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A Relationship of Monoamine Oxidase-A with Serotonin in Violent Antisocial Behavior in Iraqi Prisoners

Ali Majeed Zaal*, Asmaa Mohammed Saud
Department of Biotechnology, College of Science, University of Baghdad, Baghdad, Iraq

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Abstract

It is thought that the monoamine oxidase-A (MAOA) enzyme, which catalyzes key brain signaling chemicals like serotonin, noradrenaline, and dopamine, indirectly influences antisocial behavior by disrupting the neurotransmitter balance in brain regions and neural networks. This study aims to assess the MAOA enzyme level in serum and serotonin linked to antisocial behavior in cases in the prison of Baghdad City, Iraq. Blood samples were collected from (63) prisoners and (27) control groups, ages 18 years to 65 years, with a mean ± SD of 37.8 ± 8.8, all males, with different prison terms and different crimes for prisoners in the prison at Baghdad City, Iraq. MAOA and serotonin levels were measured in serum in prisoners and healthy men, and the results showed the serum levels of MAOA enzyme and serotonin were decreased in prisoners compared to the healthy (11.5 IU/ml vs. 19.5 IU/ml) and (79 IU/ml vs. 439 IU/ml), respectively, with the observed difference being significant ($P < 0.001$). The results of the relationship between education and social violence were: illiterate 11.1%, primary school 27%, secondary 52.4%, and university 9.5%. The median serum level of MAOA and serotonin in the age group 18–39 years was (11.3 IU/ml, 68.3 ng/ml), respectively, and in the age group 40–65 years was (13 IU/ml, 139 ng/ml), respectively.

Keywords: Antisocial Behavior, MAOA, Personality, Serotonin, Violence.

علاقة انزيم أوكسيديز أحادي الأمين مع السيروتونين بالسلوك العنيف المعادي للمجتمع لدى السجناء العراقيين

علي مجيد زعال*، اسماء محمد سعود
قسم التقنيات الاحيائية، كلية العلوم، جامعة بغداد، بغداد، العراق

الخلاصة

يعتقد ان انزيم أوكسيديز أحادي الأمينA ، الذي يحفز المواد الكيميائية الأساسية لإشارات الدماغ مثل السيروتونين والنورادرينالين والدوبامين، يؤثر بشكل غير مباشر على السلوك المعادي للمجتمع عن طريق تعطيل توازن النواقل العصبية في مناطق الدماغ والشبكات العصبية، تهدف هذه الدراسة الى تقييم مستوى انزيم أوكسيديز أحادي الأمين A والسير وتونين في مصل الدم المرتبط بالسلوك العنيف المعادي للمجتمع في

*Email: Ali.Majeed1106a@sc.uobaghdad.edu.iq

عينات من المساجين في سجون مدينة بغداد–العراق. تم جمع عينات الدم من (63) سجينًا و (27) مجموعة السيطرة تتراوح أعمارهم بين 18 عامًا و65 عامًا بمتوسط ± انحراف معياري (37.8±8.8) كانوا جميعًا من الذكور وبأحكام سجن مختلفة وجرائم مختلفة للسجناء في سجن مدينة بغداد – العراق. تم قياس مستويات انزيم أوكسيديز أحادي الأمين A والسيروتونين في مصل الدم لدى السجناء والرجال الأصحاء، وأظهرت النتائج انخفاض مستويات إنزيم أوكسيديز أحادي الأمين A والسيروتونين في المصل لدى السجناء مقارنة بمجموعة الاصحاء (11.5 وحدة دولية / مل,19.5 وحدة دولية / مل) (79 وحدة دولية / مل, 439 وحدة دولية / مل)، على التوالي ما يوضح فرق معنوي ملحوظ (P<0.001). وكانت نتائج العلاقة بين التعليم والعنف المجتمعي لغير المتعلمين 11.1٪، والتعليم الابتدائي 27٪، والثانوي 52.4٪، والدراسة الجامعية 9.5٪. كان متوسط مستوى أوكسيديز أحادي الأمين A والسيروتونين في مصل الدم في الفئة العمرية 18–39 سنة (11.3 وحدة دولية / مل، 68.3 نانوجرام / مل) على التوالي، وفي الفئة العمرية 40–65 سنة (13 وحدة دولية / مل، 139نانوجرام / مل)، على التوالي.

1. Introduction

The term "antisocial behavior" is general and encompasses a range of harmful actions, the majority of which endanger another person or violate others' rights [1]. Violence and crime are persistent socioeconomic problems that have negative effects on society. Violence and crime have a severe negative impact on social connections and the established moral order [2]. Aggressive behavior is a significant societal problem, and understanding its contributing factors is crucial to preventing violence. Pathological aggression, including violent and antisocial behaviors, is strongly influenced by genes, particularly the MAOA gene, often known as “the warrior gene.” This gene can produce monoamine oxidase-A, which may be found on the X chromosome [3]. A few instances of aggressive behavior include fighting, bullying, harshly treating others or animals, using weapons, and pressuring someone into having sex. Aggression is viewed as a sign of a mental condition when it is not a reaction to an obvious threat [4]. MAOA has been linked to psychopathology through low-activity variants or hypomorphic mutations associated with antisocial behavior and violent actions. The initial connection between MAOA and pathological aggression was made through the observation of Brunner syndrome [5]. Serotonin, dopamine, and norepinephrine are among the significant neurotransmitters that are broken down by the mitochondrial enzyme MAOA. These neurotransmitters regulate emotions, aggression, and cognition and are strongly associated with psychiatric disorders [6]. MAOA degrades these monoamines via oxidative deamination. Abnormal MAOA enzyme function due to variations in the MAOA gene is often linked to aggressive behavior [7]. The oxidative deamination of biogenic and dietary amines, monoamine hormones, neurotransmitters, and several trace amines like tyramine, tryptamine, and 2-phenylethylamine is catalyzed by monoamine oxidases (MAOs), which are mammalian flavoenzymes [8]. In order to effectively remove hazardous compounds from circulation, monoamine oxidase simultaneously inactivates and solubilizes them [9]. Serotonin is a vital monoamine neurotransmitter that regulates mood, sleep, appetite, and cognition. In the central nervous system (CNS), depression, anxiety, and obsessive-compulsive disorders might be a result of serotonin depletion. Increasing serotonin levels is an essential strategy in treating depression, and this is typically achieved by inhibiting the serotonin transporter, or MAO A. [10]. Serotonin is important and essential for many mental processes, such as memory, learning, pain, and emotions [11]. Serotonin (5-hydroxytryptamine, 5-HT) has a significant role in regulating behavior, and psychopathology has made advances in its biology that are critical for progress in psychopharmacology [12, 13]. Impulsive and aggressive people have low levels of serotonin in their cerebrospinal fluid (CSF), which is a sign of their personality [14]. The monoamine oxidase (MAO) enzyme catalyzes the deamination oxidation reaction to produce “5-hydroxy-3-indolacetaldehyde” (5-HIAAL), which is the primary pathway for serotonin (5-HT) metabolism. The present study

aims to investigate the importance of the MAOA enzyme and serotonin in antisocial behavior. Tryptophan, a basic amino acid, is used to create serotonin. Typically present in foods like nuts, cheese, and red meat, this amino acid must be consumed by the body through the diet [15].

2.Materials and Methods

Study design

The levels of serotonin and total serum MAOA in healthy and prison inmates in Baghdad were examined in this study. A questionnaire was used in the study's design to gather data. Inmates and controls made up the research population. All participants' blood was extracted, and the serum was separated. The serum levels of MAO and serotonin in each sample were measured using the enzyme-linked immunosorbent assay (ELISA) method**.**

Sample collection

Between December 2021 and March 2022, 63 inmates were referred to the inpatient-outpatient clinic at the Iraqi Reform Department health facility, and the 27 controls were chosen from the Units of Healthcare in Baghdad. A questionnaire was taken from people included in the study. It included age, marital status, education level, quality of life, and smoking. All clinical and analytical evaluations were completed. Written informed consent to be a part of the study has been given to each participant. The Department of Biotechnology, College of Science, and University of Baghdad's Ethics Committee accepted the study's protocol on January 29, 2021 (CSEC/0121/001). In the present study, data from commonly used inclusion criteria, such as age 18 and a criminal report, were applied. In both patients and controls, serotonin and total serum levels of MAOA were measured. Blood was drawn from all participants; 3 ml were placed into sterile gel tubes and waited for 10 minutes. To separate the serum, the sample was centrifuged at 3000 rpm for 15 minutes. The serum was then kept at -20 °C until it was analyzed.

Determination of MAOA

ELISA was used to measure the monoamine oxidase (MAO) serum levels in each sample (BioSource Inc., United States) (Catalog Number: MBS700291). This was done according to the manufacturer's instructions. The technique assessed the minimal detectable level of human MAOA; this is extremely sensitive and accurate, generally less than 0.225 IU/mL. A relatively low titer of MAOA in serum was also discovered. The lowest protein concentration that could be distinguished from zero is known as the lower limit of detection (LLD) of the test. It was found that the 20 duplicates of the zero standards' mean O.D. value had three standard deviations added to it.

Determination of Serotonin

The ELISA technique was used to assess the serotonin serum levels in each sample (BioSource Inc., United States) (Catalog Number: MBS494377). Quantitative acylation occurs in serotonin. The format for the following competitive ELISA kit is microtiter plates. The solid phase of the microtiter plate is coated with the antigen. The acylated standards, controls, samples, and solid-phase-bound analytes all look for a certain number of sites where they can bind to antiserum. Once the system has reached equilibrium, washing is used to remove free antigen and free antigen-antiserum complexes. Using TMB as a substrate, an anti-rabbit IgG-peroxidase conjugate finds the antibody attached to the solid phase. At 450 nm, the reaction is observed.

3.Statistical analysis

Statistical Package for the Social Sciences (SPSS), version 26, was used to examine the subjects' data. The data were examined for normality using the quantitative variables (serum MAOA and serotonin levels) and the Shapiro-Wilk and Kolmogorov-Smirnov tests. The area under the curve (AUC) is measured using the receiver operating characteristic curve (ROC), the optimal cutoff value. The significance of differences between medians was determined by the nonparametric Mann-Whitney-U test with a probability value (p-value) of 0.05.

Results:

Distribution of subjects according to age

A total of 90 individuals were all male, including 63 (70%) prisoners with different prison terms and different crimes in different cases and 27 (30%) control groups. The mean ± S.D. age of the participant's cases and controls was 38.2 ± 9.4 and 36.8 ± 7.4 years, respectively. The participants were divided into two age groups: 18–39 and 40–65 years. In these age categories, the prevalence of cases was 44 (69%) and 19, respectively. In contrast, according to Table 1, there were 18 (66%) and 9 (33%) control participants for the same age groups, respectively. The rate of hostile behavior significantly decreased with age, as demonstrated by our findings. Age has an impact on criminal behavior as well. After reaching its peak in late adolescence and the early twenties, the offense rate starts to fall. [16]. People tend to grow more sensible and intelligent if they get married, have kids, and obtain a full-time job [17].

Table 1: Distribution of Subjects According to Age and Age Group

Groups	Case (N=63), %	Controls (N=27)	p-value
Age (mean ± S. D) year	38.2 ± 9.4	36.8 ± 7.4	**<0.05***
Age Group (N, %): 18-39 years 40-65 years	44(69%) 19(31%)	18(66%) 9(33%)	

N: Frequency: %: percentage; S.D; Standard Deviation, * (P<0.05)

Levels of Education for Prisoners

This study showed that the majority of prisoners, according to education level, were not very educated: illiterate 11.1%, primary school 27%, secondary 52.4%, and university 9.5%, as shown in Table 2. This may indicate a potential association between lower education levels and criminal behavior, although further research is needed to confirm this relationship. Because of their high level of knowledge and the fact that prisoner No. 4 was imprisoned for violating military orders rather than a violent crime, the results in this case came close to being under control. In the elementary and middle school grades, children with low academic performance, low commitment to school, and low educational aspirations are at higher risk for child delinquency and violent behavior than are other children [18, 19].

Table 2: Education Level and Criminal Behavior

Education Level	Frequency	Percent %
Illiterate	7	11.1
Primary	17	27.0
Secondary	33	52.4
University	6	9.5
Total:	63	100 %

Effect of MAOA and serotonin in violent antisocial behavior

The serum levels of the MAOA enzyme and serotonin are two crucial factors in the diagnosis of violent behavior in prisoners. Serotonin and total MAOA enzyme concentrations

in the cases' serum are contrasted with those in the controls in Table 3. Serotonin levels in the case group's median blood samples were 79 ng/ml, and their median serum levels of MAOA were 11.5 IU/ml, compared with 19.5 IU/ml in the control group. In contrast, it was 439 ng/ml in the control group. According to these findings, the case group's serotonin levels were considerably lower than those of the control group (P< 0.001). Aggressive and violent individuals were highlighted with low levels of MAO [20]. When MAOA is damaged, large amounts of 5-HT (serotonin), which is crucial for regulating mood and aggression, are created, along with a wide range of phenotypical aberrations that are very similar to the symptoms of Brunner syndrome. It is crucial to consider additional variables that might have affected the outcomes, such as sample size, demographic traits, and environmental variables. Many factors may affect levels of the MAOA enzyme, such as exercise, diet, and stress [21], [22], [23]. Consequently, changes in MAOA activity and a higher risk of developing aggressive behavior could result from the interaction of a genetic predisposition with specific environmental circumstances [24]. Dysregulations in serotonin (5-hydroxytryptamine; 5-HT) neurotransmission appear to be part of the neurobiological basis for aggression [25]. Based on the results of preclinical and clinical research, there may be a strong link between aggressive reactions and problems with 5-HT release, signaling, or turnover [26]. Most evidence shows that aggression is caused by a drop in 5-HT levels. For example, limiting the 5-HT precursor tryptophan in the diet makes it harder for aggressive people to process their emotions and makes them more likely to act out [27, 28]. Overall, these findings suggest that there may be an association between decreased levels of MAOA and serotonin and certain health conditions or violent antisocial behavior.

Table 3: Total MAOA and Serotonin Concentrations in the Serum of Cases and Controls

Groups	No. of subjects	MAOA (IU/ml) Median, (min-max)	Serotonin (ng/ml) Median, (Min-max)
Cases	63	11.5(9.4-23.1) IU/ml	79, (30.30-1459.00) ng/ml
Control	27	19.6 (16.2-27.2) IU/ml	439, (229-1605) ng/ml
	P -value< 0.001 **		

Min: Minimum; mix: Maximum; p-value: probability; No.; Number; MAOA: mono amine oxidase-A IU**;** International Units; ml: Milliliter; ng: nano gram, * (P<0.05), ** (P<0.01)

The study of ROC for the cases

The "Receiver Operator Characteristic" (ROC) curve was analyzed in this study to determine the optimal cut-off value for MAOA (cut off = 16.15) and serotonin (cut off = 220) and showed an excellent AUC (above 0.9) (p<0.001).

(A) (B)

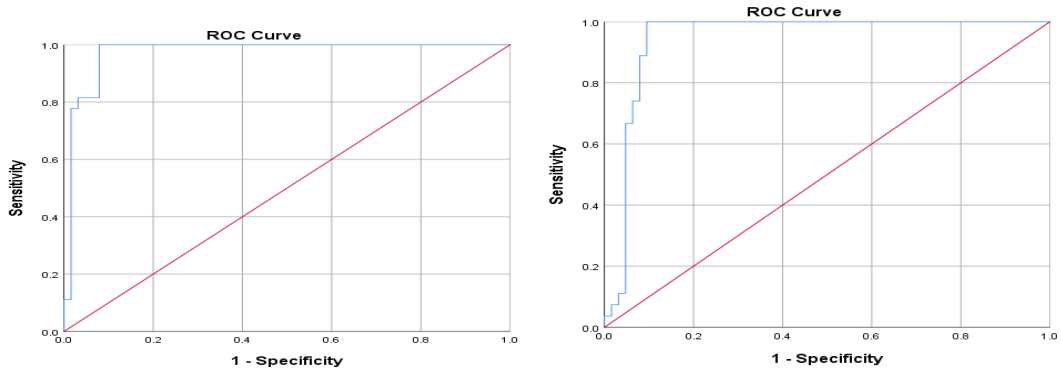

Figure 1: **A**: Receiver Operating Characteristic Curve Analysis of MAOA in Cases Versus Control**B**: Receiver Operating Characteristic Curve Analysis of Serotonin in Cases versus Control

Correlation of Age with Serotonin and MAOA

Tables 4 and 5 illustrate the connections between age groups and the median serum levels of serotonin and MAOA. The median serum level of MAOA in the age group 18–39 years was (11.4 IU/ml), whereas in the age group 40–65 years it was (12.3 IU/ml); similarly, the median serum level of serotonin in the age group 18–39 years was (68.3 ng/ml). Whereas in the age group 40–65 years, it was 134 ng/mL. These findings showed that the case group had considerably less MAOA serotonin than the control group ($P < 0.05$). When compared to the matching controls, the findings revealed a substantial difference between MAOA and serotonin in the age groups (18–39) and (40–65). There may be an association between age and MAOA/serotonin levels, and this association may be related to certain health conditions or violent antisocial behavior. The correlation between the age groups and levels of MAOA and serotonin suggests that the decrease may occur across different age groups of individuals with criminal behavior. MAOA increases with aging [29]. Reports were published in which MAO variations in the human brain during aging were studied using approaches different from the measurement of enzymatic activity using high-resolution enzyme radioautography to quantify MAOA [30].

Table 4: Correlation of MAOA level (IU/mL) with Age Groups of Study

	Patients				Control			
	No.	**Median MAOA IU /ml**	**Min**	**Max**	**No.**	**Median maoa IU /ml**	**Min**	**Max**
Age Group:								
18-39 years	41	11.4	9.4	23.1	18	19.4	16.7	26.2
40-65 years	22	12.3	8.4	18.8	9	19.7	16.2	23.4
p-value	<0.05*							

Min: Minimum; mix: Maximum; p-value: probability; No.; Number; MAOA: mono amine oxidase; IU: international unit. * ($P<0.05$)

Table 5: Correlation of Serotonin Level (ng/ml) with Age Groups of Study

	Patients				Control			
	No.	**Median serotonin ng /ml**	**Min**	**Max**	**No.**	**Median serotonin ng /ml**	**Min**	**Max**
Age Group:								
18-39 years	41	68	30.3	618.3	18	449.5	228	1605
40-65 years	22	134	54.0	1459.0	9	431	298	489
p-value	<0.05*							

Min: Minimum; mix: Maximum; p-value: probability; No.; Number oxidase; ng: nanogram; * ($P<0.05$).

Conclusion:

According to the current study, there appears to be a correlation between low levels of MAOA and serotonin in prisoners and increased violence compared to the control group. The analysis of the ROC, which revealed an excellent AUC, confirmed this prediction. Additionally, there seems to be a relationship between violence, age, and education in the cases compared to the control group.

Recommendation

recommend studying serotonin and MAOA and their relationship to violence in females too.

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