وزارة التعليم العالي والبحث العلمي

جامعة بابل / كلية الطب

فرع الفسلجة والفيزياء الطبية

تقييم التغييرات الحاصلة في تخطيط الدماغ الكهربائي لدى المرضى الذين يعانون من اضطراب الإدمان

رسالة مقدمة الى

مجلس كلية الطب ـ جامعة بابل

وهي جزء من متطلبات نيل درجة ماجستير علوم الفسلجة الطبية

من قبل

زينب ولاء صاحب مبارك

بكالوريوس في الطب والجراحة العامة

جامعة بابل / كلية الطب / 2016

بأشراف

الأستاذ الدكتورة — **الأستاذ المساعد الدكتور**

فرح نبيل عباس الصادق — **وليد عزيز العميدي**

2022 م — **1444 هـ**

Republic of Iraq

Ministry of Higher Education and

Scientific Research

University of Babylon

College of Medicine

Department of Medical Physiology

Evaluation of Electroencephalographic Changes among Patients with Substance-Related Disorders

A Thesis

Submitted To the Council of the College of Medicine, University of Babylon in Partial Fulfillment of the Requirements for the Degree of Master of Sciences in Medical Physiology

By

Zainab Walaa Sahib Mubarak

M.B.Ch.B.

University of Babylon / College of Medicine /2016

Supervised by

Prof.
Dr. Farah Nabil Abbas

Asst. Prof.
Dr. Waleed Aziz Al-Ameedy

1444 A.H **2022 A.D**

بسم الله الرحمن الرحيم

﴿يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ

وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ

وَاللَّهُ بِمَا تَعْمَلُونَ خَبِيرٌ﴾

صدق الله العلي العظيم

سورة المجادلة: الآية (11)

Acknowledgments

After thanking our great GOD , I'm so grateful to professor Farah Nabil Abass the supervisor who have been supportive and engorged me to catch up my study goals and who worked actively to provide me with help to pursue those goals. A sincere gratitude and appreciation to my supervisor Dr. Waleed Azeez Al – Ameedi , for helping me in collecting the cases and scientific supervision as well as overcoming any obstacle throughout the course of this study.

Many thanks for all professors in department of medical physiology who taught me during the course.

My gratitude goes to all members of Neurophysiological Unit at Al Imam Al Sadiq Teaching Hospital . I'm so thankful to all patients who I'm quite sure that they are so awesome and beneficial to our society if they are treated well and I hope my study will help even a little bite in understanding the substance related disorder and eventually make it a curable disorder.

Special thanks to to Dr. Azhar Al Akam for his help in collecting cases and scientific support and my special thanks for all members of neurophysiology department who had participate in this study; without them the study wouldn't be achieved .

الخلاصة:

يمكن أن تنشأ الاضطرابات المرتبطة بالمواد المخدرة عندما تأخذ الأدوية التي تنشط نظام المكافأة في الدماغ بشكل مباشر وبالتالي تسبب السعادة . يُعترف الآن بتعاطي المخدرات على أنه مرض دماغي يؤدي إلى تآكل نفس الدعامة العصبية التي تمكن من ضبط النفس واتخاذ القرار المناسب. وبالتالي ، فإن الوقاية والكشف المبكر والتدخل مهمان من خلال تدخلات فعالة شاملة ومتعددة التخصصات. يعد تخطيط الدماغ الكهربائي طريقة غير مكلفة وغير جراحية تسمح بتسجيل نشاط الدماغ الكهربائي التلقائي من عدة أقطاب كهربائية موضوعة فوق فروة الرأس. على الرغم من الدقة المكانية المحدودة ، فهي أداة سريرية قيّمة للتشخيص بسبب الدقة الزمنية الممتازة ، مما يجعلها طريقة الخط الأول لاستبعاد تشخيص الصرع أو التسمم بالعقاقير أو اضطرابات النوم لدى المرضى النفسيين.

يهدف الباحث في هذه الدراسة إلى تحديد وجود ونوع التغيرات في تخطيط الدماغ الكهربائي بين المرضى الذين يعانون من اضطراب الادمان، وتقييم الخصائص الاجتماعية والديموغرافية والسريرية للمرضى الذين يعانون من اضطراب الادمان.

أجريت الدراسة في الفترة من الأول من سبتمبر 2021 إلى الأول من أغسطس 2022 في وحدة الفسلجة العصبية في مستشفى الإمام الصادق التعليمي في مدينة الحلة – محافظة بابل لتحديد وجود ونوع التغيرات الكهربائية الدماغية لدى المريض المصاب باضطراب الادمان). تم إجراء دراسة مقطعية قائمة على الملاحظة على 112 مريضاً (104 ذكور و 8 إناث). تم تشخيص المريض من قبل الأطباء النفسيين وفقًا للدليل التشخيصي والإحصائي للاضطرابات العقلية ، الإصدار الخامس (هو تحديث 2013 للدليل التشخيصي والإحصائي للاضطرابات العقلية ، أداة التصنيف والتشخيص التي نشرتها الجمعية الأمريكية للطب النفسي).

أظهرت النتائج أن معدل تكرار التغيرات في تخطيط كهربية الدماغ كان 57.1٪ بينما تلك التي لم تتغير بنسبة 42.9٪. أولئك الذين حصلوا على الدرجة 2 أو متوسطة الشدة كانت 53.6٪. بينما تم العثور على تشوهات خطيرة في 3.5٪ من المرضى. كان هناك ارتباط معنوي بين التغيير الكهربي للدماغ ونوع المادة التي يتم تناولها بقيمة P (0.008) ، أي أن معظم التغييرات كانت الدرجة الثانية في جميع أنواع المادة باستثناء مادة متعددة (موجودة في الغالب بدرجة 0 أو بدون تغييرات) . أوضحت الدراسة الارتباط بين التغير الكهربائي للدماغ ومدة تناول المادة ، بقيمة P قدرها (0.0001) والتي كانت معنوية (كلما طالت مدة تعاطي المخدرات كانت التغييرات اشد) ، وكذلك الارتباط بين هذه التغييرات ومدة الامتناع عن تناول المواد. كانت معنوية ، بقيمة P قدرها (0.0001) ، (أقصر فترة للامتناع عن المواد المخدرة ارتبطت بمعظم التغييرات).

كان هناك ارتباط معنوي بين نوع تعاطي المخدرات والعمر (القيمة الاحتمالية = 0.002) ، وبين نوع تعاطي المخدرات والحالة الاجتماعية بقيمة P تبلغ (0.028) ، وبين نوع تعاطي المخدرات والتعليم مع قيمة P لـ (0.042) والتي كانت ذات دلالة. العلاقة بين نوع تعاطي المخدرات والجنس والإقامة والمهنة كانت غير ذات دلالة إحصائية.

خلصت هذه الدراسة إلى أن التغيرات غير الطبيعية في تخطيط كهربائية الدماغ كانت ذات انتشار مرتفع للمرضى الداخليين المصابين باضطراب الادمان. كان الشذوذ الأكثر شيوعًا هو الدرجة الثانية (شدة معتدلة) ، وكانت المادة الأكثر شيوعًا مع تغيرات غير طبيعية في تخطيط كهربائية الدماغ هي الأمفيتامين.

Summary

Substance-related disorders can arise when drugs that directly activate the brain's reward system are taken for the feelings of pleasure they induce. Substance abuse is now recognized as brain disease which erodes the same neural scaffold that enables self- control and appropriate decision making. Thus, prevention and early detection and intervention are of importance through effective comprehensive and multidisciplinary interventions.

Electroencephalography is an inexpensive and non-invasive method allowing the recording of spontaneous electrical brain activity from multiple electrodes placed over the scalp. Despite limited spatial resolution, it is a valuable clinical tool for diagnosis due to its excellent temporal resolution, making it a first-line method to exclude diagnoses of epilepsy, drug intoxication or sleep disorders in psychiatric patients.

This study aims to determine the presence and the type of EEG changes among patients with substance-related disorders .and evaluating the sociodemographic and the clinical characteristics of patients with substance-related disorder.

This observational cross sectional study was conducted on 112 patient (104 male and 8 female) from the first of September 2021 to the first of August 2022 in neurophysiology department of Al Imam Al Sadiq Teaching Hospital in Al-Hilla city, Babylon Governorate.

The patients were diagnosed by psychiatrists according to The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (is the 2013 update to the Diagnostic and Statistical Manual of Mental Disorders, the taxonomic and diagnostic tool published by the American Psychiatric Association).

The results showed that the frequency of electroencephalographic changes was 57.1% while those without any changes was 42.9%. Those with score 2 or moderate severity were 53.6%. While severe abnormalities were found in 3.5%of patient. There was a significant association between the electroencephalographic change and the type of substance taking with P value of (0.008),that is most of the changes was score two in all type of the substance except multiple substance (present mostly with score 0 or no

changes). The study showed significant association between the electroencephalographic change and duration of substance taking, with P value of (0.0001) (the longer duration of substance abuse , the most the changes), also the association between these changes and duration of substance abstinence was significant, with P value of (0.0001),(the shorter abstinence period associated with most changes).

There were significant associations between the type of substance taking and age (p value=0.002), between the type of substance taking and marital status with P value of (0.028), and between type of substance taking and education with P value of (0.042) which was a significant.

The associations between type of substance taking and gender, residence and occupation were non-significant.

This study concluded that the abnormal electroencephalographic changes were of high prevalence in-patient with substance related disorder. The most common abnormality was score two (moderate severity).Among the tested substances; amphetamine was associated with most of the EEG changes.

List of Abbreviations

Abbreviation	Complete term
APA	American Psychiatric Association
DSM-V	Diagnostic and Statistical Manual of mental disorders, fifth edition
EEG	Electroencephalography
EMG	Electromyogram
GBD	Global Burden of Disease
HV	Hyperventilation
MA	Methamphetamines
RAS	Reticular Activating System
SAMHSA	Substance Abuse and Mental Health Services Administration
SUDs	Substance Use Disorder
VTA	Ventral Tegmental Area
WHO	World Health Organization

List of contents

List of Tables

List of Figures

Dedication

To my wonderful father and mother

Who supported me in everything in my life

To my husband

who helped me from the beginning of the passage until this moment and supported me in my scientific profession

To my son (Yousif) and daughter (Dhay)

To my sisters

To all my family

To my friends and teachers who supported me to accomplish this study

To everyone who believe that education does not stop at any point of our life and learning is infinity.

I dedicate this work.

Zainab

1.1. Introduction:

Substance abuse refers to the harmful or hazardous use of psychoactive substances, including alcohol and illicit drugs. It is now a major public health challenge all over the world (WHO, 2014).

Substance use, misuse, and alcohol or drug use are chronically relapsing disorders, characterized by the compulsive use of addictive substances despite adverse consequences to the individual and society and major contributors to the burden of disease in the United States and worldwide (GBD, 2018).

Drug use disorders carry a lifetime prevalence of about 10% in the general American population, representing more than 23 million adults who are struggling with problematic drug use (SAMHSA, 2019).

It is expounded that psychoactive drugs are mood altering and used for purposes of recreation or self-medication. These substances affect the central nervous system, and therefore alter the user's mood and sensory perceptions in some cases. For this reason, the major drugs of misuse, activator or inhibitor imitate the structure of neurotransmitters, the chemicals in the brain that give people pleasure (Van Wormer and Davis, 2008).

Studies on populations subjected to conflict and displacement suggest that exposure to war and violence increases the risk for substance use (Ezard, 2012). There is growing concern about the impacts of conflict and war on substance use in Iraq. Previous community-based information about prevalence and patterns of tobacco, alcohol and drug use in Iraq are lacking (Aqrawi and Humphreys, 2009).

Electroencephalography (EEG) is a noninvasive electrophysiological monitoring tool that is used for recording electrical activity of the brain. It measures voltage fluctuations arising in the brain due to the ionic currents flowing through the neurons of the brain. It is often used for diagnosing epilepsy, depth of anesthesia, coma, sleeping disorders, encephalopathies, brain death and neuropsychiatric conditions (Davenport, 2019).

There has been many upsurge of neuroimaging research seeking to examine the risk-factors, neural mechanisms, and neuropathological outcomes of dependence and substance abuse. Neuroimaging studies such as EEG of drug-abusing and drug-dependent individuals have revealed significant alterations in brain structure (Suckling and Nestor, 2016).

Standard-EEG is a far more widely available approach and costs less overall for processing and interpretation,it is an insightful estimation for mental health in patients with substance use disorder (Minnerly *et al*., 2021).

Although excess beta activity and increase in theta frequency may be the most common EEG alterations associated with medication, more remarkable changes may also appear. Although changes such as diffuse delta, triphasic waves, bisynchronous spikes or polyspikes, burst suppression or electrocerebral inactivity may indicate a dismal prognosis under many circumstances; these patterns may fully resolve to a normal EEG if drug administration is the unique or principal cause was stopped (Blume, 2006).

1.2. Aims of the study:

1. Determining the presence and the type of EEG changes among patients with substance-related disorders.
2. Evaluating the sociodemographic and the clinical characteristics of patients with substance-related disorder.
3. EEG changes among the type of substances taking.

Review of literature:

2.1 Substance related disorder

A maladaptive pattern of substance use leading to clinically significant impairment or distress, manifested by the presence of at least two of 11 criteria in a 12-month period (DSM-V, APA 2013).

It is one of the important social pathologies, which not only endangers the health of the individual and society, but also leads to mental and ethical decline. It refers to the improper, excessive, irresponsible, or self-damaging use of addictive substances (Visser & Routledge, 2007).It is the most common psychiatric conditions resulting in serious impairments in cognition and behavior (APA 2013).

Brain is affected in a particular manner by chronic alcohol and drug use; there is extensive research evidencing prefrontal damage, alterations in mesocorticolimbic pathways or fronto-cerebellar circuits (Wang *et al.*, 2015), as well as psychophysiological alterations in terms of brain evoked potentials or brain rhythm changes (Kamarajan & Porjesz, 2015). These alterations can be related to clinical aspects such as impulsivity (Wang *et al.*,2015), dependence severity, and vulnerability toward relapse (Courtney *et al.*, 2013).

2.1.1 Some terminology:

2.1.1.1 Substance dependence:

Includes more severe forms of substance use disorders, and usually involves a marked physiological need for increasing amounts of a substance to achieve the desired effects. On the other hand, substance dependence means that an individual will show a tolerance for a drug and experience withdrawal symptoms when the drug is unavailable (Boland, 2021).

2.1.1.2 Tolerance:

Is the need for increased amounts of a substance to achieve the desired effects, which results from biomedical changes in the body that affects the rate of metabolism and elimination of substance from the body (Butcher, *et al*., 2007).

2.1.1.3 Substance Intoxication:

Substance intoxication is the diagnosis used to describe a syndrome characterized by specific signs and symptoms resulting from recent ingestion or exposure to the substance (Juhnke, 2017).

2.1.1.4 Substance Withdrawal :

Substance withdrawal is the diagnosis used to describe a substance-specific syndrome that results from the abrupt cessation of heavy and prolonged use of a substance (Laura and APAP , 2019).

2.1.2 Brain Areas Associated With Substance Use and Addiction:

The brain is made up of a multiple areas with strong connections to the addiction process. These areas are :

2.1.2.1 The Basal Ganglia :

The basal ganglia are a group of structures located deep within the brain that play an important role in keeping body movements smooth and coordinated. They are also involved in learning routine behaviors and forming habits. Two sub-regions of the basal ganglia are particularly important in substance use disorders: The nucleus accumbens, which is involved in motivation and the experience of reward, and The dorsal striatum, which is involved in forming habits and other routine behaviors (Kalivas and Volkow, 2005).

2.1.2.2 The Amygdala:

The extended amygdala and its sub-regions, located beneath the basal ganglia, regulate the brain's reactions to stress-including behavioral responses like “fight or flight” and negative emotions like unease, anxiety, and irritability. This region also interacts with the hypothalamus, an area of the brain that controls activity of multiple hormone-producing glands, such as the pituitary gland at the base of the brain and the adrenal glands at the top of each kidney. These glands, in turn, control reactions to stress and regulate many other bodily processes (Davis et al., 2009).

2.1.2.3 The Prefrontal Cortex:

The prefrontal cortex is located at the very front of the brain, over the eyes, and is responsible for complex cognitive processes described as “executive function.” Executive function is the ability to organize thoughts and activities, prioritize tasks, manage time, make decisions, and regulate one's actions, emotions, and impulses (Ball *et al* .,2011).

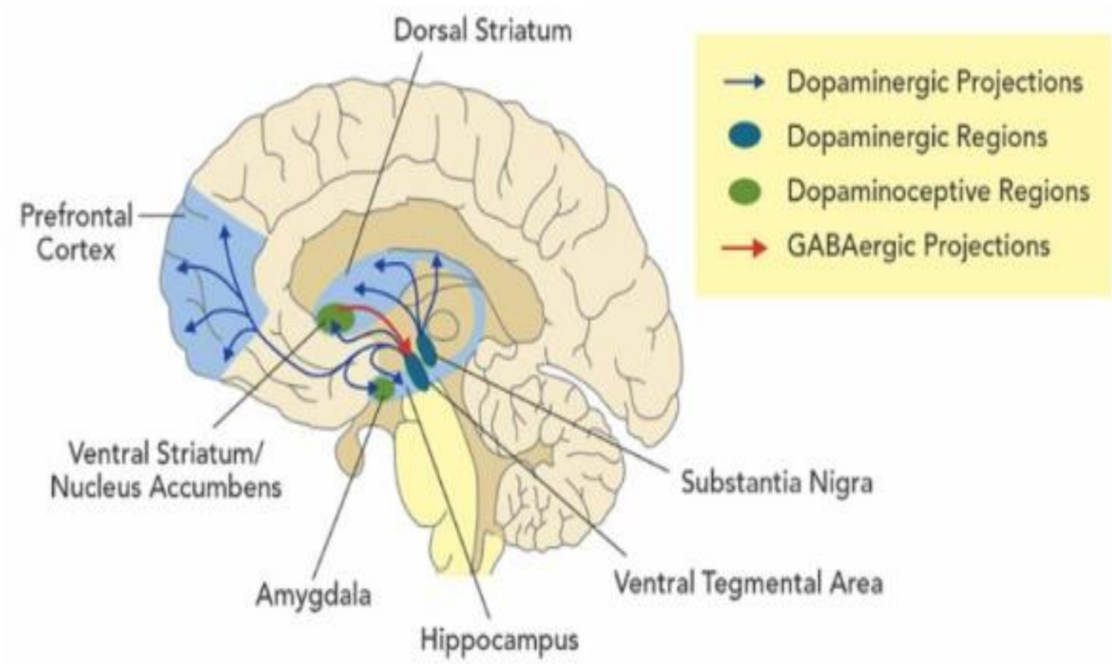

Figure (2-1) Brain area associated with reward system (Tomkins, *et al* ., 2001).

2.1.3 Etiology of substance abuse

2.1.3.1 Social factor:

An established relationship exists between substance abuse and delinquency risk factors .As many as 80% of youth in trouble with the law are using alcohol and other drugs (CASA , 2004), and substance use disorders are among the most commonly diagnosed disorders within the juvenile justice system (Palermo, 2009). Young people are particularly vulnerable to harm from substance abuse due to culture, customs and values , increased risk of substance abuse due to challenges such as academic failure and deviant peer relationships (Mason, *et al*., 2007), as well as early aggressive behavior, instability, and poverty (Dodgen & Shea, 2000).Other factors are behind substance use, such as low socioeconomic status, formless time with peers، parental influences, psychosocial factors and community (Alhyas , *et al*., 2015) , accessibility, lack of knowledge, negative attitudes and beliefs are problems associated with substance abuse among the youth (Jiloha, 2018).

2.1.3.2 Genetic factor:

Strong evidence from studies of twins, adoptees, and siblings brought up separately indicates that the cause of alcohol abuse has a genetic component. Many less conclusive data show that other types of substance abuse or substance dependence have a genetic pattern in their development.Researchers have used restriction fragment length polymorphism (RFLP) in the study of substance use disorders, and preliminary results show associations with genes that affect dopamine production (Boland , 2021).

2.1.3.3 Neurochemical Factors:

While pharmacological differences exist among the various classes of abused drugs, the one-shared factor among all drugs with a strong dependence potential is a rewarding or reinforcing property by acting on dopamine receptor. Dopamine (DA) is the neurotransmitter that has been classically associated with the reinforcing effects of drugs of abuse and may have a key role in triggering the neurobiological changes associated with addiction. This notion reflects the fact that all of the drugs of abuse increase the extracellular concentration of DA in the nucleus accumbens. Increases in DA levels have an important role in coding reward and prediction of reward, in the motivational drive to procure the reward, and in facilitating learning (Wise, 2002). Research on the neurobiology of addiction has shown that the reinforcing properties of most misused drugs are mediated by activation of the mesolimbic dopaminergic system, the orbitofrontal cortex, and the extended amygdala (Cunha-Oliveira, *et al*., 2008). Alterations in the intracellular messenger pathways, transcription factors, and immediate early gene expression in these reward circuits are believed to be important for the development of addiction and chronic drug abuse (Koob & Volkow, 2010). There are several lines of evidence suggesting that dopaminergic pathways are implicated in at least some reward circuits, and various drugs may activate or "switch on" the circuits at different points (Preedy,2016).

2.1.4 Epidemiology of substance related disorder:

Alcohol misuse alone was found to be the 7th leading risk factor for mortality and DALYs (GBD, AC, 2018).In general, more men than women abuse substances. Those who use substances earlier are more likely to develop a disorder. Among ethnic and racial groups in the United States, the highest lifetime rate is among American Indian or Alaska Natives; whites are more affected than blacks or African Americans. There is a sociodemographic effect as well. For example, those with some college education use more substances than those with less education, and the unemployed have higher rates than those with either part time or full-time employment (Culter, 2016).

Developing countries are highly susceptible to drug dependence and its consequences (Aggleton *et al*., 2005). Studies have shown that adolescence and early adulthood ages are critical stages of life. The use of illegal substances is more common among young adults (18–25 years of age) and featured with higher vulnerability to a variety of psychological diseases and drug abuse (Delgadillo *et al*., 2015). Most abused substances can be administered by a number of routes. Routes that provide quick access to the bloodstream, and hence the brain, are often preferred by abusers (e.g., sniffing into the nose "snorting" and smoking rather than ingesting recently the method of use is shifting from smoking to intravenous injection (Sanchez *et al*., 2006).

There is growing concern about the impacts of conflict and war on substance use in Iraq (Ezard, 2012). Another report, from the Iraqi community epidemiology work group, suggests that there has been increased use of alcohol and prescription and illicit drugs in Iraq Since 2009, especially among adolescents (Al-Hemiary, *et al*., 2014). According to the final report of the Iraq National Household Survey on Alcohol and Drug use (INHSAD) (including Kurdistan region),the lifetime prevalence rates of tobacco use, alcohol consumption، nonmedical use of prescription drugs, and use of illicit drugs were 28.8%, 8.1%, 2.9%, and 0.7%, respectively (Al-Hemiary, *et al*.,2014).

2.1.5 Clinical and behavioral signs of addict :

The prominent signs of addict depend on the type of substances including reductions of both body weight, food intake and increased water intake. Irritability, anxiety, and dysphoria are key negative emotional states that characterize the withdrawal syndrome in humans, which arises when access to the drug is prevented and contributes to drug relapse . Irritability has also been reported to be greater in adolescents at higher risk for substance use (Ruginsk, *et al*., 2015).

Irritability-like behavior has also been shown to increase during exposure to cannabinoids in adolescence and adulthood, suggesting that cannabinoid exposure in adolescence induces long-lasting neurobehavioral adaptations. Numerous studies demonstrate that early cannabis use is associated with greater vulnerability to the later development of drug addiction, psychiatric illness and mental health disorders. Adolescents exhibiting violent behavior were found to live in high risk or vulnerable communities, such as communities with drug addicts (Xue *et al*., 2018)

2.1.6 Diagnosis of substance related disorder

According to the (DSM-5) there are 11 symptoms for each substance class (except for caffeine) that are used to make a substance use disorder diagnosis within a 12-month period. (DSM- V , 2013) Symptoms include:

- Substance is taken in larger amounts or over longer periods than was intended.
- There is a persistent desire or unsuccessful effort to cut down or control substance use.
- A great deal of time is spent in activities necessary to obtain substance, use substance, or recover from its effects.
- Craving, or a strong desire or urge to use substance.
- Recurrent use of the substance is resulting in a failure to fulfill major role obligations at work, home, or school.
- Continued use of substance despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance.
- Important social, occupational, or recreational activities are given up or reduced because of substance use.
- Recurrent substance use in situations in which it is physically hazardous.
- Substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
- Tolerance.
- Withdrawal symptom.

The diagnosis is made along a continuum—mild , moderate, or severe—based on the number and severity of the symptoms.

Specify current severity based on the following guidelines:

Mild: presence of 2 or 3 symptoms

Moderate: presence of 4 or 5 symptoms

Severe: presence of 6 or more symptoms

2.1.7 Treatment:

Prevention and management of substance use disorder have been considered one of the top priorities. Internationally, the WHO and the United Nations have been at the forefront with many efforts in synthesizing evidence and developing guidelines and frameworks to combat this public health crisis. Both non-pharmacological and pharmacological Methods, have been well-documented, for the treatment of substance related disorder (Jain *et al* , 2013).

In terms of tobacco use, along with nicotine replacement therapies, non-pharmacological treatments such as “counseling”, "self-help”, and “behavioral therapies” have been proven as effective therapies that can maintain smoking cessation more than 6-month follow up (Schmelzle, 2008).

Similarly, non-pharmacological approaches including “skills training ”, "cognitive behavior therapy” and “family and couple therapy” are used widely to improve alcohol dependence (Jiloha,2007). For drug use disorder, substitution treatments including methadone, buprenorphine or naltrexone maintenance treatment are used commonly as replacement therapies, ongoing vitamin supplementation, antidepressants (and other medications) for psychiatric co-morbidities along with traditional medicine and motivational enhancement therapies (Lu L , 2009).

Hospitals are increasingly filled with people suffering from medical complications of substance use disorders (SUD) (Tedesco *et al* ., 2017). One in seven patients in general hospitals has a substance use disorder (Walley, *et al* ., 2012). Amphetamine use is now the fourth most common reason to seek drug treatment in the United States, after alcohol, opioid, and marijuana use (Rockville,2018).

Trends in hospitalizations related to amphetamine use (ie, hospitalizations in which a clinician identified current amphetamine dependence or abuse, or amphetamine poisoning, as one of the issues relevant to the hospital stay (Villapiano, *et al* ., 2017). Compared with all other hospitalizations, amphetamine-related hospitalizations were associated with a 29% higher rate of adjusted in-hospital mortality. Higher in-hospital mortality may be associated with the known cardiovascular effects of amphetamine use. In recent years, a small number of medical centers ,predominantly in urban settings, have developed inpatient addiction consultation services (Englander, *et al*., 2017). Persons admitted to inpatient care usually have severe medical conditions e.g., severe withdrawal symptoms, Psychiatric disorder due to drug abuse (Bhalla, *et al*., 2017) intoxication-related injury or trauma, complications of substance use, including opioid overdose and injection-related infections such as endocarditis that may require weeks of intravenous (IV) antibiotic therapy (Ronan & Herzig, 2016).

2.1.8 Complication:

Substance abuse and cigarette smoking are nowregarded as major public health problems (Volkow,*et al* ., 2017). Communicable diseases such as hepatitis B, hepatitis C, and HIV are continuously adding up to the global burden of dis eases, because of the intravenous illicit drug abuse (Degenhardt,2017). Furthermore, opium, tobacco, and alcohol users have a higher risk for esophageal squamous cell carcinoma (Xie,2018).

The use of Tobacco and amphetamine-type stimulants is a known risk factor for myocardial infarction and other cardiovascular diseases like cardiomyopathy(Attard,2017).Mental health problems are also a concern, as the use of cannabis is a risk factor for psychosis (Murray,*et al* ., 2017). Substance abuse in non-fatal doses can result in morbidity and serious health consequences, thus affecting the quality of life.In 2016, approximately 18.45 million and 21.89 million healthy years of life were estimated to be lost due to alcohol abuse and drugs abuse disorders, respectively.

In addition, drug abuse is associated with a multitude of social, psychological, and economical sequelae. The most serious outcome of alcohol and drug abuse is death, which respectively accounted for 0.26% and 0.28% of all-cause mortality on the global scale in 2016(Mattiuzzi and Lippi ,2019).

2.1.9 Classification of substance:

2.1.9.1 Depressants or Sedatives

This category of drugs includes alcohol, barbiturates and benzodiazepines .These drugs depress the central nervous system, reduce anxiety at low dosages, and can induce anesthesia and death at high dosages (van wormer *et al*., 2008). Some of these drugs such as alcohol can be purchased legally by adults. Other drugs such as barbiturates can be used legally under medical supervision (Butcher,*et al*., 2007), depressants slow the central nervous system to induce relaxation, drowsiness, or sleep, but when they are abused, they can be extremely dangerous (Johnson, 2004).

2.1.9.1.1 Alcohol:

Alcohol is a potent drug that causes both acute and chronic changes in almost all neurochemical systems. Thus alcohol abuse can produce severe, temporary psychological symptoms including depression, anxiety, and psychoses. Increasing levels of regular alcohol consumption can cause tolerance. Chronic use can cause such intense adaptation of the body that stopping drinking can precipitate withdrawal syndromes, including insomnia, autonomic nervous system hyperactivity, and anxiety (Boland,2021).

Excessive alcohol consumption imposes a tremendous burden on society in terms of economic cost and increased morbidity and mortality rates (CDC,2015). In most regions of the world, most adults consume alcohol at least occasionally (WHO,2018). Alcohol is among the leading causes of preventable death worldwide, with 3 million deaths per year attributable to alcohol. In the United States, more than 55% of those aged 26 and older consumed alcohol in a given month , and one in four adults in this age group engaged in binge drinking (defined as more than four drinks for women and five drinks for men on a single drinking occasion) . The morbidity and mortality associated with alcohol are largely due to the high rates of alcohol use disorder in the population (NSDUH , 2018).

2.1.9.2 Hallucinogens

Humans have used psychedelics (also known as serotonergic hallucinogens) for thousands of years. Nonetheless, scientists became interested in these substances only after Albert Hofmann discovered the psychoactive properties of lysergic acid diethylamide (LSD) in 1943 (Begola and Schillerstrom, 2019). Although hallucinogens are derived from multiple structural families, they are known as powerful agents producing profound changes in consciousness, perception, and mood (Halberstadt, 2015).

According to their chemical backbone, psychedelics can be divided into the following categories: mescaline-like phenylalkylamines, psilocybinlike tryptamines, and a small subclass of LSD-like ergolines , since 2010, a new class of powerful synthetic N-(2-methoxybenzyl)-2,5-dimethoxyphenethylamine (NBOMe) hallucinogens has been present on the drug market and has been used as a legal substitute for LSD ,The iodine derivative, 4-iodo-2,5-dimethoxy-N- (2-methoxybenzyl) phenethylamine (25I-NBOMe), is one of the three NBOMe representatives most readily available to drug users (Lawn *et al*. 2014). Like other psychedelics, 25I-NBOMe acts as 5-HT2A and 5-HT2C receptor agonist due to its high in vitro binding affinity for these receptors (Rickli, *et al*., 2015).

Marked perceptual distortion (charging Shapes, colors…),Hallucinations (visual,Tactile…), False sense of achievement and strength depersonalization, derealization euphoria, anxiety, panic tachycardia ,hyp ertension ,cerebellar signs ,wide pupils ,hyperemic conjunctiva,blurred vision, hyperthermia and piloerection are the main effect of hallucinogens.(Herian,2021).

2.1.9.3 Cannabis

Worldwide it is currently the most widely used illicit drug (Smart & Pacula 2019; Carliner *et al.* 2017; United Nations Office on Drugs and Crime 2019). As its name suggests, the cannabis plant is unique in its ability to produce a plethora of molecular compounds called cannabinoids. Cannabis *sativa* is the most widely used illicit drug in the world. The main psychoactive component of cannabis is delta-9-tetrahydrocannabinol (THC), and this compound is primarily responsible for the cognitive and peripheral effects contributing to the "high" achieved by recreational use(Kesner,2021).

The main forms of cannabis are marijuana and hashish which are either smoked or eaten, and the differences in the effects they produce depend primarily on their concentration of the active ingredient tetrahydrocannibinol (THC) Kesner,2021).

The most common route of cannabis administration in humans is smoking; either via inhalation of smoke from burning the plant, or vapors from vaporization of phytocannabinoids in plants or extracts. Other common routes include oral consumption of cannabis infused foods or tablets, sublingual oromucosal absorption of tinctures, and transcutaneous absorption of topical creams or dermal patches(Kesner,2021).

A significant population of regular cannabis users will develop cannabis use disorder (CUD). These individuals experience many of the hallmarks of substance use disorders including tolerance and withdrawal symptoms. It cause changes in the societal attitudes (Hasin *et al.* 2019).

Regardless of the route of administration, the acute behavioral effects of cannabis use in first-time or inexperienced users occur within minutes of smoking, or obviously longer with other administration routes, and can last for several hours(Solowij, *et al.*, 2019).These effects include euphoria, decreased anxiety and depression, and increased sociability (Ashton,2001). Conversely,it is not uncommon for new users to experience negative affective processes such as general anxiety and aggravation, and in more extreme cases, panic, paranoia, and other forms of psychosis (Johns 2001).

Some individuals experience positive and others negative psychological effects early in cannabis use (Cooper & Williams, 2019). In addition to profound behavioral effects in the awake state, acute administration of cannabis produces alterations during sleep (Kesner and Lovinger,2020).Another effects of acute cannabis use include conjunctival injection ("red-eye"), increased appetite, dry mouth, and tachycardia (APA, 2013).

2.1.9.4 Opiates or Narcotics:

- **opium • heroin**

- **morphine • codeine • pethidine • methadone • pentazocine**

Some of these compounds are naturally occurring (e.g. opium, codeine) while the others are synthetic or semi – synthetic. Some of theses substances have medical uses (e.g. Pethidine), while others are solely substances of abuse (e.g. heroin). Opiates/opioids. Opiates are a group of chemicals derived from the opium poppy (Papaver somniferum) which is similar to synthetic compounds. They have potent analgesic properties (e.g., morphine) as well as drugs of abuse (e.g., heroin), the effects of opiates can be euphoria, pleasurable apathy and dreamy, drowsy warmth (Nelson, 2012).

Opiates users inject, smoke or snort substance for maximum effect, whereas some mix heroin and cocaine by shooting it, which is an extremely dangerous practice called "speedballing" (van wormer, *et al*., 2008). Many synthetic opioids have been manufactured, including meperidine, methadone, pentazocine, and propoxyphene. Opioids are subjectively addictive because of the euphoric high (the rush) that users experience, especially those who take the substances intravenously. The associated symptoms include a feeling of warmth, heaviness of the extremities, dry mouth, itchy face (especially thenose), and facial flushing. A period of sedation follows the initial euphoria, known in street parlance as "nodding off." (Boland,2021).

Opioid use in the United States has steadily risen since the late 1990s, along with staggering increases in overdose fatalities (Kolodny,2015). The use of illicit opioids such as heroin and fentanyl has increased dramatically, contributing to opioid-related morbidity and mortality with approximately 115 Americans dying each day from an opioid overdose, this epidemic is now considered a public health emergency (Volkow,2019).

2.1.9.5 Stimulants:

Are central nervous system activators that include caffeine, nicotine, amphetamines, methamphetamines and cocaine & khat (Qat) . It increase alertness, and relieving fatigue (Nelson, 2012). Amphetamines and other stimulant drugs are second only to cannabis as the most widely used class of (illicit) drugs globally, accounting for 68 million past-year consumers and it is a well-known stimulant that mainly produces its effects through increasing the availability of norepinephrine and dopamine (Koob,*et al*., 2014).Amphetamines refer to both amphetamine (AMPH) and the structurally similar methamphetamines (MA), both of which are used extra-medically. Methamphetamine is considered a more potent derivative of AMPH, with a longer duration of action and increased ability to cross the blood–brain barrier; and global shifts in the illicit stimulant market have resulted in the predominance of MA (Stoneberg,2018).

Amphetamines act on the central nervous system (CNS) and acute effects include a heightened sense of alertness; increased energy; heightened curiosity; anorexia; decreased fatigue; elevated mood; dose-dependent effects on focus, attention and concentration; and elevated interest in environmental stimuli(Silber,2006).Methamphetamine is a highly addictive central nervous system stimulant. Methamphetamine use is associated with a range of health harms, including psychosis and other mental disorders, cardiovascular and renal dysfunction, infectious disease transmission, and overdose(Degenhardt,2017).Methamphetamine is now available in different forms such as ice, powder, and pills, with different pharmacokinetic characteristics that make them popular among certain types of individuals.(Chomchai,2015).

Captagon, the trademark name for the synthetic stimulant Fenethylline1–6, was first reported by a German pharmacist in 1961 for the potential treatment of hyperactivity, depression and narcolepsy (Wenthur,*et al*., 2017). It is used in the form of pills or injection, and like amphetamine, it is mainly consumed for its euphoric and energizing effects (Katselou, *et al* ., 2016).

2.2 Reticular Activating System (RAS):

The RAS is a component of the reticular formation, found in the anterior-most segment of the brainstem between the brainstem and the cortex. Multiple neuronal circuits ultimately contribute to the RAS.(Yeo *et al*., 2013). These circuits function to allow the brain to modulate between slow sleep rhythms and fast sleep rhythms, as seen on EEG .The reticular formation receives input from the spinal cord, sensory pathways, thalamus, and cortex and has efferent connections throughout the nervous system. The RAS itself is primarily composed of four main components that each contain groupings of nuclei. These are the locus coeruleus, raphe nuclei, posterior tuberomammillary hypothalamus, and pedunculopontine tegmentum (Garcia ,*et al* ., 2013).

Each is unique in the neuropeptides they release. In large part, these centers are activated by the lateral hypothalamus (LH), which releases the neuropeptide orexin in response to the light hitting the eyes, which then stimulates arousal and the transition from sleep to waking (Nishino , 2011).

The locus coeruleus is located within the upper dorsolateral pons of the brainstem. It is activated directly by orexin from the lateral hypothalamus, and in response, releases norepinephrine. Its excitatory functions are widely distributed within the brain, acting on both the alpha and beta receptors of neurons and glial cells distributed throughout the cortex. It functions primarily upon waking and in arousal (Giorgi , *et al*., 2017).

The raphe nuclei are located midline throughout the brainstem within the pons, midbrain, and medulla. The majority of neurons located in the raphe nuclei are serotonergic. The more rostral raphe nuclei appear to be important in various bodily functions, including pain sensation and mood regulation. In the context of the RAS, these nuclei communicate with the suprachiasmatic nucleus, playing a role in circadian rhythms, and contributing to arousal and attention (Hornung , 2003).

The tuberomammillary nucleus is located within the posterior aspect of the hypothalamus. The neurons that make up these nuclei are primarily histaminergic and serve as the primary source of histamine projections in the brain. They are important in both wakefulness and cognition, projecting in large part to the forebrain where they play an important role in arousal (Fujita , *et al* ., 2017).

The lateral and dorsal pedunculopontine tegmentum contains primarily cholinergic neurons in neighboring groups within the midbrain and pons. Cholinergic neurons project to the thalamus and cortex, promoting desynchronization of the brain, allowing the body to switch from slow sleep rhythms to high frequency, low amplitude wake rhythms (Vincent,2000).

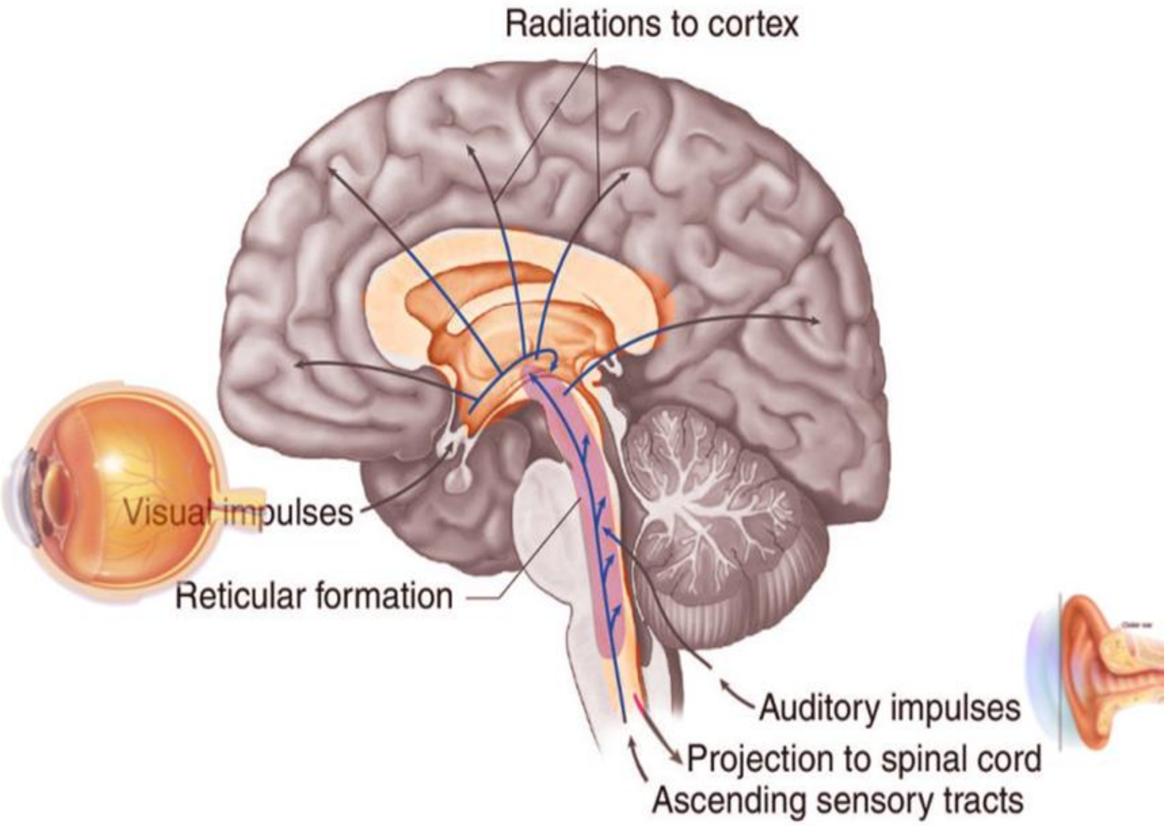

Figure (2-2): The Reticular Activating System (Arguinchona, 2021).

2.3 The brain electrical activity:

The brain is one of the largest and most complex organ of human body. More than 100 billion neurons are contained in it . Electrical activity is generated through communication process between neurons, resulting in the human electroencephalographic signals. The spontaneous electrical activity of the brain is due largely to graded summated postsynaptic potentials in the many hundreds or thousands of brain neurons that underlie the recording electrode at the surface of scalp (Boron ,2016).

The cells of the nervous system can be divided into two major categories: neurons and neuroglial cells. The neuron is the building block of the nervous system. Neurons are various in type, communicated, adaptable, and therefore, as aggregates, give rise to the spectacular brain complexity. A convoluted system is gifted with advancing characteristics— that is, characteristics that emerge only in companies as opposed to being exist completely in the separate component. Their cell bodies of neurons are situated in gray matter areas of the CNS, while the white matter consists of fibers joining neurons from various areas. Excitability is one of the Neurons properties (Raz and Perouansky, 2019).

Afferent neurons are neurons that carry information into the circuit, whereas efferent neurons are neurons signaling information away from the circuit. The electrical signaling within neuronal circuits produce spontaneous and evoked electrical activity that is routinely measured in the clinical neurophysiology laboratory (Blum, *et al*.,2007).) Neurons communicate in trillions of connections called synapses in which, the neurotransmitters are released(Yuste ,*et al*., 2014). Many receptors and neurotransmitter systems are involved with substance use disorder and addiction, including dopamine, serotonin, norepinephrine, glutamate, gamma-aminobutyric acid (GABA), acetylcholine, the endogenous opiate system, and the cannabinoid system (Pinel, 2013).

2.4 Normal Brain oscillation or waves :

Normal EEG wave formes are generally classified according to their frequency , amplitude, shape, and their location on the scalp at which they are recorded, the most familiar classification is that uses EEG waveform frequency which are: alpha, beta, theta, and delta (Müller-Putz,2020).

2.4.1The alpha wave:

The alpha rhythm is characterized by an average frequency of (8–13Hz). It is detected throughout resting periods in which the eye is closed and basically indicates states of relaxed wakefulness in healthy adults.). it is called the "posterior basic rhythm" (also termed the "posterior dominant rhythm" or the "posterior alpha rhythm"), observed in the posterior regions of the head on both sides, developed in amplitude on the dominant side (Tiago-Costa, *et al*., 2016). In addition to its domination in the occipital region it can be documented from the frontal and parietal regions (Schomer and Silva, 2018). Further more to the posterior basic rhythm, there are other normal alpha rhythms such as the mu rhythm (alpha activity in the contralateral sensory and motor cortical areas) that arises when the hands and arms are sluggish and the "third rhythm" (alpha activity in the temporal or frontal lobes). Alpha can be abnormal for example, an EEG that has spread alpha occurring in coma and is not reactive to external stimuli is referred to as "alpha coma" (Basar, 2012).

2.4.2 Beta wave:

Beta waves occur at frequencies greater than 14 cycles/ sec and as high as 80 cycles/sec. They are recorded mainly from the parietal and frontal regions during specific activation of these parts of the brain (Gyton ,2021). Beta activity is closely associated to motor behavior and is generally attenuated through active movements. Low amplitude beta with multiple and varying frequencies is often related with active, busy or anxious thinking and active concentration (Tiago-Costa, *et al*., 2016).

2.4.3Theta waves:

It has low-frequency activity (4–8Hz) Theta is observed normally in young children. It may be detected in drowsiness or arousal in children who are older and adults. Extra theta for age denotes abnormal activity (Brilla, 2019). It linked to mental effort, signifying that attention is directed to an existing stimulus. Overall, the amplitude of theta waves is naturally between 8 and 10Mv. It can be detected as a focal disturbance in focal subcortical lesions; it can be perceived in common distribution in diffuse disorder or midline disorders, metabolic encephalopathy or some cases of hydrocephalus.it characteristically associated with drowsiness, particular sleep states , and meditation, also relaxed, and creative states. (Cahn & Polich, 2006).

2.4.4 Gamma wave:

Gamma oscillations are characterized by very high-frequency activity (30–200 Hz) but typically not measurable by EEG when higher than 100Hz) ,while many of the low-frequency oscillations have been associated with functional inhibition, faster gamma-band oscillations are believed to reflect cortical activation, depending on the exact cortical region, gamma oscillations are closely related to attentive processing of information ,active maintenance of memory contents, conscious perception(Herrmann *et al*., 2016).

2.4.5 Delta waves:

Delta waves are characterized by very low-frequency activity (below 1–4Hz), which usually relates to deep and unconscious sleep in healthy humans It is also detected normally in babies. Delta wave (amplitude can be several tenths of mV) are also associated with pathologic neural states, such as coma or the loss of consciousness. It may happen focally with subcortical lesions and in general distribution with defuse lesions, metabolic encephalopathy hydrocephalus or deep midline lesions. Generally, delta activity diminishes with increasing age, which suggests that delta activity is primarily an inhibitory mechanism (Britton ,*et al.*, 2016). It is frequently most prominent frontally in adults (e.g. FIRDA – frontal intermittent rhythmic delta) and posteriorly in children (e.g. OIRDA – occipital intermittent rhythmic delta) (Cahn & Polich, 2006).

2.4.6 Mu :

Range is 8–13 Hz and partially overlaps with other frequencies. It reveals the synchronous firing of motor neurons in rest state (Brilla, 2019). Mu suppression is believed to reflect motor mirror neuron systems, because when an action is detected, the pattern extinguishes, perhaps because the normal and mirror neuronal systems "go out of sync" and affect with one other (Oberman, *et al*., 2005). The mu rhythm is an exam "Ultra-slow" or "near-DC" (Direct current) activity is recorded using DC amplifiers in some research contexts. It is not typically recorded in a clinical context because the signal at these frequencies is susceptible to a number of artifacts (Abou-Khalil, *et al*., 2006).

2.4.7 Lambda wave:

Are electropositive potentials seen in the occipital regions. They are sharp, symmetrical and seem to be similar to epileptic potentials. They are produced by visual scanning of a picture. When a subject explores interesting things lambda waves are elicited. They are visual potentials evoked (Paszkiel, *et al* .,2020).

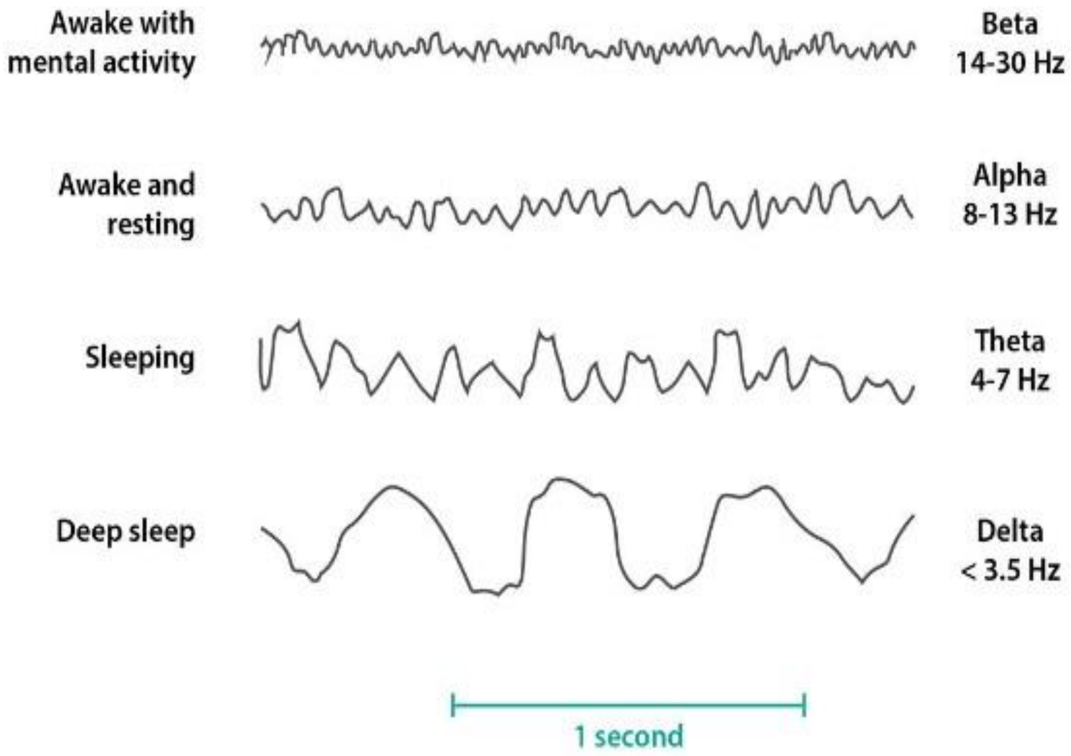

Figure (2-3) Different EEG waves patterns (Hu *et al* .,2019)

2.5 The electroencephalogram:

The EEG is direct, actual monitoring and standard methods that are used for measurement of electrical activity produces by the firing of neurons within the brain. It is non invasive neurophysiological test that measure brain activity with a set of electrodes placed on the scalp surface (Placidi, *et al*.,2021).

The EEG readings are one of the widely used modalities to diagnose brain-related neural irregularity. Electroencephalography has been extensively used for early diagnosis of a diversity of brain conditions such as epileptic seizures, ADHD, dementia, depression, schizophrenia, Alzheimer's, and sleep-related disorders (Mannan, *et al*., 2018).

2.5.1 History of EEG

The first human EEG was obtained in 1929 by Hans Berger a German neurologist and psychiatrist (1873–1941) (Stone and Hughes, 2013). From that time, various discoveries and developments have made the application of EEG in the clinical management of patients. Berger first described the alpha rhythm and its correlation to eye closure in 1924 and put out his findings in 1929 (Berger, 1929).

In the 1930s, Gibbs, Lennox, and Jasper denoted different patterns regarding generalized spike-and-wave activity and focal epileptiform discharges (EDs) as markers of epilepsy (Stone and Hughes, 2013). At 1940s invasive methods such as the use of distinctive implanted or depth electrodes to be an indicater for the exploration of deep intracerebral regions. In the 1980s digitalization and recording of the EEG was happen, allowing ambulatory procedures. Through the 1990s the first-generation commercial digital EEG systems were introduced (Lodder, *et al*., 2014).

At the turn of the century, Remot EEG interpretation became available by mean of computed networking with simultaneous video recording. This stimulated prolonged EEG and hurled the growth of continuous (cEEG) monitoring(Feyissa, *et al*., 2017). In the last few decades, complex algorithms using quantitative EEG (qEEG) analyses increased the diagnostic yield of EEG (Thakor andTong, 2004).

2.5.2 Physiological mechanism:

The EEG records oscillations in brain electrical activity over time. This electrical activity typically between -100 and +100 micro volts. The data appears as positive and negative deflections that may be analyzed for frequency and magnitude, all of which could have psychological, neurological, or physiological implications. (Read & Innis, 2017). Differences of electrical potentials are caused by summed PSPs from pyramidal cells that create electrical dipoles between soma (body of neuron) and apical dendrites (neural branches) (Teplan, 2002), these PSPs are the voltages that emerge from a nerve impulse when transmitters are discharged and attach to a postsynaptic neuron, affecting the movement of ions along a cellular membranes. (Ganong et al., 2019).

Neurons of the cortex are grouped in a columnar arrangement with their electrical fields oriented in the same direction. This allows for the summation of signals from numerous neurons. (Aminoff, 2012). Only the activity at the ends of electrical dipoles of simultaneously discharging neurons that are positioned perpendicular to the scalp can be detected by EEG. The contra-polar dipole are not detected (Guyton, 2020).

Certain cortical neurons, such as those in the amygdala, are not organized in this columnar fashion and hence cannot be spotted by EEG. Dipoles having conflicting polarity directed toward one other cancel each other out, resulting in none of the dipole being recorded. (Read & Innis, 2017). Electrodes are placed on the scalp and linked to the EEG recording system to pick up this activity. Brain complex, cortico-spinal fluid, cranium, and scalp form a volume conductor that modifies the magnitude and shape of the electrical signal generated by cortical neurons.(Sazgar & Young, 2019). According to estimate, a potential is captured at the scalp if 6 cm2 of cortical surface area is simultaneously stimulated (Misulis, 2014).

2.6 Abnormal adult EEG

Abnormal EEG findings may be focal or generalized and are subdivided into non-epileptiform , interictal epileptiform and ictal patterns. Interictal epileptiform discharges are characterized by the presence of spikes and sharp waves, with or without after-going slow waves and are strongly associated with epilepsy. These discharges may also be seen in from 0% to 6.6% of healthy adult without epilepsy Burkholder *et al.*, 2016). In those with a first seizure، epileptiform discharges provide level evidence of the likelihood of recurrence (Krumholz, *et al.,* 2015). Nonepileptiform EEG abnormalities are characterized by several patterns, including focal slow activity, regional or generalized bisynchronous slow activity, generalized asynchronous slow activity, and focal or generalized suppression of the background activity. These patterns provide valuable information in the setting of acute brain insults، diffuse encephalopathy, coma, brain death, and epilepsy (Britton ,*et al*., 2016).

2.7 EEG artifacts:

Signal artifacts are further significant while collecting EEG data from recording systems (Johal & Jain, 2016 and Jebelli, *et al*., 2018).These artifacts can contaminate the feature of EEG data. In this regard, a comprehensive knowledge of the kinds of artifacts is requisite to remove the artifacts or noise efficiently (Jebelli, *et al*., 2018).

Artifacts are unwanted signals which are chiefly originated from environment noise, experimental error and physiological artifacts. Since, the environment artifacts and experiment error, which originate from external factors, are classified as extrinsic artifacts, while the physiological from body itself (e.g., eye blink ,muscle activity, heart beat) can be characterized as intrinsic artifacts (Islam, *et al*., 2016).

The environment artifacts can be removed by a simple filter due to the frequency of such artifacts are inconsistent with wanted signals (Uriguen & Garcia, 2015). Proper procedure and planning can reduced experimental error simply. Though, the physiological artifacts are more difficult to be removed as they necessitate particular algorithms (Jebelli, *et al*., 2018).

2.7.1 Physiologic intrinsic Artifacts like:

2.7.1.1-muscle (Electromyogram) Activity:

Contamination of EEG data by muscle activity is a well-predictable tough problem as it arises from diverse type of muscle groups (Hamal & bin Abdul Rehman, 2013).These MAs stem from the subject itself as a consequence of various muscle contraction activities, for instance, swallowing, chewing, talking, clenching, sniffing, and head movements (Bisht , *et al* 2018).Theoretically, muscle artifacts measured by electromyogram (EMG) have an extensive distribution from 0 Hz to >200 Hz (Uriguen & Garcia, 2015). These artifacts are characterized as high frequency activity normally acknowledged in the range above 20 Hz and exist in multiple EEG channels due to volume conduction (Chen , *et al*.,2019).The degree of muscle contraction and stretch will disturb the amplitude and waveform of artifacts. It is exceedingly difficult to obtain the activity from a single channel measurement matching to EOG and eye-tracking. Hence, EMG artifacts are particularly challenging to eliminate. Additionally, EMG contamination and EEG have substantial statistical independence from all other both temporally and spatially. This imply that the Independent Components Analysis might be an appropriate methods to remove EMG contamination (Chen, *et al*., 2016).

2.7.1.2 Ocular Artifacts

Ocular artifacts produce significant artifacts in the EEG recordings. The origin of ocular artifacts is eye movement and blinks which can spread over the scalp and be recorded by EEG activity. Further specifically, eye movement artifacts produce by variations in orientation of the retina and cornea dipole, and blink artifacts produced by ocular conductance due to the alterations of contact of the cornea with eyelid (Jiang, *et al*., 2019).

In addition, because of volume conduction effect, together ocular artifact and EEG activity propagated to head surface and record by the electrodes. Such ocular signals can be documented using electrooculogram (EOG). The amplitude of EOG is usually many times greater than EEG and its frequency are like with the frequency of EEG signals (Hamal & bin Abdul Rehman, 2013).

2.7.1.3 Cardiac artifacts

Cardiac artifacts can be presented when the electrodes is placed on or close a blood vessel in which the movement of expansion and contraction due to the heart. Such artifacts called pulse artifacts, whose frequency is about 1.2 Hz, can occur within EEG as a like waveform, hence it is hard to remove (Hamal & bin Abdul Rehman, 2013).

Additional cardiac activity known as ECG measure the electrical signal out pushed from the heart. In difference to pulse artifacts, ECG can be measured with characteristic regular pattern, and be recorded aside cerebral activity, therefore removing such artifacts may be at ease just using a reference waveform (Lee, *et al*., 2015).

2.7.1.4 Skin Artifacts:

Biological processes may change impedance and cause artifacts. Sweat is a common cause. Lactic acid and sodium chloride from sweating react with the metals of the electrodes and generate large and very slow (generally 0.5 Hz) baseline sways (Benbadis, 2006).

2.7.2 Extrinsic Artifacts

Moreover to the artifacts mentioned above, external source of artifacts similarly have a harmful effect on EEG measurement. Instrument artifacts as a kind of extrinsic artifacts originate from the electrode misplacement and cable movements. These artifacts can be removed by suitable procedure and planning. The electromagnetic interference emitted from surroundings is additional type of external artifact that affect the EEG recordings. Such artifacts from environmental sources can be simply=- removed by a simple filter due to its distinguishable frequency band. (Nolte, *et al*., 2004).

In spite of the wide frequency band of white noise, a high-frequency filter still can remove most of artifacts. Then the activity of brain area can be observed in numerous channels, the coherence among EEG channels will introduce volume conduct artifact (Dong, *et al*., 2017).The environment artifacts can be removed by a simple filter due to the frequency of such artifacts are inconsistent with wanted signals (Uriguen & Garcia, 2015). Proper procedure and planning can reduced experimental error simply. Though, the physiological artifacts are more difficult to be removed as they necessitate particular algorithms (Jebelli, *et al*., 2018).

2.8 Limitations of EEG:

Electroencephalography has several limitations. Most important is its poor spatial resolution. EEG is most sensitive to a particular set of post-synaptic potentials: those generated in superficial layers of the cortex, on the crests of gyri directly touching the skull and radial to the skull. Dendrites, which are deeper in the cortex, inside sulci, in midline or deep structures (such as the cingulate gyrus or hippocampus), or producing currents that are tangential to the skull, have far less contribution to the EEG signal (Kondylis , 2014).

2.9 Abnormal brain waves associated with substance related disorder:

The effect of the illicit drug on the EEG can be measured as specific types of alteration that are described as a change from control or baseline state. One type of this change development of new wave form with predominant frequency or emergence of new event such as spikes , seizure like activity or spindle slow wave / high amplitude burst of activity (Ceballos,2009)

2.10 EEG finding in patient with substance related disorder:

Although excess beta activity and a mild theta increase may be the most common EEG alterations associated with substance use , more remarkable changes may also appear such as diffuse delta, triphasic waves, bisynchronous spikes or polyspikes, burst suppression can be present(Van-Cott and Brenner, 2003).

EEG as a powerful tool used to study opioid- (OUD), methamphetamine- (MUD), and alcohol-use disorders (AUD) has been ventured over the past few decades. Most efforts were made to identify frequency bands in relationship with EEG potentials in the closed-eye (i.e.,resting) state. Opioid abuse can cause a loss of GABAergic inhibitory control over postsynaptic excitatory potentials, including cortical pyramidal neurons (Liao, 2005). Also resulting in an alteration of electrical synchronization between cortical neurons (Baldo,*et al.*,2016). By analysis of delta/δ, theta/θ, alpha/α, beta/β, and gamma/γ waves, it was found that all of the five spectral powers was elevated with almost equipotency in the frontal, central, temporal, parietal, and occipital sub-regions of patients with OUD (Wang, 2015). However, others demonstrated that it was only certain spectra, but not all, that were elevated in the cortical subregions (Motlagh,2018). The selective effects are also reported in MUD and AUD.

Methamphetamine (METH) exposure for a long period time may cause a reduction in dopamine transporters in the brain (McCann UD, 1998).The delta/δ and theta/θ bands, but not others, were elevated almost globally in the cortical subregions (Khajehpour, *et al.*, 2019).

Alcohol is believed to be inhibitory, mimicking GABA's effect on postsynaptic GABA receptors (Olsen,2017).The gamma/γ powers, but not other frequency bands, were elevated across the cortex of patients with AUD (Bauer, 2001). However there was a reduction in alpha/α power while an increase in gamma/γ powers (Ko,2018). Also reduction took place in the delta/δ and theta/θ bands (Coutin-Churchman ,*et al* .,2006) . An augmentation of voltage, field distribution, and persistence of normally appearing 15 to 25 Hz Beta activity most commonly indicates Barbiturates and benzodiazepines taking drugs (Van-Cott and Brenner, 2003) ;(Bauer and Bauer, 2005).

3.1. Materials:

3.1.1. Study design and subjects:

This observational cross sectional study was conducted on patients with substance-related disorder.The study extended from the beginning of September 2021 to the beginning of August 2022 in the Department of Neurophysiology of Imam Al-Sadiq Teaching Hospital in Babylon Province. Recognition of patients with substance-related disorder was done at the psychiatric outpatient clinic, dependence ward in the hospital. The referrals of patients mainly from psychiatrist, and from our psychiatric outpatient department. They were diagnosed according to DSM-5 criteria for substance related disorder (DSM-5, APA,2013)

3.1.1.1 Sample size calculation

The study's sample size will be calculated according to the following formula:

$N=Z^2 P (1-P)/d^2$ Where: N: Sample size.

Z: Statistic corresponding to level of confidence, which equals to 1.96 as the level of confidence is 95%

P: Expected prevalence of substance related disorder which equals to about 10%, obtained from previous studies, (SSAI ,2015).

d: Precision which equals to 5% as the prevalence of disease is between 10-90%.

Accordingly, the calculated sample size will be about 138 patients. The exact number of the patients in this study were 112 because the remainder of them were excluded.

3.1.2 Inclusion criteria

All patients who:

- Take substance for at least 12 months.
- Abstinence duration not more than four weeks.
- Diagnosed according to DSM-V criteria for substance related disorder.

3.1.3. Exclusion criteria:

All patients with:

- Past medical history of neurological disease such as multiple sclerosis.
- Patient with space occupying lesions in the brain.
- Patient with head trauma
- Patients having cerebrovascular accident, epilepsy and diabetes mellitus.
- Psychological disorders like depression.
- Patient on medication like antipsychotic, antidepressant, antiepileptics , etc.

3.1.4 Ethical approval:

All patients involved in this work were informed consent and the agreement were obtained verbally from them or their family before the collection of samples. This study was approved by the Committee on Publication Ethics in Imam Al-Sadiq Teaching Hospital and College of Medicine-University of Babylon, Iraq according to the document number 7266 (including the number and the date in 08/09/2021) to get this approval.

3.2 Methods

3.2.1 Data collection tools:

3.2.1.1 Questionnaires:

A list of socio demographic and other relevant questionnaires was used in the study as in table (3-1):

Sociodemographic	Psychological and medical history
Name	Type of the substance use
Age	Single or multiple use
Sex	Duration of substance taking

Address	Substance abstinence and its duration.
Marital state	History of chronic medical disease Like epilepsy, DM , CVA.
Education	History of head trauma
Occupation	History of surgery to the brain
	History of brain lesion and previous EEG
	History of psychological illness (Depression, schizophrenia , ect)
	History of taking medication (anti psychotic,antiepileptic ,antidepressants.
	History of comorbidity (antisocial personality disorder, anxiety disorder, suicide).

3.2.1.2 Psychiatric assessment and clinical examination

Subjects were carefully chosen to prevent the impacts of the patients' medical histories and the medications they were taking. Sociodemographic history like name, age, address, marital status, educational level, occupation, along with history of type of substance taking and the duration of the disorder, as well as previous EEG record was taken from all of the patient. All of them were sent for CT scan to rule out any brain lesions. For this study, patients were chosen who had been diagnosed with substance related disorder according to (DSM5) approved by American Psychiatric Association (APA, 2013).All subjects were recruited from the outpatient department and given verbal consent after being informed of the electrographic examination's goals and protocols.

3.2.1.3 Electrophysiological assessment

Awake EEG recordings were made in accordance with the guidelines of the American Electroencephalographic Society, using a traditional 10/20 scheme for electrode placement, which is 21; bipolar montages were used (American Electroencephalographic Society, 1986). The following electroencephalographic electrical activity was recorded: 0=no abnormality; 1=mild abnormality (generalized or frontal symmetrical theta slowing); 2=moderate abnormality (theta and delta slowing, increased delta/alpha frequency activity, that is, higher delta and lower alpha synchronization, decreased activity of alpha or beta, asymmetry increase activity of alpha or beta, increase activity of delta and theta, asymmetrical focal theta or delta, generalized 3=extreme abnormality (spike discharges or spike-and-wave activity, either alone or with the moderate abnormality) (AES, 1986) ;(Centorrino *et al* .,2002).

3.2.2 Equipment:

- EEG machine.
- Abrasive electrolyte gel.
- Distilled water.
- Disinfectant solution.
- EEG acquisition software.
- Digital EEG amplifier.
- Computers (see EEG acquisition program documentation for system requirements.).
- Electrode cap.
- Flexible tape measure.
- Printer.
- Elefix Paste for EEG Z-401CE.

3.2.3 EEG Machine:

The Nihon One EEG was used in the neurophysiologic unit of Imam Al-Sadiq Teaching Hospital for this study, which was prepared in Japan by Nihon Kohden. In a 36 channel clinical EEG system and 2 lead ECG, it combines functional sophistication and flexibility. It has automatic measurement, a multipurpose flash light with a USB connection, and manual or automatic control. The Nicolet One Nic36 amplifier has a thin, long-lasting fiber-optic interface that is resistant to electrical, radio, and magnetic interference. (Müller-Putz,2020).It consist of

- Head or jack box.
- Connectors (flexible cables).
- Recording machine (Laptop, software).
- Electrodes (grounding, reference).
- Suppliers.
- Amplifiers.

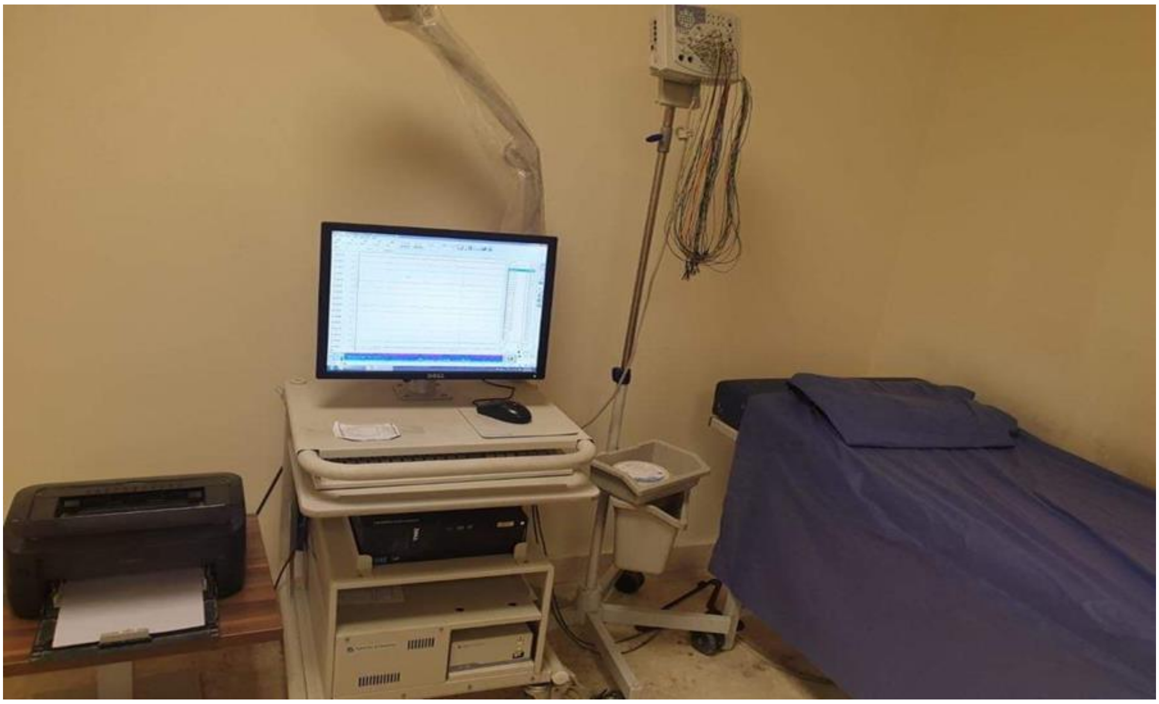

Figure (3-1) Photograph for the EEG system (finding in neurophysiology units of Imam Al-Sadiq Teaching Hospital in Al-Hilla City)

3.2.3.1 Electrodes Used in EEG:

The Clips recording cap Ag/AgCl comes with XS (18.5-20") silver electrodes, elefix Paste for EEG Z-401CE, soothed needles for gel application, and a disc ground electrode. The electrodes, which are made of a 7 mm cup disc and are connected to amplifiers via cables, record the signal from the surface of the head. Amplifiers push the microvolt into the range where it can be precisely digitalized. A converter converts the analog signals to digital signals, and the system computer stores and displays the collected data (Britton, *et al* .,2016).

3.2.4 The procedure:

3.2.4.1 Preparation for the test:

It is so important to prepare the patient before the EEG procedure (Degabriele and Lagopoulos,2008).

- All measurements were taken in a quiet examining room with a temperature controlled between 25 and 28 °C, and they were kept there for at least 15 minutes before being examined.
- Caffeine-containing foods and beverages, such as coffee, tea, or cola, must be avoided for at least 8-12 hours before the procedure, but the patient should not fast the night before or on the day of the test, since low blood sugar might alter the findings.
- The patient must wash his or her hair before the EEG and avoid using any hair products such as conditioners, sprays, or gels.
- To assist the patients stay comfortable, the exam room should be quiet with dark lighting. The patient has the option of sitting or lying down. The electrodes were placed in the right location after taking a head measurement. Following that, about 21 electrodes are put on the scalp. Using alcohol to gently clean the scalp to obtain proper recording with low impedance (Ferree *et al*.,2001). A specific paste will be used to adhere each electrode.
- The technologist can identify and document clinical data with proper equipment preparations and positioning. Reduce artifacts and interference.

Figure (3-2) Photograph for elefix Z-401CE paste used in this study

3.2.4.2 Technique:

- All patients were examined using a digital electroencephalography (EEG) equipment, bipolar montages, and the EEG record was carefully evaluated.
- The test should be performed by an EEG technician with appropriate and relevant training.
- The subject was told that the test would be painless, and he or she was permitted to relax and recline comfortably on the couch at 45 degrees.
- After cleaning the electrodes with rectified spirit, they were put on the scalp and conductive paste was utilized to minimize resistance.
- A minimum of 21 electrodes is recommended by the American Clinical Neurophysiology Society (ACNS) (Sinha *et al*., 2016). The International Federation of Clinical Neurophysiology's general assembly advises that EEG be performed using the International 10-20 method, which places electrodes in standard intervals of measurement constituted of 10% or 20%.A letter and a numerical value are assigned to each electrode location. The letters F 1/4 frontal, T 1/4 temporal, P 1/4 parietal, and O 1/4 occipital indicate which lobe of the brain the electrode location covers. Even-numbered electrodes are on the right side of the head, while odd-numbered electrodes are on the left, with two linked mastoid process

electrodes (M1 & M2) serving as reference electrodes and one forehead (FPz) electrode serving as ground electrode. With band frequencies of 0.5-30 Hz.

- During the recording, various activation procedures are performed in order to trigger epileptiform abnormalities and other EEG changes. These include eye-opening and closure, hyperventilation, and photic stimulation (Rubboli *et al*., 2004).
- The EEG channels are displayed following different montages, and each channel records the electrical potential difference between the two components (electrodes) of each channel. Electroencephalography should be reviewed using different types of montages (mainly bipolar and referential montages) in order to accurately isolate and localize abnormal discharges (Foldvary, *et al* .,2000). The digitalization of EEG has significantly improved the ease of reformatting and re-montaging per the electroencephalographer's requirements for interpretation purposes (Halford, *et al*., 2016).
- The recorded EEG waves were averaged, amplified, and filtered. The EEG trace is stored and analyzed afterwards.
- After about 20-30 minute ,When the test is finished, the electrodes will be removed and the scalp will be cleaned.

3.2.4.3 EEG Recoding:

3.2.4.3.1 Resting with eyes closed.

Resting states are the most commonly used method for obtaining EEG readings.The subject is instructed to remain completely calm, typically sitting in a 45 degree in a quiet area, before the EEG signal is recorded. The simplicity of the procedure is what makes it useful. There are no other prerequisites or instructions; however, the environment must be peaceful, and the participant must be free of mental activity or concern; otherwise, the results will be skewed. Nonetheless, the resting state can be used as a baseline EEG activity for the other activities in the preprocessing step (Acharya, et al.,2016) .

3.2.4.3.2 Open-eyed hyperventilation.

The patient is hyperventilated by breathing deeply for 2-3 minutes at a rate of 18-24 breaths per minute. Patients with severe cardiac or pulmonary illness, uncontrolled hypertension, sickle cell anemia, active asthma, or a recent ischemic event (such as myocardial infarction, stroke, transient ischemic attack, or subarachnoid hemorrhage) should not take HV (Holmes *et al*., 2004). Hypocapnia and alkalosis caused by HV may result in decreased cerebral perfusion or vasospasm, which may further impair circulation. A typical HV response includes theta or delta background slowing (buildup), which is accentuated when fasting (relative hypoglycemia). The EEG usually returns to baseline within 2 minutes after HV. During HV, focal EEG alterations that do not resolve are investigated.

3.2.4.3.3 Photic stimulation

It is a technique for activation. The standard approach for intermittent photic stimulation is a sequence of photic flashes delivered by a strobe light at a specified distance of 20-30cm from the patient's face during eye closure (IPS)(Kasteleijn-Nolst Trenite *et al*., 2012).

3.2.4.4 Montages

A montage is a topographic map of the electrical activity of the brain composed of a uniform array of recording electrodes. The most common types are referential and bipolar montages (Acharya, *et al*.,2016).

3.2.4.4.1 Mono polar or Referential Technique:

A referential montage's channels represent the electrical difference between an active electrode (G1) and an inactive reference (G2) (Acharya et al., 2016). Frequent reference montages include the vertex Cz recording montage, ipsilateral ear/mastoid processes, and a shared average reference. In a common average reference, an electrode is compared to a weighted average of the signal from all other recording electrodes on the scalp. A significant advantage of digital EEG is the ability to evaluate numerous bipolar and referential electrode configurations after the patient recording has been collected using a common reference montage (Britton *et al*., 2016).

3.2.4.4.2 Bipolar Technique:

A bipolar montage captures the comparison of two active electrodes in each channel (Britton *et al*., 2016). The longitudinal bipolar montage (also known as a "double banana") is the most common, so named because the electrode layout resembles a banana placed front to back over each of the brain hemispheres. A bipolar montage is formed by chaining together nearby electrodes to form an array that can be anterior to posterior (longitudinal bipolar) or side to side (transverse bipolar). Each of these has advantages and limitations when used alone; combining bipolar and reference montages is recommended (Sinha *et al*., 2016) to obtain the most information. At the very least, the ACNS advises that a conventional EEG recording contain a longitudinal bipolar montage, a transverse bipolar montage, and a referential montage (Acharya *et al*., 2016).

Both type of montage are used in our test.

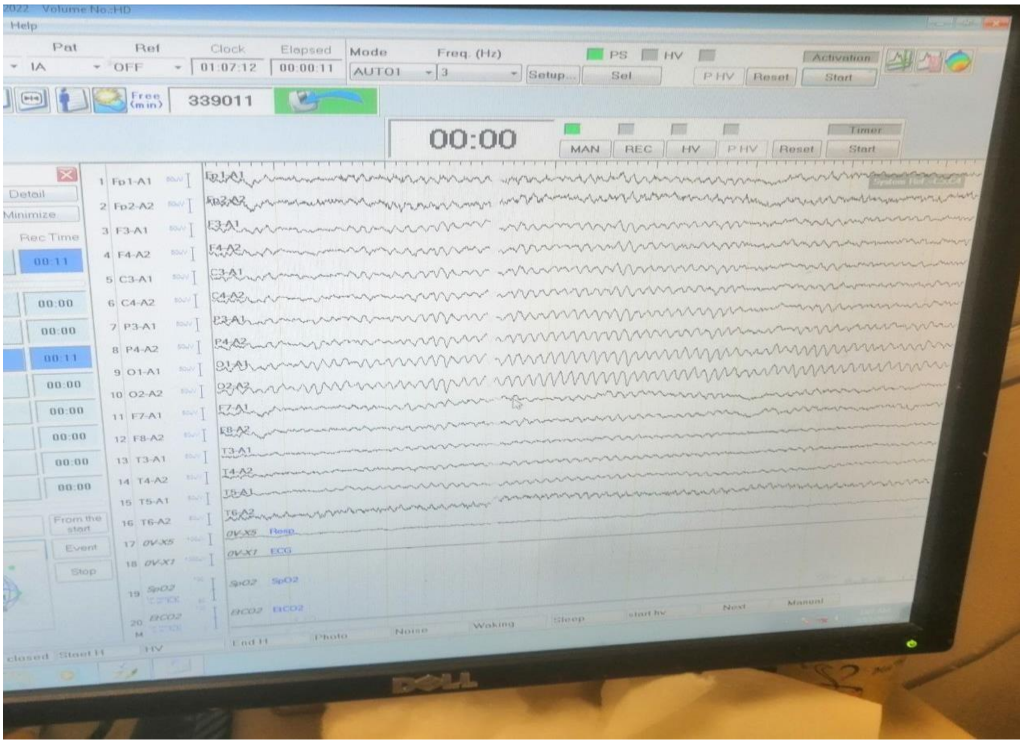

Figure (3-3): Electrodes placement (montage) used in pattern reversal Electroencephalography (EEG).

3.3. Statistical analysis:

The data were analyzed by using computerized SPSS (Statistical Package for Social science) program, version 25. Categorical variables were addressed as percentages (no. (%)).“Chi-square test was used to compare between the study groups, and a P value of less than 0.05 was considered statistically significant” (Daniel & Cross, 2018).

The Results:

4.1 The distribution of patients according to socio-demographic characteristics

The total number of participants in this study were 112 (104 males and 8 females). The age were be most common in (15-25) and (26-35) years with frequency of 41% for each category. The frequency of patients who were living in urban area was (80.4%),while the frequency of the study participants who were single was (50%). Most of the study participants were unemployed (87.5 %). Secondary school was the most common educational level of the study participants (62.5%).

4.1.1 Age distribution:

There were be four age group patient:

1- (15-25) years, there number were 46 with frequency of 41%.
2- (26-35) years, there number were 46 with frequency of 41%
3- (36-45) years, there number were 16 with frequency of 14.4%
4- More than 45 yeares, there were 4 with frequency of 3.6%.

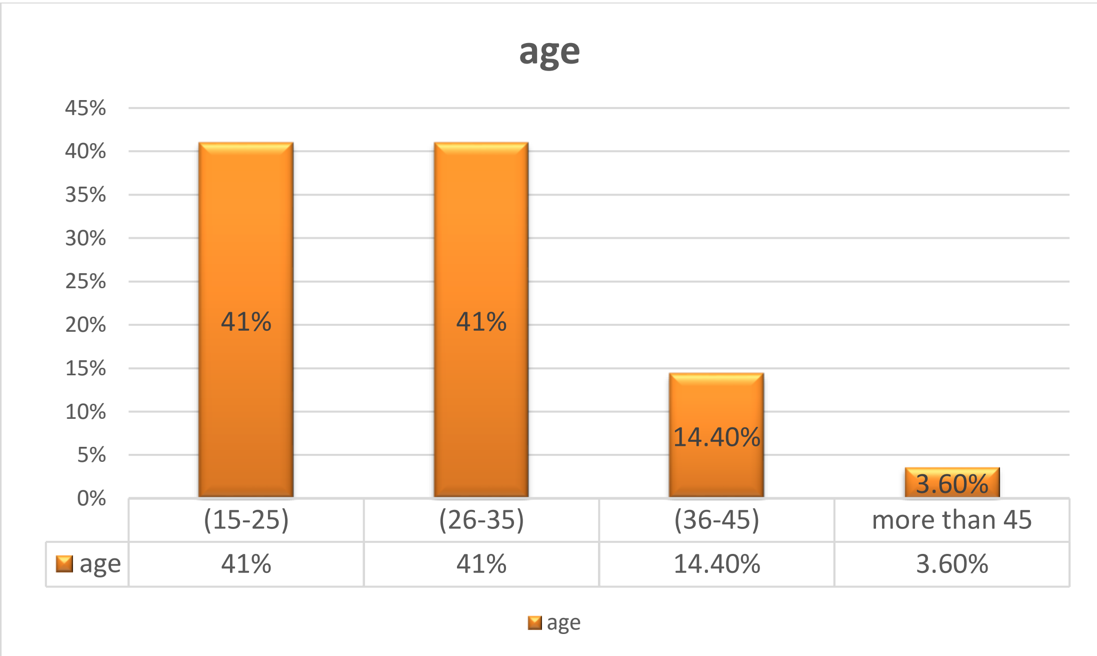

figure (4-1) the age distribution of the patients.

4.1.2Gender distribution:

The patient divided in to 104 male and 8 female with frequency of 92.9% and 7.1% respectively.

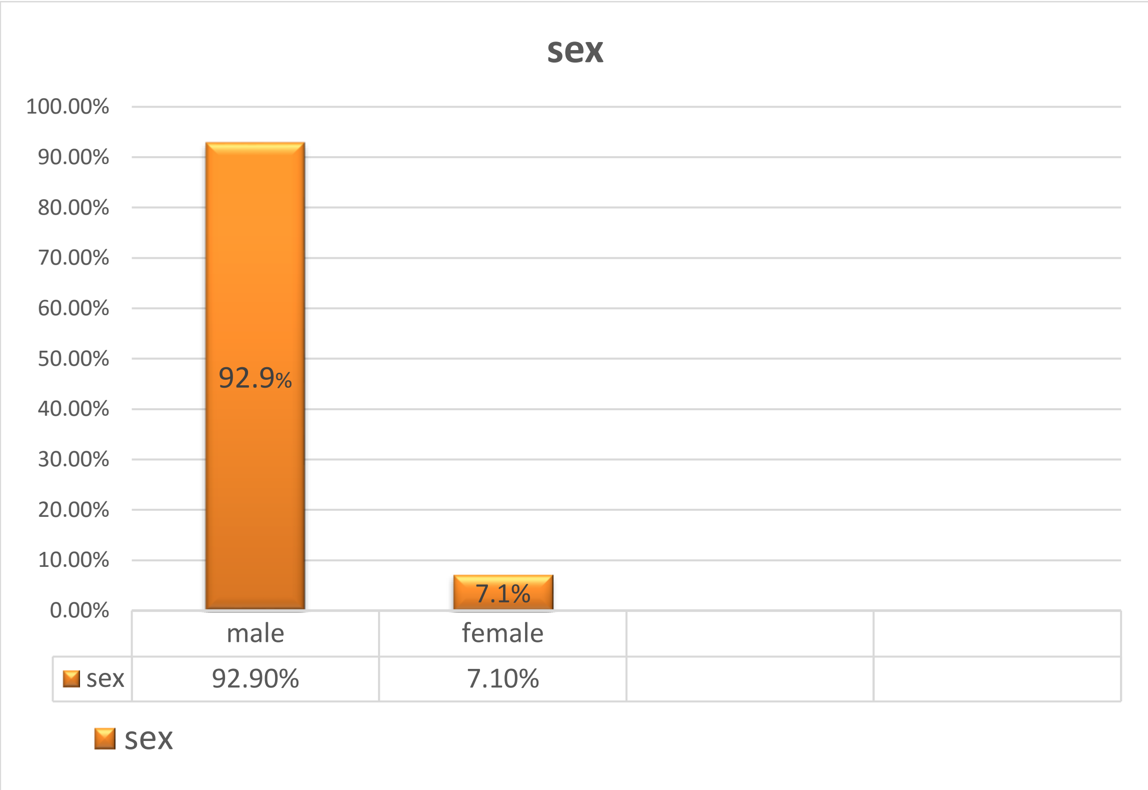

Figure (4-2) the distribution of patients according to their sex.

4.1.3 Marital state distribution:

Half of the total number of the patients were married and the other were single with equal frequency (50%) for both.

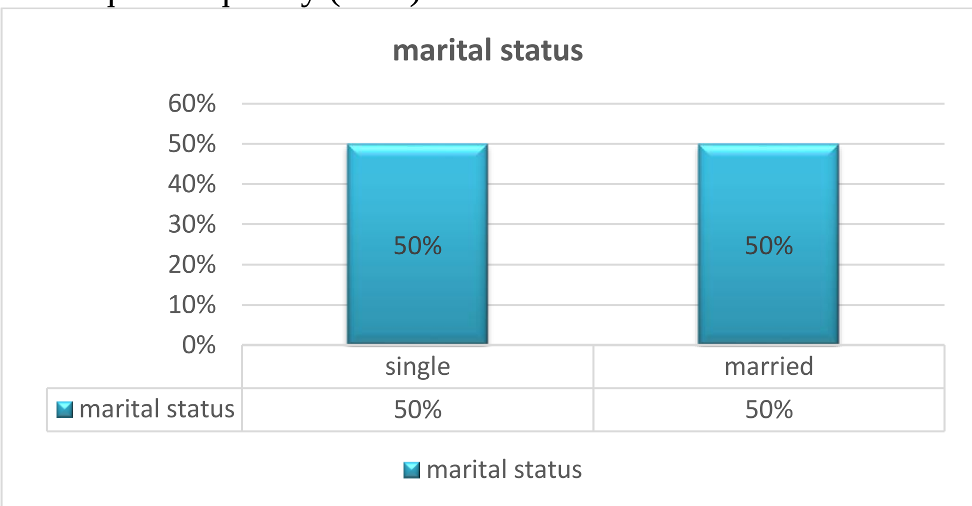

Figure (4-3) the patient frequency according to marital status.

4.1.4 Residence distribution:

The total number of the patients lived in urban area were 90 with frequency of 80.4%,while the patients that lived in rural area were 22 with frequency of 19.6%.

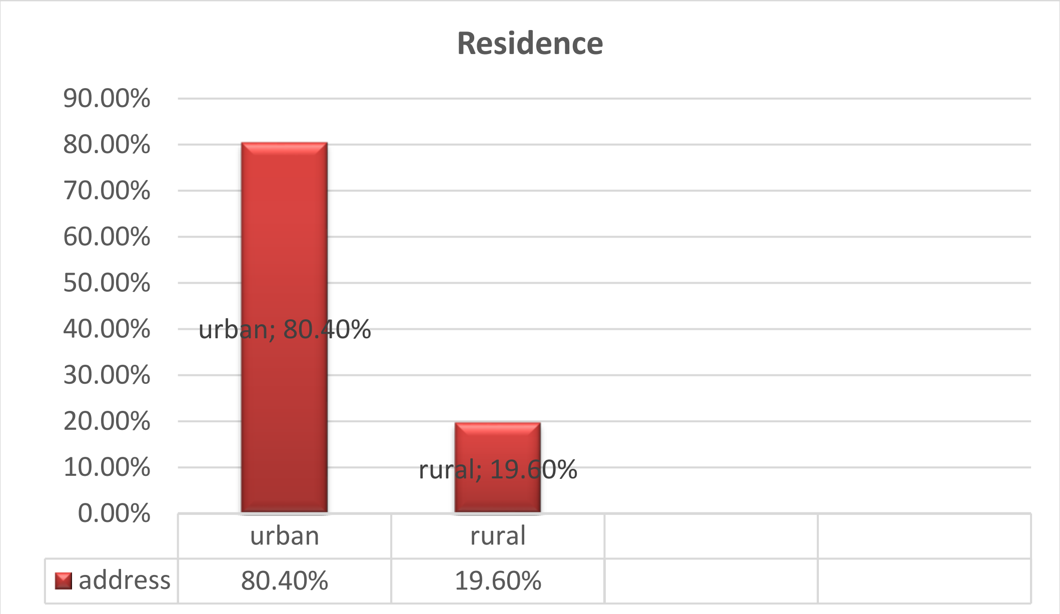

Figure (4-4) the frequency of the patients by their address

4.1.5 The distribution according to education:

The major number of the patients had secondary school educational level which were 70 with frequency of 62.5%, while the remainder were 4 illiterate (3.6 %) , primary school 24 (21.4%) , college 14 (12.5%).

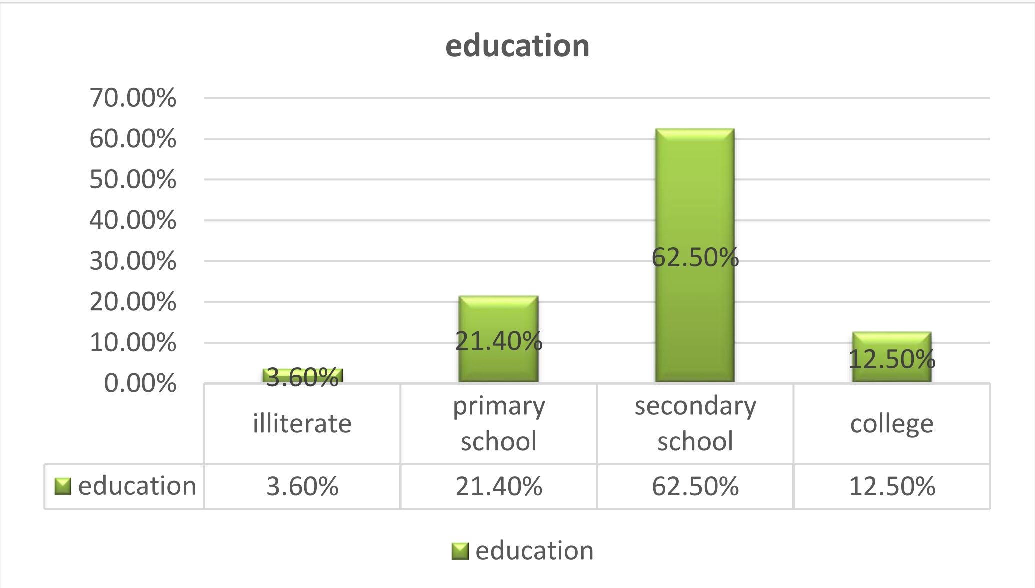

Figure (4-5) the frequency of the patients cording to their educational level.

4.1.6 Occupation distribution:

98 of the total number of the patients were unemployed with frequency of 87.5%, while the other 14 were employed with frequency of 12.5%.

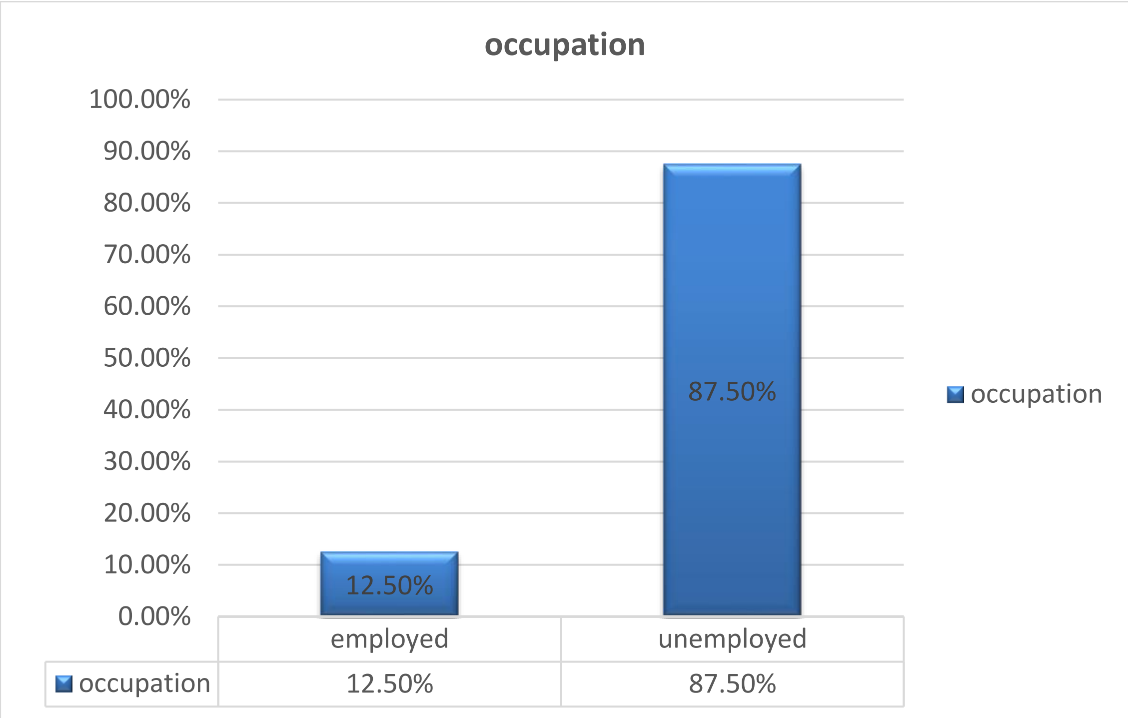

Figure (4-6) the distribution of the patients according to the occupation

4.2The distribution of the patient according to the clinical characteristics.

In this study (44.6%) of participants were used amphetamine. The duration of taking the substance for most of the patient were 2 and 3 years with frequency of 33.9% for each one. Most of the study participants had an abstinence duration of one weak (55.4%). The most common EEG change in this study was score 2 which mean moderate change (the frequency of the patient with moderate EEG change were 42.9%.

4.2.1 The distribution of the patients according to the type of substance.

In this study, there were be four type of the substance taken by the patient which consist of

1- Amphetamine: the patients number were 50 with 44.6% frequency.
2- Alcohol: the patients number were 24 with 21.4% frequency.
3- Benzodiazepine: the patients number were 10 with 9% frequency.
4- Poly substance: the patients number were 28 with 25% frequency.

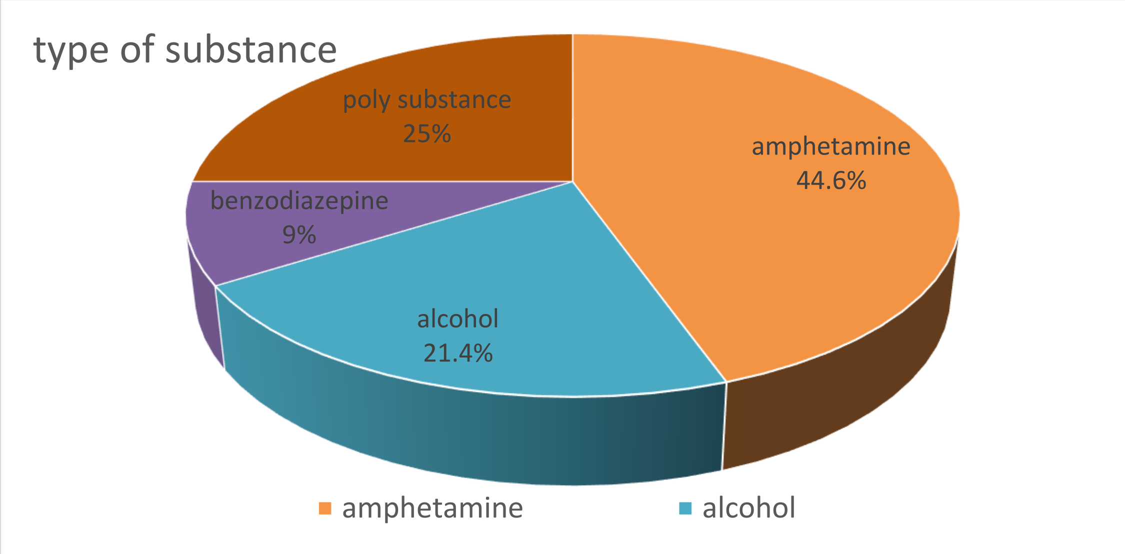

Figure (4-7) the distribution of the patient according to the type of substance.

4.2.2 The distribution of patients according to the duration of substance taking

The frequency of the patients who take the substance for one year 17.9%
The frequency of the patients who take the substance for two year 33.9%
The frequency of the patients who take the substance for three year 33.9%
The frequency of the patients who take the substance for four year 14.3%

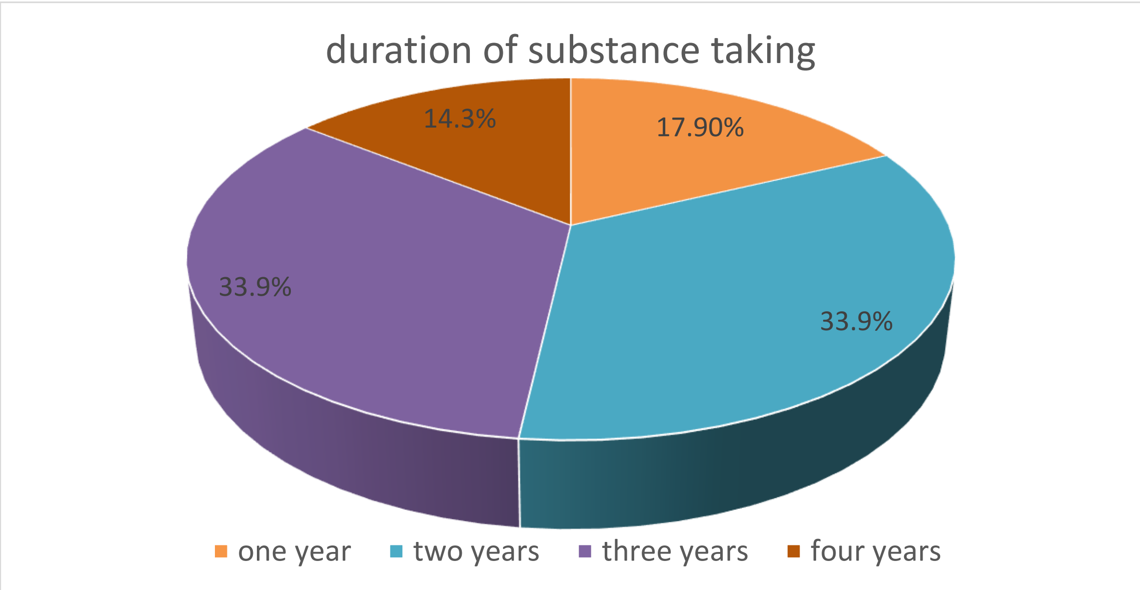

Figure (4-8) the frequency of patient according to the duration of substance taking.

4.2.3 The distribution of the patient according to duration of substance abstinence:

The patients were distributed in to three groups according to the duration of substance abstinence which include one week duration with a number of 62 and frequency of 55.4% , two weeks with 32 patients and frequency of 28.6% , and three weeks of 18 patients with a frequency of 16%.

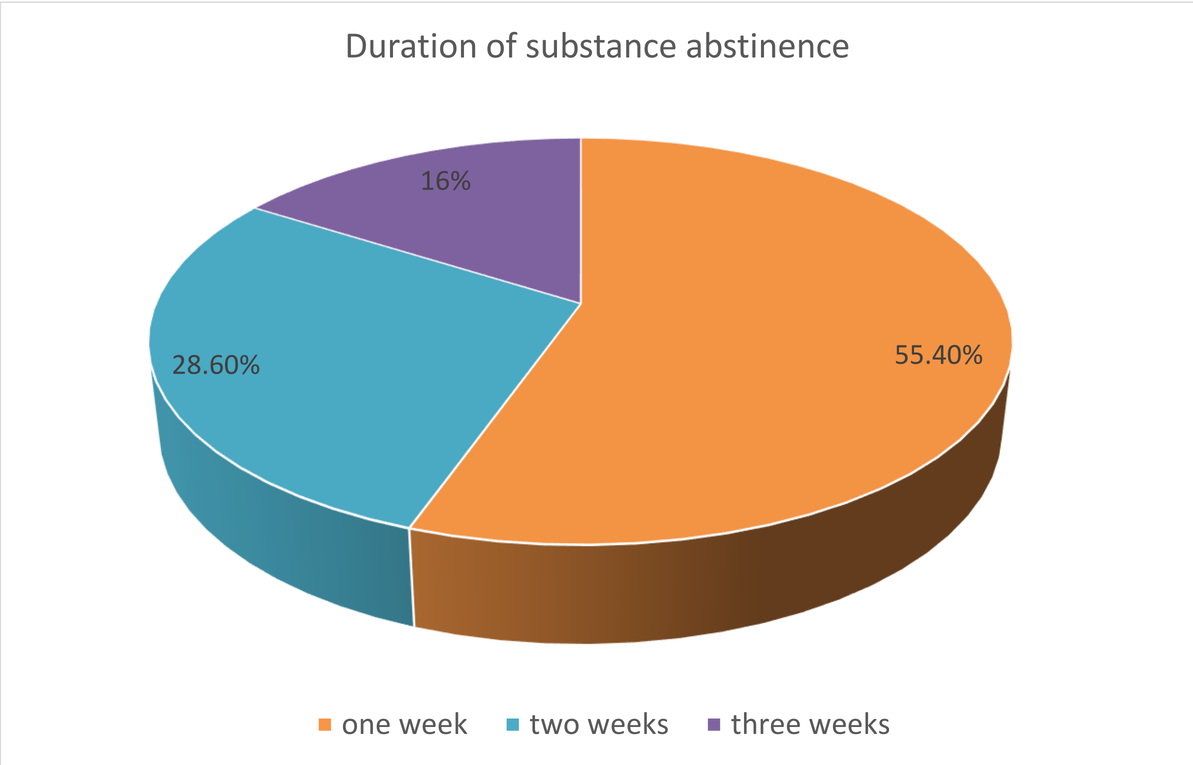

Figure (4-9) the frequency of the patient according to the duration of substance abstinence.

4.2.4 The distribution of the patient according to the EEG changes

None of the participants showed score 1 EEG changes, the rest showed changes as in figure (4-10)

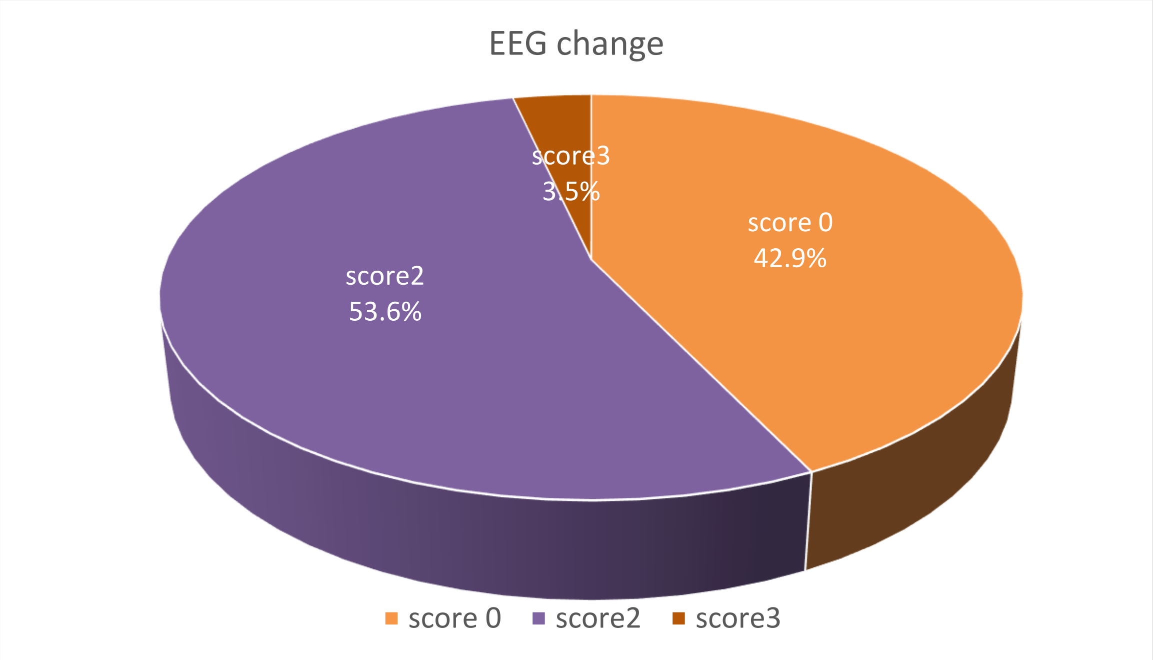

Figure (4-10) the distribution of the patient according to the EEG change.

4.2.5 The distribution of the patient according to the history of comorbidity (antisocial personality disorder, anxiety disorder, suicide etc.):

As in figure (4_11) there were 31% of the participants had a history of comorbidity while the remaining 69% of them did not have comorbidity.

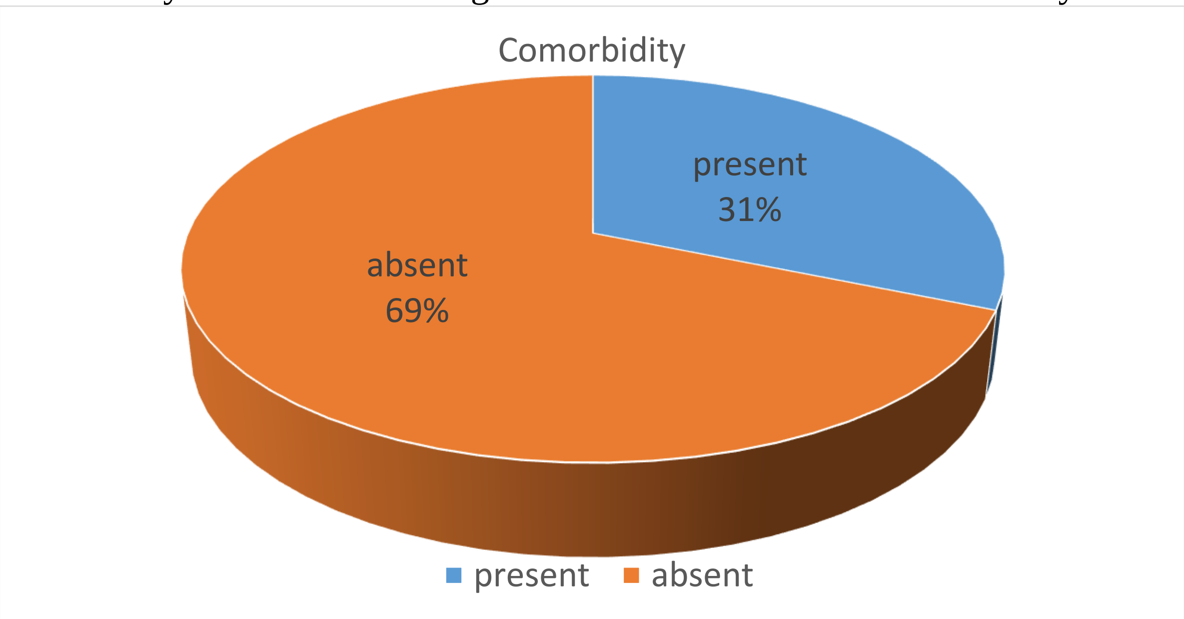

Figure (4-11) the distribution of the patients according to the history of comorbidity

4.3 The association between the type of substance and sociodemographic characteristics:

4.3.1 The distribution of patients according to type of substance taking in correlation with age

As in table (4-1) ,There was a significant difference between the type of substance taking and age (p value=0.002).

Table (4-1) The distribution of patients according to type of substance taking in correlation with age.

	Age group				Total	P value
Type of substance	15-25	26-35	36-45	More than 45		
Alcohol	4 16.7%	12 50.0%	4 16.7%	4 16.7%	24 100.0%	0.002
Amphetamine	24 48.0%	20 40.0%	6 12.0%	0 .0%	50 100.0%	
Benzodiazepine	2 20.0%	4 40.0%	4 40.0%	0 .0%	10 100.0%	
Multiple substances	16 57.1%	10 35.7%	2 7.1%	0 .0%	28 100.0%	
Total	46 41.1%	46 41.1%	16 14.3%	4 3.6%	112 100.0%	

4.3.2 The distribution of patients according to type of substance taking in correlation with gender:

Table (4-2) demonstrate the frequency of the patient according to type of substance taking in correlation with gender, The study showed no association between the type of substance and gender, p value was (0.447) which was non-significant.

Table (4-2): the association between type of substance and gender

Type of substance	Gender		Total	P value
	Males	Females		
Alcohol	22 91.7%	2 8.3%	24 100.0%	0.447
Amphetamine	48 96.0%	2 4.0%	50 100.0%	
Benzodiazepine	8 80.0%	2 20.0%	10 100.0%	
Multiple substances	26 92.9%	2 7.1%	28 100.0%	
Total	104 92.9%	8 7.1%	112 100.0%	

4.3.3 The distribution of patients according to type of substance taking in correlation with marital status:

Table (4-3) shows the association between type of substance taking and marital status with P value of (0.028) which was a significant.

Table (4-3) the association between type of substance taking and marital status

Type of substance	Marital status		Total	P value
	Single	Married		
Alcohol	6 25.0%	18 75.0%	24 100.0%	0.028
Amphetamine	26 52.0%	24 48.0%	50 100.0%	
Benzodiazepine	6 60.0%	4 40.0%	10 100.0%	
Multiple substances	18 64.3%	10 35.7%	28 100.0%	
Total	56 50.0%	56 50.0%	112 100.0%	

4.3.4 The distribution of patients according to type of substance taking in correlation with residence:

The study showed no association between the type of substance and residence, p value was (0.129) which was non-significant.

Table (4-4) The association between type of substance taking and residence

Type of substance		Residence		Total	P value
		Urban	Rural		
Alcohol	Count	22	2	24	0.129
	%	91.7%	8.3%	100.0%	
Amphetamine	Count	38	12	50	
	%	76.0%	24.0%	100.0%	
Benzodiazepine	Count	6	4	10	
	%	60.0%	40.0%	100.0%	
Multiple substances	Count	24	4	28	
	%	85.7%	14.3%	100.0%	
Total	Count	90	22	112	
	%	80.4%	19.6%	100.0%	

4.3.5 The distribution of patients according to type of substance taking in correlation with occupation:

The study showed no association between the type of substance and occupation, p value was (0.108) which was non-significant.

Table (4-5) The association between type of substance and occupation

Type of substance	Occupation		Total	P value
	Unemployed	Employed		
Alcohol	22 91.7%	2 8.3%	24 100.0%	0.108
Amphetamine	44 88.0%	6 12.0%	50 100.0%	
Benzodiazepine	6 60.0%	4 40.0%	10 100.0%	
Multiple substances	26 92.9%	2 7.1%	28 100.0%	
Total	98 87.5%	14 12.5%	112 100.0%	

4.3.6 The distribution of patients according to type of substance taking in correlation with education:

Table (4-6) shows the association between type of substance taking and education with P value of (0.042) that was a significant.

Table (4-6) The association between type of substance taking and education

Type of substance	Type of education				Total	P value
	Not read and write	Primary school	Secondary school	College		
Alcohol	0 .0%	8 33.3%	14 58.3%	2 8.3%	24 100.0%	0.042
Amphetamine	2 4.0%	6 12.0%	32 64.0%	10 20.0%	50 100.0%	
Benzodiazepine	0 .0%	2 20.0%	6 60.0%	2 20.0%	10 100.0%	
Multiple substances	2 7.1%	8 28.6%	18 64.3%	0 .0%	28 100.0%	
Total	4 3.6%	24 21.4%	70 62.5%	14 12.5%	112 100.0%	

4.4 The distribution of patients according to the clinical characteristics:

4.4.1 The correlation of duration of substance taking and EEG changes:

The study showed the association between type of substance taking and EEG change, with P value of (0.008) which was significant.

Table (4-7) The association between type of substance taking and EEG change:

	EEG changes			Total	P value
	Score 0	Score 2	Score 3		
Alcohol	8 33.3%	12 50.0%	4 16.7%	24 100.0%	0.008
Amphetamine	22 44.0%	28 56.0%	0 .0%	50 100.0%	
Benzodiazepine	2 20.0%	8 80.0%	0 .0%	10 100.0%	
Multiple substances	16 57.1%	12 42.9%	0 .0%	28 100.0%	
Total	48 42.9%	60 53.6%	4 3.6%	112 100.0%	

4.4.2 The correlation of the EEG changes and duration of substance taking:

The study showed the association between the EEG change and duration of substance taking , with P value of (0.0001) which was significant.

Table (4-8) the association between the EEG change and duration of substance taking

EEG	Duration of substance taking				Total	P value
	One year	Two years	Three years	Four years		
Score 0	12 25.0%	26 54.2%	10 20.8%	0 .0%	48 100.0%	0.0001
Score 2	8 13.3%	12 20.0%	26 43.3%	14 23.3%	60 100.0%	
Score 3	0 .0%	0 .0%	2 50.0%	2 50.0%	4 100.0%	
Total	20 17.9%	38 33.9%	38 33.9%	16 14.3%	112 100.0%	

4.4.3 The correlation of EEG changes and duration of substance abstinence:

The study showed the association between the EEG change and duration of substance abstinence, with P value of (0.0001) which was significant.

Table (4-9) The correlation between the EEG change and duration of substance abstinence

EEG		Duration of substance abstinence			Total	P value
		One week	Two weeks	Three weeks		
EEG	Score 0	16 33.3%	14 29.2%	18 37.5%	48 100.0%	0.0001
	Score 2	42 70.0%	18 30.0%	0 .0%	60 100.0%	
	Score 3	4 100.0%	0 .0%	0 .0%	4 100.0%	
Total		62 55.4%	32 28.6%	18 16.1%	112 100.0%	

Discussion:

5.1 Distribution of patients according to socio-demographic characteristics

5.1.1 Age distribution:

The study result reflecting the fact that substance related disorder is a problem in adolescence and early adulthood.

Adolescence (10–19 years) is characterized by a series of developmental changes, which are highly impacted by social, cultural, and nutritional influences (Hamidullah,*et al*.,2020). A vast array of neurodevelopmental changes occur during this time, including cortical thinning, gray matter volume reductions, increases in white matter volume, synaptic pruning, and reorganization within cortical and limbic regions (Hamidullah,*et al*.,2020). These neurodevelopmental changes give rise to characteristic behaviors during adolescence, such as improvements in cognition and executive functions, increases in reward sensitivity, novelty-seeking, risk-taking behavior, and a tendency to spend more time with peers (Romer ,2010). Some of these behavioral characteristics, in turn, contribute to a greater likelihood of initiating substance use (Garofoli,2020).

Our result were in agreement with other study such as:

Zaki *et al*. (2021) study the sociodemographic characteristics of a sample of patients with substance use disorders stated that the mean age of the participant were 29 years with the youngest subject being 14 years old and the oldest 63 years.

Ibrahim *et al*. (2018) said that the majority of the participant abuser (73%) were 21-40 years of age and only 6.5% were adolescents under the age of 20 years.

Hamdi *et al*. (2016) presented in their review that : Substance use and abuse have higher lifetime prevalence among young and middle aged males.

Survey of Substance Abuse in Iraq (2015) showed that Most of the participant were in the (18_34) age group.

5.1.2 Gender distribution

The frequency of male patient was more than female in this study, the reason for that largely difference was that male were more than female seeking help from hospital, female refusal for social , religious attitude. Male were spent a lot of time outside the home, socialize with friends, and are more present in the café than female.

Research on substance use disorders (SUDs) has disproportionately focused on males. However, there are numerous biological, psychological and social differences between men and women that may affect the development, maintenance and treatment of SUDs (Greenfield, Brooks, *et al.*, 2007).

Recent clinical studies in SUD analyzing sex differences reveal neurobiological changes that are differentially impacted in common reward processing regions such as the striatum, hippocampus, amygdala, insula, and corpus collosum (Cornish and Prasad,2021).

Zaki *et al*.(2021) showed that males accounted for 96.6 percent of the cases, while females accounted for only 3.4 percent. Previous research (Khalil *et al*., 2008) has explained the significant male predominance among substance users as a result of Egyptian customs and traditions, which give men more freedom while restricting women's movement, and being slightly more tolerant of male substance use than females, where it is associated with social stigma.

Hamdi *et al*. (2016) said that the majority of the sample (20.6 percent) was from the age group (26-35 years old), with a male preponderance in all phases, i.e. 67.5 percent of the total sample was male. The male-to-female ratio was approximately 7:1. These ratios can be explained by the theory that females suffer more than males from internalizing problems (anxiety and depression), while males suffer more from externalizing problems (substance use and aggression).

Survey of Substance Abuse in Iraq (2015) showed that most of the refusals of the participant were from females (90.0%) in Baghdad governorate. Reasons for refusal included not having permission to participate from male guardians، Suspicions about the nature of the interview, and religious reasons (females thought that talking with a stranger without the presence of a male family member would be sinful).

The result of the study mentioned above were as similar as our study.

5.1.3 Marital status distribution

In this study, there was no difference between being married or single and having substance related disorder. The responsibility of marriage, it's problems made the individual under pressure lead him to seek for substance. On the other hand being single, away from family, lack of emotional support, curiosity and other problems increased the risk of substance abuse.

Numerous studies have been conducted to identify trends in drug dependence among single and married groups, and it has been discovered that an individual's marital status can indeed influence their likelihood of becoming a victim of drug abuse. Many studies have found that marriage hastens the decline in drug use when compared to those who remain single. However, some studies discovered negative outcomes. Marriage has been concluded to be a protective factor against drug use, but several factors, including qualitative spare time, a more mature relationship, a sense of commitment, and intimacy, have influenced this (Sinha,2019).

Zaki *et al*.(2021) in a study conducted on stated that 57% of the participant were married.

Salvatore *et al*.(2019) said that when compared to being divorced/separated or single, marriage was associated with significant reductions in substance use, and these reductions began prior to marriage. The co-twin comparison and within-person models ruled out the alternative explanation of confounding background familial and individual factors as the cause of marriage effects. These findings provide compelling evidence that the social role expectations associated with marriage reduce the use of psychoactive substances. This is contrast to our study.

Ibrahim *et al*. (2018) showed that the married abuser were more than the single one.

Survey of Substance Abuse in Iraq (2015) showed the married participants more prone to substance use (78% of the participants were married).

Liang and his collegeous.(2012) discovered that having never been married, divorced, or separated was a strong predictor of risky alcohol consumption behaviors. Young and middle-aged people's marital status could be a useful screening tool for health professionals looking to identify patients at high risk of alcohol-related problems.

5.1.4 Distribution of education

The majority of the patient had secondary educational level, clarified that individuals with some level of education are more prone to substance related disorders.

Zaki *et al*. (2021) stated that less educated people are more common users of substance.

Ibrahim *et al*. (2018) reported that most of the abuser had a secondary or higher school level of education.

Hamdi *et al*. (2016) showed that the less educated people were more common users of substance(s). In the United States, the annual prevalence of use of any illicit drug was 39 percent for college students and 44 percent for non-college respondents in 2014. (Johnston, *et al.*, 2015). These findings may lend credence to the notion that education protects against substance abuse, education assists people in developing risk perceptions and skills.

Survey of Substance Abuse in Iraq (2015) showed the secondary educational level was dominant supporting the result of our study.

5.1.5 Distribution of occupation:

Most participants of our study were unemployed. This is due to the pressure or problem of free work that lead to substance gaiting.

Ibrahim *et al*. (2018) found a high prevalence of abuse in unemployed participant.

Previous Egyptian studies Zaki *et al*.(2021) ,(Bassiony *et al*., 2016; Abou El-Magd *et al*., 2018; El-Wasify *et al*., 2018) reported most of their sample to be manual workers probably due to their belief that drugs can help them overcome fatigue and hardship of their work.

Hamdi *et al*. (2016) supposed that the enormous stress, rejection, fear, and frequent bouts of depression that often accompany being unemployed and single are high risk factors for developing a drug use problem. Many people who are unemployed and single turn to alcohol or drugs to alleviate their discomfort and sense of helplessness.

In contrast to this study, Survey of Substance Abuse in Iraq (2015) showed the majority of the participant were employed.

5.1.6 Residence distribution:

The majority of participant were from urban area this is duo to easy availability of substances. People in the urban were under stress more than those lived in rural region, this stress may be familial pressure, educational or employment problem.

Zaki *et al*. (2021) clarified that 54% of the sample were from rural areas and this disagreed with our study.

Hamdi *et al*. (2016) showed that as regards the regions of residence, most substance users were living in urban areas, and hence in agreement with the present study.

5.2 The distribution of the patient according to the clinical characteristics.

5.2.1The distribution of the patient according to the type of substance:

In this study, the result showed that the amphetamine was the most common used substance followed by multiple substance then alcohol and lastly benzodiazepine substance.

The use of amphetamines and their derivatives has been linked to an increase in aggression, violent behavior, psychosis, and impulsiveness (Harro, 2015). Our respondents' reasons for using psychoactive substances included relief from depression, increased alertness, staying awake at night, peer pressure, and improved sexual performance. These were similar to findings reported in previous studies for the initiation of substance use and included academic pressure, peer group temptation, stress relief, and increased pleasure during sex (Osman *et,al*.,2016).

Jones *et al*.(2020) showed that methamphetamine is a highly addictive stimulant of the central nervous system. Although overall population rates of methamphetamine use in the United States have remained relatively stable in recent years (SAMHSA,2019), Methamphetamine availability and methamphetamine-related harms have increased in the United States in recent years (Gladden and colleagues, 2019).

Al-wateefee (2019) study the Screening of addiction associated drug among suspected prisoners , said that amphetamine is hugely used among Babylon addicts.

Ibrahim *et al*. (2018) said that when compared to previous Saudi Arabian studies, there was an increase in polysubstance and amphetamine use and a decrease in prescription drug abuse. The prevalence of heroin and alcohol was decreasing. Benzodiazepines and volatile inhalants were the least commonly abused drugs.

Survey of Substance Abuse in Iraq (2015) showed that the main substance use in the north region was cannabis while in south and middle region of Iraq was captagon.

5.2.2 The distribution of patient according to the duration of substance taking:

The main result was increasing frequency for taking the substance for two and three years. This is could be due to the recent availability of illicit drugs in Iraq.

All addictive substances have strong brain effects. These effects account for the euphoric or intensely pleasurable feelings that people experience when first using alcohol or other substances, and these feelings motivate people to use those substances again and again, despite the risks of serious harm. As people continue to abuse alcohol or other substances, progressive changes in the structure and function of the brain, known as neuroadaptations, occur. These neuroadaptations impair brain function and also drive the transition from controlled, occasional substance use to chronic, difficult-to-control substance abuse. Furthermore, these brain changes last long after a person stops using substances. They may cause ongoing, periodic cravings for the substance, which can lead to relapse. More than 60% of people treated for a substance use disorder relapse within the first year after leaving treatment (Hubbard *et al*., 2003), and a person can be at high risk of relapse for many years (Friedman,*et al*.,2009).

Ibrahim *et al*. (2018) found sixty-five percent of the participant abuse the substance for (0-10) years.

5.2.3 The distribution of the patient according to duration of substance abstinence:

Most of the participant in this study had abstinence period of one week, this result could be due to most of our cases came voluntarily or compulsively by their family to dependence ward to seek treatment.

It is important to note that the duration of abstinence was longer among participants who were convinced and encouraged to quit the habit as opposed to those who were forced to quit (Adinoff, *et al*.,2016). Choose abstinence over their option. Apart from a variety of other bio-psycho-social factors that contribute to relapse, social/peer pressure and negative emotions from family are the most prevalent.

Positive reinforcement from family members increases confidence, emotional stability, and develops an optimistic approach in addicts, motivating them to quit drug abuse. It is critical to motivate drug users to quit, but it is also critical to educate members on how to identify negative behaviors and approaches so that the individual's rehabilitation and abstinence is more effective, efficient, and long-lasting (Chan, *et al*.,2019).

Allsop et al.(2016) Uses EEG to Explore moderators of recovery during cannabis abstinence EEG was tested before and after 2 weeks of abstinence and found abstinence only led to increase beta activity in later onset users.

5.2.4 The distribution of the patient according to the EEG changes:

The study result showed that there were EEG abnormality associated with substance related disorder; these changes classified into four scores.

Score 2 or moderate abnormality was the most common finding, followed by score zero or no change and lastly score 3 or severe changes. The explanation for this is that the abnormal finding may be non-specific, for different drugs may affect the reward system, cognitive behavior, multiple neurotransmitters and specific brain area.

Substance abuse is a complex set of disorders with frequent psychopathological comorbidities and various types of EEG abnormalities (Egorov,2004). Substances' effects on the EEG vary and are frequently dose dependent. Effects on the EEG are generally predictable and include : no effect, accentuation of beta activity, background slowing with decreased amplitude and/or frequency of the alpha rhythm, intermixed theta and/or delta activity, decreased seizure activity, and lower seizure threshold with increased spike and wave discharges. In cases of severe overdose, the EEG may show alpha/theta coma, burst suppression, or even a "flat" EEG pattern (Banoczi,2005).

Liu (2022) stated that long-term substance use, such as alcohol, tobacco, cannabis, cocaine, opioids, heroin, methamphetamine, is associated with a wide range of resting-state EEG abnormalities, the majority of which cannot be recovered automatically after brief abstinence(1 to 2 weeks). The similarities and differences in findings for different drugs may reflect their shared and distinct effects on neurotransmitters and brain regions.

5.2.5 The distribution of the patient according to comorbidity (antisocial personality, anxiety disorder, suicide, etc.).

In this study about thirty one percent of participant had history of comorbidity (antisocial personality disorder, anxiety disorder and suicide). The patient who took the substance may be socially isolated, anxious and may be at increasing the risk for suicide.

This agreed with (Saha *et al*. 2021) who found robust and consistent evidence of an increased risk of comorbidity between many combinations of mood and substance-related disorders.

Co-occurring substance use disorders and other mental health conditions (dual disorders) are very common, and these patients typically have more severe clinical and psychosocial problems than patients with only substance use disorders.

Depression, anxiety, post-traumatic stress disorder, personality disorders (primarily antisocial and borderline), and suicide are the most common psychiatric comorbidities among people with substance use disorders(Torrens, *et al* .,2011)؛(Magidson *et al*., 2012).

5.3 The association between the type of substance and sociodemographic characteristics:

5.3.1 The distribution of patients according to type of substance taking in correlation with age:

The study showed the significant association between type of substance and age, most of amphetamine and multiple substance abuser were in (15-25) years. While alcohol and benzodiazepine abuser were in (26_35) years. This clarified that the use of illicit drugs are more common among adolescents.

Adolescence is defined by an increased interest in new experiences combined with poor inhibitory control, which may promote impulsive actions and, as a result, increase the chances of experimenting with drugs (for example, alcohol), making adolescents more vulnerable to addiction (Beil-Gawelczyk *et al*., 2014) and other related problems (Green *et al*., 2016; Silins *et al*., 2018).

Board *et al*.(2020) concluded that national stimulant dispensing rates increased from 2014 to 2019, driven by notable increases among females and adults aged ≥20 years. These trends should be considered when prescribing stimulants given growing concerns over prescription stimulant diversion, misuse, and related health harms.

Nair *et al*. (2016) said there was a significant linear decline in the age at onset of alcohol use and use disorder. The mean age at onset of alcohol use and alcohol use disorder declined from17 to 24 years and 21 to 46 years, respectively.

Austic (2015) said that the peak annual incidence rates for nonmedical use of prescription stimulants were observed between the ages of 16 and 19 years. There is reason to initiate interventions during the earlier adolescent years to prevent youths from starting nonmedical use of prescription stimulants.

Degenhardt (2007) showed that young people in Australia using amphetamine at age 24 years are highly likely to be significant polydrug users. The risks for both initiation of young adult amphetamine use, and maintenance of such use, pertain to the heavy use of other drugs.

5.3.2 The distribution of patients according to type of substance taking in correlation with gender:

The study showed no association between the type of substance and gender, this reflect that substance related disorder is a problem in both sex and this result could be due to sample size (The larger the sample size, the greater the chance of a woman being present in our study) and as was mentioned previously most of female in our society did not seek help for treatment from abuse duo to stigma, cultural religious customs and traditions.

Gender differences in substance use have been consistently observed in the West, in general population as well as in the treatment-seeking samples, with men exhibiting significantly higher rates of substance use, abuse, and dependence (Brown,*et al* ., 2000).

The relative proportion of different drugs used by females varies by region. Women's alcohol use is more socially acceptable in some countries, such as the United States, but women have always been a minority when it comes to other drugs (Wilsnack, *et al*., 2015). Other countries, such as India, have much lower rates of alcohol consumption than the West.

Lal *et al* (2015) stated that drug abuse although is commonly thought to be a male phenomenon, it exists among women and appears to be associated with patterns of drug abuse similar to that of men in current urban settings. Though drug use in women generally begins later or is introduced iatrogenically, it follows a more rapid downhill trajectory, with rapid progression through the stages of dependence and more associated psychological and physical morbidity. The stigma of being a "fallen angel" makes these women easy prey for society's ills and keeps them from seeking help early in the course of the illness.

5.3.3 The distribution of patients according to type of substance taking in correlation with occupation, residence:

There were no significant association between type of substance abused and occupation, residence. Most of the participant were from urban area and unemployed and we could not confirm our result because of the sample size (The larger the sample size, the more accurate the results).

5.3.4 The distribution of patients according to type of substance taking in correlation with education:

There were significant association between type of substance used and education that most of the participant had secondary school education reflected that poor educational level were associated with increasing risk for substance use disorder.

Ibrahim *et al*. (2018) showed that most of participant with amphetamine, alcohol, poly substance had secondary high school level.

5.4 The distribution of patients according to type of substance taking in correlation with EEG change:

The result showed the association between type of substance taking and EEG change, which was significant.

Most of amphetamine participant had score 2 or moderate severity. We found that amphetamine could change the EEG result by causing increase in beta band activity, this is due to increasing in dopamine activity which caused by most of the stimulant drugs.

The study result is in consistent with (Van-Cott and Brenner,2003);(Bauer,2005) who said that central nervous system stimulants such as cocaine, amphetamines, and methylphenidate as well as tricyclic antidepressants may evoke greater beta activity at low voltage.

Other our finding was that increase in delta and theta band this is in agreement with one study reported (Newton *et al*. 2003) that methamphetamine dependent volunteers with 4 days of abstinence had increased EEG power in the delta and theta but not in the alpha and beta bands. Within the methamphetamine dependent group, a majority of the conventional EEGs were abnormal (64%), compared to 18% in the non methamphetamine using group suggesting that methamphetamine abuse is associated with psychomotor slowing and frontal executive deficits (Kalechstein *et al*. 2003).

Other studies such as (Ahmadlou *et al*. 2013) revealed that the gamma band differences between meth-user and normal control may be related to abstinent duration and withdrawal effect rather than the meth abuse effect.

Khajehpour *et al*. (2019) study results show that the beta band waves are abnormally changed in methamphetamine MDIs versus normal controls.

In this study alcoholic participant were associated with score two or moderate severity (include increasing in beta band activity, slow wave activity) and some had score three or severe EEG changes (spike and sharp waves). The spike and sharp waves due to seizure activity which may be occur due to the effect of the substance or due to the withdrawal symptoms.

(Liu, *et al*.,2022) stated that the most predominant finding is the well-documented increased beta power, especially in the frontal and central regions. Increased beta rhythms were seemed to reflect cortical hyperexcitability or disinhibition (Edenberg,2004). Neurophysiological similarities of these groups suggest that binge drinking and hazardous alcohol consumption might be a transition stage into addiction.Though the positive family history of AUD (Rangaswamy ,2014) and medicine intake (eg, benzodiazepines)(Bauer ,2001) were also related to increased beta rhythms.

Affan *et al*.(2018) concluded that binge drinking in young adults is associated with dysregulation of the spontaneous EEG signal, as evidenced by a slowing of the alpha peak and increased power in the theta and beta bands. This, combined with evidence of increased beta power in people with AUD and their relatives, and the reported genetic link between beta oscillations and GABA receptor markers, suggests that beta power may be associated with vulnerability to alcoholism.

Acute withdrawal of alcohol may elicit bursts of spikes and polyspikes, particularly as a photo paroxysmal response (Van Cott and Brenner, 2003; Bauer and Bauer, 2005), this was in agreement with our finding.

An increase in voltage, field distribution, and the persistence of normally occurring 15 to 25 Hz Beta activity most commonly indicates the presence of an EEG medication effect; benzodiazepines are the most prominent producers of this effect (Van Cott and Brenner, 2003; Bauer and Bauer, 2005)

The beta and gamma bands are linked to perception (Sedley and Cunningham 2013), learning (de Souza *et al*. 2013), and attention (de Souza *et al*. 2013).

5.5 The association between the EEG change and duration of substance taking

There was a significant association between EEG change and duration of substance taking. The frequency of the participants who take the substance for two years was within normal (score o or no changes) while moderate severity or score 2 were found with those who take the substance for three years, and lastly participant took the substance for four years were associated with score 3 or sever EEG change). This reflect the fact that taking the substance for long duration may be associated with changes in brain area or neurotransmitters.

Long-term substance use, with or without a diagnosis of substance use disorder, was found to be associated with broad intrinsic neural activity alterations, which were typically manifested as neural hyperactivation and decreased neural communication between brain regions (Liu ,2022).

Liu *et al* (2022) stated that long-term substance use, including alcohol, tobacco, cannabis, cocaine, opioids, heroin, methamphetamine, is associated with a wide range of resting-state EEG abnormalities, the majority of which cannot be recovered automatically after a short period of abstinence. The similarities and differences in findings for different drugs may reflect their shared and distinct effects on neurotransmitters and brain regions.

5.6 The distribution of patients according to the EEG change and its association with duration of substance abstinence:

There was a significant correlation between duration of substance abstinence and EEG changes. Most of the participant with EEG changes whether moderate or severe had one-week duration while those with normal EEG changes had longer abstinence period (3weeks). These changes were duo to either the effect of the substance use or the abstinence period.

Although EEG recorded during abstinence may be confounded with the subacute and withdrawal effects, it is usually associated with neural hypoactivation (ie, increased power for low-frequency bands), which may be due in part to withdrawal drowsiness. Some substances (e.g., alcohol) appear to have a greater recovery effect than others (e.g., cannabis), which may reflect differences in neurotoxicity (Liu, *et al*.,2022).

Allsop *et al*.(2016) Uses EEG to Explore moderators of recovery during cannabis abstinence EEG was tested before and after 2 weeks of abstinence and found abstinence only led to increase beta activity in later onset users.

Liu *et al* (2022) found that chronic methamphetamine use has been linked to long-term deficits in the dopaminergic and serotonergic systems Nordahl and colleagues, 2003). These deficits could explain some of the EEG changes observed in the reviewed studies, such as increased lower frequency band (eg, delta, theta) power (Newton *et al*., 2003), global hypersynchronization in the gamma band (Ahmadlou *et al*.,2013), and reduced neural network integration81 after a short period of methamphetamine abstinence (mean 1 month).

5.7Limitations

- Difficulty in collecting the sample because of patient refusal, or not coming at the day of the appointment duo to feeling of embarrassment.
- Crowding of other patient on the same EEG machine, which make it difficult for our patient to get an appointment.

6.1 Conclusions:

1. EEG is an advisable tool in all patients with substance related disorders, because the EEG changes were of high prevalence in those patient.

2. The most common abnormalities in EEG changes were moderate severity and those affected by the duration of substance taking and abstinent period.

3. The most common substance with an abnormal EEG changes was amphetamine.

4. Most of patient with substance related disorder were single, at adolescence and early adulthood, and had secondary education.

6.2 Recommendations

1. Increasing the sample size to include more females gender in the future study.
2. Assessing the severity of substance related disorder and it's correlation with EEG changes.
3. Studying the effect of another type of the substance on the EEG.
4. Continuous EEG monitoring to get more accurate results.
5. Future EEG study might be needed to assess the EEG changes before and after short abstinence period as well as long abstinence period (more than six months).

Abou El-Magd S., Khalil M., Gohar S., Enaba D., Abdelgawad T., Hasan N. M., Miotto K. & Rawson R. (2018). Tramadol misuse and dependence in Egypt and the UAE: user characteristics and drug-use patterns. International Addiction Review; 2 (1): 6-13.

Abiu-Khalil, B., HEMDAL, P. and PRIVITERA, M.D. (2003). An open-label study of levetiracetam at individualised doses between 1000 and 3000 mg day−1 in adult patients with refractory epilepsy. Seizure, 12(3), pp.141–149.

Acharya, J., Hani, A., Thirumala, P. and Tsuchida, T. (2016). American Clinical Neurophysiology Society Guideline 3: A Proposal for Standard Montages to Be Used in Clinical EEG. Journal of Clinical Neurophysiology, [online] 33(4), pp.312–316.

Adinoff, B., Carmody, T., Walker, R., Donovan, D., Brigham, G. and Winhusen, T.(2016). Decision-making processes as predictors of relapse and subsequent use in stimulant-dependent patients. The American Journal of Drug and Alcohol Abuse, 42(1), pp.88–97.

Affan, R., Huang, S., Cruz, S., Holcomb, L., Nguyen, E. and Marinkovic, K. (2018). High-intensity binge drinking is associated with alterations in spontaneous neural oscillations in young adults. Alcohol, 70, pp.51–60

Aggleton, P., Jenkins, P. and Malcolm, A. (2005). HIV/AIDS and injecting drug use: Information, education and communication.International Journal of Drug Policy, 16, pp.21–30.

Ahmadlou M, Ahmadi K, Rezazade M, Azad-Marzabadi E. (2013).Global organization of functional brain connectivity in methamphetamine abusers. Clin Neurophysiol 124(6):1122–1131

Ahmady, A., Fadaizadeh, L., Heydari, G., Masjedi, M., Leischow, S.,Lando, H. and Shadmehr, M. (2015). Quit smoking experts′

opinions toward quality and results of quit smoking methods provided in tobacco cessation services centers in Iran. International Journal of Preventive Medicine, 6(1), p.74.

Al-Hemiary, N., Al-Diwan, J., Hasson, A. and and Rawson, R. (2014). Drug and alcohol use in Iraq: findings of the inaugural Iraqi Community Epidemiological Workgroup. Substance use & misuse, 49(13), pp.1759-1763..

Alhyas, L., Al Ozaibi, N., Elarabi, H., El-Kashef, A., Wanigaratne, S., Almarzouqi, A., Alhosani, A. and Al Ghaferi, H. (2015). Adolescents’ perception of substance use and factors influencing its use: a qualitative study in Abu Dhabi. JRSM Open, [online] 6(2), p.205427041456716.

Allsop, D. and Copeland, J. (2015). Age at first cannabis use moderates EEG markers of recovery from cannabis. Journal of Substance Use, 21(4), pp.400–406.

Al-Wateefee A. (2019). Rapid Screening of Addiction Associated Drug Among Suspected Prisoners. A Research Submitted to the College of Science/University of Babylon

American Electroencephalographic Society,(1986): Guidelines in EEG and evoked potentials. J Clin Neurophysiol; 3(suppl 1):1– 152

American Psychiatric Publishing (2013). American Psychiatric Association, Diagnostic and Statistical Manual for Mental Disorders ed. 5.

Aminoff, M. J. (2012). Aminoff’s Electrodiagnosis in Clinical Neurology SIXTH EDITION (6th editio). Elsevier Inc.

Aqrawi, R. and Humphreys, K. (2009). Responding to Rising Substance Misuse in Iraq. Substance Use & Misuse, 44(12), pp.1744–1748.

Arguinchona J, Tadi P(2021). Neuroanatomy, Reticular Activating System. [Updated 2021 Jul 26].

Ashton, C.(2001). Pharmacology and effects of cannabis: A brief review. British Journal of Psychiatry, [online] 178(2), pp.101–106.

Attard, R., Dingli, P., Doggen, C., Cassar, K., Farrugia, R. and Wettinger, S. (2017). The impact of passive and active smoking on inflammation, lipid profile and the risk of myocardial infarction. Open Heart, 4(2), p.e000620.

Aurlien, H., Gjerde, I., Aarseth, J., Eldøen, G., Karlsen, B., Skeidsvoll, H., Gilhus, N. (2004). "EEG background activity described by a large computerized database". Clinical Neurophysiology.

Austic, E.(2015). Peak ages of risk for starting nonmedical use of prescription stimulants. Drug and Alcohol Dependence, 152, pp.224–229.

Baldo, B., Spencer, R., Sadeghian, K. and Mena, J. (2015). GABA-Mediated Inactivation of Medial Prefrontal and Agranular Insular Cortex in the Rat: Contrasting Effects on Hunger- and Palatability-Driven Feeding. Neuropsychopharmacology, 41(4), pp.960–970.

Ball, G., Stokes, P., Rhodes, R., Bose, S., Rezek, I., Wink, A., Lord, L., Mehta, M., Grasby, P. and Turkheimer, F. (2011). Executive Functions and Prefrontal Cortex: A Matter of Persistence? Frontiers in Systems Neuroscience, [online] 5.

Banoczi, W.(2005). How Some Drugs Affect theElectroencephalogram (EEG). American Journal of Electroneurodiagnostic Technology, 45(2),pp.118–129.

Başar, E. (2012). A review of alpha activity in integrative brain function: Fundamental physiology, sensory coding, cognition and pathology.International Journal of Psychophysiology, [online] 86(1), pp.1–24.

Bassiony, M., Youssif, U., Hussein, R. and Saeed, M. (2016).Psychiatric Comorbidity Among Egyptian Patients With Opioid Use Disorders

Attributed to Tramadol. Journal of Addiction Medicine, 10(4), pp.262–268.

Bauer G, Bauer R. (2005).EEG Drug Effects and Central Nervous System Poisoning. In: Niedermeyer, E and Lopes da Silva, F.Electroencephalography. 5th Edition. Philadelphia: Lippincott, Williams and Wilkins,:701–724.

Bauer, L. (2001). Predicting Relapse to Alcohol and Drug Abuse via Quantitative Electroencephalography. Neuropsychopharmacology, [online] 25(3), pp.332–340.

Begola , M. and Schillerstrom, J. (2019). Hallucinogens and Their Therapeutic Use. Journal of Psychiatric Practice, [online] 25(5), pp.334–346.

Beil-Gawelczyk, J., Bratek, A., Banach, M., & Beil, S. (2014). EPA1511-Association of early drinking onset with subsequent alcohol abuse. European Psychiatry, 29(Suppl. 1).

Benbadis S. (2006). Introduction to EEG. In sleep: a comprehensive Handbook. Lee-Chiong T (Ed.). Wiley and Sons, NJ, USA. 9891024.

Berger, H. (1929). Über das Elektrenkephalogramm des Menschen. Archiv für Psychiatrie und Nervenkrankheiten, 87(1), pp.527–570.

Bhalla, I., Stefanovics, E. and Rosenheck, R.(2017). Clinical Epidemiology of Single Versus Multiple Substance Use Disorders. Medical Care, 55, pp.S24–S32.

Bisht, A., Kaur, C. and Singh, P. (2019). Recent Advances in Artifact Removal Techniques for EEG Signal Processing. Advances in Intelligent Systems and Computing, pp.385–392.

Blum, Andrew, S. and Rutkove, S. (2007). Neurophysiology Primer. Vol. 388. Springer..

Blume, W. (2006). Drug effects on EEG. Journal of Clinical Neurophysiology: Official Publication of the American Electroencephalographic Society, [online] 23(4), pp.306–311.

Board, A., Guy, G., Jones, C. and Hoots, B. (2020). Trends in stimulant dispensing by age, sex, state of residence, and prescriber specialty — United States, 2014–2019. Drug and Alcohol Dependence, [online] 217, p.108297.

Boland, R. (2021). Kaplan & Sadock's Synopsis Of Psychiatry. New York: Wolters Kluwer Medical.

Boron, W.F. and Boulpaep, E.L. (2016). Medical Physiology E-Book. [online] Google Books. Elsevier Health Sciences. Available at: https://books.google.iq/books?id=6QzhCwAAQBAJ&printsec=fro ntcove r [Accessed 19 Jul. 2022].

Brilla, R. (2019). Electroencephalography (EEG). Pain, Springer, 201–203..

Britton JW, Frey LC, Hopp JL et al. (2016). In: EK St. Louis, LC Frey (Eds.), Electroencephalography (EEG): an introductory text and atlas of normal and abnormal findings in adults, children, and infants .American Epilepsy Society, Chicago

Brown, C., Madden, P., Palenchar, D. and Cooper-Patrick, L. (2000). The Association between Depressive Symptoms and Cigarette Smoking in An Urban Primary Care Sample. The International Journal of Psychiatry in Medicine, 30(1), pp.15–26. doi:10.2190/ny79-cj0h-vbay5m1u.

Burkholder, D., Britton, J., Rajasekaran, V., Fabris, R.,Cherian, P., Kelly-Williams, K., So, E, Nickels, K., WongKisiel, L., Lagerlund, T., Cascino, G., Worrell, G. and Wirrell, E. (2016). Routine vs extended outpatient EEG for the detection of interictal epileptiform discharges. Neurology, 86(16), pp.1524–1530. doi:10.1212/wnl.0000000000002592.

Butcher, R., Mineka, T.F. and Hooley, T.S. (2007). Introduction to psychology. Boston: Allyn & Bacon.

Cahn, B. and Polich, J. (2006). Meditation states and traits: EEG, ERP, and neuroimaging studies. Psychological bulletin, [online] 132(2), pp.180– 211. doi:10.1037/0033-2909.132.2.180.

Carliner, H., Brown, Q., Sarvet, A. and Hasin, D. (2017). Cannabis use, attitudes, and legal status in the U.S.: A review. Preventive Medicine, 104, pp.13–23. doi:10.1016/j.ypmed.2017.07.008.

Center on Addiction and Substance Abuse (2004). Criminal neglect: Substance abuse, juvenile justice, and the children left behind. New York: Columbia University

Centorrino, Franca, Bruce H Price, Margaret Tuttle, Won-Myong Bahk, John Hennen, Matthew J Albert, and Ross J Baldessarini.(2002). ―EEG Abnormalities during Treatment with Typical and Atypical Antipsychotics.‖ American Journal of Psychiatry 159 (1):109–15).

Ceballos N, Bauer L, Houston R .(2009). Recent EEG and ERP findings in substance abusers. Clin EEG Neurosci. Apr;40(2):122-8.

Chan, G., Lo, T., Tam, C. and Lee, G. (2019). Intrinsic motivation and Psychological Connectedness to Drug Abuse and Rehabilitation: The Perspective of Self-Determination. International Journal of Environmental Research and Public Health, 16(11), p.1934. doi:10.3390/ijerph16111934.

Chen, X., Liu, A., Chiang, J., Wang, Z., McKeown, M. and Ward, R. (2016). Removing Muscle Artifacts From EEG Data: Multichannel or Single-Channel Techniques? IEEE Sensors Journal, 16(7), pp.1986– 1997. doi:10.1109/jsen.2015.2506982.

Chen, X., Xu, X., Liu, A., Lee, S., Chen, X., Zhang, X., McKeown, M. and Wang, Z. (2019). Removal of Muscle Artifacts From the EEG: A Review and Recommendations. IEEE Sensors Journal, [online] 19(14), pp.5353–5368. doi:10.1109/jsen.2019.2906572.

Chomchai, C. and Chomchai, S. (2015). Global patterns of methamphetamine use. Current Opinion in Psychiatry, 28(4), pp.269–274.

Conway, K., Compton, W., Stinson, F. and Grant, B. (2006). Lifetime Comorbidity of DSM-IV Mood and Anxiety Disorders and Specific Drug Use Disorders. The Journal of Clinical Psychiatry, 67(02), pp.247–258. doi:10.4088/jcp.v67n0211.

Cooper, Z. and Williams, A. (2019). Cannabis and Cannabinoid Intoxication and 1101 Toxicity. In: Cannabis Use Disorders, pp. 103-111.

Cornish, J. and Prasad, A. (2021). Sex Differences in Substance UseDisorders: A Neurobiological Perspective. Frontiers in Global Women's Health, 2. doi:10.3389/fgwh.2021.778514.

Courtney, K. , Ghahremani, D. , & Ray, L. (2013). Frontostriatal functional connectivity during response inhibition in alcohol dependence. Addiction Biology, 18(3), 593–604. https://doi.org/10.1111/adb.12013 .

Coutin-Churchman, P., Moreno, R., Añez, Y. and Vergara, F. (2006).Clinical correlates of quantitative EEG alterations in alcoholic patients.

Clinical Neurophysiology, 117(4), pp.740–751. doi:10.1016/j.clinph.2005.12.021.

Cunha-Oliveira, T., Rego, A. and Oliveira, C. (2008). Cellular and molecular mechanisms involved in the neurotoxicity of opioid and psychostimulant drugs. Brain Research Reviews, 58(1), pp.192–208. doi:10.1016/j.brainresrev.2008.03.002.

Cutler , J. (2016). Kaplan and Sadock's Synopsis of Psychiatry, Eleventh Edition. Journal of Psychiatric Practice, 22(1), pp.68–69. doi:10.1097/pra.0000000000000126.

Daniel, W., & Cross, C. (2018). Biostatistics: a foundation for analysis in the health sciences.11th edition, Wiley, 254.

Davenport, G. (2019). Electroencephalography : principles and clinical applications. Forest Hills, Ny: Foster Academics.

Davis, M., Walker, D., Miles, L. and Grillon, C. (2009). Phasic vs

Sustained Fear in Rats and Humans: Role of the Extended Amygdala in Fear vs Anxiety. Neuropsychopharmacology, 35(1), pp.105–135. doi:10.1038/npp.2009.109.

Degabriele, R. and Lagopoulos, J. (2008). Techniques for effective EEG subject preparation. Acta Neuropsychiatrica, 20(4), pp.218–219

Degenhardt, L., Coffey, C., Carlin, J., Moran, P. and Patton, G. (2007). Who are the new amphetamine users? A 10-year prospective study of young Australians. Addiction, 102(8), pp.1269–1279. doi:10.1111/j.1360-0443.2007.01906.x.

Degenhardt, L., Peacock, A., Colledge, S., Leung, J., Grebely, J., Vickerman, P., Stone, J., Cunningham, E., Trickey, A., Dumchev,

K., Lynskey, M., Griffiths, P., Mattick, R., Hickman, M. and Larney, S. (2017). Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. The Lancet. Global health, [online] 5(12), pp.e1192–e1207. doi:10.1016/S2214-109X(17)30375-3.

Degenhardt, L., Sara, G., McKetin, R., Roxburgh, A., Dobbins, T., Farrell, M., Burns, L. and Hall, W. (2016). Crystalline methamphetamine use and methamphetamine-related harms in Australia. Drug and Alcohol Review, 36(2), pp.160–170. doi:10.1111/dar.12426.

Delgadillo, J., Gore, S., Ali, S., Ekers, D., Gilbody, S., Gilchrist, G., McMillan, D. and Hughes, E. (2015). Feasibility Randomized Controlled Trial of Cognitive and Behavioral Interventions for Depression Symptoms in Patients Accessing Drug and Alcohol Treatment. Journal of Substance Abuse Treatment, 55, pp.6–14. doi:10.1016/j.jsat.2015.02.008.

Dinis-Oliveira, R.J. and Magalhães, T. (2020). Abuse of Licit and Illicit Psychoactive Substances in the Workplace: Medical, Toxicological, and Forensic Aspects. Journal of Clinical Medicine, 9(3), p.770.

Dodgen, C. and Shea, W.(2000). Substance use disorders:Assessment and treatment. San Diego, CA: Academic Press.

Dong, L., , , Liu, Q., Wen, X., Lai, Y., Xu, P. and Yao, D. (2017).

MATLAB Toolboxes for Reference Electrode Standardization Technique (REST) of Scalp EEG. Frontiers in Neuroscience, 11. doi:10.3389/fnins.2017.00601.

Edenberg, H., Dick, D., Xuei, X., Tian, H., Almasy, L., Bauer,L. , Crowe, R., Goate, A., Hesselbrock, V., Jones, K., Kwon, J., Li,T.-, Nurnberger, J., O'Connor, S., Reich, T., Rice, J., Schuckit,M. A., Porjesz, B., Foroud, T. and Begleiter, H. (2004). Variations In GABRA2, Encoding the α2 Subunit of the GABAA Receptor, Are Associated with Alcohol Dependence and with Brain Oscillations. The American Journal of Human Genetics, 74(4), pp.705–714.

Egorov, A. and Tikhomirov, T. (2004). Profiles of brain functional asymmetry in patients with alcoholism and drug addiction. Journal of Evolutionary Biochemistry and Physiology, 40(5), pp.557–562.

El Wasify, M., Fawzy, M., Barakat, D., Youssef, U., El Wasify, M., Saleh, A., and Hamed, S. (2018). The sociodemo-graphic and clinical characteristics of tra-madol dependence among Egyptians and their relationship to the associated inso-mnia. Addictive Disorders & Their Treat-ment, 17(2), 98-106.

Emad Hamdi , Noha Sabry, Albert Sedrak, Aref Khowailed, Nasser Loza, Menan Rabie and Hisham Ramy,(2016) .SociodemographicIndicators for Substance Use and Abuse in Egypt.Journal of Addiction & Prevention, 4(1) Eng 14(4):046002

Englander, H., Wilson, T., Collins, D., Phoutrides, E., Weimer, M., Korthuis, P., Calcagni, J. and Nicolaidis, C. (2018). Lessons learned from the implementation of a medically enhanced residential treatment (MERT) model integrating intravenous antibiotics and residential addiction treatment. Substance Abuse, 39(2), pp.225–232. doi:10.1080/08897077.2018.1452326.

Ezard, N. (2012). Substance use among populations displaced by conflict: a literature review. Disasters, 36(3), pp.533–557. doi:10.1111/j.14677717.2011.01261.x.

Fantegrossi, W.E., Murnane, K.S. and Reissig, C.J. (2008). The behavioral pharmacology of hallucinogens. Biochemical Pharmacology, 75(1), pp.17–33. doi:10.1016/j.bcp.2007.07.018.

Ferree T, Luu P, Russell G, Tucker D.(2001).Scalp electrode impedance, infection risk, and EEG data quality. Clin Neurophysiol. Mar;112(3):536-44. [PubMed]

Feyissa, A., Britton, J., Van Gompel, J., Lagerlund, T., So, E., Wong-Kisiel, L., Cascino, G., Brinkman, B., Nelson, C., Watson, R. and Worrell, G. (2017). High density scalp EEG in frontal lobe epilepsy. Epilepsyresearch,129,pp.157-161.

Fisher RS, Harding G, Erba G et al. (2005). Photic- and pattern induced seizures: a review for the Epilepsy Foundation of America Working Group. Epilepsia 46: 1426–1441.

Foldvary N, Caruso A, Mascha E, Perry M, Klem G, McCarthy V, Qureshi F, Dinner D. (2000).Identifying montages that best detect electrographic seizure activity during polysomnography. Sleep. Mar 15;23(2):221-9. [PubMed].

Friedman, D. (2009). Drug Addiction: A Chronically Relapsing Brain Disease. North Carolina Medical Journal, 70(1), pp.35–37. doi:10.18043/ncm.70.1.35.

Fujita, A., Bonnavion, P., Wilson, M.H., Mickelsen, L., Bloit, J., de Lecea, L. and Jackson, A. (2017). Hypothalamic Tuberomammillary Nucleus Neurons: Electrophysiological Diversity and Essential Role in Arousal Stability. The Journal of Neuroscience, 37(39), pp.9574–9592. doi:10.1523/jneurosci.0580-17.2017.

Ganong, W. Barrett, K. Barman, S. Brooks, H.& Yuan, J. (2019). ganong`s review of medical physiology. In McGraw-Hill Education (26th ed., Issue 26).

Garcia-Rill, E., Kezunovic, N., Hyde, J., Simon, C., Beck, P. and Urbano, F. (2013). Coherence and frequency in the reticular activating system (RAS). Sleep Medicine Reviews, 17(3), pp.227–238. doi:10.1016/j.smrv.2012.06.002.

Garofoli, M. (2020). Adolescent Substance Abuse. Primary Care: Clinics in Office Practice. doi:10.1016/j.pop.2020.02.013.

Giorgi, F., Ryskalin, L., Ruffoli, R., Biagioni, F., Limanaqi, F., Ferrucci, M., Busceti, C., Bonuccelli, U. and Fornai, F. (2017). The Neuroanatomy of the Reticular Nucleus Locus Coeruleus in Alzheimer's Disease. Frontiers in Neuroanatomy, 11. doi:10.3389/fnana.2017.00080.

Gladden, R., O'Donnell, J., Mattson, C. and Seth, P. (2019). Changes in Opioid-Involved Overdose Deaths by Opioid Type and Presence of Benzodiazepines, Cocaine, and Methamphetamine — 25 States, July–December 2017 to January–June 2018. MMWR. Morbidity and Mortality Weekly Report, 68(34), pp.737–744. doi:10.15585/mmwr.mm6834a2.

Global Burden of Disease and Prevention , Alcohol Collaborators.(2018). Alcohol use and burden for 195 countries and territories, 19902016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 392 (10152), 1015–1035

Green, M. , Leyland, A. , Sweeting, H., & Benzeval, M. (2016). Adolescent smoking and tertiary education: Opposing pathways linking socio-economic background to alcohol consumption. Addiction, 111(8), 1457-1463. https://doi.org/10.1111/add.13365

Greenfield, S., Brooks, A., Gordon, S., Green, C., Kropp, F., McHugh, R., Lincoln, M., Hien, D. and Miele, G. (2007). Substance abuse treatment entry, retention, and outcome in women: A review of the literature. Drug and Alcohol Dependence, [online] 86(1), pp.1–21. doi:10.1016/j.drugalcdep.2006.05.012.

Guyton, M. (2020). Guyton and Hall Textbook of Medical Physiology (14th ed.).

Halberstadt, A. (2015). Recent advances in the neuropsychopharmacology of serotonergic hallucinogens. Behavioural Brain Research, 277, pp.99–120. doi:10.1016/j.bbr.2014.07.016.

Halford J, Sabau D, Drislane F, Tsuchida T, Sinha S. (2016). American Clinical Neurophysiology Society Guideline 4: Recording Clinical EEG on Digital Media. Neurodiagn J. ;56(4):261-265. [PubMed].

Hamal, A. and bin Abdul Rehman, A. (2013). Artifact Processing of Epileptic EEG Signals: An Overview of Different Types of Artifacts. 2013 International Conference on Advanced Computer Science Applications and Technologies, 358–361.

Hamidullah, S., Thorpe, H., Frie, J., Mccurdy, R. and Khokhar, J.(2020). Adolescent Substance Use and the Brain: Behavioral, Cognitive and Neuroimaging Correlates. Frontiers in Human Neuroscience, 14. doi:10.3389/fnhum.2020.00298

Harro J. (2015).Neuropsychiatric Adverse Effects of Amphetamine and Methamphetamine. Int Rev Neurobiol.;120:179-204. doi: 10.1016/bs.irn.2015.02.004. Epub 2015 Mar 12.

Hasin, D., Shmulewitz, D. and Sarvet, A. (2019). Time trends in US cannabis use and cannabis use disorders overall and by sociodemographic subgroups: a narrative review and new findings. The American Journal of Drug and Alcohol Abuse, pp.1–21. doi:10.1080/00952990.2019.1569668.

Herian, M., Skawski, M., Wojtas, A., Sobocińska, M., Noworyta, K. and Gołembiowska, K. (2021). Tolerance to neurochemical and behavioral effects of the hallucinogen 25I-NBOMe. Psychopharmacology, 238(8), pp.2349–2364. doi:10.1007/s00213-021-05860-5.

Herrmann, C., Strüber, D., Helfrich, R. and Engel, A. (2016). EEG oscillations: From correlation to causality. International Journal of Psychophysiology, [online] 103, pp.12–21. doi:10.1016/j.ijpsycho.2015.02.003.

Holmes M, Dewaraja A, Vanhatalo S (2004). Does hyperventilation elicit epileptic seizures? Epilepsia 45: 618–620.

Hornung, J. (2003). The human raphe nuclei and the serotonergic system. Journal of Chemical Neuroanatomy, 26(4), pp.331–343. doi:10.1016/j.jchemneu.2003.10.002.

Hser, Y., Hoffman, V., Grella, C. and Anglin, M. (2001). A 33Year Follow-up of Narcotics Addicts. Archives of General Psychiatry, 58(5), p.503. doi:10.1001/archpsyc.58.5.503.

Hu, Li, and Zhiguo Zhang. (2019). EEG Signal Processing and Feature Extraction. Springer.

Huang Y, Mohan A, De Ridder D, Sunaert S, Vanneste S. (2018). The neural correlates of the unified percept of alcohol-related craving: a fMRI and EEG study. Sci Rep 8(1):923

Hubbard, R., Craddock, S.Gail. and Anderson, J. (2003). Overview of 5-year followup outcomes in the drug abuse treatment outcome studies (DATOS). Journal of Substance Abuse Treatment, 25(3), pp.125–134. doi:10.1016/s0740-5472(03)00130-2.

Ibrahim Y, Hussain S, Alnasser S, Almohandes H, Sarhandi I.(2018). Patterns and sociodemographic characteristics of substance abuse in Al Qassim, Saudi Arabia: a retrospective study at a psychiatric rehabilitation center. Ann Saudi Med 2018; 38(5): 319-325.

Islam, M., Rastegarnia, A. and Yang, Z. (2016). Methods for artifact detection and removal from scalp EEG: A review. Neurophysiologie Clinique/Clinical Neurophysiology, [online] 46(4-5), pp.287–305. doi:10.1016/j.neucli.2016.07.002.

Jafari Giv, M. (2017). Exposure to Amphetamines Leads to Development of Amphetamine Type Stimulants Associated Cardiomyopathy (ATSAC). Cardiovascular Toxicology, 17(1), pp.13–24. doi:10.1007/s12012-0169385-8.

Jain R, Majumder P, Gupta T.(2013). Pharmacological intervention of nicotine dependence. –278392.

Jebelli, H., Hwang, S. and Lee, S. (2018). EEG-based workers' stress recognition at construction sites. Automation in Construction, 93, pp.315– 324. doi:10.1016/j.autcon.2018.05.027.

Jiang, X., Bian, G. and Tian, Z. (2019). Removal of Artifacts from EEG Signals: A Review. Sensors (Basel, Switzerland), [online] 19(5), p.987. doi:10.3390/s19050987.

Jiloha R. (2007).Non-Pharmacological Treatment of Alcohol Dependence. Delhi Psychiatry J.;10:119–22.

Jiloha, R. and Kukreti, P. (2018). Psychiatry in Delhi: History and current status. Indian Journal of Psychiatry, 60(6), p.218. doi:10.4103/psychiatry.indianjpsychiatry_452_17.

Johns, A. (2001).Psychiatric effects of cannabis. Br J Psychiatry 178, 116122.

Johnson, H., (2004). Psyche and synapse expanding worlds: The role of neurobiology in emotions, behaviour, thinking, and addiction for non-scientists (2nd ed.).

Johnston, L., O'Malley, P. and Bachman, J. (2003). Monitoring the Future: National Results on Adolescent Drug Use: Overview of Key Findings. FOCUS, 1(2), pp.213–234. doi:10.1176/foc.1.2.213.

Johnston L, Malley P, Miech R, Bachman J, and Schulenberg J. (2015). Monitoring the Future national survey results on drug use, 1975-2015: Overview, key findings on adolescent drug use. Ann Arbor: Institute for Social Research, The University of Michigan.

Jones, C., Compton, W. and Mustaquim, D. (2020). Patterns and Characteristics of Methamphetamine Use Among Adults — United States, 2015–2018. MMWR. Morbidity and Mortality Weekly Report, 69(12), pp.317–323. doi:10.15585/mmwr.mm6912a1.

Juhnke, G. (2017). Substance Abuse Assessment and Diagnosis A Comprehensive Guide for Counselors and Helping Professionals.

Routledge.

Kalechstein, A. , Newton, T. , & Green, M. (2003). Methamphetamine dependence is associated with neurocognitive impairment in the initial phases of abstinence. Journal of Neuropsychiatry & Clinical Neurosciences, 15, 215–220.

Kalivas, P. and Volkow, N. (2005). The Neural Basis of Addiction: A Pathology of Motivation and Choice. American Journal of Psychiatry, 162(8), pp.1403–1413. doi:10.1176/appi.ajp.162.8.1403.

Kamarajan, C., and Porjesz, B. (2015). Advances in electrophysiological research. Alcohol Research: Current Reviews, 37(1), 53–87.

Kasteleijn-Nolst Trenite D, Rubboli G, Hirsch E et al. (2012) . Methodology of photic stimulation revisited: updated European algorithm for visual stimulation in the EEG laboratory. Epilepsia 53: 16–24.

Katselou, M., Papoutsis, I., Nikolaou, P., Qammaz, S., Spiliopoulou, C. and Athanaselis, S. (2016). Fenethylline (Captagon) Abuse - Local Problems from an Old Drug Become Universal. Basic & Clinical Pharmacology & Toxicology, 119(2), pp.133–140. doi:10.1111/bcpt.12584.

Kesner, A. and Lovinger, D. (2020). Cannabinoids, Endocannabinoids and Sleep. Frontiers in Molecular Neuroscience, 13. doi:10.3389/fnmol.2020.00125.

Kesner, A. and Lovinger, D. (2021). Cannabis use, abuse, and withdrawal: Cannabinergic mechanisms, clinical, and preclinical findings.Journal of Neurochemistry, 157(5), pp.1674–1696. doi:10.1111/jnc.15369.

Khajehpour, H., Mohagheghian, F., Ekhtiari, H., Makkiabadi, B., Jafari, A., Eqlimi, E. and Harirchian, M.(2019). Computer-aided classifying and characterizing of methamphetamine use disorder using resting-state EEG. Cognitive Neurodynamics, 13(6), pp.519–530. doi:10.1007/s11571-019-09550-z.

Khalil, A., Okasha, T., Shawky, M., Haroon, A., Elhabiby, M., Carise, D.,... & Rawson, R. (2008). Characterization of substance abuse patients presenting for treatment at a University Psychiatric Hospital in Cairo, Egypt. Addictive Disorders & Their Treat-ment, 7(4), 199-209.

Ko, S. and Park, W. (2018).Effects of Quantitative Electroencephalography Based Neurofeedback Training on Autonomous Regulations in Patients with Alcohol Use Disorder. Asian Nursing Research, 12(2), pp.136–144. doi:10.1016/j.anr.2018.05.003.

Kolodny, A., Courtwright, D., Hwang, C., Kreiner, P., Eadie, J., Clark, T. and Alexander, G.(2015). The Prescription Opioid andHeroin Crisis: A Public Health Approach to an Epidemic of Addiction. Annual Review of Public Health, 36(1), pp.559–574. doi:10.1146/annurevpublhealth-031914-122957.

Koob, G., Arends, M. and Le Moal, M. (2014). Chapter 4 - Psychostimulants. Drugs, Addiction, and the Brain. San Diego: Academic Press; . p. 93-132..

Koob, G. and Volkow, N. (2010). Neurocircuitry of Addiction.Neuropsychopharmacology,35(1),pp.217–238.doi:10.1038/npp.2009.110.

Krumholz, A., Cole, A., Shinnar, S., French, J., Gronseth, G., Wiebe, S. and Cascino, G.(2015). Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy SocietyCommentary Author Response. Neurology, 85(17), pp.1526–1527. doi:10.1212/01.wnl.0000473351.32413.7c.

Laura W and American Psychiatric Association Publishing (2019). The American Psychiatric Association Publishing textbook of psychiatry. Washington, Dc: American Psychiatric Association Publishing.

Lal, R., Deb, K. and Kedia, S. (2015). Substance use in women: Current status and future directions. Indian Journal of Psychiatry, 57(6), p.275.

Lawn, W., Barratt, M., Williams, M., Horne, A. and Winstock, A. (2014). The NBOMe hallucinogenic drug series: Patterns of use, characteristics of users and self-reported effects in a large international sample. Journal of Psychopharmacology, 28(8), pp.780–788. doi:10.1177/0269881114523866.

Lee, K., Park, C. and Lee, B. (2015). Elimination of ECG artifacts from a single-channel EEG using sparse derivative method. IEEE International Conference on Systems, Man, and Cybernetics, 2384–2389..

Liang, W. and Chikritzhs, T. (2011). Brief report: marital status and alcohol consumption behaviours. Journal of Substance Use, 17(1), pp.84–90. doi:10.3109/14659891.2010.538463.

Liao, D., Lin, H., Law, P. and Loh, H. (2005). Mu-opioid receptors modulate the stability of dendritic spines. Proceedings of the National Academy of Sciences, 102(5), pp.1725–1730. doi:10.1073/pnas.0406797102.

Liu, Y., Chen, Y., Fraga-González, G., Szpak, V., Laverman, J., Wiers, R. and Richard Ridderinkhof, K. (2022). Resting-state EEG, Substance use and Abstinence After Chronic use: A Systematic Review. Clinical EEG and Neuroscience, p.155005942210763. doi:10.1177/15500594221076347.

Lodder, S., Askamp, J. and van Putten, M.(2014). ComputerAssisted Interpretation of the EEG Background Pattern: A Clinical

Evaluation. PLoS ONE, 9(1), p.e85966. doi:10.1371/journal.pone.0085966.

Lu, L., Liu, Y., Zhu, W., Shi, J., Liu, Y., Ling, W. and Kosten, T. (2009). Traditional Medicine in the Treatment of Drug Addiction. The American Journal of Drug and Alcohol Abuse, 35(1), pp.1–11.

Magidson, J., Liu, S.-M., Lejuez, C. and Blanco, C. (2012). Comparison of the course of substance use disorders among individuals with and without generalized anxiety disorder in a nationally representative sample. Journal of Psychiatric Research, 46(5), pp.659–666. doi:10.1016/j.jpsychires.2012.02.011.

Mannan, M., Kamran, M. and Jeong, M.(2018). Identification and Removal of Physiological Artifacts From Electroencephalogram Signals: A Review. IEEE Access, [online] 6, pp.30630–30652. doi:10.1109/ACCESS.2018.2842082.

Mason, W., Hitchings, J., McMahon, R. and Spoth, R. (2007). A Test of Three Alternative Hypotheses Regarding the Effects of Early Delinquency on Adolescent Psychosocial Functioning and Substance Involvement. Journal of Abnormal Child Psychology, 35(5), pp.831–843. doi:10.1007/s10802-007-9130-7.

Mattiuzzi, C. and Lippi, G. (2019). Worldwide epidemiology of alcohol and drugs abuse. European Journal of Internal Medicine, [online] 70, pp.e27–e28. doi:10.1016/j.ejim.2019.10.019.

McLellan, A., Lewis, D., O'Brien, C. and Kleber, H. (2000). Drug Dependence, a Chronic Medical Illness. JAMA, 284(13), p.1689. doi:10.1001/jama.284.13.1689.

Micheal J.Aminoff (2005), Electrodiagnosis in clinical neurology, fifth edition, Churchil Livingstone publisher, U.S.A.

Minnerly, C., Shokry, I., To, W., Callanan, J. and Tao, R. (2021). Characteristic changes in EEG spectral powers of patients with opioid-use disorder as compared with those with methamphetamine- and alcohol-use disorders. PLOS ONE, 16(9), p.e0248794. doi:10.1371/journal.pone.0248794.

Misulis, K. E. (2014). Atlas of EEG, Seizure Semiology, and Management (SECOND EDI). Oxford University Press 2014.

Motlagh, F., Ibrahim, F., Rashid, R., Shafiabady, N., Seghatoleslam, T. and Habil, H. (2018). Acute effects of methadone on EEG power spectrum and event-related potentials among heroin dependents.Psychopharmacology, 235(11), pp.3273–3288.

Müller-Putz, G. (2020). Electroencephalography. Brain-Computer Interfaces, pp.249–262. doi:10.1016/b978-0-444-63934-9.00018-4.

Murray, R., Englund, A., Abi-Dargham, A., Lewis, D., Di Forti,M., Davies, C., Sherif, M., McGuire, P. and D'Souza, D.(2017). Cannabis-associated psychosis: Neural substrate and clinical impact. Neuropharmacology, 124, pp.89–104.

Nair, U., Vidhukumar, K. and Prabhakaran, A. (2016). Age at Onset of Alcohol Use and Alcohol Use Disorder: Time-trend Study in Patients Seeking De-addiction Services in Kerala. Indian Journal of Psychological Medicine, 38(4), pp.315–319. doi:10.4103/0253-7176.185958.

National Survey on Drug Use and Health.(2020), SAMHSA, Quarter 4,Center for Behavioral Health Statistics and Quality,.

Newton, T., Cook, I., Kalechstein, A., Duran, S., Monroy, F., Ling, W. and Leuchter, A. (2003). Quantitative EEG abnormalities in recently abstinent methamphetamine dependent individuals. Clinical Neurophysiology, 114(3),pp.410–415. doi:10.1016/s13882457(02)00409-1.

Nishino, S. (2011). The hypothalamic peptidergic system, hypocretin/orexin and vigilance control. Neuropeptides, 41(3), pp.117– 133. doi:10.1016/j.npep.2007.01.003.

Nolte, G., Bai, O., Wheaton, L., Mari, Z., Vorbach, S. and Hallett, M. (2004). Identifying true brain interaction from EEG data using the imaginary part of coherency. Clinical Neurophysiology, 115(10), pp.2292– 2307. doi:10.1016/j.clinph.2004.04.029.

Nordahl, T., Salo, R. and Leamon, M. (2003). Neuropsychological Effects of Chronic Methamphetamine Use on Neurotransmitters and Cognition: A Review. The Journal of Neuropsychiatry and Clinical Neurosciences, 15(3), pp.317–325. doi:10.1176/jnp.15.3.317.

Oberman, L., Hubbard, E., McCleery, J., Altschuler, E., Ramachandran, V. and Pineda, J.(2005). EEG evidence for mirror neuron dysfunction in autism spectrum disorders. Cognitive Brain Research, 24(2), pp.190–198. doi:10.1016/j.cogbrainres.2005.01.014.

Olsen, R. and Liang, J. (2017). Role of GABAA receptors in alcohol use disorders suggested by chronic intermittent ethanol (CIE) rodent model. Molecular Brain, 10(1). doi:10.1186/s13041-017-0325-8.

Ostenveld R, Praamstra P (2001). The five percent electrode system for high-resolution EEG and ERP measurements. Clin Neurophysiol 112: 713–719.

Osman, T., Victor, C., Abdulmoneim, A., Mohammed, H., Abdalla, F., Ahmed, A., Ali, E. and Mohammed, W. (2016). Epidemiology of Substance Use among University Students in Sudan. Journal of Addiction, 2016, pp.1–8. doi:10.1155/2016/2476164.

Palermo, G. (2009). Delinquency: Risks and protective factors. International Journal of Offender Therapy and Comparative Criminology, 53, 247-248. doi:10.1177/0306624x09335886.

Park SM, Lee JY, Kim YJ, Lee JY, Jung HY, Sohn BK, Kim DJ, Choi Paszkiel, and Szczepan. (2020). Analysis and Classification of EEG Signals for Brain-Computer Interfaces. Springer.

Peacock, A., Leung, J., Larney, S., Colledge, S., Hickman, M., Rehm, J., Giovino, G., West, R., Hall, W., Griffiths, P., Ali, R., Gowing, L., Marsden, J., Ferrari, A., Grebely, J., Farrell, M. and Degenhardt, L. (2018). Global statistics on alcohol, tobacco and illicit drug use: 2017 status report. Addiction, 113(10), pp.1905–1926. doi:10.1111/add.14234.

Placidi, G., Cinque, L. and Polsinelli, M. (2021). A fast and scalable framework for automated artifact recognition from EEG signals represented in scalp topographies of Independent Components. Computers in Biology and Medicine, 132, p.104347. doi:10.1016/j.compbiomed.2021.104347.

Preedy, V.(2016). Neuropathology of Drug Addictions and Substance Misuse Volume 1: Foundations of Understanding, Tobacco, Alcohol, Cannabinoids and Opioids.

Rangaswamy, M. and Porjesz, B. (2014). Understanding alcohol use disorders with neuroelectrophysiology. Handbook of Clinical Neurology, pp.383–414. doi:10.1016/b978-0-444-62619-6.00023-9.

Raz, A. and Perouansky, M. (2019). Central Nervous System Physiology: Neurophysiology‘, in Pharmacology and Physiology for Anesthesia. Elsevier, pp. 145–173.

Read, G. L., & Innis, I. J. (2017). Electroencephalography (EEG). https://doi.org/10.1002/9781118901731.iecrm0080.

Rickli, A., Luethi, D., Reinisch, J., Buchy, D., Hoener, M. and Liechti, M. (2015). Receptor interaction profiles of novel N-2methoxybenzyl (NBOMe) derivatives of 2,5-dimethoxy-substituted phenethylamines (2C drugs). Neuropharmacology, [online] 99, pp.546– 553. doi:10.1016/j.neuropharm.2015.08.034.

Roberts, L.W(2019). The American Psychiatric Association Publishing textbook of psychiatry. Washington, Dc: American Psychiatric Association Publishing. Journal of Psychiatric Practice, 25(5), pp.414– 415. doi:10.1097/pra.0000000000000407.

Rockville, M(2014). Substance Abuse and Mental Health Services Administration; 2016. https://wwwdasis.samhsa.gov/ dasis2/teds_pubs/2014_teds_rpt_natl.pdf. Accessed May 10, 2018.

Romer, D. (2010). Adolescent risk taking, impulsivity, and brain development: Implications for prevention. Developmental Psychobiology, [online] 52(3), p.n/a-n/a. doi:10.1002/dev.20442.

Ronan, M. and Herzig, S. (2016). Hospitalizations Related To Opioid Abuse/Dependence And Associated Serious Infections Increased Sharply, 2002–12. Health Affairs, 35(5), pp.832– 837. doi:10.1377/hlthaff.2015.1424.

Rubboli G, Parra J, Seri S et al. (2004). EEG diagnostic procedures and special investigations in the assessment of photosensitivity. Epilepsia 45 (Suppl. 1): 35–39.

Ruginsk, S., Vechiato, F., Uchoa, E., Elias, L. and Antunes-Rodrigues, J. (2015). Type 1 cannabinoid receptor modulates water deprivation-induced homeostatic responses. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 309(11), pp.R1358–R1368. doi:10.1152/ajpregu.00536.2014.

Saha, S., Lim, C., Degenhardt, L., Cannon, D., Bremner, M., Prentis, F., Lawrence, Z., Heffernan, E., Meurk, C., Reilly, J. and McGrath, J. (2021). Comorbidity between mood and substance-related disorders: A systematic review and meta-analysis. Australian & New Zealand Journal of Psychiatry, p.000486742110547.

Salvatore, J., Gardner, C. and Kendler, K.(2019). Marriage and reductions in men’s alcohol, tobacco, and cannabis use. Psychological Medicine, 50(15), pp.2634–2640. doi:10.1017/s0033291719002964.

Sanchez, J., Todd, C., Bautista, C., Botros, B., Khakimov, M., Giyasova, G., Yakubov, S., Abdulaeva, M., Saad, M., Graham, R., Carr, J. and Earhart, K. (2006). High HIV prevalence and risk factors among injection drug users in Tashkent, Uzbekistan, 2003–2004. Drug and Alcohol Dependence, 82, pp.S15–S22. doi:10.1016/s0376-8716(06)80003-7.

Sazgar, M., & Young, M. G. (2019). Absolute Epilepsy and EEG Rotation Review. In Absolute Epilepsy and EEG Rotation Review.

Schmelzle J, Rosser WW, Birtwhistle R. (2008). Update on pharmacologic and nonpharmacologic therapies for smoking cessation. Can Fam Phys Med De Famille Canadien.;54:994–9.

Schomer, D. and Silva, F.(2018). Niedermeyer’s Electroenc- ephalography : Basic Principles, Clinical Applications, and Related Fields. [online] Google Books. Oxford University Press. Available at:https://books.google.iq/books?id=y3o7DwAAQBAJ&printsec=frontco ver.

Schumacker, R. , & Lomax, R. (2010). A beginner's guide to structural equation modeling (3rd ed.). New York, NY: Routledge/Taylor & Francis Group

Schomer, D. and Silva, F.(2018). Niedermeyer’s Electroencephalography: Basic Principles, Clinical Applications, and Related Fields. [online] Google Books. Oxford University Press. Available at: https://books.google.iq/books?id=y3o7DwAAQBAJ&printsec=frontcover [Accessed 23 Jul. 2022].

Silber, B., Croft, R., Papafotiou, K. and Stough, C. (2006). The acute effects of d-amphetamine and methamphetamine on attention and psychomotor performance. Psychopharmacology, 187(2), pp.154–169. doi:10.1007/s00213-006-0410-7.

Silins, E., Horwood, L. , Najman, J. , Patton, G. , Toumbourou, J., Olsson, C. A., Hutchinson, D. , Degenhardt, L., Fergusson, D., Becker, D., Boden, J. , Borschmann, R., Plotnikova, M., Youssef, G. , Tait, R. , Clare, P., Hall, W. , Mattick, R. , & Cannabis Cohorts Research Consortium. (2018). Adverse adult consequences of different alcohol use patterns in adolescence: an integrative analysis of data to age 30 years from four Australasian cohorts. Addiction, 113(10), 1811-1825. https://doi.org/10.1111/add.14263

Sinha SR, Sullivan L, Sabau D (2016). American clinical neurophysiology society guideline 1: minimum technical requirements for performing clinical electroencephalography. J Clin Neurophysiol 33: 303–307.

Sinha N. (2019), Effect of Marital Status on Substance Abuse - A Review. Int J Recent Sci Res. 9(5), pp. 27012-27015

Smart, R. and Pacula, R. (2019). Early evidence of the impact of cannabis legalization on cannabis use, cannabis use disorder, and the use of other substances: Findings from state policy evaluations. The American Journal of Drug and Alcohol Abuse, 45(6), pp.1–20. doi:10.1080/00952990.2019.1669626.

Solowij, N., Broyd, S., Greenwood, L., van Hell, H., Martelozzo, D., Rueb, K., Todd, J., Liu, Z., Galettis, P., Martin, J., Murray, R., Jones, A., Michie, P. and Croft, R. (2019). A randomised controlled trial of vaporised Δ9-tetrahydrocannabinol and cannabidiol alone and in combination in frequent and infrequent cannabis users: acute intoxication effects. European Archives of Psychiatry and Clinical Neuroscience, 269(1), pp.17–35. doi:10.1007/s00406-019-00978-2.

Stone, J. and Hughes, J. (2013). Early History of Electroence-phalography and Establishment of the American Clinical Neurophysiology Society. Journal of Clinical Neurophysiology, [online] 30(1), pp.28–44. doi:10.1097/WNP.0b013e31827edb2d.

Stoneberg, D., Shukla, R. and Magness, M.(2017). Global Methamphetamine Trends. International Criminal Justice Review, 28(2), pp.136–161. doi:10.1177/1057567717730104.

Substance Abuse and Mental Health Services Administration (2020). Key Substance Use and Mental Health Indicators in the United States: Results from the 2019 National Survey on Drug Use and Health. Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services.

Substance Abuse and Mental Health Services Administration. (2019).Results from the 2018 National Survey on Drug Use and Health. Rockville, MD: US Department of Health and Human Services, https://www.samhsa.gov/data/report/2018-nsduh-detailed-tables

Substance Abuse and Mental Health Services Administration.(2016).National Admissions to Substance Abuse Treatment Services. Treatment Episode Data Set (TEDS). 2004-2014. Rockville, MD: https://wwwdasis.samhsa.gov/dasis2/teds_pubs/2014_teds_rpt_natl .pdf. Accessed May 10, 2018.

Suckling, J. and Nestor, L.(2016). The neurobiology of addiction: the perspective from magnetic resonance imaging present and future. Addiction, 112(2), pp.360–369. doi:10.1111/add.13474.

Survey of Substance Abuse in Iraq (2015). Final report

Tedesco, D., Asch, S., Curtin, C., Hah, J., McDonald, K., Fantini, M. and Hernandez-Boussard, T. (2017). Opioid Abuse And Poisoning:

Trends In Inpatient And Emergency Department Discharges. Health Affairs, 36(10), pp.1748–1753. doi:10.1377/hlthaff.2017.0260.

Thakor, N.and Tong, S. (2004). Advances in Quantitative Electroencephalogram Analysis Methods. Annual Review of Biomedical Engineering, 6(1), pp.453–495.

Teplan, M. (2002). FUNDAMENTALS OF EEG MEASUREMENT. Institute of Measurement Science, Slovak Academy of Sciences, Volume 2.

Tiago-Costa, E., Quelhas-Costa, E. and Santos-Baptista, J. (2016). Changes in EEG amplitude (Alpha and Beta waves) with Thermal environment. DYNA, 83(197), p.87. doi:10.15446/dyna.v83n197.57590.

Tomkins D, Sellers E.(2001). Addiction and the brain: the role of neurotransmitters in the cause and treatment of drug dependence. CMAJ.;164(6):817-21.

Torrens, M., Gilchrist, G. and Domingo-Salvany, A. (2011). Psychiatric comorbidity in illicit drug users: Substance-induced versus independent disorders. Drug and Alcohol Dependence, 113(2-3), pp.147–156. doi:10.1016/j.drugalcdep.2010.07.013.

U.S. Department of State. (2011). International narcotics control strategy report (Iraq). Available at http://www. state.gov/j/inl/rls/nrcrpt/2011/vol1/156361.htm. Accessed on May 6, 2015.

Urigüen, J. and Garcia-Zapirain, B. (2015). EEG artifact removalstate-of-the-art and guidelines. Journal of neural engineering, [online] 12(3), p.031001. doi:10.1088/1741-2560/12/3/031001.

Van Wormer, K., and Davis, D. (2008). Addiction treatment: a strengths perspective, 2nd ed. , Belmont, USA: Brooks/Cole.

Venkatesh‹, D. and Sudhakar, H. (2018).,Textbook of Medical Physiology. Second edition

Villapiano, N., Winkelman, T., Kozhimannil, K., Davis, M. and Patrick, S.(2017). Rural and Urban Differences in Neonatal Abstinence Syndrome and Maternal Opioid Use, 2004 to 2013. JAMA Pediatrics, 171(2), p.194. doi:10.1001/jamapediatrics.2016.3750.

Vincent, S. (2000). The ascending reticular activating system — from aminergic neurons to nitric oxide. Journal of Chemical Neuroanatomy, 18(1-2), pp.23–30. doi:10.1016/s0891-0618(99)00048-4.

Volkow, N., Jones, E., Einstein, E. and Wargo, E.(2019). Prevention and Treatment of Opioid Misuse and Addiction. JAMA Psychiatry, [online] 76(2), p.208. doi:10.1001/jamapsychiatry.2018.3126.

Volkow, N., Poznyak, V., Saxena, S. and Gerra, G. (2017). Drug use disorders: impact of a public health rather than a criminal justice approach. World Psychiatry, [online] 16(2), pp.213–214. doi:10.1002/wps.20428.

Walley, A., Paasche-Orlow, M., Lee, E., Forsythe, S., Chetty, V., Mitchell, S. and Jack, B.(2012). Acute Care Hospital Utilization Among Medical Inpatients Discharged With a Substance Use Disorder Diagnosis. Journal of Addiction Medicine, 6(1), pp.50–56.

Wang, G., Kydd, R., Wouldes, T., Jensen, M. and Russell, B. (2015). Changes in resting EEG following methadone treatment in opiate addicts. Clinical Neurophysiology, [online] 126(5), pp.943–950.

Wenthur, C., Zhou, B. and Janda, K. (2017). Vaccine-driven pharmacodynamic dissection and mitigation of fenethylline psychoactivity. Nature, 548(7668), pp.476–479.

Wilsnack, S. and Wilsnack, R. (2015). International Gender and Alcohol Research: Recent Findings and FutureDirections. [online]pubs.niaaa.nih.gov.

Wise R.(2002). Brain reward circuitry: insights from unsensed incentives. Neuron.; 36(2):229-240.

World Health Organization (2014). Substance Abuse. Available on http://www.who.int/topics/substance_ abuse/en/. Accessed October 12th , 2017

World Health Organization (2010). Atlas of substance use disorders.Country profile: Iraq. Retrieved November 7, 2013World Health Organization.(2018). Global Status Report on Alcohol and Health2018;www.who.int/substance_abuse/publications/global_alcohol _report/en/.

Xie, S.and Lagergren, J. (2018). Risk factors for oesophageal cancer.Best Practice & Research Clinical Gastroenterology, [online] 36-37, pp.3–8.

Xue, S., Kallupi, M., Zhou, B., Smith, L., Miranda, P., George, O. and Janda, K. (2018). An enzymatic advance in nicotine cessation therapy. Chemical Communications, 54(14), pp.1686–1689.

Yang, M., Mamy, J., Gao, P. and Xiao, S. (2015). From Abstinence to Relapse: A Preliminary Qualitative Study of Drug Users in a Compulsory Drug Rehabilitation Center in Changsha, China. PLOS ONE, 10(6), p.e0130711. doi:10.1371/journal.pone.0130711.

Yang, X., Wang, Y., Li, Q., Zhong, Y., Chen, L., Du, Y., He, J., Liao, L., Xiong, K., Yi, C. and Yan, J. (2018). The Main Molecular Mechanisms Underlying Methamphetamine- Induced Neurotoxicity and Implications for Pharmacological Treatment. Frontiers in Molecular Neuroscience, 11. doi:10.3389/fnmol.2018.00186.

Yeo, S., Chang, P. and Jang, S.(2013). The Ascending Reticular Activating System from Pontine Reticular Formation to the Thalamus in the Human Brain. Frontiers in Human Neuroscience, 7. doi:10.3389/fnhum.2013.00416.

Yun, K., Park, H., Kwon, D., Kim, Y., Cho, S., Cho, H.-, Peterson, B. and Jeong, J. (2012). Decreased cortical complexity in methamphetamine abusers. Psychiatry Research: Neuroimaging, 201(3), pp.226–232. doi:10.1016/j.pscychresns.2011.07.009.

Yuste, Church, R. and George, M. (2014). 'The new century of the brain'(PDF). Scientific American. 310 (3): 38– 45..

Zaki, A., Abdel-Fadeel, N., Helmy, M. and Kamal, A. (2021).Sociodemographic Characteristics of a Sample of patients with Substance Use Disorders. Minia Journal of Medical Research, 32(2), pp.36–39. doi:10.21608/mjmr.2021.230563.