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Research Article

Beta-Endorphin and Serotonin Levels in Individuals with Methamphetamine use Disorder

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Abstract

Background: Alterations in the levels of beta-endorphins and serotonin are heavily involved in the mood dysregulation regularly observed in individuals with methamphetamine use disorder, with lower levels of these neurotransmitters contributing to mood disturbances commonly seen in addiction. Such neurochemical imbalances may also disrupt normal mood regulation pathways, leading to the emotional and psychological challenges often experienced by individuals struggling with addiction.

Objective: To investigate the relationship between beta-endorphin and serotonin levels in individuals with methamphetamine addiction, and to evaluate their potential roles in mood regulation and addiction-related behaviors.

Methods: This observational study assessed the serum levels of beta-endorphin and serotonin in individuals with methamphetamine use disorder compared to healthy controls. Fifty patients with confirmed methamphetamine use disorder and fifty matched healthy individuals were recruited. ELISA (Enzyme-linked immunosorbent assay) was used to measure serum serotonin and beta-endorphin levels. Research permission was obtained with ethical approval from the Health Research Ethics Committee.

Results: The results showed significantly lower levels of both neurotransmitters in the addiction group with mean ± SD (11.84 ± 3.64) of beta endorphin and means of 10.28 ± 3.21, of serotonin. A strong positive correlation between serotonin and beta-endorphin was also noted. These findings suggest a critical role of these neurochemicals in the mood disturbances associated with methamphetamine addiction.

Conclusion: Mood regulation and addictive behaviors in methamphetamine addiction were impacted by changes in beta-endorphin and serotonin levels. Understanding these neurochemical changes help to develop more effective treatments for changes in mood and addictive behaviors.

Keywords: Beta-endorphin; ELISA; Methamphetamine addiction; Mood regulation; Neurotransmitters; Serotonin.

Introduction

Methamphetamine (METH) is a synthetic central nervous system stimulant with a significant abuse potential and robust neurotoxic effects(1). METH addiction impairs cognition, memory, and attention while causing long-term neural damage. Because of its lipophilic nature, METH readily crosses the blood brain barrier and accumulates in the brain, where it primarily increases the release of both central and peripheral neurotransmitters, including glutamate, serotonin, dopamine, and norepinephrine (2). Repeated METH administration promotes behavioral sensitization, which besides addiction includes behavioral abnormalities such as drug seeking, relapse, and psychotic episodes; in rare cases, psychotic symptoms can remain for months or years long after the addict stops using methamphetamine (3). Frequent methamphetamine misuse affects dopaminergic, serotonergic nerve endings in many parts of the brain, as well as increasing anxiety and sadness as mood disorders; these symptoms are particularly common during the withdrawal period. Neurochemical markers of this toxicity include decreases in serotonin and beta-endorphin(4)(5). Serotonin, a neurotransmitter, is essential and performs a crucial role in emotional well-being. Despite promoting emotional stability and general well-being, it also influences mood, malnutrition, and sleep management (6). Beta-endorphin is a peptide that functions as both a neurotransmitter and a neuromodulator in the brain. It is an endogenous opioid generated and stored predominantly in the anterior pituitary gland. Beta-endorphins are vital for pain management, mood enhancement, and stress response. Evidence suggests that beta-endorphins are partially responsible for the euphoric or pleasurable sensations that frequently occur in response to exercise (7), (8).

This study aimed to investigate the relationship between beta endorphin and serotonin levels in individuals with methamphetamine addiction, and to evaluate their potential roles in mood regulation and addiction-related behaviors.

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Patients and Methods

This study was analytical observational research conducted by College of Medicine, University of Baghdad, from January to October 2024. In this study 50 persons with methamphetamine use disorder were included in the study, with duration of abuse for more than 6 months on different doses of addiction. The diagnosis of methamphetamine use disorder was made by a specialist psychiatrist according to the DSM-5-TR diagnostic criteria in Ibn-Rushed Psychiatric Teaching Hospital. Fifty individuals as healthy controls were selected. The age range (18-60) years old of all participants in the study. Serum levels of beta endorphin and serotonin were measured using the Enzyme-linked Immunosorbent assay (ELISA). Blood samples were collected, and serum was separated using a centrifuge. The isolated serum was then stored at -20°C for six months prior to analysis, with all samples analyzed simultaneously. Research permission was obtained with ethical approval from the Health Research Ethics Committee at College of Medicine, University of Baghdad, according to the code number (418). In addition, consents were obtained from the hospital and participants. Exclusion criteria were hepatic, renal, or cardiac disease, alcohol dependence, and comorbid substance use disorders.

Statistical analysis

Data analysis was performed with SPSS software version 16.0. Data were presented as Mean ± SD to compare serum levels based on analysis of variance is different from t-test for each study. Pearson correlation analysis was performed to see if there was a significant association between the parameters. The alpha level for statistical significance was established at a threshold of $P < 0.05$.

Results

In table (1) there were no statistically significant differences in age distribution between the methamphetamine use disorder group and control groups ($P<$ 0.74). The measurements of neurochemicals in the two groups reveal significant variations, indicating distinct biochemical profiles among these cohorts. These differences highlight the neurochemical imbalances that are associated with methamphetamine use disorder. Beta endorphin concentrations show the significantly lowest level in the addiction group with mean ± SD (11.84 ± 3.64) and the highest in controls with mean ±SD (35.18 ± 5.89) *P*-value (<0.001) as shown in Figure (2). Serotonin exhibited a significant group difference, with means of 10.28 ± 3.21 (addiction) and 32.82 ± 8.45 (control) *P*-value (<0.001) as shown in Figure (1). These results emphasize the role of Beta-endorphin and serotonin in reward pathways and mood regulation, which are disrupted in addiction due to substance dependence.

Table (1): Comparison of measurements across addicts and control group

Parameters	Addiction (n=50)	Control (n=50)	*P*-value
Age (year)	33.2 ± 10.8	32.8 ± 11.4	<0.74
Serum Endorphin (ng/L)	11.84 ± 3.64	35.18 ± 5.89	<0.001*
Serum Serotonin (ng/mL)	10.28 ± 3.21	32.82 ± 8.45	<0.001*

Note. Values presented as Mean ± SD. *Significant Value $P<0.05$

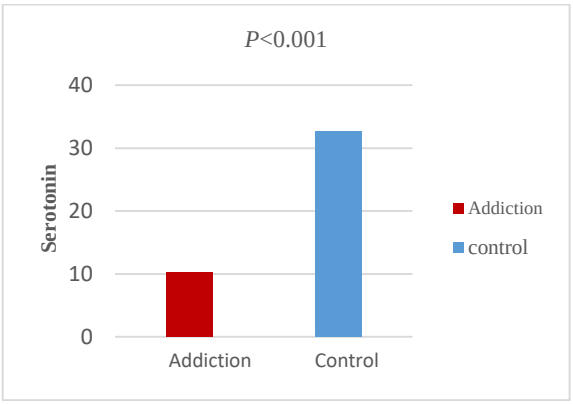

Figure (1) Comparison of Mean Serotonin across groups.

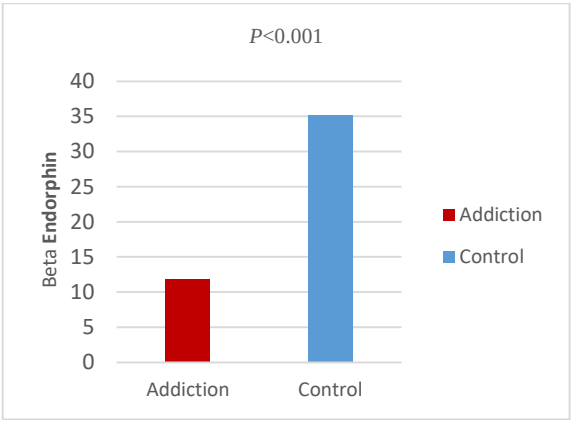

Figure 2: Comparison of Mean endorphin across groups.

In Figure (3) there is a correlation analysis between beta endorphin and serotonin in the group, shown strong significant positive correlation between two parameter levels (r=0.76, $P<0.001$). This result demonstrated that both parameters impacted by methamphetamine addiction and there is a relationship between them in mood regulation.

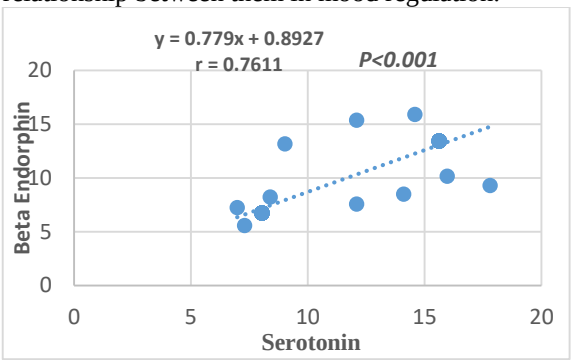

Figure 3: Correlation between beta endorphin and serotonin in addicts group

Discussion

The results presented in the study demonstrated significant biochemical differences between individuals with methamphetamine addiction and healthy controls, providing important insights into the neurochemical disruptions associated with addiction. The absence of a significant difference in age between the two groups supports the validity of the comparison, ensuring that age-related factors did not confound the findings. This allows for a more accurate evaluation of the specific impact of methamphetamine addiction and depression on neurochemical systems; there are no age-related influences in this study, which agreed with a previous study (9).

The most significant findings were reductions in serum levels of both beta endorphin and serotonin in the addiction group, compared to the control group. The addiction group exhibited much lower concentrations of beta-endorphin and serotonin compared to the control group (beta endorphin, serotonin, with *P*-values less than 0.001 for both biomarkers. Previous studies explained that chronic methamphetamine use causes significant neurotoxicity by damaging nerve endings at different sites of the brain disturbs various neurotransmitter systems through various mechanisms including dopaminergic and serotonergic mechanisms, resulting in reward processing and mood regulation (10)(11). Another clinical studies indicated that the increase in the levels of serotonin, norepinephrine and endogenous opioid peptides, specially beta-endorphins in METH abusers is responsible for neurogenesis and reduces the level of stress, and subsequently alleviating depression and anxiety (3).

The present study demonstrated a strong positive correlation between beta endorphin and serotonin levels in the addiction group, indicating a significant link between these two biomarkers in the context of methamphetamine addiction.

Methamphetamine induces oxidative stress in the brain, largely through the generation of reactive oxygen species (ROS), which impair cellular function and contribute to neurotoxicity. When METH penetrates neurons, it displaces dopamine and serotonin from their vesicles, causing an excessive release of these neurotransmitters into the synaptic cleft. This elevated neurotransmitter activity increases ROS production, leading to oxidative damage that is a primary factor in the deterioration of neurochemical neurons. As these neurons lose, they release neuromelanin, which further promotes neuroinflammation and accelerates neurodegeneration. In cases of METH overdose, the combined effects of oxidative stress, neurotoxicity, and inflammation extend to β-endorphin-producing neurons, resulting in their destruction and acute depletion. Thus, the interplay between serotonin release, oxidative stress, and β-endorphin neuron loss underlies much of the neurotoxic damage caused by methamphetamine overdose(12). A previous study investigating the role of beta-endorphin therapy in cocaine-addicted mice showed that they have low levels of beta-endorphin. The findings highlight that beta-endorphin mediates cocaine reward and relapse behaviors, potentially informing targeted addiction treatments. Since cocaine is a central nervous system stimulant, which could apply to the current study of methamphetamine as a central nervous system stimulant (13). Serotonin is essential for mood regulation, influencing emotional responses and cognitive functions. Low beta-endorphin and serotonin levels are associated with depression and irritability, while selective serotonin reuptake inhibitors (SSRIs) and physical exercise, which increase the levels of serotonin and beta-endorphin respectively, are well established modalities in the treatment of mood disorders (6). This explains that β-Endorphin indirectly enhances dopamine release in reward pathways; simultaneously, β-Endorphin modulates serotonergic activity, which is critical for emotional resilience during stress (14). Prior studies suggested that chronic methamphetamine addiction involves complex neurochemical changes that disrupt and make difficulty in mood and emotional regulation, leading to increased relapse, which impairs an individual's capacity for pleasure and emotional regulation, and increases susceptibility to continuous METH use to restore emotional stability, and reward sensitivity (15).

Limitations of this Study:

1. The sample size of future research should be to include more individuals in order to produce more reliable and accurate diagnostic findings.

2. Targeted Treatment Approaches Treatment strategies for methamphetamine addiction should prioritize the restoration of neurochemical imbalances, particularly concerning the observed alterations in beta-endorphin and serotonin levels.

3. Routine assessment of serotonin and beta-endorphin levels may be incorporated into treatment regimens to identify persons at increased risk of mood disorders.

Conclusion

The results of the current research highlighted the significant decrease of beta endorphin and serotonin that were associated with methamphetamine addiction compared with controls. The observed decreases in both neurochemicals in the addiction group were consistent with previous research, emphasizing addiction's deleterious impact on mood regulation and the reward system. Moreover, the significant association between these two measurements implies that changes in one system could exacerbate mood dysregulation and compulsive behaviors by causing disruptions in the other. These findings supported the necessity of therapeutic approaches that target the serotonin and beta endorphin systems in order to restore equilibrium in these neurochemical pathways and, eventually, enhance the effectiveness of therapy for methamphetamine addicts. In order to lessen the emotional and behavioral difficulties associated with addiction, future studies should keep examining the

mechanisms causing these disruptions and look into cutting-edge methods of modifying these neurochemicals.

Authors' declaration

We confirm that all the Figures and Tables in the manuscript belong to the current study. Besides, the Figures and images, which do not belong to the current study, have been given permission for re-publication attached to the manuscript. Authors sign on ethical consideration's Approval-Ethical Clearance: The project was approved by the local ethical committee of (College of Medicine, University of Baghdad & Ibn-Rushed Psychiatric Teaching Hospital) according to the code number (418) on (29/ 12/ 2024).

Conflict of Interest: None

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Author contributions

Study conception & design: (Noor H. Talib, Maysaa J. Majeed, Mahir M. Hussein). Literature search: (Noor H. Talib, Maysaa J Majeed, Mahir M. Hussein). Data acquisition: (Noor H. Talib, Maysaa J. Majeed, Mahir M. Hussein). Data analysis & interpretation: (Noor H. Talib, Maysaa J. Majeed, Mahir M. Hussein), Manuscript preparation: (Noor H. Talib, Maysaa J. Majeed, Mahir M. Hussein). Manuscript editing & review: (Noor H. Talib, Maysaa J. Majeed, Mahir M. Hussein).

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مستويات بيتا إندورفين والسيروتونين في مدمنين الميثامفيتامين

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الخلاصة:

خلفية البحث: تلعب التغيرات في مستويات بيتا إندورفين والسيروتونين دورا مهما في اضطراب المزاج الذي لوحظ لدى الأفراد الذين يعانون من إدمان الميثامفيتامين ، حيث تساهم المستويات المنخفضة من هذه الناقلات العصبية في اضطرابات المزاج التي تظهر عادة في الإدمان. قد يعطل أيضا عمليات تنظيم المزاج العادية, مما يؤدي إلى التحديات العاطفية والنفسية التي غالبا ما يواجهها الأفراد الذين يعانون من الإدمان.

الاهداف: التحقيق في العلاقة بين مستويات بيتا إندورفين والسيروتونين لدى الأفراد الذين يعانون من إدمان الميثامفيتامين ، وتقييم أدوارهم المحتملة في تنظيم الحالة المزاجية والسلوكيات المرتبطة بالإدمان.

المرضى وطرق العمل: شملت هذه الدراسة القائمة على الملاحظة ، التي أجرتها كلية الطب بجامعة بغداد (من يناير إلى أكتوبر 2024) ، 50 مدمنا على الميثامفيتامين و 50 اصحاء تتراوح أعمارهم بين 18 و 60 عاما. استخدم المشاركون الميثامفيتامين لأكثر من ستة أشهر وتم تشخيصهم من قبل أخصائي. تم قياس مستويات بيتا الإندورفين والسيروتونين في المصل باستخدام جهاز الايلايزا.

تم الحصول على الموافقة الأخلاقية ، وتم استبعاد الأفراد الذين يعانون من أمراض الكبد أو الكلى أو القلب أو تعاطي الكحول أو إدمان المخدرات الأخرى.

النتائج: لم يتم العثور على فروق عمرية معنوية بين المجموعات ذات دلالة احصائيةز كانت مستويات بيتا اندورفين والسيروتونين اقل بشكل ملحوظ في مجموعة الادمان ذات دلالة احصائية مقارنة بالمجموعة الضابطة. لوحظ وجود علاقة ايجابية قوية بين بيتا اندورفين والسيروتونين في مجموعة الادمان.

الاستنتاجات: تشير النتائج إلى أن مستويات بيتا إندورفين والسيروتونين المتغيرة تؤثر على تنظيم الحالة المزاجية وسلوكيات الإدمان في إدمان الميثامفيتامين. يمكن أن يؤدي فهم هذه التغييرات الكيميائية العصبية إلى علاجات أكثر فعالية تستهدف عدم تنظيم المزاج والرغبة الشديدة.

مفتاح الكلمات: المدمنين, بيتا اندورفين, ميثامفيتامين,كيميائيات عصبية, سيروتونين.