RESEARCH ARTICLE

# The Neuropsychological Effects of Pregabalin (Lyrica) and Tramadol Addiction Among Youth: A Clinical Study

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**Abstract**

This clinical study investigates the neuropsychological effects associated with addiction to Pregabalin (Lyrica) and Tramadol among young individuals. Specifically, the research examines the psychological and neurocognitive alterations observed in individuals both before and after substance dependency. The study focuses on two clinical cases selected purposively and systematically from the Addiction Treatment Department at Abu Bakr Al Razi Hospital in Annaba, Algeria. Both individuals presented with significant neuropsychological dysfunction due to excessive use of Pregabalin and Tramadol without medical oversight.

The assessment tools used include the Hamilton Anxiety Rating Scale, Beck Depression Inventory, and a custom Pregabalin Symptom Checklist. A qualitative clinical approach was adopted to explore the underlying psychopathological manifestations and behavioral changes in the participants. The results revealed a strong association between addiction to Pregabalin and Tramadol and a wide range of neuropsychological disorders, including depression, generalized anxiety, sleep disturbances, impaired memory, social maladjustment, and neuromotor symptoms such as tremors. These dysfunctions were further linked to increased vulnerability to suicide risk, schizophrenia spectrum disorders, borderline personality disorder, and antisocial personality disorder.

In conclusion, the findings underscore the thin boundary between misuse and full-blown addiction. A considerable number of users transition from therapeutic use to dependency, particularly among individuals with a pre-existing history of substance abuse. The study calls for more comprehensive clinical attention to the neuropsychological consequences of non-prescribed use of Pregabalin and Tramadol among youth.

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## 1. Introduction :

An individual's life faces a set of challenges and pressures that negatively impact his balance and stability, leading them to experience various imbalances and illnesses that can reach dangerous levels. In order to prevent this, humans resort to defensive mechanisms, coping strategies, and resistant behaviors that can sometimes be pathological and harmful. Among the most prominent manifestations of this is the trap of drug abuse. This phenomenon has evolved and diversified in terms of forms and types over the ages. Substances with intoxicating effects, known to humanity since ancient times, initially represented a means to attain pleasure, euphoria, and a loss of reality.

However, today the situation is extremely dire. Drugs have taken on a criminal dimension due to exploitation by criminal organizations, given the substantial financial gains they yield, and the rapid growth in the number of

consumers. Additionally, they are employed in modern warfare strategies by flooding societies and undermining public health through drug trafficking.

This phenomenon now affects all strata of society and all age groups—women, men, children, and teenagers are not exempt. Everyone is susceptible to this cursed epidemic, which has escalated due to the introduction of new types of high-quality drugs and narcotics through methods previously unknown to communities. Among these are pharmaceutical opioids like buprenorphine and tramadol, which have become alarmingly prevalent in Algeria. This situation demands a serious examination to understand this phenomenon and its resulting consequences.

## 2. Problem Statement :

Addiction is defined as a chronic relapsing disorder characterized by compulsive drug-seeking and use despite severe consequences due to its neuropsychological effects. Addiction is considered a brain disorder involving functional changes in brain circuits related to reward, stress, and self-control. These changes can persist for a long time even after a person stops using drugs. Addiction, to a large extent, resembles other diseases, such as heart diseases, as both impair the normal and healthy functioning of a body organ. They both have serious harmful effects, and in many cases, can be prevented and treated. If they are left untreated, they can persist throughout life and may lead to death. (1)

One of the distinguishing features of these "new" psychoactive substances is the unprecedented rate of globalization. By September 2015, the United Nations Office on Drugs and Crime reported the presence of over 613 "new" psychoactive substances in 101 countries. Materials were reported in Europe more than any other region, according to a study conducted in China, Japan, Korea, and Taiwan. Between 2007 and 2015, out of a group of 940 reported "new" psychoactive substances, only 25% were controlled in four countries at that time, with Japan and Korea being the most active in regulation.

The production, distribution, or non-medical use of many psychoactive drugs is subject to control or prohibition outside the channels sanctioned by law. Psychoactive drugs have varying degrees of restrictions based on their health risks and therapeutic benefits. They are classified according to hierarchical schedules at national and international levels. Internationally, there are drug control treaties concerned with monitoring the production and distribution of psychoactive drugs : the Single Convention on Narcotic Drugs of 1961, as amended by the 1972 Protocol, the Convention on Psychotropic Substances of 1971, and the 1988 Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances.

The unsupervised use of psychoactive drugs is associated with significant health risks that can lead to drug use disorders, particularly when left untreated, resulting in increased rates of impairment and death for individuals. This, in turn, leads to substantial suffering and weaknesses in personal, familial, social, educational, professional, or other functional domains.

Drug use disorders are associated with significant societal costs due to decreased productivity, premature death, increased healthcare expenditures, criminal justice costs, social care, and social consequences. 2

In Algeria, the misuse of Pregabalin and Tramadol has increased significantly over the past decade. Although several studies have confirmed the neurological and psychological effects of Pregabalin and Tramadol, the effects of Pregabalin have not been thoroughly studied.

Through our professional practice at the Abu Bakr El Razi Psychiatric Hospital, we have observed that substance abuse is an extremely prevalent and serious issue among young people, ultimately leading to significant psychological, neurological, social, national, and legal problems. This prompted us, as mental health practitioners at the Abu Bakr El Razi Psychiatric Hospital, to choose this study topic based on our expertise, aiming to leverage our skills in the field to delve into this unique clinical experience. Our presence in addiction treatment facilities and our familiarity with handling the unique characteristics, preferences, and personal traits of patients motivated us to explore this area.

Over the past two decades, the proliferation of this issue has sharply risen in Algeria due to social and economic instability. Consequently, Algerian health authorities have included both Pregabalin and Tramadol in the list of highly addictive substances. Based on the aforementioned problem statement and relying on available previous studies on Pregabalin and Tramadol, the aim is to determine the extent of addiction effects on individuals and to identify the resulting neuropsychological impacts. Hence, the following question is posed :

What are the neuropsychological effects of addiction to Pregabalin (Lyrica) and Tramadol ?

## 3. Study Hypotheses :

### 3.1. General Hypothesis :

"The consumption of Pregabalin and Tramadol has neuropsychological effects."

### 3.2. Specific Hypotheses :

Addiction to Pregabalin and Tramadol results in psychological effects (depression, anxiety, social maladjustment).

Addiction to Pregabalin and Tramadol leads to neurological effects (sleep disturbances, memory impairments, tremors).

## 4. Study Objectives :

- Identify the Neuropsychological effects on Pregabalin and Tramadol addicts .
- Understand the aspects of Neuropsychosocial disorders that Pregabalin and Tramadol addict may experience before and after addiction.
- Determine the significant psychological characteristics exhibited by an addict to these substances.

## The Significance of This Study :

- The importance of the study is evident in the following points :

- This study addresses an important variable, examining the neuropsychological impact on Pregabalin and Tramadol addicts, significantly affecting their lives.

- The relevance of the specific group under study, which comprises two adult male addicts.

- This research contributes to identifying key neuropsychological disorders in addicts, offering current insights to further the field and guide specialists.

There is a notable focus on addressing this problem, aiding individuals struggling with addiction, and developing counseling programs for proper guidance. This includes generating recommendations that should be scientifically examined and implemented.

## 5. Study Definitions :

### * Pregabalin : Pregabalin (Lyrica)

It is a medicinal drug similar to gamma-aminobutyric acid used as an antiepileptic and nerve pain relaxant. The mechanisms of action are not well understood, especially those mediated by the anti-seizure and analgesic effects of pregabalin. Recent data indicate that one of the potential contributing mechanisms may involve modification at the level of the voltage-gated calcium channel through interactions with subunits symbolized by the α28-1. 3

Lyrica is the first trade name for the drug pregabalin, which was approved in 2004 by the U.S. Food and Drug Administration (FDA) for Pfizer Pharmaceuticals. It is available in liquid form of 20 mg/mL or capsules ranging from 25 to 300 mg, taken orally and can also be consumed through the throat or inhalation. 4

The drug Pregabalin is available in Algeria under several trade names such as 150/300, 50/75 mg LYRIZIN, alongside Gabalyse 300 mg, Leptica 300 mg, Prégabaline Beker Regab 300 mg, in various doses of 50, 150, 300 mg. Addicts often refer to it as "rocket," "taxi," Double signature, CRB. The majority of the confiscated types of Pregabalin by security authorities originate from foreign sources, entering the country through smuggling, especially across the eastern and southeastern borders of Algeria.

*** Tramadol :**

It is a capsule, half white and half orange, produced by Memphis company. Or a green capsule produced by October Pharmaceuticals.

**- Amadol** : a yellow, light-colored capsule.

**- Contramal** : capsules of 50 mg or tablets of 200 mg produced by Sigma company.

**- Tamol** : white tablets in a transparent box of 200 mg produced by Al-Kan company.

**- Trama SR**: white tablets in a non-transparent white box produced by GNB company.

**- Tramal** : capsules, half orange and half green, in a non-transparent white box, also available as drops produced by Minapharma company.

**- Tramax** : capsules divided into half white and half blue in a transparent box produced by High Pharm company.

**- Tramodine** : white tablets in transparent boxes produced by MUB company.

**- Altradol** : flat rectangular pills available as tablets in small jars or as water-like injections found in transparent bottles.

Tramadol is known as a very potent pain reliever that acts on morphine receptors, providing a pain-relieving effect similar to morphine. It alleviates chronic conditions, especially in digestive system tumors and severe bone fractures. Its prescription and dosage are precisely determined by the treating doctor. Tramadol interacts with chemicals responsible for nerve signal transmission between brain cells, causing disruptions and dysfunction in brain functions. These disturbances manifest in severe physical and mental complications. Initially, Tramadol gives users a sense of euphoria, but with continued use, this feeling diminishes gradually, leading users to seek increased dosage. 5

*** Neuropsychological Effects** : Neuropsychological effects refer to the psychological and nervous system changes caused by the use of drugs or medications affecting the central nervous system. These changes can impact an individual's mental and physical health, behavior, and overall life."

## 6. Previous Studies :

Previous studies are one of the most critical elements in scientific research and theses that affect reviewers and assessors responsible for deciding whether to approve and publish these works or not. The importance of previous studies lies in their multifaceted implications, indicating that the researcher has been exposed to a diverse range of ideas and opinions on the subject matter, enriching the content of the dissertation or research. Additionally, reliance on information obtained from well-known and reliable sources enhances confidence in the data. By reviewing numerous previous Arab and foreign studies and research, we were able to narrow down studies relevant to the current research, aiding in formulating its hypotheses and interpreting its results. Thus, in this article, we attempted to highlight some studies that addressed the changes in psychological disorders and their relationship with substance abuse and subsequently commented on them.

**Here is a brief presentation of some of the previous studies and research :**

6.1. A study by Amina Al-Khalaf, Ranem Al-Bukhari, Ilham Al-Shahri, and Aisha Farim Badr in **2021** titled "**Misuse of Gabapentin in Saudi Arabia After Restriction on Pregabalin Usage** : A Cross-Sectional Study." The

study concluded that the restriction on pregabalin usage led addicts to turn to Gabapentin as an alternative. Half of the participants reported misuse of pregabalin for non-medical purposes. Most of the sample indicated that the drug has mental effects, and motivations for its use included pleasure and peer pressure. The study recommended a shift from pregabalin addiction to gabapentin after the ban on selling the former without a medical prescription in Saudi Arabia and the necessity of revising pharmaceutical regulations to include gabapentin within the category of psychoactive substances. 6

6.2. A study by Jovenovic et al. (2006) titled "**Psychiatric Features Associated with Tramadol Addiction in Young Drug Users**." The study comprised 57 individuals using tramadol over three years, aged between 16 and 43, males and females. The researcher utilized a psychopathological characteristics scale and found that tramadol addicts, regardless of gender, suffered from hand tremors, tension, anxiety, and psychotic episodes.

6.3. A study by Lynn et al. From Ireland in 2020 titled "**A Retrospective Study of Factors Associated with Deaths Due to Pregabalin Poisoning in Ireland**." Researchers analyzed reports of deaths due to drug overdose from 2013 to 2016. They found that one out of six deceased individuals had indications of pregabalin poisoning, with a significant rise in the presence of pregabalin in blood analysis from 4.5% in 2013 to 26% in 2016. Mixing pregabalin with opioid substances contributed to reversing its effects, unlike when combined with alcohol. The researchers concluded the necessity of enhancing training and treatment, especially for individuals using multiple types of drugs alongside pregabalin.

6.4. The study by Karen Mariam in 2000, titled **"Psychological Characteristics of Tramadol Addicted Women,"** aimed to identify certain psychological characteristics associated with tramadol addiction among a sample of women. The study involved a sample of 64 women who were users of various medications, including tramadol. The researcher utilized tests for depression and self-esteem. The study found that these women suffered significantly from depression and had lower self-esteem levels.

**Commentary on Previous Studies :**

The current study shares similarities with some aspects of previous studies while differing in terms of the community, sample, and the utilized scale. Consequently, we benefited from these prior studies in constructing the theoretical framework for our current study and employed some of the results from previous studies to interpret certain aspects of the current research.

**7. The Theoretical Framework : Addiction:**

**7.1. General Concept of Addiction:** Addiction is defined as a condition of periodic or chronic poisoning that harms the individual and society, resulting from repeated misuse of natural or synthetic drugs. It manifests with an uncontrollable desire or need to continue using the drug, earnestly seeking it through any means possible, often escalating the dosage, and causing both psychological and organic dependency. 7

**WHO's Definition of Addiction**: The World Health Organization describes addiction as a mental and sometimes organic condition resulting from an individual's interaction with a substance, leading to behavioral patterns characterized by a constant urgent desire to use the substance to experience its psychological and desired organic effects. The individual also aims to avoid the threatening effects of withdrawal and the discomfort caused by its absence, often leaning towards increased dosage. 8

**Definition of Drug Addiction :** Drug addiction represents an advanced stage where there is an urgent desire by the addict to obtain the drug through any means. At this point, the individual becomes dependent, whether physically or psychologically, often relying on the drug to maintain balance. Abrupt cessation leads to severe withdrawal symptoms and could even result in fatality. 9

Drug addiction is a state of intoxication that arises from the repeated use of pills, with an intense desire to increase the dosage each time, resulting in the person's inability to quit these hallucinogenic pills. Eventually, the addict's life revolves around these substances taken in an abnormal and illegal manner, starting from experimental use to addiction (untranslated).

**7.2. Concepts Related to Addiction :**

**Craving:** A strong desire to obtain the effects of a drug or alcoholic beverage. Craving often involves obsessive thoughts that persistently haunt the addict and are typically accompanied by negative feelings. 10

**Dependence:** A mental state, sometimes organic, resulting from the interaction between a living being and a psychotropic substance. This condition is characterized by persistent responses or behaviors always containing an element of an overpowering desire for continuous or periodic substance use. 11

Sometimes, the term "dependence syndrome" is used as one of the psychiatric diagnostic categories for a group of disorders associated with substance use. Its mention is found in the classification issued by the World Health Organization for mental and behavioral disorders known as ICD 10.

**Psychological Dependence:** This is a state where there is a feeling of satisfaction with a psychological drive that requires continuous or periodic intake of a particular substance to stimulate pleasure or avoid troubles. This psychological state is considered the strongest factor in chronic poisoning by psychotropic substances, and in some of these substances, this condition is the sole factor involved in the situation. 12

**Physical Dependence:** This is an organic condition that reveals itself with the appearance of severe organic disruptions when a specific psychotropic substance is absent or when its effects are countered due to the individual taking an antagonist drug. The disturbances referred to as withdrawal symptoms consist of a set of organic and psychological signs and symptoms specific to each category of psychotropic substances. These symptoms and signs can be alleviated by the individual returning to the intake of the same psychotropic substance or another substance with a similar pharmacological effect within the same category as the original psychotropic substance. Physical dependence is considered a strong factor in supporting psychological dependence and its impact on either continuing the intake of the psychotropic substance or relapsing into its consumption after withdrawal attempts.

**Potential Dependence :** These are the characteristics present in any psychotropic substance based on its pharmacological effects on several psychological or organic functions. The potential for dependence on this substance is determined by its pharmacological characteristics, which can be measured through specific procedures on both animals and humans.

**Dependency Responsibility :**

The possibility of a psychological substance dependency in animals and humans, when assessing the possibilities of dependency on any psychological substance, takes into account the potential dependency of this substance and prevailing social habits.

**Dependency produced by medications :**

Substances capable of interacting with living organisms, causing a psychological, organic, or combined dependency. This psychological substance can be discussed in a medical or non-medical context without necessarily resulting in dependency. However, once a state of dependency arises, its characteristics will vary depending on the category of the involved psychological substance. Some substances, including those found in coffee and tea, can potentially induce dependency to a significant extent. Such a condition is not necessarily harmful, but there are other categories of substances that affect the central nervous system in stimulating, linked, or disruptive ways in perception, mood, thinking, or movement. These substances, if used in certain contexts, are known to cause individual and general problems simultaneously. These substance categories have the potential to induce significant levels of dependency. 13

**Neuroadaptation :**

The total neural changes accompanying both tolerance and the appearance of withdrawal symptoms. In some cases, these changes can be highly distressing, as with opioids, and "neuroadaptation" can occur without any noticeable cognitive or behavioral aspects.

**7.3. Stages of Addiction :**

**Tolerance Stage :** The addict's need to increase the drug dosage day by day to achieve the same desired effects. The addict might consume a quantity of the drug to reach their goal. If given to a normal person, it could lead to immediate death and the process of acquiring the drug through any means, meaning behavior that involves lying, cheating, forgery, deceit, and theft could culminate in a crime to obtain the hallucinogenic substance.

**Addiction Warning Stage, Psychological Dependency :** A psychological phenomenon where an individual becomes accustomed to the drug without dangerously relying on it. Compounds leading to dependency are

numerous, including sedatives and stimulants. This dependency can be easily removed in certain cases, while in others, it might be extremely challenging, as with opioid compounds where psychological dependency interferes, providing the drug user with a sense of euphoria and elation.

**Stage of Physical Organic Dependency:**

It refers to the deviation of normal actions and functions of the body's organs due to prolonged drug use, leading to addiction. The addict becomes reliant on the drug, and it becomes an inevitable necessity. If the addict abandons the drug, it leads to severe hardships, requiring significant sacrifices to obtain it. 14

The stages of addiction progress through the addict's increasing need for a higher drug dosage to achieve the desired effect, leading to psychological and physical dependence. With repeated actions, it may even lead to death.

### 7.4. Neurological Disorders Resulting from Addiction to Pregabalin (Lyrica) and Tramadol :

**These disorders manifest as follows:**

#### 7.4.1. Tremors :

It refers to involuntary, somewhat repetitive movements due to muscle contractions. This involves relaxation and back-and-forth movements (oscillations or tingling) in one or more parts of the body. It serves as evidence and a symptom of other neurological disorders, attributed to drug use such as tramadol, pregabalin, serotonin inhibitors, and caffeine. 15

#### 7.4.2. Memory Disorders :

Anterograde Amnesia, sometimes referred to as "Consolidation Amnesia," where the patient is unable to acquire or retain new information, although they can recall their past experiences with accuracy. This condition prevents the individual from remembering daily life events and situations, evident in their conversation despite displaying the possibility of implicit acquisition. This memory impairment manifests immediately after the information enters the memory. The patient struggles to recall information heard, seen, or felt after a minute or two, although immediate repetition is possible in this case. This type of forgetting pertains more to the loss of temporal orientation than spatial.

Retrograde Amnesia, also known as "Recall Amnesia," where the individual cannot recall experiences or recognize events and previously acquired information before the onset of the disease or disorder. In this type, there is difficulty and inability in recall. This disorder becomes apparent when questioning the patient about their life history, political events they were inclined towards, or educational achievements. 16

#### 7.4.3. Sleep Disorders :

**Sleep Paralysis** : Sleep paralysis is defined as a state of losing the ability to move that occurs while one is between sleep and wakefulness. During this state, the sleeper may dream that a thief is attacking them or that a predator is approaching, yet they are unable to shout or move. This state lasts from seconds to minutes, and these moments pass extremely slowly.

**Nightmares:** Previously known as anxiety dream disorders, nightmares are dreams loaded with anxiety. Nightmares cause severe distress, especially during drug withdrawal stages, in the presence of psychological pressure or physical exhaustion.

**Insomnia :** It is a more common condition among addicts, especially during treatment periods, characterized by severe sleep loss to the extent that it interferes with an individual's daytime performance. There are three types of insomnia : (difficulty falling asleep), (difficulty staying asleep), and the final type, early awakening and inability to return to sleep. Scientifically, insomnia should not occur during sleep or lead to the development of other mental disorders like major depressive disorder.

There are other disorders, including sleep hallucinations, restless leg syndrome, sleep drunkenness, and head-banging disorders. 17

**Psychological Disorders Resulting from the Addiction to Pregabalin (Lyrica) and Tramadol :**

Depressive Disorders : Psychological heritage in the field of addiction points to a strong relationship between drug abuse and depression. Depression is a common complaint among these patients. Psychologists embrace Simmel's statement that addiction joy is a form of hypomania, meaning that addiction joy is a defensive mechanism to overcome and get rid of depression.

Empirical studies have supported the theoretical heritage of a strong relationship between drug use and depression. Studies have found a fundamental link between depression and the misuse of substances like heroin, cannabis, alcohol, barbiturates, and amphetamines. 18

**Anxiety Disorder** :

Drug users suffer from anxiety symptoms, which can be attributed to either poisoning orwithdrawal. Patients with anxiety disorders may become dependent on sedative drugs such as barbiturates, leading to complex diagnostic issues regarding anxiety

(Bolo, 1991) refers to panic and fear disorders in open spaces being common among alcohol addicts, leading to prolonged feelings of anxiety and tension, which in turn lead to using alcohol as a self-treatment for this anxiety. Miller (1991) also clarified that acute alcohol withdrawal typically involves anxiety, depression, irritability, and insomnia.

Additionally, poisoning from cocaine, amphetamines, marijuana, and various hallucinogenic pills can lead to symptoms of anxiety and panic, manifested through palpitations, severe tension, sweating, increased body temperature, and dilated pupils. The Diagnostic and Statistical Manual DSM-5 also noted that the cessation of drug use after addiction to amphetamines or the reduction in the quantity consumed leads to an anxious mood, perhaps depression, emotional upheaval, severe insomnia, and psychomotor agitation. 19

### 7.4.4. Social Maladjustment :

The consumption of pregabalin and tramadol affects the social performance of individuals, placing a burden on society as well. These disorders contribute to medical or psychological conditions, disability, death due to accidents or diseases caused or exacerbated by the consumption of these drugs, high suicide rates, all of which affect society. Other social problems associated with consumption include instability, homelessness, criminal behaviors (victim or perpetrator), imprisonment, transmission of HIV due to consumption of these substances, or high-risk behaviors, unemployment, or reliance on welfare. The costs associated with these social problems are staggering, creating an economic burden on governments or funders who spend substantial amounts on addiction treatments, medical or psychological disorders, and other related problems such as those associated with reliance on social care.

Numerous individual and group therapies for pregabalin and tramadol consumption address social recovery issues, as they have implications for relapse and life quality. These interventions may address issues such as avoiding or reducing contact with high-risk individuals, places, or events; resolving relationship problems; developing new friendships; developing a recovery network of reliable friends and supportive individuals; resisting social pressure to use substances; improving communication or assertiveness skills; seeking help and support from others; engaging in drug-free social activities; engaging in mutual support programs; and/or compensating victims of sudden death. 20

## 8. Field Study Procedures :

### 8.1. Study Methodology :

In our study, we relied on the clinical approach using the case study technique to comprehend the clinical characteristics of each case, as required by the study. This method involves collecting extensive and comprehensive data and information about an individual case or a limited number of cases, aiming to achieve a deeper understanding of the studied phenomenon and similar phenomena. Data is gathered about the current situation of the case under study, as well as its past and relationships, to gain a deeper and better understanding of the represented community. 21

### 8.2. Case Selection :

To evaluate the neuropsychological impact on addicts of pregabalin and tramadol, we deliberately chose the cases. Sometimes, a researcher aims to achieve a specific goal or purpose in their study, so they select cases that serve this goal or purpose.

The two cases were as follows : the first case was 26 years old, while the second case was approximately 22 years old. Both individuals had severe addiction. These cases were selected from the Abu Bakr Al Razi Addiction Treatment Department and the Intermediate Center in Boukhadra for Addiction Treatment.

**Table No. 01 : Presentation of the Study Cases and their Characteristics.**

| Name of the Case | case (01) | case (02) |
|---|---|---|
| Gender and Age | Male, 26 years old | Male, 34 years old |
| Substance Used | Lyrica 300 Mg. Tramadol 100 Mg | Lyrica 300 Mg. Tramadol 50 Mg |
| Quantity of the Substance | Lyrica 14 tablets per day, Tramadol 08 tablets per day | Lyrica 08 tablets per day, Tramadol 04 tablets per day |
| Accompanying Disorder | Depression, Anxiety, Sleep Disorder, Tremor | Depression, Anxiety, Sleep Disorder |

### 8.3. Fields of Spatial and Temporal Study :

Our study was conducted in the specialized psychiatric institution - Abu Bakr Al Razi - and the intermediate center for drug addiction treatment located in Boukhadra. This center takes on the psychological and medical care of drug addicts.

The study commenced from 18/03/2023 until 21/05/2023. We examined one case at the psychiatric hospital for addiction treatment - Addictology- and another case at the Boukhadra Intermediate Center, affiliated with the aforementioned psychiatric facility in Annaba Algeria.

### 8.4. Research Tools :

#### Observation :

To facilitate observation, we attended sessions and classes with the cases, recording direct and indirect observations. Our direct observations of both cases focused on their outward appearance, hygiene, and their receptiveness to interactions, including how they responded to assessments. Additionally, we noticed pronounced shivering, dark circles under their eyes, indicative of sleep deprivation and anxiety.

Indirect observations helped us verify the obtained results through various activities aiding the treatment process, such as group therapy and relaxation therapy.

#### Interviews :

Interviews are common data collection tools utilized in various scientific research domains. In this phase, we interviewed the cases, the psychological specialist, and the treating physician. These interviews provided us with comprehensive information regarding the cases' histories.

#### Scales :

#### Beck Depression Inventory :

This scale, translated into Arabic by Dr. Abdel Sattar Ibrahim, provides an accurate and rapid assessment of depression levels. It comprises 21 questions, each with a graded series of four alternatives representing different levels of depressive symptoms, scored from 0 to 3, indicating the symptom severity.

#### Hamilton Anxiety Rating Scale :

His scale was developed by the psychiatrist Max Hamilton in 1959 for use with patients previously diagnosed with anxiety. It gives a quantitative score based on the presence of certain physical and psychological symptoms. When used correctly, these scores serve as a reliable indicator to record the patient's improvement. The application of the scale relies on the skill of the examiner and their ability to identify diverse symptoms through questioning the patient and assessing the severity of those symptoms based on the patient's self-perception.

The scale consists of 14 composite items, the sum of their scores quantifies the level of anxiety. It's typically administered before the start of treatment and then periodically afterward to assess the extent of improvement.

**The Pregabalin Scale:**

It measures the extent of withdrawal experienced by Pregabalin users after ceasing drug intake within hours. During this time, the quantity of the neurotransmitter dopamine decreases, initiating a return to its natural state. However, this return comes with a cost manifested in several symptoms that necessitate a medicinal program. This scale aims to treat drug withdrawal symptoms without pain and includes 13 indications : intense drug cravings, flu-like symptoms, depression, mood swings, vomiting and nausea, increased heart rate, rapid breathing, muscle spasms, severe anxiety, insomnia, agitation and aggression, severe body aches, and paranoia.

## 9. Presentation and Discussion of Study Results :

**Table illustrating the measurements' results for the first condition :**

| The First Condition | The Degree | Description of the degree |
|---|---|---|
| Hamilton Anxiety Scale | 32 | High |
| PEK Depression Scale | 49 | Severe depression |
| Pregabalin Symptoms Scale | 49 | Neurological and psychological symptoms |

### 9.1. Quantitative Analysis :

The table illustrates the results of the applied measurements in the first condition. After applying the Anxiety Scale, we obtained a high anxiety score of 32, which indicates a very high level of anxiety. A score of 25 and above is considered a serious indicator.

Regarding the Depression Scale, a score of 46 or higher represents extremely severe depression. Similarly, in the Breggin Scale, a score of 36 represents a high degree.

### 9.2. Qualitative Analysis :

After explaining the measurements and thoroughly training the individual on these measures, the case showed no difficulty in responding to the assessments. It became evident that the individual was suffering from pathological anxiety accompanied by suicidal thoughts resulting from severe depression, mixed with neurological symptoms and memory disturbances. This was evident in the neurological scale, indicating damage resulting from the use of Pregabalin and Tramadol.

**A table illustrating the results of the measurements for the second condition :**

| The Second Condition | The Degree | Description of the degree |
|---|---|---|
| Hamilton Anxiety Scale | 34 | High |
| Depression Scale | 46 | Severe depression |

| | | |
|---|---|---|
| Pregabalin Symptoms Scale | 43 | Neurological and psychological symptoms |

### 9.3. Quantitative Analysis :

The table illustrates the results of the applied measures with the second case. Following the administration of the anxiety scale, the case obtained a score of 34, indicating a high level of anxiety. Additionally, a score of 46 was recorded on the depression scale, representing extremely severe depression, and a score of 43 on the Pregabalin Symptoms Scale, which is considered highly elevated.

## 10. Discussion of Results in Light of Hypotheses :

### 10.1. First Hypothesis :

"Pregabalin and Tramadol addiction lead to psychological effects, depression, anxiety, and social maladjustment."

According to the study's findings, both quantitatively, through the application of the anxiety and depression scales, and qualitatively, through clinical interviews with the two cases under study, the psychological effects are evident in both cases. This can be inferred from the results obtained from the application of the three scales or through observations across various sessions conducted with the cases.

The different facets constituting the personalities of the two cases under study depict a state best described as severe distress (cognitive, emotional, and behavioral imbalance), with difficulties in maintaining close relationships, especially within their families. Their social lives are marked by conflicts, reflecting an overall inability to socially adapt.

The aforementioned supports the study's partial hypothesis that addiction to Pregabalin and Tramadol has psychological effects such as anxiety, depression, and social maladjustment, proving to be devastating for individuals addicted to these substances.

This result is in line with what was demonstrated by studies such as El Abboudi, Salima, and Wanas (2019), which confirmed the psychological effects of Pregabalin on an addict suffering from schizophrenia or schizoaffective disorder. Similarly, the study by Al-Khalaf, Al-Bukhari, Al-Shahri, Al-Shahri, and Pharm (2021), from a psychological perspective, confirmed the neuropsychological effects of the drug Pregabalin. Even foreign studies like the study by Hickey & Tomas (2012), which, in turn, demonstrated the psychological effects of Pregabalin with a secondary diagnosis for a woman resulting from Pregabalin use. Additionally, the findings presented by Raphael and others indicated the psychological effects of the drug Tramadol. The partial hypothesis of the study aligns with what was found in the study by Karen Mariam (2000), which proved the psychological effects of Tramadol. Also, a study by Jovenovic et al. (2006), in its psychological segment, demonstrated the neuropsychological effects of Tramadol.

### 10.2. The second hypothesis :

**Addiction to Pregabalin and Tramadol leads to neurological effects such as sleep disorders, memory disturbances, and tremors.**

According to the results obtained in the study, following the administration of the anxiety scale, depression scale, Pregabalin symptoms scale, and clinical interviews with the two cases under study, neurological effects are evident in both cases. This can be observed through the observations recorded across various sessions conducted with the cases or even through the items of the three scales related to sleep and memory. It can be said that the clear neurological damage experienced by the cases under study manifests in limb tremors, memory impairment, which is notably evident in the inability to recall recent events or confirm recent dates, and recurring complaints regarding the inability to sleep, insufficient hours of sleep, or irregular sleep patterns. What can be deduced is that the second partial hypothesis of the study has been validated, indicating that addiction to Pregabalin and Tramadol has neurological effects such as sleep disorders, memory disturbances, and tremors. This aligns with neurological effects as found in Susanne Philippsohn and Tillmann H C Kruger's study (2012), which highlighted the neurological effects of Pregabalin on sexual function.

### 10.3. The general hypothesis :

Both hypotheses have been confirmed, indicating that the general hypothesis of the study has been fulfilled, which states : "**Addiction to Pregabalin and Tramadol has neuropsychological effects**." There is a high common impairment between Pregabalin and Tramadol use and disorders including depression, anxiety, social maladjustment, sleep disturbances, memory impairment, and tremors. These accompanying psychological and neurological impairments may be associated with an increased risk of suicide, schizophrenia, borderline personality disorder, antisocial personality disorder, and this is at the core of the observations we recorded from the two cases at the Abu Bakr El Razi Psychiatric Hospital in Annaba. The use of Pregabalin and Tramadol is becoming a growing source of concern on a wide scale, and its consequences can be severe and dire.

### 10.4. General Analysis of Results :

Through our applied study, which delved into the neuropsychological effects on addicts of Pregabalin and Tramadol, the clinical study results of individuals addicted to these drugs, in light of the hypotheses, personal and familial data, and conclusions derived from the applied measurements with these cases, after analyzing and discussing the results, and in light of modern neurological theories suggesting that psychoactive substances lead to sensations and changes in mental and behavioral activity due to their impact on the brain, studies have shown that drugs are associated with specific sites on the surface of nerve cells called receptors. Consequently, serious neurological damage occurs, as covered in this study, such as sleep disorders, memory disturbances, and tremors.

Furthermore, the use of Pregabalin and Tramadol leads to various psychological effects, including susceptibility to mental illnesses like chronic anxiety, depression, social maladjustment, where users might appear with cheerful trends and broad smiles, but, in reality, they are in a state of mental fog. Additionally, individuals under the influence of these drugs might imagine things that aren't real and swim in a sea of unrealistic dreams and impossible occurrences. One of the significant reasons prompting their use is the lack of customary satisfaction, leading to the addict experiencing anxiety attacks that hinder their social adaptation, and negative thoughts dominate their mind, believing themselves rejected and despised, leading to a cycle of anxiety, tension, fear, and alienation.

As the study by Mohammed Rafat (1986) highlighted that drug addiction leads to psychological disorders such as depression, anxiety, and despair... This was reinforced by Miller, Shilts, and Cox's study (1980) on depression among delinquents, where researchers found that 60.07% of the research sample used drugs, particularly marijuana and alcohol, to alleviate feelings of depression. Dr. Mohammed Mashabaqa (2007) pointed out in a study on addicts that addiction causes deterioration in vital body functions and mental faculties, affecting the addict's productivity and efficiency, often leading to an absolute inability to work. Another study in 2012 discussed tremors as a disease affecting the central nervous system, resulting from dopamine deficiency, leading to the death of nerve cells in the substantia nigra in the brain, which in turn affects motor functions (tremors).

Ultimately, sleep disorders, memory disturbances, tremors, depression, social maladjustment, and anxiety are among the most common neurological disorders observed in Pregabalin (Lyrica) and Tramadol addicts, as addressed in our study.

## 11. Conclusion :

In our current study, we aimed to address a pressing issue, one of the most significant social afflictions of our time. It is characterized by rapid and widespread expansion, where the reported figures and statistics from specialized agencies, some of which we have referred to, represent only a fraction of the actual numbers. Despite the sensitivity of this type of addiction for several reasons, such as its legal repercussions, societal dissatisfaction with victims, the lack of acceptance by families, and the failure to acknowledge their role in aiding or potentially failing the addict.

While the use of Pregabalin and Tramadol increases the likelihood of misuse and addiction, problems arise with these substances when taken in high doses outside their known therapeutic context or when combined with other substances. Pregabalin and Tramadol, when misused or abused, can lead to severe issues. There is a fine line between misuse and addiction, and many individuals end up using Pregabalin and Tramadol without realizing it.

Moreover, many cases of addiction to these substances have occurred in individuals who already rely on illegal substances.

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