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Effect of Serotonin and Thyroid Stimulating Hormone in Criminal Behavior of Iraqi Males

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By

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Certification

I certify that this reserch entitled **"Effect of Serotonin and Thyroid Stimulating Hormone in Criminal Behavior of Iraqi Males"** was prepared by **Mohammed Ahmed Radhi Assi** under my supervision at the College of Science, University of Babylon, as a partial requirement for the degree of **Higher Diploma in Forensic Evidence.**

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Committee Certification

We, the examining committee, certify that we have read the thesis entitled **"Effect of Serotonin and Thyroid Stimulating Hormone in Criminal Behavior of Iraqi Males"** and examined the student**(Mohammed Ahmed Radhi)** in its contents and that our opinion it is accepted as a thesis for a degree of high diploma in forensic evidences with **excellent** degree.

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DEDICATION

TO WHOM LEARN ME THE

SUCCESS AND PATIENCE...

MY PARENTS...

TO MY FAMILY...

TO EVERYONE SUPPORTED ME...

Mohammed 2021

Acknowledgments

Thanks and praise be to
Allah, and prayer and peace
upon his messenger Mohammed, and his household and best companions.

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Finally my gratitude to all the responsable staff in prisons for their cooperation in achieving this study.

Mohammed 2021

Summary

The aim of the present study was to investigate the effects of serotonin and thyroid stimulating hormone and their relationship with criminal behavior in Iraqi males prisoners and their matched controls. Blood samples were taken from total number of subjects involved in this study was 80 (40 prisoners and 40 healthy control). All prisoners and control were from the same ethnic group (Arabic).

The results showed that the (21-30) age group of criminals prisoners were more frequent 17(42.5%) than control 3(7.5%) followed by age group 31-40 year which was 13(32.5%) compared to control 24(60%), whereas the percentage was 10 (25 %) in 41-50 years group compared to control group 13(32.5%).

When separating the criminals prisoners according to educational level, most of them were had no degree 15(37.5%) or at primary school 15(37.5%) followed by those with secondary school 10(25%) compared to the control group in which who had primary school 16(40%) was more frequent followed by who had university degree 11(27.5%) then secondary school 8(20%) and diploma degree was 5(12.5%) .

According to the residence, it was found that most of them was in urban area 21(52.5%) than in rural area which was 19(47.5%) compared to control group which was 29(72.5%) and 11(27.5%) in urban and rural areas respectively.Moreover, according to marital status, most of criminals prisoners were married 24(60%) while singles were 16(40%) compared to control group in which the married persons were 29(72.5%) and singles was 11(27.5%).

The distribution according to their type of crime recorded that both murders and drug abuse were 20(50%). Also,15(37.5%) of prisoners had previous delinquency while 25(62.5%) without previous delinquency. The distribution according to their duration of imprisonment recorded that 6-10 years were 15 (37.5%) was more frequent

The results showed that the mean of TSH concentration for all criminals prisoners was 2.04± 0.23 µIU/L which nonsignificantly high ($P>0.05$) than control (1.89 ± 0.17 µIU/L) whereas serotonin concentration (78.39±6.77 ng/ml) was significantly elevated ($P\leq0.05$) compared to control (62.73 ± 3.9) ng/ml Further more,the results revealed that serotonin positively correlated with TSH (r=0. 1) but the correlation was non significant.

In conclusion, many reasons contribute to the criminal behavior and serotonin with TSH has impact in the criminal behavior of Iraqi prisoners.

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List of Abbreviation

Abbreviation	Complete Name
WHO	World Health Organization
Da	Dopamine
HPT	hypothalamic-pituitary thyroid
TH	Thyroid hormones
GABA	γ-aminobutyric acid
CNS	central nervous system
HPG	hypothalamic-pituitary-gonadal
OFC	orbitofrontal cortex
PFC	prefrontal cortex
T4	Thyroxin
T3	Triiodothyronine
TSH	thyroid-stimulating hormone
TRH	thyrotropin-releasing hormone
TBG	thyroid-binding globulin
CSF	cerebrospinal fluid
ELISA	enzyme linked immonosorbant assay
APD	antisocial personality disorder

Chapter One
Introduction

1.1 Introduction

Aggressiveness can be defined as the generation of a behavior that aims at causing physical or psychic harm to somebody else (Ferguson & Beaver, 2009). The social inequality, poverty and the environment as the main reasons for the display of an aggressive and criminal behavior (Okami & Shackelford, 2001). Unfortunately, aside from homicides, some forms of violence are part of the day to-day of our society: violence against one's partner, sexual abuse at childhood and adolescence, early involvement with alcohol and drugs, kidnappings, and violence against the elderly (Mari *et al*., 2008).

The World Health Organization (WHO) declared violence a major public health problem. Violence rates, whose main victims are the youth, women and children, have been increasing. The WHO defines violence as "the intentional use of physical force or power, threatened or actual, against oneself, another person, or against a group or community, that either results in or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment or deprivation" (WHO, 2002).

However, the previous research in neurosciences uncovered the biological, i.e. the genetic and neurophysiological mechanisms implicated in aggressive behavior، it became evident that both social and environmental factors are not the only reasons explaining the development of aggressive and anti-social behavior. As a matter of fact, what happens is an interaction between the biological and socio-environmental factors that modulate violent behavior. Several factors are involved in the development of aggressive behavior as well as a combination of these factors may be implicated in the development of aggressive, violent and antisocial behavior (Mendes *et al*., 2009).

There are many neurotransmitters that have been implicated in emotional and crime related behaviour (Glick, 2015). A number of studies indicate that dopamine (DA) and

serotonin systems interact closely at a basic neurophysiological level (Kapur & Remington, 1996; Daw *et al*., 2002) and the impairment of the serotonin system function can lead to dysregulation of the dopamine system (De Simoni *et al*., 1987). These lines of evidence suggest that aggression and its comorbid disorders may come from an underlying neurobiology, specifically serotonin and dopamine interaction in the prefrontal cortex of brain. Other biological factors, such as norepinephrine (Barrett *et al*, 1990) and testosterone may also contribute to aggression (Giammanco *et al*., 2005).

Moreover, various factors cause aggression, which can be related to hormone imbalance T3 and T4, which can act as neurotransmiters are reported to be elevated during aggression. Moreover mental and behavioural disorders possibly occur in individuals with impairment in thyroid hormone balance (Acar, 2018). Disorders of the thyroid gland are frequently associated with severe mental disturbances (Whybrow & Bauer,2000; Whybrow & Bauer,2001). There is intimate association between the thyroid system and behavior and the role of the hypothalamic-pituitary thyroid (HPT) axis in the pathophysiology of mood disorders. Thyroid hormones (TH) have a profound influence on behavior and mood (Bauer *et al*., 2001; Whybrow & Bauer,2001). Furthermore, the thyroid has a modulating impact on the brain serotonin system. Thus it is postulated that one mechanism, through which exogenous thyroid hormones may exert their modulatory effects in affective illness is via an increase in serotonergic neurotransmission, specifically by reducing the sensitivity of serotonin receptor (5-HT1A), and by increasing 5-HT2 receptor sensitivity. Also, the thyroid status impacts the serotonin system in the adult brain and the increasing thyroid hormone levels increase serotonin neurotransmission (Bauer *et al*., 2002).

1.2: The Aim of the Study

The aim of the present study was to investigate the effects of serotonin and thyroid stimulating hormone and their relationship with criminal behavior in Iraqi males prisoners and their matched controls. This aim was achieved by the following objectives-:

1- The information were taken as questionnaire including the age, marital status, ethnicity, duration of imprisonment, residence, previous delinquency (aggression history), educational level, type of crime.
2- Collection of the blood samples from Iraqi prisoners who divided into murders and drug abuse.
3- Measurement of serotonin concentrations was performed for criminals and control groups .
4- Determination of thyroid stimulating hormone (as indicator for thyroid gland function) in the criminals and control groups.
5- Study the correlation between studied parameters.

Chapter Two

Literature Review

2.1: Neurotransmitters and Aggressive Behavior

Neurotransmitters are signaling molecules in the nervous system. Their function as signaling molecules depends on receptors that are specific to each neurotransmitter in the synaptic cleft include serotonin (5-HT), dopamine (DA), γ-aminobutyric acid (GABA),) norepinephrine, and acetylcholine, among many others. These molecules are key factors in a wide range of behaviors. The role of neurotransmitters in aggression was well defined (Mehta &Beer, 2009).

Most neurotransmitters are made within the brain, derived from a variety of different chemical compounds known as the neurotransmitter's precursors usually from an amino acid (protein) and other micronutrients (vitamin and minerals). If the precursor is not available, the brain will be unable to create the neurotransmitter. This will leads that the brain cell will be unable to communicate correctly (Demelash, 2017).

Aggression plays a critical role in the manifestation of violent and criminal behavior and is considered an important psychopathological symptom of several mental disorders including antisocial personality disorders (Linnoila & Virkkunen, 1992; Coccaro & Siever, 2000). In fact, aggression is a key symptom in a numerous psychiatric disorders such as mood disorders and personality disorders (Veenema & Neumann, 2007). Drug abuse, schizophrenia, autism, and bipolar disorder are just a few examples (Soyka, 2011; Voravka, 2013). In humans, aggressive behavior has seemed to exponentially increase in the last few decades. Previous reports showed that at least 700000 people die each year as victims of aggressive assault (Bartolomeos *et al*., 2007). Moreover, aggression is a complex behavioral phenotype and multiple brain systems may contribute to its etiology and its high comorbidity with other disorders (Linnoila & Virkkunen, 1992; Seo & Patrick *et al*., 2008) including depression, suicidal behavior, substance abuse, and suicidality, which suggest that these comorbid disorders have a common biological correlates. This association between impulsive aggression and its comorbid

disorders may result from biological predisposing factors, such as an imbalance among the functions of different neurochemical systems, or dysfunction in activities of executive brain regions (Seo and Patrick *et al*., 2008).

Many neurobiological abnormalities have been reported in patients with violent and criminal behaviour. Strong associations exist between aggressive/violent behaviour and brain dysfunction. Due to the advances in technology, researchers have been able to establish a clear link between abnormalities in brain functioning and the increase of incidences of crime and violence (Reddy *et al*., 2018).

The regulation of aggression by a wide spectrum of neurotransmitters is well known. The most commonly neurotransmitter studied is dopamine because its functionally associated to the regulation of behavior that may affect crime and offending. Dopamine can sometimes enhance aggression and sometimes reduce the impulsivity that might lead to abnormal aggression (Beaver , 2006). Previous studies focuses on the roles played by three neurotransmitters (dopamine, serotonin, and γ-Aminobutyric acid (GABA)) in aggressive behavior and analyzing aggressive behavior (Narvaes & de Almeida, 2014). Furthermore, serotonin has shown both inhibitory and stimulating effects on aggressive behavior, depending on the brain region measured and specifc receptors where it acts. Dopamine can sometimes enhance aggression and sometimes reduce the impulsivity that might lead to abnormal aggression. γ-Aminobutyric acid (GABA) is the main inhibitory neurotransmitter, and its relationship with aggressive behavior is extremely complex and highly associated with serotonin (Narvaes and de Almeida, 2014).

2.2: Serotonin

2.2.1: Structure and functions of Serotonin

Serotonin or 5-hydroxytryptamine (5-HT) is a monoamine neurotransmitter that plays a role in several complex biological functions (David & Gardier, 2016). Its biological function is complex and multifaceted, modulating mood, cognition, reward, learning, memory, and numerous physiological processes such as vomiting

and vasoconstriction (Young , 2007). Serotonin forms from the hydroxylation (i.e., the addition of -OH group) and decarboxylation of the tryptophan amino acid (Figure 2-1). Serotonin induces changes in the cell by its action on the serotonergic receptors, which are coupled to different G proteins mediating intracellular changes (Smith & Smith *et al*., 2020). Also, 5-HT is a key neurotransmitter related to aggressive behavior. Serotonergic neurons originate from raphé nuclei in the brain stem. The axons of serotonergic neurons in raphé nuclei in the midbrain reach almost every structure in the brain. The relationship between serotonin and aggression is extremely complex. Different neural pathways can present different reactions to the same pharmacological manipulation depending on the receptor subtypes that are present in the pathway. There are currently seven known families of 5-HT receptors: 5-HT1, 5-HT2, 5-HT3, 5-HT4, 5HT5, 5-HT6, and 5-HT7 (Celada *et al*., 2013).

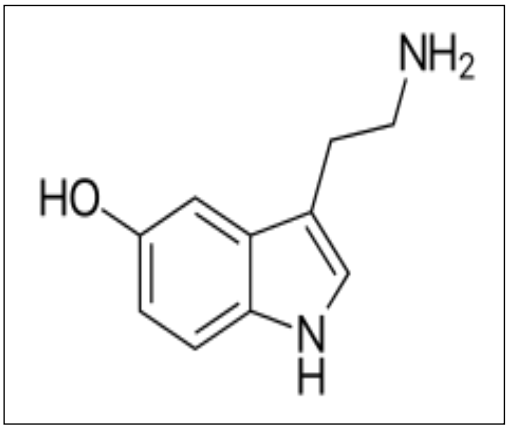

Figure (2-1): Chemical structure of serotonin (Young , 2007).

2.2.2: Serotonin and Criminal Behavior

The main biological risk factors leading to the development of aggressive behavior were genetic (low expression of the monoamine oxidase gene and the serotonin transporter gene, variations in transporter and dopamine receptor genes), exposure to substances during intrauterine development (tobacco, alcohol and cocaine) and nutrition (malnutrition) (Mendes *et al*., 2009). Beitchman *et al*. (2006) evaluated the association of polymorphisms in the transporter gene of serotonin and aggressive behavior at both infancy and adolescence who were genotyped for 5HTTLPR and 5-HTT variable-number-tandem-repeat polymorphisms. The presence of alleles with a low genic expression in the transcription control site in the serotonin transporter gene 5-HTTLPR (S/S, LG/S, Lg/Lg) was strongly associated to a risk twice as large of aggressiveness at infancy compared to individuals with high expression alleles (n = 77, p = 0.049, OR = 2.37، CI = 1.10-5.8). Similar results were shown by Haberstick *et al*.(2006) who concluded that the allele S-5HTTLPR was associated to high levels of aggressive behavior in school-aged children. Other studies have established the same association with aggressiveness at adulthood (Retz *et al*., 2004) thus leading to the conclusion that the presence of low expression alleles of S-5HTTLPR in adults is indeed associated with extreme violence (Mendes *et al*., 2009).

Furthermore, the strong neuronal connections promote the functional modulation of 5-HT over DA activities in the neural network (Kelland & Chiodo, 1996). For example, the 5 HT2 receptors inhibit DA activity, whereas the 5 HT2 receptor antagonists counteract the inhibition of the DA activity (Shi *et al*., 1995). Further, administration the 5-HT2 antagonist results in increased dopamine levels in the frontal cortex of rats, indicating an inhibitory effect of the serotonergic system on frontal dopamine activity (Millan *et al*.,1998). Moreover, there was significant increase in dopamine concentration in Iraqi criminal prisoners (Abdullah, 2019).

In relation to this, dopaminergic hyperactivity may exert an additive effect on proneness to aggressive behavior, that is, secondary to serotonergic dysfunction. Given that the serotonergic system modulates dopaminergic activity, hyperactivity in the dopamine system in aggressive individuals may be attributed to disinhibition of the dopamine activity from deficient serotonergic function (Seo and Patrick *et al*., 2008) whereas another previous study revealed heightened serotonin activity through the elevation of serotonin precursor levels, serotonin reuptake inhibition, or 5-HT1A receptor agonism is known to reduce aggressive behavior (Nelson & Trainor, 2007). The receptors 5-HT1B are mostly located presynaptically on serotonergic neuron terminals in the raphé nuclei to modulate the release of serotonin (Suzuki *et al*., 2010). The activation of 5-HT1B receptors inhibits aggressive behavior, independent of serotonin levels. Presumably, the behavioral effects regulated by 5-HT1B receptors reflect the modulation of systems associated with other neurotransmitters (Nelson &Trainor, 2007).

Previous study have demonstrated that 5-HT1A receptor agonists potently inhibit aggressive behavior suggests that the inhibition of serotonergic neurons in the raphé nuclei through these autoreceptors may be a marker in individuals with high levels of aggression. Therefore, pharmacological manipulations that target these autoreceptors could be used to lower aggressive behavior. Data that showed that serotonin inhibits aggression(Caramaschi *et al*., 2007).

One particularly interesting fnding is that serotonin not only regulates the levels of aggressive behavior but also regulates the reaction to aggressive behavior (Narvaes and de Almeida, 2014). The hypothalamic-pituitary-gonadal (HPG) axis regulates testosterone levels in the organism (Mehta & Josephs, 2010). The significant increasing in the concentration of testosterone in Iraqi criminal prisoners in comparison with the control group was recorded (Al Shwaliy, 2019). High testosterone levels can decrease the activity of the medial region of the orbitofrontal cortex (OFC) within the prefrontal cortex (PFC) and stimulate aggressive behavior (Mehta &Beer, 2009). One of the possible mechanisms by

which testosterone can reduce the activity of the OFC is by regulating serotonin. Androgens have been previously shown to downregulate serotonin receptor mRNA expression and serotonin turnover in the medial PFC (mPFC) (Ambar & Chiavegatto, 2009). Previous data also support the involvement of serotonin in defensive aggression(Crockett *et al*., 2008).

In fact, the reduction of defensive aggression levels over generations leads to abnormal serotonin metabolism (Popova, 2009; Olivier, 2004)

2.3: Thyroid Hormones and Thyroid Stimulating Hormone

The thyroid gland is an endocrine gland that synthesizes and releases thyroxin(T4) and its vigorous derived triiodothyronine (T3), through the stimulation of pituitary thyrotropin or thyroid-stimulating hormone (TSH) which in turn lie under the control of hypothalamic thyrotropin-releasing hormone (TRH) (Kopp, 2005). The regulation of thyroid function depends on regular function of the hypothalamic-pituitary-thyroid axis(through a negative feedback loop), T3 and T4have an inhibitory action on both TRH and TSH secretion (Annika *et al*., 2014) and serum thyrotropin has a high sensitivity to small changes in the concentrations of thyroid hormone (Santisteban, 2005). Thyrotropin or thyroid stimulating hormone (TSH) is the main sensitive and valuable test for thyroid function (Baskin *et al*., 2002**)**

Serum thyrotropin level is a sensitive indicator of thyroid function. High and low TSH concentration refers to hypo and hyper function of the thyroid gland, respectively(Annika *et al*.,2014 ; Alves and Manoel , 2017). T3 is the active form of Thyroid Hormone (TH) and has a shorter half-life one day in the circulation compared with T4 which is 7 days, in the body T3 results from deiodination of T4 and the majority of circulating TH bounds to proteins of plasma, mainly thyroid-binding globulin (TBG) (Woeber . 2005) .Small changes in the function of thyroid gland may be vital for the body mass index and obesity incidence in the general

population (Sanyal and Raychaudhuri, 2016; Al-Musa, 2017). Thyroid hormones influence on growth, development, metabolism bone and physiology of heart (Damiano *et al*., 2017). Dysfunction of thyroid gland can lead to hyperthyroidism and hypothyroidism (Pedro *et al*., 2011; Alves and Manoel, 2017).

2.3.2: Relationships between Thyroid Hormones and Criminal Behavior

Many studies aiming to clarify and control the biological basis of aggression. Thyroid hormones have been indicated to play a role in the development of aggression. The mean score of free T3 level in the criminal antisocial personality disorder (APD) group was found to be significantly higher than that in the noncriminal APD group. APD subjects with higher free T3 levels also had higher aggression scores (Evrensel *et al*., 2016).

Aggression is among the symptoms of hyperthyroidism (Brand *et al*., 2013). There are few studies that indicate a correlation between serum thyroid hormone levels and aggression and tendency to commit a crime. The incidence of crime in individuals with high serum T3 levels is 3.8 times greater than that in those swith normal erum T3 levels (Eklund *et al*., 2005). Testosterone, cortisol، and T4 levels were found to be significantly high in individuals exhibiting antisocial behavior (Mazur *et al*., 1995).

Previous study investigate the relationship between aggression and serum thyroid hormone levels in patients with APD. T3 levels were significantly associated with criminality. Juvenile delinquents who displayed persistent criminal behavior were found to have higher mean T3 levels than juvenile delinquents who did not display criminality in adulthood and non-criminal controls. Former juvenile delinquents with T3 levels above the mean level found in the controls were registered for criminality 3.8 times more often than juvenile delinquents with T, levels below the mean level found in the control group. The results are discussed in terms of elevated T3 levels representing a compensatory or stress phenomenon for low social adaptive ability of individuals who display persistent criminal behavior (Alm *et al*., 1996).

In addition, the relation between thyroid function and depression has long been recognized. Patients with thyroid disorders are more prone to develop depressive symptoms and conversely depression may be accompanied by various subtle thyroid abnormalities. Traditionally, the most commonly documented abnormalities are elevated T4 levels, low T3, elevated T3, a blunted TSH response to TRH, positive antithyroid antibodies, and elevated CSF TRH concentrations. While patients with hypothyroidism commonly manifest features of depression, hyperthyroidism presents with a wider spectrum of neuropsychiatric symptoms including both depression and anxiety (Hage and Azar, 2012).

ChapterThree

Materials and Methods

3: Materials and Methods

3.1: Kits

The kits that used in the current study are listed in the Table 3-1. The enzyme linked immonosorbant assay (ELISA) technique was used for estimation of serotonin and TSH.

Table (3-1): Kits used in the present study.

Kit	Company name
Serotonin	IBL International -Germany
TSH	SD Biosensor- Korea

3.2: Study design

The study subjects comprised 40 prisoners with age ranged from (20-50) years and the age-matched group control group comprised 40 apparently healthy individuals with age ranged from (20-50) years. All prisoners selected from Iraqi prisons (Babylon&Alnasiriyah) Prisons. Samples collection was performed under appropriate ethical guidelines. A permission was taken from all subjects of control group after they were told about the aim and advantages of this study. All prisoners and control were from the same ethnic group (Arabic).

The prisoners were asked to provide informations as questionnaire taken including their age, marital status, ethnicity, occupation, duration of imprisonment,

residence, previous delinquency (aggression history), educational level, accusation type. The experimental design was shown in Figure 3-1.

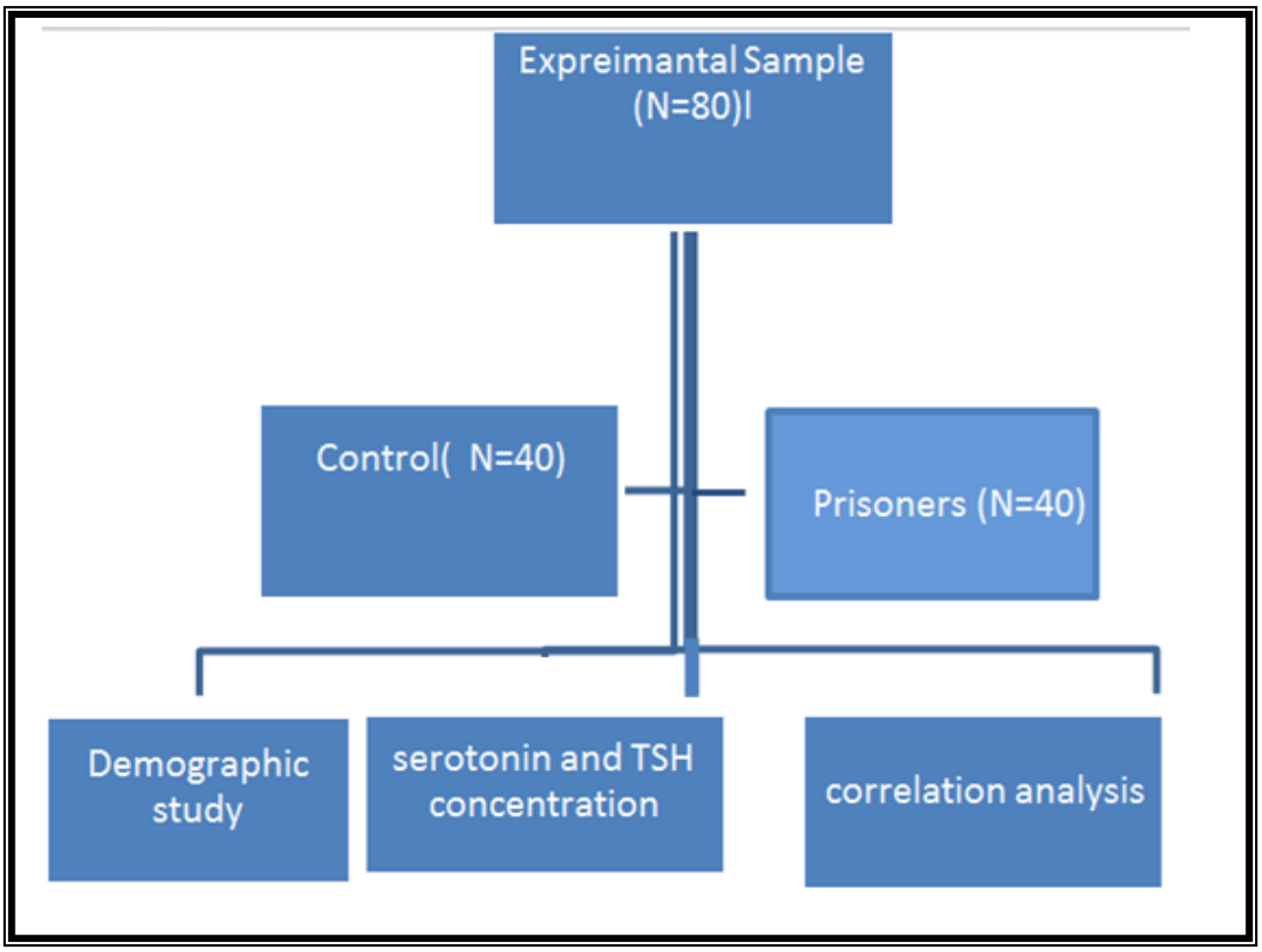

Figure (3-1): Experimental design.

3.3: Blood sampling

Five ml of blood were obtained from each each prisoners and control groups by vein puncture by vein puncture and the pushed slowly into disposable tubes containing separating gel. Then, blood in the gel containing tubes was allowed to clot at room temperature for (30) minutes and then centrifuged at 2000×g for approximately (15) minutes then the sera were obtained and stored at (-20˚C) until analyses.

3.4: Measurement of serum serotonin concentration

The IBL International laboratory kit components was used to detect human serotonin concentration in this study by the enzyme linked immonosorbant assay (ELISA) technique.

3.4.1: Test Principle

The sample preparation (derivatization of serotonin to N-acylserotonin) is part of the sample dilution and is achieved by incubation of the respective sample with the Acylation Reagent.

The assay procedure follows the basic principle of competitive ELISA whereby there is competition between a biotinylated and a non-biotinylated antigen for a fixed number of antibody binding sites. The amount of biotinylated antigen bound to the antibody is inversely proportional to the analyte concentration of the sample. When the system is in equilibrium, the free biotinylated antigen is removed by a washing step and the antibody bound biotinylated antigen is determined by use of streptavidine alkaline phosphatase as marker and p-nitrophenyl phosphate as substrate.

3.4.2: Test Procedure

1. Fifty (50) µL had been pipetted of each Standard, acylated Control and acylated sample into the respective wells of the Microtiter Plate.
2. Fifty (50) µL had been pipetted of Serotonin Biotin into each well.
3. Fifty (50) µL had been pipetted of Serotonin Antiserum into each well.
4. The plate was cover with adhesive foil and incubated 90 min at RT (18-25 °C) on an orbital shaker (500 rpm).
5. The adhesive foil was removed and the incubation solution was discarded. The plate 3 x was wash with 250 µL of diluted Wash Buffer with removing excess solution by tapping the inverted plate on a paper towel.
6. The freshly prepared Enzyme Conjugate (150 µL) into each well.

7. The plate was cover with adhesive foil with Incubation 60 min at RT (18-25 °C) on an orbital shaker (500 rpm).

8. The adhesive foil was removed with discarding incubation solution and wash plate 3 x with 250 µL of diluted Wash Buffer. The excess solution was removed by tapping the inverted plate on a paper towel.

10. The PNPP Substrate Solution (200 µL) was added into each well.

11. Incubation was carried out 60 min at RT (18-25 °C) on an orbital shaker (500 rpm).

12. The substrate was stopped reaction by adding 50 µL of PNPP Stop Solution into each well. Briefly mix contents by gently shaking the plate.

13. The optical density was measured with a photometer at 405 nm within 60 min after pipetting of the Stop Solution.

3.5: Determination of Thyroid Stimulating Hormone(TSH)

3.5.1: Principle:

The assay principle is a one-step enzyme immunoassay sandwish method with a final fluorescent detection (ELFA). The solid phase Receptacle (SPR) which contain anti-TSH and serves as the solid phase as well as the pipetting device for the assay. Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent strips. All of the assay steps are performed automatically

by the instrument. The reaction medium is cycled in and out of the SPR several times. The sample is transferred into the well containing anti-TSH antibody labeled with alkaline phosphatase (conjugate) .The sample/conjugate mixture is cycled in and out of the SPR. The antigen binds to antibodies coated on SPR and to the conjugate forming a sandwich. Unpound components are eliminated during the washing steps. During the final detection step, the substrate (4- methyl-umbelliferyl phosphate) is cycled in and out of the SPR. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-Methyl-umbelliferone) the fluorescence of which is measured at 450 nm . The intensity of the fluorescence is proportional to the concentration of antigen present in the sample. At the end of the assay, the results are automatically calculated by the instrument in relation to the calibration curve stored in memory, and then printed out.

3.5.2: Procedure:

1- The required reagents were removed from the refrigerator and leave it at room temperature for at least 30 minutes.

2- A mount of 200 µL of was taken from each calibrator, control and samples and mix them.

3- The TSH SPRs and TSH strips were insert into the instrument.

4-Then all assay steps were performed automatically in the instrument.

5- The SPRs and strips were removed from the instrument and dispose them into appropriate recipient.

6- When the assay complete, TSH results were calculated automatically by the instrument.

3.6: Statistical analysis

Statistical analysis was carried out by using SPSS version (20). Categorical variables were presented as frequencies and percentages. Continuous variables were presented as Means ± SE. Student's t-test was used for comparison of means between the study groups. Pearson's linear correlation coefficient (r) was used to find correlation between two continuous variables. A p-value of ≤ 0.05 was considered as significant.

Chapter Four
Result

4. Results

4.1: Distribution of Study Groups by Socio-Demographic Characteristics

In this study, the distribution of Iraqi prisoners compared with control groups according to socio-demographic characteristics was showed in Table 4-1. The 21-30 age group of criminals prisoners were more frequent 17(42.5%) than control 3(7.5%) followed by age group 31-40 year which was 13(32.5%) compared to control 24(60%), whereas the percentage was 10 (25 %) in 41-50 years group compared to control group 13(32.5%).

When separating the criminals prisoners according to educational level, most of them were had no degree 15(37.5%) or at primary school 15(37.5%) followed by those with secondary school 10(25%) compared to the control group in which who had primary school 16(40%) was more frequent followed by who had university degree 11(27.5%) then secondary school 8(20%) and diploma degree was 5(12.5%) .

According to the residence, it was found that most of them was in urban area 21(52.5%) than in rural area which was 19(47.5%) compared to control group which was 29(72.5%) and 11(27.5%) in urban and rural areas respectively.

Moreover, according to marital status, most of criminals prisoners were married 24(60%) while singles were 16(40%) compared to control group in which the married persons were 29(72.5%) and singles was 11(27.5%).

Table (4-1): The demographic characteristics of study groups.

Age group	control	prisoners
21- 30	3(7.5%)	17(42.5%)
31- 40	24(60%)	13(32.5%)
41- 50	13(32.5%)	10 (25 %)
Total	40(100%)	40(100%)
Educational level		
No degree	0	15(37.5%)
Primary school	16(40%)	15(37.5%)
Secondary school	8(20%)	10(25%)
Diploma	5(12.5%)	0
University	11(27.5%)	0
Total	40(100%)	40(100%) %
Residence		
Urban	29(72.5%)	21(52.5%)
Rural	11(27.5%)	19(47.5%)
Total	40(100%)	40(100%)
Marital status		
Married	29(72.5%)	24(60%)
Single	11(27.5%)	16(40%)
Total	40(100%)	40(100%)

4.

The distribution according to their type of crime recorded that both murders and drug abuse were 20(50%).

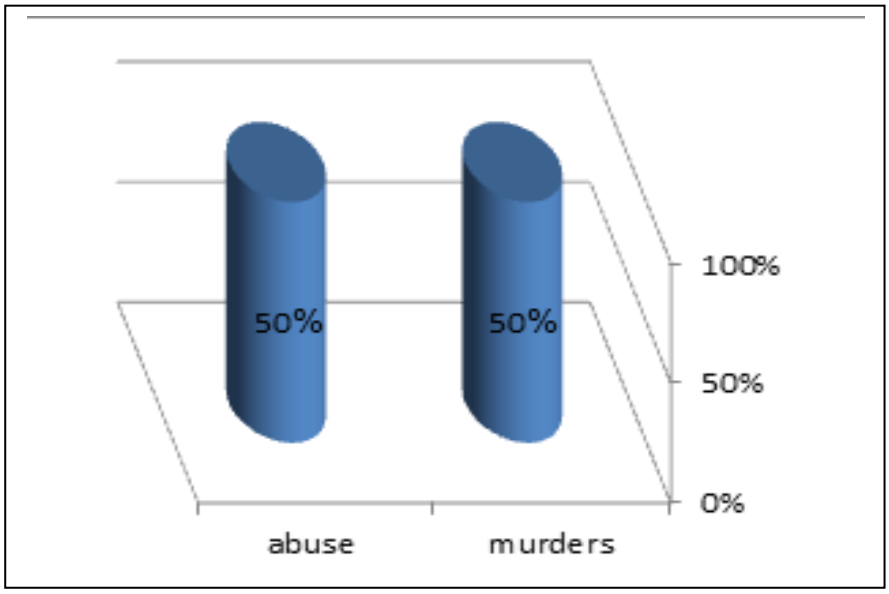

Figure (4-1): Distribution of criminals prisoners according to Type of crime.

4.3: Distribution of criminals prisoners according to previous delinquency and duration of imprisonment.

Figure (4-2) revealed that 15(37.5%) of prisoners had previous delinquency while 25(62.5%) without previous delinquency. The distribution according to their duration of imprisonment recorded that 1-5 years were 10(25%), 6-10 years were 20 (33.3%),11-15 years were 11(27.5%) and for death was 4(10%) as shown in Figure (4-3).

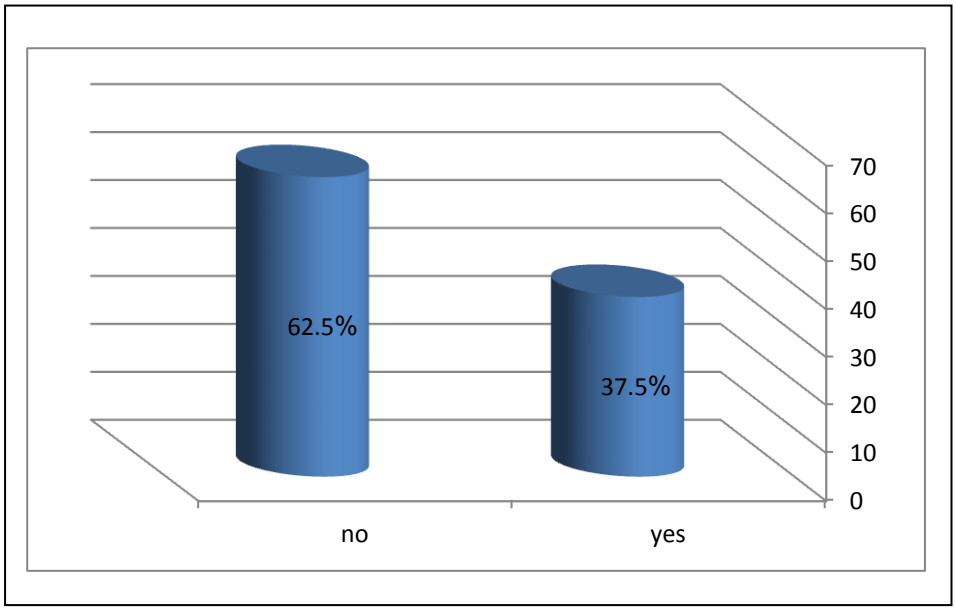

Figure (4-2): Distribution of criminals prisoners according to previous delinquency.

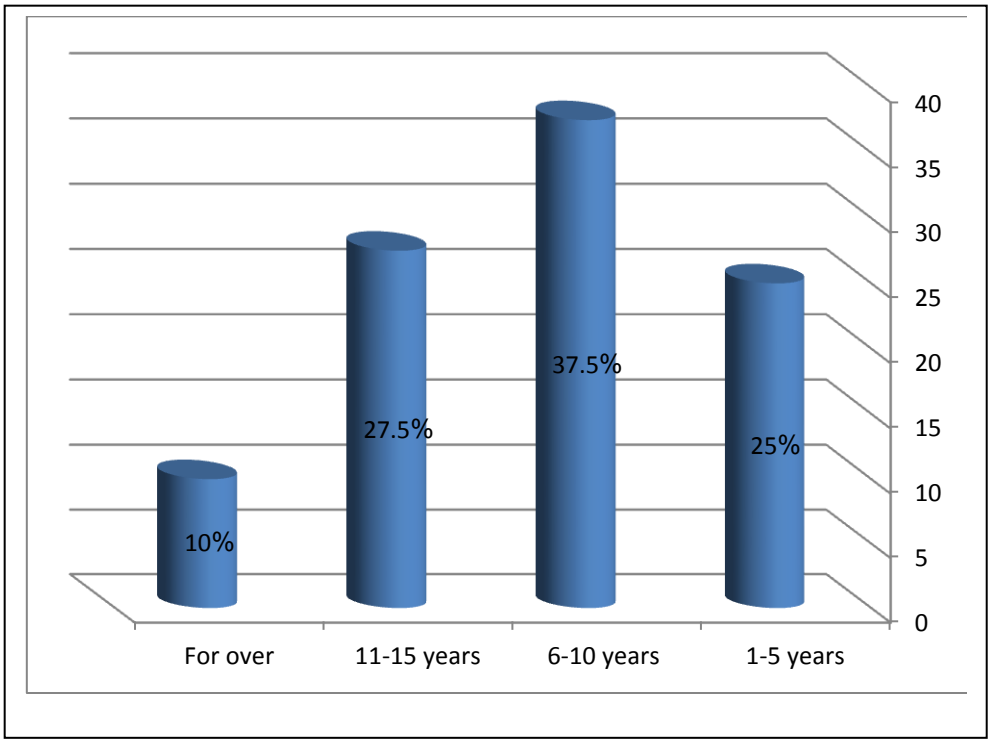

Figure (4-3): Distribution of criminals prisoners according to duration of imprisonment.

4.4: Mean Differences of TSH and Serotonin Concentration Between Study Groups

The results in Table (4-2) showed that the mean of TSH concentration for all criminals prisoners was 2.04± 0.23 µIU/L which nonsignificantly high (P<0.05) than control (1.89 ± 0.17 µIU/L) whereas serotonin concentration (78.39±6.77 ng/ml) was significantly elevated (P≤0.05) compared to control (62.73 ± 3.9 ng/ml).

Table (4-2): Mean differences of TSH and serotonin concentration between criminals prisoners and control groups.

Group	Control Mean ± SE	Prisoners Mean ± SE	P-value*
TSH (µIU/L)	1.89 ± 0.17	2.04± 0.23	0.6
Serotonin (ng/ml)	62.73 ± 3.9	78.39±6.77	**0.04**

***P-value ≤ 0.05 was significant**

When separating criminals prisoners according type of crime and comparing TSH and serotonin concentrations between them according type of crime, the statistical analysis revealed no significant differences between them (P>0.05) as shown in Table (4-3).

Table (4-3): Mean differences of TSH and Serotonin between subgroup of prisoners according to type of crime.

Subgroup of prisoners	Murders Mean ± SE	Drug abuse Mean ± SE	P-value*
TSH (µIU/L)	2.17 ± 0.36	1.91 ± 0.29	0.58
Serotonin (ng/ml)	88.55 ± 10.7	68.23 ± 7.97	0.13

4-5: The correlation of serotonin with TSH in the study group

The results revealed that serotonin positively correlated with TSH (r=0. 1) but the correlation was non significant as shown in figure 4-4

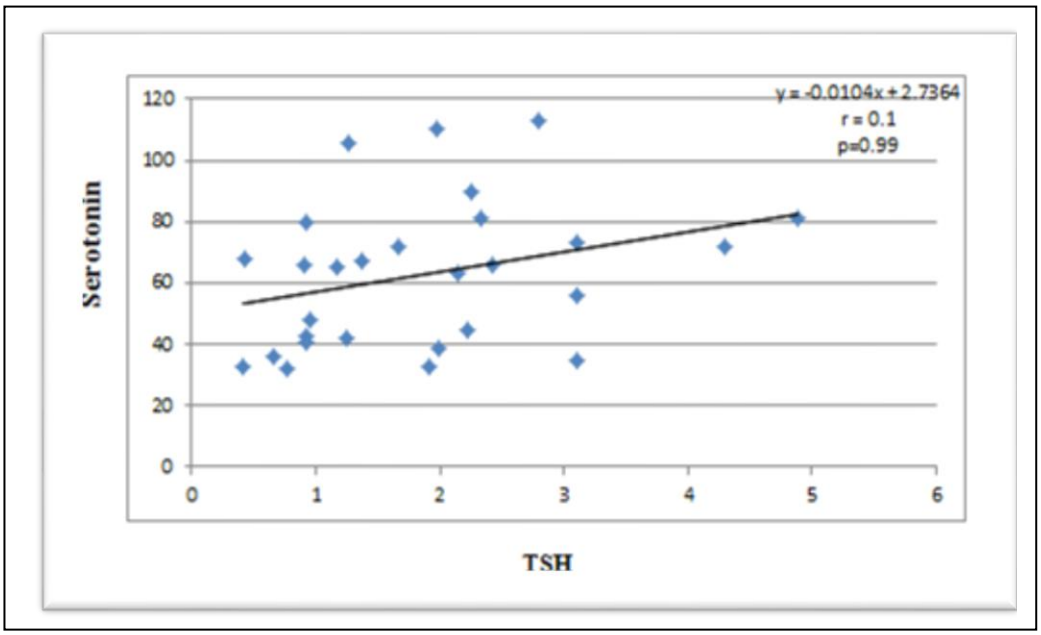

Figure (4-4):The correlation of serotonin with TSH was positively non significant correlation.

Chapter Five
Discussion

5. Discussion

5.1: Distribution of Study Groups by Socio-Demographic Characteristics

In the current study, some of the demographical characteristics were assessed. The age group(21-30) years of criminals prisoners were more frequent 17(42.5%) followed by age group 31-40 which was 13(32.5%) then 13(32.5%) in 41-50 years.

Social statisticians identified a strong relationship between age and crime. The official crime rates rise in adolescence to a peak in the late teenage years and then decline rapidly through adulthood (Steffensmeier *et al*., 1989). Blumstein and colleagues (1988) referred to the initiation of criminal behavior, and have focused on age of onset as an important element of the criminal career. In particular, research has examined whether individuals who initiate their offending early in life are more likely to become long-term or high-rate offenders.

The current results did not in agreement with previous report which demonstrated that criminal activity peaks at age 17year and then gradually declines. However, criminologists have long observed a strong correlation between age and crime. It is necessary to include sociological, psychological, and environmental elements into the understanding of the age and crime relationship (Corneliu *et al*., 2017). Finally, it is a truism that age is one of the strongest factors associates with criminal behavior. In fact, some have claimed that age-crime is invariant, or universal across groups, societies, times. Also, age has a direct effect on crime and on other social factors proposed to explain crime (Hirschi & Gottfredson, 1983), and that this invariance signals that age-crime relationship is strongly biologically

determined (Kanazawa & Still, 2000). Age is confound in regard to changing response and actual levels of hormones (Farrington et al., 2012).

According to the residence, it was found that the percentage of them more frequent in urban area 21(52.5%) than in rural area that may be due to a powerful relationship between residing in a different environment and participating in criminal acts (McCord *et al*., 2001).

According to educational level of the criminals prisoners, most of them were had no degree 15(37.5%) or at primary school 15(37.5%) followed by those with secondary school 10(25%) but decrease in higher educational level. Moreover, according to marital status, most of criminals prisoners were married 24(60%) while singles were 16(40%). This result didn't agree with result of Hirschi and Gottfredson (1983) who suggested that an apparent relationship between marriage and reduced offending is spurious, in other words, this relationship appears only because individuals get married and begin to age out of crime at the same time.

According to aggression history, the Figure (4-2) revealed that 15(37.5%) of prisoners had previous delinquency while 25(62.5%) without previous delinquency. Hahn and colleagues (2007) noted that the problems at school can lead to delinquency and children with low academic performance, low obligation to school, and low educational aims during the primary and secondary school grades are at higher risk for child delinquency than other children. Sampson and Laub (2003) identify graduating from high school or college, serving in the military, getting married, or having children as turning points in life that directly alter one's trajectory. Further, these turning points can result in a trajectory away from criminality as crime is often not conducive to the achievement of each of these turning points.

Moreover, aggression has been linked with depression as well as violent acts (Mammen *et al*., 2002). Individuals who have exhibited suicidal behavior in the past demonstrate more impulsive and aggressive traits (Carballo *et al*., 2005). More specifically, violent suicidal behavior has been linked to elevated levels of impulsivity and lifetime aggression (Dumais *et al*., 2005).

The main environmental factors were child abuse, poverty, crime and antisocial behavior at childhood. The interaction between biological and environmental factors can be catalyzed by a hostile environment, thus increasing the risk for the development of aggressive behavior (Mendes *et al*., 2009).

5.2: Serotonin concentration

The results revealed a significant increasing in the mean of serotonin concentration in prisoners compared to control groups (Table 4-2). Also, the mean of serotonin concentration had nonsignificant differences between prisoners subgroups when divided according to type of crime as shown in table (4-3).

This result may due to that neurotransmitters molecules which are key factors in a wide range of behaviors. Both neurotransmitters serotonin and dopamine are involved not only in aggressive behavior but also in coping with stress. Both pleasant and stressful events activate the mesocorticolimbic dopamine system (Miczek *et al*., 2004).

The results of current study didn't agree with previous study showing a negative correlation between serum serotonin concentration and aggressive behavior in a variety of animal species that show impulsive aggression (Amat *et al*., 2010).

Beitchman *et al*. (2006) evaluated the association of polymorphisms in the transporter gene of serotonin and aggressive behavior at both infancy and adolescence. The sample was comprised of 82 individuals aged between 5 and 15 years who were genotyped for 5HTTLPR (n = 77) and 5HTT variable-number-tandem-repeat polymorphisms (n=78). The presence of alleles with a low genic expression in the transcription control site in the serotonin transporter gene 5-HTTLPR (S/S, LG/S, Lg/Lg) was strongly associated to a risk twice as large of

aggressiveness at infancy compared to individuals with high expression alleles (n = 77, p = 0.049, OR = 2.37, CI = 1.10-5.8). Similar results were shown by Haberstick *et al.* (2006) who conducted that the allele S-5HTTLPR was associated to high levels of aggressive behavior in school-aged children (p=0.0779). Other studies have established the same association with aggressiveness at adulthood (Retz *et al*., 2004) thus leading to the conclusion that the presence of low expression alleles in adults is indeed associated with extreme violence (Mendes *et al*., 2009).

The relationship between serotonin hypofunction and impulsive aggression is a consistent finding in clinical neuroscience. In relation to this, dopaminergic hyperactivity may exert an additive effect on proneness to aggressive behavior, that is, secondary to serotonergic dysfunction. Given that the serotonergic system modulates dopaminergic activity, hyperactivity in the dopamine system in aggressive individuals may be attributed to disinhibition of the dopamine activity from deficient serotonergic function (Seo and Patrick, 2008).

5.3: Thyroid hormone and thyroid stimulating hormone

The results revealed non significant increasing in the mean of TSH concentration in prisoners compared to control groups (Table 4-2). Many studies aiming to clarify and control the biological basis of aggression. Thyroid hormones have been indicated to play a role in the development of aggression. The mean score of free T3 level in the criminal antisocial personality disorder (APD) group was found to be significantly higher than that in the noncriminal APD group. APD subjects with higher free T3 levels also had higher aggression scores (Evrensel *et al*., 2016).The crimes were 3.8 times more frequent in former juvenile delinquents with high T3 levels than in those with low T3 levels. The mean TSH levels did not differ between crime groups. Furthermore, almost all of prisoners subjects were heavy smokers, in contrast to the control subjects, 50% or more of whom did not consume nicotine at all, and relatively few were heavy smokers. Cigarette smoking is reported to cause subtle changes in tests of thyroid function. With discontinuation of smoking there was a small increase in TSH but no change in T3 levels. Heavy smokers

displayed lower tetra- and triiodothyronine levels than light smokers and control subjects. In patients with Grave's disease, no effect of smoking on thyroid hormones could be detected. Thus differences in the mean levels of the thyroid hormones between the present groups were probably not caused by differences in nicotine consumption (Alm *et al*., 1996).

Elevation of T3 levels has been observed among young, serious-crime recidivists and in the older, moderately criminally loaded males, who were no longer engaging in criminal behaviour, and almost all of whom were apparently functioning within socially accepted boundaries of behavior at the time of the investigation. T3 levels appear to differ between subjects with deviant/criminal behaviour and subjects with normal social behavior as well as between subjects exposed to extremely stressful psychotraumatic events. Thus it might be assumed that the experience of complete powerlessness as a small child, or exposure to combat in war, is a characteristic shared by criminals and combat veterans.

During acute stress, T3 levels may change very rapidly. Generalized resistance to thyroid hormones should be borne in mind as a possible reason for elevated T3 levels. This might be over-represented among offenders, since it is associated with attention deficit hyperactivity disorder, which is a risk factor for criminal behavior. However, in most of the subjects with this disturbance there is a general elevation of the levels of all hormones in the HPT axis.

Criminality and psychopathy as related to thyroid activity in former juvenile delinquents. T3 levels were significantly associated with criminality but not with psychopathy-related personality traits. TSH levels were not related to any of these variables. Juvenile delinquents who displayed persistent criminal behaviour were found to have higher mean T3 levels than juvenile delinquents who did not display criminality in adulthood and non-criminal controls. Former juvenile delinquents with T3 levels above the mean level in the controls were registered for criminality 3.8 times more often than juvenile delinquents with T3 levels below the mean level found in the control group (Alm *et al*., 1996; Eklund *et al*., 2005).

The mutations in the thyroid receptor beta-gene characterized by reduced responsiveness of peripheral and pituitary tissues to the action of thyroid hormone may `associated with attention deficit hyperactivity disorder which is found to be a risk factor in the development of criminal behavior. In sons of familial alcoholics, TRH stimulation tests have shown significantly higher basal and peak levels of TSH than those found in control boys (Hauserp *et al*., 1993).

The previous study assess if high T3, high T4, and low TSH hormones could have an effect on aggression-related crime tendency. Hence, the association of thyroid hormone levels, pulse rate, TSH, T3/T4 ratio and presence of toxic goitre with crime type in prisoners (Acar, 2018).

Significantly more frequent substance-alcohol abuse, self-mutilation, tattoos, and suicide attempts as well as significantly lower levels of education were found in the violent offenders group. The free T4 and cortisol levels of the case group were found to be significantly higher than those of the control group, whereas the free T3 level was lower (Eklund *et al*., 2005).

5.4: Correlation between serotonin and TSH

In experimentally-induced hypothyroid states the 5-HT1A (presynaptic) receptor density in the brainstem and midbrain was not altered. In contrast, examined animals after thyroidectomy, which resulted in an elevated serotonin turnover rate; in these animals, T3 replacement resulted in a significant decrease in the 5-HIAA/5-HT ratio in the brainstem (Henley et al., 1997). Also, the receptors studies indicate that thyroid hormone application may increase cortical 5-HT2 receptor sensitivity. Cortical 5-HT2 receptor densities were only increased after prolonged treatment with relatively high doses of thyroid hormone in thyroidectomized rats. Serotonin-HPT system interaction in patients with major depression. The interaction of the 5-HT system and thyroid axis function was investigated in patients with major depression. In summary, several lines of evidence indicate that an experimentally-induced hypothyroid state in adult

rodents is associated with decreasing in cortical 5-HT serotonin concentrations and 5-HT2A receptor density (Bauer *et al*., 2002).

This interaction of thyroid hormones with the serotonin system is probably only one of the mechanisms through which thyroid hormones may have modulatory effects in mood disorders. Thyroid hormones interact with a broad range of neurotransmitter systems thought to be involved in the regulation of mood including post-receptor and signal transducing processes, as well as gene regulatory mechanisms. In addition to the important role of the serotonin system in the pathogenesis of depression, the serotonin system may be involved in the mood modulating effects of thyroid hormones among patients with affective disorders (Bauer *et al*., 2002).

Conclusion

1- By measuring serotonin concentration, the significant increase in its concentration in Iraqi criminal prisoners reflect its role in their criminal behavior.

2- By measuring TSH, although there was an non significant increase in the its concentration, but this result give indicator to the variation in the pituitary-thyroid-axis in Iraqi criminal prisoners.

3- There were many reasons contribute to the criminal behavior including biological and environmental factors.

Recommendation

1- To further understand the neurobiological bases of aggression, future researches should investigate the nature of interactions of between serotonin with another neurotransmitters in individuals exhibiting aggression behavior .

2- Measurement of another neurotransmitters in the Iraqi criminals.

3- Measurement of serotonin and TSH in the Iraqi criminal women.

4- Further studies that investigates levels of another hormones related with aggressive and violence behavior.

5- Re-examine the relationship between serotonin and TSH with criminal behavior in a larger sample of criminals.

6- Further investigation to assessment of some gene polymorphism and their impact on violence behavior in Iraqi prisoners.

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