity-weighted mean frequency (IWMF), intensity weighted bandwidth (IWBW), spectral edge frequency (SEF), spectral entropy (SE), peak frequency, power ratio, and bandwidth [93-116]. Table (2) shows these features. The relationship between specific electroencephalographic frequencies can be employed to differentiate between EEG signals of healthy and addicted individuals. There are differences in the patterns of brain cortical activity between healthy and addicted individuals. One of the frequencies and brain waves that can be recorded is event-related potentials or evoked potentials, which are a set of brain waves recordable at the scalp level. These waves occur simultaneously with the presentation of a distinct stimulus. Event-related signals have a low amplitude, which is improved by averaging. The baseline signal is obtained by averaging, while the event-related signal is preserved. This averaging process allows limited-domain ERPs to be plotted quantitatively as voltage over time. Conventionally, these ERPs are named according to their latency and polarity. One of these waves, which has been the subject of extensive studies, is called P3 or P300 because when averaged in ERP, it appears as the third positive wave and has a latency of approximately 300 milliseconds. These components are highly useful for detecting sensory impairments in addicted individuals and can be used in diagnostic research for various problems and disorders [117-122].

On the other hand, since electroencephalogram reflects the simultaneous activity of neurons, it can be assumed that EEG power is a tool that can reflect the processing capacity of cortical information. However, it should also be noted that power measurement is influenced to a large extent by various factors such as skull thickness or cerebrospinal fluid volume, technique-dependent factors, or methodological factors. However, more specific factors such as age, motivation, and actual performance during operation have a significant impact. It appears that another suitable tool for detection in spectral power signals [130-135].

A) Main study and innovation

This paper discusses human neurophysiological experiments conducted to examine the effects of addiction on individuals and evaluates them based on the used method and ERP/EEG patterns. Findings related to cognitive impairments and abnormal brain activities due to chronic substance abuse are also investigated. In this study, the characteristics of electroencephalogram signals and ERP changes related to cognitive, emotional, and craving aspects of information processing are examined in the subjects. By understanding these changes and differences between healthy individuals and addicts, suitable diagnostic methods can be developed to distinguish between healthy individuals and addicts. Additionally, they can be used to develop therapeutic protocols in neurofeedback.

B) Research highlights

In this study more than 160 papers related to the topic have been selected, and the review has been done by studying them. This review can help researchers to conduct future research studies. The prominent aspects of this study include the following:

- Investigating the extraction of time and frequency domain features from electroencephalogram signals.
- Examining the effects of addiction on electroencephalogram signal features.
- Investigating the impact of extracted features in attention, dynamics, and their effects on different brain regions and sub-bands.
- Providing several key recommendations for future research.

Table.2.
Frequency characteristics extracted from electroencephalogram signal

Ref.	***Explanations***	***Subcategories***
[123]	Energy is extracted from certain specific frequency ranges.	Energy
[124]	Measuring the weighted average of frequencies in estimating power spectral density	Weighted average frequency
[125]	Calculation of bandwidth associated with weighted average frequency characteristic	Bandwidth weighted intensity
[126]	Using the power spectrum amplitude components of time series for entropy evaluation and quantifying the spectral complexity of the EEG signal	Spectral entropy
[127]	This criterion can be used for discrimination.	Peak frequency
[128]	The dominant frequency bandwidth is defined as the FWHM (Full width at half maximum) band corresponding to the peak frequency.	Bandwidth
[129]	The brain's activity power in abnormal states and periods is usually greater than its natural state.	Power ratio

C) Paper structure and research method

The structure of the paper is as follows. After stating the problem and the importance of the subject in the introduction section, since the changes in the electroencephalogram signal and different brain regions have been mentioned, several studies on the impact of addiction on the electroencephalogram signal are discussed in the second section from three perspectives: attention disorder changes, dynamical changes, and changes in recorded regions. The results are presented in the third section. The conclusion is provided in the fourth section.

2. Impact of Addiction on the EEG Signal

Drug addiction is typically accompanied by psychological disorders. For example, concurrent cocaine use is associated with attention deficit hyperactivity disorder, while simultaneous heroin use is linked to post-traumatic stress disorder [136,137]. Reference [138] has demonstrated that substance abuse leads to functional abnormalities, particularly in alpha band neural oscillations, especially after heroin withdrawal. Additionally, the intensity of psychiatric symptoms may increase as a result of substance abuse [139,140]. Numerous studies have examined the effects of addiction on electroencephalogram signals [141,142]. The impact of addiction on the brain is investigated from various perspectives [143]. These changes can include attention disorders, dynamics of extracted features from the electroencephalogram, and their effects on different brain regions, including brain channels and extracted sub-bands from the electroencephalogram signals. One way to investigate attention impairment due to substance abuse is through the examination of the P300 component in the electroencephalogram. Furthermore, to analyze the dynamics of features, time and frequency domain characteristics are extracted from the signals. Finally, through the examination of these features, differences between different brain regions and sub-bands are revealed. The following paragraphs briefly discuss the impact of addiction within these three categories.

A) Attention Disorder

Attention disorder has been identified as one of the impairments caused by drug addiction. The P300 component extracted from event-related potentials can be used to detect attention [144,145]. In [146], the P300 component was examined during a short-term memory test in individuals addicted to heroin, individuals who had quit heroin use, and healthy individuals. During the preliminary evaluation of short-term memory, the P300 component was investigated in 20 patients with a history of drug addiction (at least 6 months after quitting addiction), 18 current heroin users, and 20 healthy individuals who matched in terms of age, gender, and education level. The results showed a significant reduction in the P300 amplitude in the central frontal region in individuals who had quit heroin compared to the other two groups. Although demographic information and its impact on brain signals were examined in this study, only the P300 component was investigated, while the impact of addiction on other components is also evident.

In [147], EEG signals of individuals who had undergone heroin withdrawal were examined. In this study, the P300 amplitude was investigated, and the results showed a normalization of P300 in the group of healthy individuals and those who had quit heroin, indicating a continued trend of recovery during heroin withdrawal. The analysis was performed in the time domain and within the signal's amplitude range. EEG signals are highly susceptible to noise and artifacts, thus the amplitude of the EEG signal is also affected. Although preprocessing methods can reduce the effects of noise and artifacts, the results of the analysis will still be influenced.

In [148], they examined the P300 in individuals who were completely dependent on cocaine and heroin. Three groups of male substance-dependent volunteers and cocaine addicts were tested using an auditory pattern before and after addiction withdrawal. The results showed no difference in the P300 amplitude between addicted individuals and healthy non-substance-dependent volunteers when they were undergoing addiction withdrawal. However, after the withdrawal period, the P300 amplitude in the cocaine and heroin-dependent group was significantly lower compared to the control group of healthy non-substance-dependent individuals. Buprenorphine treatment significantly reduced the P300 amplitude after addiction withdrawal, while the P300 amplitude in individuals treated with placebo remained similar to that of depressed individuals. Placebo effect is defined as a phenomenon in which some individuals feel good after taking an inactive substance. These findings indicate that buprenorphine treatment is effective in alleviating withdrawal-related disorders. Although this drug works well in treating drug addiction, it is addictive itself. Discontinuing its use is also challenging.

In [149], ten individuals with drug and heroin use and ten healthy individuals were examined for the P300 component in the electroencephalogram EEG signal. The results show that the P300 component amplitude increases with drug use. Examining other components and sub-bands can yield better results.

Table (3) provides a summary comparison of studies on the effect of attention disorder on the electroencephalogram, focusing on the P300 component as the feature. Examining the amplitude information of EEG signals can be greatly influenced by noise and artifacts, although this challenge can be overcome with preprocessing methods, the results are still affected. The use of other time-domain features can help improve the results. Since the impact of drug addiction is more evident in the P300 component, the selected studies in Table (3) have focused on this component. This examination can be performed from a signal analysis perspective or a statistical analysis perspective. This table covers both cases.

B) *Investigation of Electroencephalogram Signal Changes*

Neural differences between individuals who have quit heroin and a healthy control group can be examined through nonlinear dynamic analysis and local source localization analysis of electroencephalogram data. This work involves extracting linear and nonlinear features in the time and frequency domains from EEG signals and comparing them between addicted and healthy individuals [150].

In [151], EEG signal analysis using the fast Fourier transform method was performed on heroin-addicted individuals, recently abstinent individuals, and normal individuals to compare and describe the characteristics of each group. The data included 60 EEG recordings from 20 current heroin users, 20 individuals who recently quit, and 20 healthy individuals.

The study focused on examining the delta-to-alpha sub-band power ratio, and the results showed that addicted individuals had higher alpha sub-band power. Those who had quit showed a decrease in alpha sub-band power, while their delta sub-band power and delta-to-alpha power ratio were relatively high. The delta-to-alpha power ratio decreased as a function of time from the beginning of quitting addiction. No significant changes were observed in the EEG signals between individuals who had quit for more than 80 days and healthy individuals.

Table.3.
Effect of attention disorder on electroencephalogram signal (P300 component amplitude feature type)

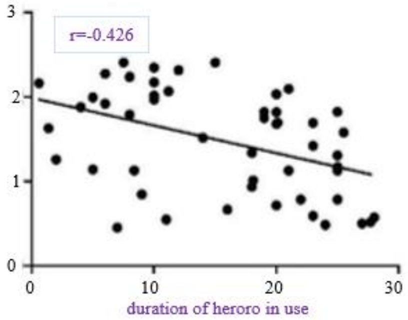
Ref.	***Explanation***	***Advantages***	***Disadvantages***	***Database specifications***
[146]	- Examination of P300 component in individuals addicted to heroin and those who have quit during a short-term memory test	- Examination of individuals from the perspective of demographic information such as age, gender, and education level.	- The examination has been conducted solely on the domain information of the P300 component.	- 20 addicted individuals, 20 healthy individuals.
[147]	- Examination of P300 component in individuals addicted to heroin and healthy individuals.	- Comprehensive study of individuals who have quit heroin.	- The examination has been conducted solely on the domain information of the P300 component.	- 48 addicted individuals, 20 healthy individuals, 59 individuals who have quit heroin.
[148]	- Examination of P300 component in three groups: individuals addicted to heroin, individuals who have quit, and healthy individuals.	- Comprehensive study of individuals in three groups and demonstrating their differences, examining the drug's effect on the P300 component.	- The examination does not consider demographic information such as age and gender.	- 15 addicted individuals, 11 healthy individuals.
[149]	- Examination of P300 component in domain feature.	- Comprehensive study of individuals who use heroin.	- The examination has been conducted solely on the domain information of the P300 component.	- 10 individuals addicted to heroin, 10 healthy individuals.

In [152], by studying EEG signals in addicted individuals, it was found that the alpha-to-theta sub-band power ratio at T6 showed a decrease. Meanwhile, the beta sub-band power at T5 showed a relative increase, suggesting improved visual perception and cognitive performance in addicted individuals.

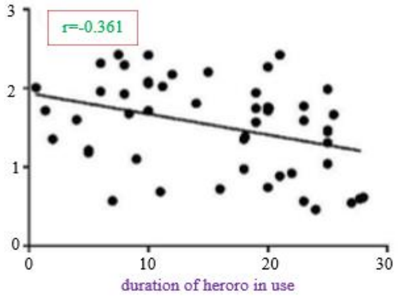
In [153], they investigated the power coherence of EEG signals in 18 heroin-dependent individuals and 12 healthy individuals. The results showed that heroin-dependent individuals had higher relative beta 2 power and gamma coherence in the left hemisphere compared to the control group.

In [154], the focus was on the temporal dynamics and frequency characteristics of electroencephalogram signals in studying addicted individuals. In this study, it was observed that the amplitude of low-frequency fluctuations (ALFF) in addicted individuals was lower compared to non-heroin-dependent healthy individuals in the bilateral anterior cingulate cortex (dACC), bilateral middle frontal cortex (BMFC), left posterior dorsolateral prefrontal cortex (dlPFC), left middle cingulate gyrus, left cingulate gyrus, posterior cingulate cortex, and left inferior frontal gyrus. Furthermore, increased ALFF was observed in the bilateral angular gyrus, bilateral fusiform gyrus, bilateral posterior cingulate cortex, and left middle frontal gyrus. Additionally, the increase in low-frequency oscillations in the bilateral parietal lobes showed a significant positive correlation with methadone dosage. Therefore, it can be concluded that the decrease in ALFF is associated with heroin use, while the increase in ALFF in the bilateral parietal lobes may be a result of methadone treatment. As shown in Fig. 2, the duration of heroin use in heroin-addicted individuals was significantly negatively correlated with ALFF in the right angular gyrus (p=0.004 and r=-0.426).

In [155], the relative power and central frequency of the alpha (α) and beta (β) sub-bands were investigated in addicted individuals and healthy individuals. The results of this study show significant differences in the examined features. The analysis of the electroencephalogram signals indicates that in over 70% of cases, a relatively low amplitude of alpha sub-band activity, increased beta activity, and a significant amount of low-amplitude waves in central brain regions are observed. Fig. 3 demonstrates the distribution of average alpha 2 frequencies in different study groups. In the healthy control group, the average alpha 2 frequency at C3 was significantly higher compared to the average alpha 2 frequencies in other derivations, including the closest ones such as Cz, F3, and P3. However, with this EEG parameter, in the more distant electrodes (T4 and T6).



(a) right angular gyrus (p=0.004, r=-0.426)



(b) left superior occipital gyrus (p=0.009, r=-0.361)

Fig. 2. Bivariate scatter plots bivariate (Demonstrating the duration of heroin use in heroin-dependent individuals with amplitude of low-frequency fluctuation in the right angular gyrus and in the left superior occipital gyrus)

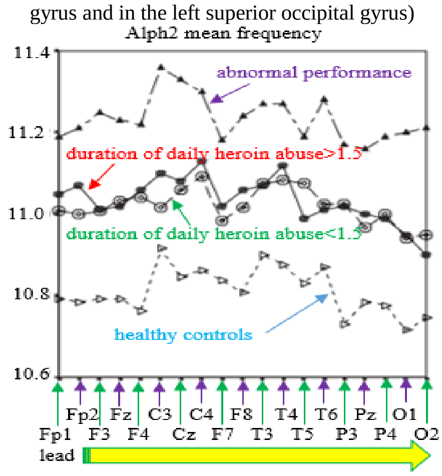


Fig. 3. Average frequency distribution of alpha2 in 19 leadsin healthy and heroin addiction people

In [156], the effects of heroin on the brain were assessed by studying the relationship between the power spectrum and average frequency of the electroencephalogram, as well as the duration of heroin use. The study participants included 33 heroin users (with durations of heroin use ranging from 4 to 44 months, intravenous injection amounts ranging from 0.04 to 1 gram per day, and withdrawal durations ranging from 6 days to 5.4 months) and 13 healthy individuals who matched the heroin users in terms of age. The research results showed that frequency changes in the alpha 2 sub-band were more prominent in the frontal and central regions and correlated with the duration of heroin use. The average frequency of the alpha 1 sub-band was significantly lower in the central, parietal, and midline regions, primarily observed in heroin-addicted individuals who used higher doses of the drug. The power spectrum of brain activity in patients corresponded with the duration of withdrawal. These findings provide a basis for the hypothesis that excessive heroin use leads to frequency changes in neural oscillations, which may contribute to the progression of antisocial behaviors and some impairments in cognitive processes in these patients. During early heroin withdrawal, there are inconsistencies in the power spectrum of the electroencephalogram signal, which usually normalizes completely after several weeks of withdrawal.

In [157], the study examined the differences in the beta sub-band (12-22 Hz) and investigated the physiological and operational relationships between different electroencephalogram frequency bands in addicted individuals. The results of the study also indicated operational differences between the various electroencephalogram bands in these individuals.

In [158], a direct correlation between the low-alpha sub-band in the central region of the brain in channels C3, C4, and CZ and the duration of heroin use in the right hemisphere of the brain (channel C4) has been demonstrated. This research shows that the structural function of the brain is immediately affected by the onset of heroin use, initially impacting the left hemisphere and then extending to the right hemisphere.

In [159], it has been shown that the relative power and central frequency of frequency sub-bands in electroencephalogram signals of addicted individuals compared to healthy individuals have significant differences in the alpha and beta sub-bands.

In [160], studies conducted on electroencephalogram signals have concluded that heroin-addicted individuals exhibit low-voltage background activity with a decrease in the alpha sub-band rhythm, increased beta activity, and an increase in theta and delta waves with a low amplitude in central regions.

In [161], after extracting the P300 component, a multi-resolution wavelet transform was used. The main objective was to investigate changes in the registered electroencephalogram signal channels. The results obtained in this study indicate that the P3 channel in individuals using heroin exhibits more changes in their wavelet transform. Figs. 4 and 5 compare the average latency and amplitude of the P300 component (addiction, control, and recovery) for each channel. As observed, the control participants have a shorter delay in comparison to other groups. Therefore, the control participants are quicker in decision-making, while others require more time for decision-making. In comparison to the control group, addicted subjects require more power for concentration. The high amplitude is presented by addicted individuals, and the low amplitude is presented by recovery individuals, indicating greater brain activity in the addiction group.

In [162], the extraction of the P300 and P600 components was used to investigate the power spectrum in these components. The results of this article show that the frequency power spectrum in the alpha 2 sub-band is greater in the frontal and central regions compared to other areas. Furthermore, a significant difference between healthy individuals and addicts is observed in this region.

A summary comparison of the studies on the effect of electroencephalogram signal changes is presented in Table (4). Based on the presented results, although multiple features have been considered for linear and nonlinear frequency characteristics, the main challenge of the Fourier transform, which is its inefficiency for non-stationary signals, is addressed. To overcome this challenge in these studies, EEG signals are divided into short-time windows with overlap, but it seems that multi-resolution transforms such as wavelet transform and short-time Fourier transform can provide more effective analysis.

C) Changes in Brain Regions

As mentioned, electroencephalogram signals are a reliable tool for assessing changes in drug-affected regions [163,164]. In [165], the differences in drug effects on channels and sub-bands of EEG signals recorded from addicted and healthy individuals have been studied extensively. In summary, it can be stated that in the central regions (channels C3, C4, and CZ) of the brains of heroin-addicted individuals, slow-wave potentials exhibit a maximum magnitude compared to healthy individuals. The investigation of the resting-state reactive behavior of heroin addicts has been examined in this study. In this study, all head regions were analyzed. The results obtained indicate that there are greater slow-wave potentials in the C3, C4, and CZ regions of the brains of heroin-addicted individuals compared to healthy individuals.

In [166], nonlinear features in the alpha sub-band during the resting state were examined in individuals who have quit heroin compared to a healthy group. It was shown that in individuals who have quit heroin, irregular neuronal oscillations lead to higher nonlinear dynamics. Nonlinear analysis results using features such as correlation dimensions, Kolmogorov entropy, and Lempel-Ziv complexity showed that the alpha sub-band EEG signals of individuals who have quit heroin are significantly more irregular. The results of this study indicate that neural activities in the alpha sub-band of individuals who have quit heroin are significantly weaker in the parietal lobe 25 (BA3 and BA7), frontal lobe 26

(BA4 and BA6), and limbic lobe 27 (BA24). Therefore, functional abnormalities in the brain, especially for alpha sub-band neural oscillations, occur after quitting heroin. To investigate the acute and short-term effects of methadone dosage, EEG sessions were recorded in two time intervals, T1 and T2. One session during the first week of methadone maintenance treatment and the second after 10 weeks. In each interval, two EEG sessions were recorded using the described paradigm. The average potentials related to pre- and post-methadone consumption events in the T1 time interval, indicating an increase in the average magnitude of the potentials related to events after the dosage compared to pre-dosage measurement, are shown in Fig. 6.

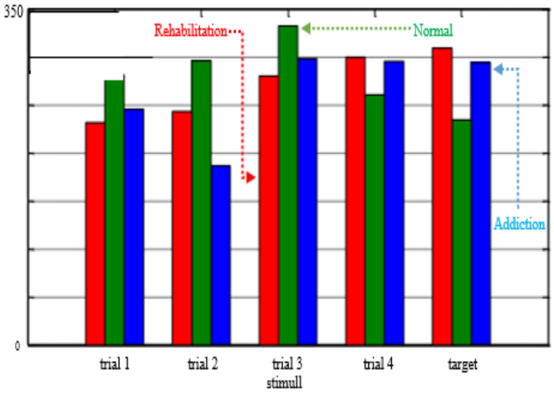


Fig. 4. Comparison of average delay for each channel

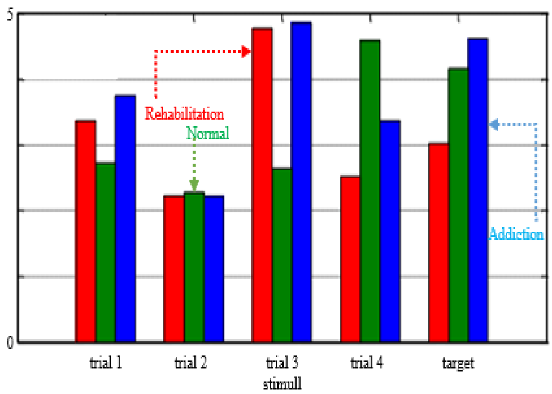


Fig. 5. Comparison of mean amplitude for each channel

In [167], disruptions in the frontal cortex and prefrontal-limbic circuits were observed in heroin-addicted individuals, indicating an imbalance between local neural activity and neuronal communication networks. Abnormal activities in the posterior cingulate cortex, right insula, gyrus, and prefrontal regions of drug-addicted individuals compared to healthy individuals have been demonstrated in this study. This effect gradually increases with increased substance use and compulsive drug consumption. Strong functional connections have been reported between the nucleus accumbency (NAc) and both the ventromedial/dorsolateral aspects of the anterior cingulate cortex (ACC) and the orbitofrontal cortex (OFC), as well as between the lateral OFC and the amygdala in addicted individuals compared to the control group.

Table (5) provides an overview of the conducted research, highlighting the advantages and disadvantages of each in investigating changes in brain regions and sub-bands. It is worth noting that the correlation between brain regions and their impact on each other in heroin-addicted individuals was not considered in these studies. Multi-feature-based analyses can further improve the results of the analysis.

3. Analysis of the Results

Electroencephalogram signals are a tool for examining brain changes in both healthy and addicted individuals. Numerous studies have been conducted using EEG signals on individuals addicted to various substances. This study provides a review of research conducted on the effects of addiction on EEG signals.

Table (6) briefly presents the results. This study examined the effects of attention deficit disorder on the electroencephalogram signal, changes in EEG signal frequency characteristics, and changes in brain regions and sub-bands. The changes in the extracted features from the EEG signal and their impact on different regions are shown in Fig. 7, representing the evaluation results for three different tests. As observed, compared to a healthy individual (HC), the changes in an addicted individual (AHA) indicate a significant influence of drugs. The changes in EEG signal frequency characteristics were investigated, and as evident, the desired changes tend to occur in the frontal region, indicated by the color red. The results shown are consistent with relevant studies and the findings presented in Table (5). Neural activity in the parietal (BA3 and BA7), frontal (BA4 and BA6), and limbic lobes (BA24) is observable in the images of the subjects. Additionally, changes in the right-sided regions of the temporal and frontal areas are observed, as depicted in this figure.

Table.4.
Examining changes in the frequency characteristic of the electroencephalogram signal (type of characteristics in the time and frequency domain)

Ref.	***Explanation***	***Advantages***	***Disadvantages***	***Database***	***Type of Feature***
[152]	- Relative power ratio of alpha to theta at T6 and T5	- Determining the difference between healthy and addicted individuals	- Considering only one feature (spectral power)	- 18 addicted individuals, 18 healthy individuals	- Time and frequency domain
[153]	- Utilizing fast Fourier transform method in heroin addicts and individuals in recovery	- Determining the difference between healthy and recovered individuals by examining all Sub-bands - Large sample population for investigating differences	- Considering only one feature (spectral power) - Inability of fast Fourier transform in detecting changes in brain signals	- 20 addicted individuals, 20 healthy individuals, 20 individuals who recovered from heroin addiction	- Utilizing Fourier transform and power spectral density
[154]	- Investigation of spectral power density coherence in determining the difference between two hemispheres	- Examining all sub-bands to determine the difference between healthy and addicted individuals in hemispheres	- Examination of only power spectral coherence feature (one feature is not sufficient)	- 18 addicted individuals, 12 healthy individuals	- Power spectral density
[155]	- Dynamics and frequency characteristics of electroencephalogram signals	- Investigation of time and frequency domain characteristics in all scalp areas and brain regions - Examining the impact of drug use in addicted and healthy individuals	- Undetermined dosage of methadone for treatment	- 51 addicted individuals, 40 healthy individuals	- Frequency domain
[156]	- Examination of relative power and central frequency of alpha and beta sub-bands	- Simultaneous investigation of two features in the frequency domain	- Differences between healthy and addicted individuals examined only in two sub-bands	- 33 addicted individuals, 12 healthy individuals, 14 individuals who recovered from addiction	- Relative power and central frequency
[157]	- Exploring the relationship between power spectrum and average frequency of electroencephalogram and duration of heroin use	- Study of drug-related disorders in treatment examining all sub-bands to determine the relationship	- Considering only one feature for investigating the relationship	- 20 addicted individuals, 12 healthy individuals	- Examination of power spectral density
[158]	- Relative power and central frequency of alpha and beta sub-bands	- Examining all sub-bands to establish the relationship	- Only central frequency feature has been examined	- 33 addicted individuals, 13 healthy individuals	- Central frequency
[159]	- Analyzing differences in beta sub-bands and investigating physiological relationships	- Investigating the physiological and/or operational interactions between bands	- Examination of differences in only beta sub-band	- 18 addicted individuals, 18 healthy individuals	- Central frequency
[160]	- Alpha sub-band in the frequency range of 10 to 13 hz in the frontal and central lobes	- Examining the relationship between Wechsler intelligence scale and changes in electroencephalogram signal power for adults	- Dysfunction in the right hemisphere exists, but the left hemisphere is occasionally involved	- 30 addicted individuals, 18 healthy individuals	- Power spectrum
[161]	- Study of background voltage activity in heroin addicted individuals	- Drug consumption in brain signal channels, investigating all scalp regions in all sub-bands	- Investigation of differences with evoked potentials, ineffectiveness of background voltage feature	- 19 addicted individuals, 14 healthy individuals	- Power spectrum
[162]	Investigation of Multiresolution Wavelet Transform in P300 Component and Amplitude Domain Feature	- Comprehensive study of individuals using heroin	- Examination conducted only with wavelet transform applied to P300	- 10 individuals addicted to heroin, 10 healthy individuals	- Multiresolution information derived from wavelet transform component P300
[163]	Analysis of Relative Power and Central Frequency of Frequency Sub-bands	- Examining all scalp regions in all available sub-bands.	- Investigations conducted only on one feature	- 19 individuals addicted to heroin, 19 healthy individuals	- Frequency power spectrum in P300 and P600s components

Table.5.
Examination of changes in brain areas and sub-bands

Ref.	Explanation	Advantages	Disadvantages	Database Specifications	Type of Feature
[165]	- Investigation of the differences induced by drug consumption in channels and sub-bands of electroencephalogram signals	- Comprehensive nonlinear analysis presented in all sub-bands - Examination of all brain regions	- Nonlinear analysis-based features extracted only in the time domain.	- 33 addicted individuals, 13 healthy individuals	- Nonlinear analysis in the time domain
[166]	- Examination of nonlinear features in the alpha sub-band during resting state in individuals who have quit heroin and healthy individuals	- Regions of interest have been fully determined in this study - Investigation of connectivity in all brain regions	- Investigations have been conducted only in the alpha sub-band.	- 18 addicted individuals, 18 healthy individuals	- Relative power
[167]	- Investigation of impairments in the prefrontal cortex and frontal-circuit pathways	- Establishing the Link between Local Neural Activity and Neuronal Communication Network	- Brain regions with high coherence in function are correlated, but correlation was not considered in this study.	- 17 addicted individuals, 15 healthy individuals	- Temporal correlation

Table.6.
Summary of the results analysis

Investigation of the Type of Change	Obtained Results
The effect of attention disorder on electroencephalogram signal	- Reduction of P300 amplitude during consumption and increase after quitting - Increase of P300 amplitude upon reuse of drugs in beta and secondary alpha sub-bands
Frequency feature changes in electroencephalogram signal	- Demonstration of power spectrum changes in heroin-addicted individuals even after quitting - Decrease in low-frequency oscillation amplitude - Significant relationship between spectral power, average frequency, and duration of heroin use in electroencephalogram
Changes in Brain Regions and Sub-bands	- Weak neural activity in alpha sub-band in parietal lobe (BA3 and BA7), frontal lobe (BA4 and BA6), and limbic lobe (BA24) - Increase in Oscillation amplitude in right-sided temporal and frontal regions among addicted individuals - Decrease in amplitude in regions such as the posterior cortex, including left supra-marginal gyrus

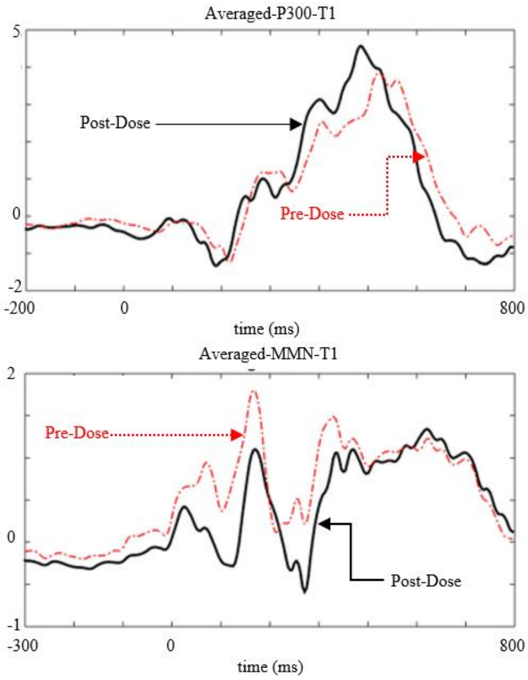


Fig. 6. Mean test event-related potential for pre- and post-dose measurements at time interval T1

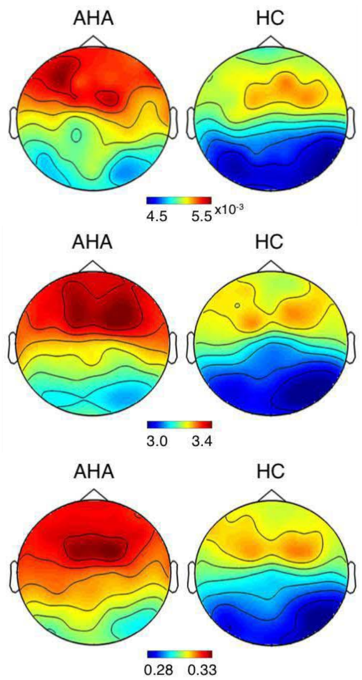


Fig. 7. Comparison of the changes made in different areas of the head compared to an addicted person

The structure of the electroencephalogram signal in different sub-bands and different brain regions has been investigated in the conducted research. To examine the electroencephalogram signals in healthy and addicted individuals, features such as the P300 amplitude, frequency power spectrum, frequency changes in different sub-bands, and power in various sub-bands have been studied in various research projects. It should be noted that these features are extracted from different regions and sub-bands. Statistical methods or other approaches, such as examining connections between regions, have been used to investigate differences in sub-bands and different regions' placement of electrodes. The results of these studies indicate differences in electroencephalogram signals between healthy and addicted individuals in various regions and sub-bands. These differences can be significant or subtle. The existing differences are present both in individuals who have quit drug addiction and those who are currently using compared to healthy individuals. For example, in the reviewed studies, it is evident that the P300 amplitude has significantly decreased during the abstinence period of individuals. Furthermore, in cases of re-use, the P300 amplitude has shown an increase. The investigations also indicate an increase in the P300 amplitude upon reusing drugs in the beta and the second alpha sub-bands.

The studies indicate that individuals' inclination and the duration of substance use also have an impact on the power of the electroencephalogram signal. Much weaker neural activity has been observed in the alpha sub-band in the parietal lobe (BA3 and BA7), frontal lobe (BA4 and BA6), and limbic lobe (BA24). Research shows a decrease in the low-frequency oscillations in addicted individuals. This decrease is observed in regions such as the posterior cortex, including the left occipital primes. Increased oscillation amplitude has also been observed in addicted individuals. This increase is present in the right-sided regions of the temporal and frontal areas. Research has demonstrated the effects of drug use and addiction symptom improvement on the EEG signal. Therefore, substance use influences the electroencephalogram signal of individuals.

In addition to the differences in the electroencephalogram across different regions of the head, differences in the electroencephalogram signals of healthy and addicted individuals have also been observed in various sub-bands. In addicted individuals, the alpha-to-theta power ratio at T6 has decreased. Significant differences have been observed in the power spectrum between the delta and alpha sub-bands. These differences are evident in individuals who have quit addiction through a decrease in alpha sub-band power. The average power spectrum and frequency of the electroencephalogram also show a significant relationship with the duration of heroin use. Each study has considered the significance level based on different statistical conditions in the population. The significance level may be 0.05 or 0.01, depending on the chosen statistical criteria. Since the value of the significance level varies depending on the statistical criteria in each study, only the significance has been mentioned. Frequency changes in the alpha 2 sub-band are more pronounced in the frontal and central regions and are related to the duration of heroin use. On the other hand, a significant decrease in the average frequency of the alpha 1 sub-band in central, parietal, and midline regions has been observed in individuals with higher addiction. The existing differences in the electroencephalogram signal can also be observed in nonlinear dynamic analysis and local analysis. These differences indicate higher irregular neuronal oscillations in nonlinear dynamics. Features such as correlation dimension, Kolmogorov entropy, and Lempel-Ziv complexity have been used to demonstrate this irregularity in the alpha sub-band.

4. Conclusion

When a change occurs in the nervous system, a related change in psychological behaviour or function, such as learning, memory, addiction, maturity, and improvement, usually occurs. Drug consumption has its own specific effects on various parts of the body. The most significant effect of drug consumption in the human body is manifested in the brain. One way to investigate these effects is through electroencephalogram signals, which require feature extraction. The aim of this article is to examine the research conducted on the effect of addiction on the brain signals of heroin addicts. It is possible to distinguish between the electroencephalogram signals of healthy individuals and addicts by examining the relationship between specific electroencephalographic frequencies. Furthermore, the time and frequency domain features of the electroencephalogram signal are different in addicted and healthy individuals. In this article, the impact of addiction on electroencephalogram signals is analyzed from three perspectives: attention disorder, examination of extracted feature dynamics, and the effect on different brain regions and sub-bands. Understanding the changes and differences in the brain signals of addicted individuals compared to healthy individuals can be helpful in providing diagnostic methods for differentiating between healthy and addicted individuals. The results indicate that drug consumption leads to attention processing, functional impairments, and brain abnormalities. Functional impairments include attention disorder. The examination of attention disorder due to drug consumption is carried out by examining the P300 component in the electroencephalogram. The results of the studies indicate a significant reduction in the P300 amplitude in the central frontal region in individuals who have quit heroin. Additionally, the P300 amplitude in individuals undergoing the quitting process approaches normal levels over time. Since the information in the domain of brain signals is highly influenced by noise, frequency domain information can be used to further investigate the signal. Linear and nonlinear frequency features have been considered to examine changes in healthy and addicted individuals. However, the Fourier transform is not applicable to non-stationary signals, which presents a significant challenge. Therefore, discrete wavelet transform and its family are recommended for further investigations into the changes in brain signals. Changes in brain signals are accompanied by increased activity in beta and alpha sub-bands, event-related P300 reduction, the influence on the power of the electroencephalogram signal, and the effect on different brain lobes. The results of previous studies indicate changes in the brain signals of heroin addicts, including a decrease in the alpha-to-theta power ratio at T6. This significant difference is also accompanied by a difference in the delta-to-alpha power ratio. Furthermore, the results of the studies indicate that the power of the electroencephalogram signal is influenced by craving and substance use history. The impact of drug use does not disappear even with quitting; it only decreases to the extent that the neural activity of individuals who have quit is significantly weaker in the parietal lobe (BA3 and BA7), frontal lobe (BA4 and BA6), and limbic lobe (BA24). Based on the conducted study, it is suggested to conduct research on designing a neurofeedback therapeutic protocol and utilize the data from this research. Additionally, the P300 component can be used as a feature for neurofeedback therapy in the treatment of addicted individuals. The expansion of machine learning methods for testing addicted individuals using brain signals in the specified region can be of interest to researchers. The correlation between brain regions, their impact, and the influence of different sub-bands on each other in heroin-addicted individuals is a challenge that has not been addressed in the articles. The above study can provide great help to researchers in further related studies.

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