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A Comparative Analysis of Serum Levels of Serotonin, Testosterone and Cortisol in Normal and Aggressive Individuals

BAKHTIAR EBRAHIMIRAD* and GHOLAMALI JELODR

[1]Department of Physiology, Faculty of Veterinary, University of Shiraz, Shiraz, Iran.
*Corresponding Author: Bakhtiar.ebrahimi@gmail.com

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ABSTRACT

Based on biological views, behavioral changes are associated with the amount of neurotransmitters and hormones. In this regard, the current article intends to perform a comparative analysis of the amount of the hormones including serotonin, testosterone, and cortisol in normal and aggressive subjects. Therefore, 70 patients (age range 20 to 40 years) were studied in two groups of aggressive and normal that none of them had the history of addiction, cardiovascular and intestinal diseases. To examine aggressive behavior, two methods including Arnold H. Buss and Mark Perry Aggression Questionnaires and also interview technique were utilized. The aggressive people were selected, in collaboration with a psychiatrist, among incarcerated people and also those referred to hospital ICU who mostly suffered from non-penetrating and penetrating trauma following injuries and clashes. To choose normal people, a questionnaire was distributed among all the people of all strata of society, and eventually after a review of the questionnaire, two groups of normal and aggressive subjects were selected. Blood samples were taken from all persons and the amount of serotonin, testosterone, and cortisol were measured by ELISA. Then, the data obtained were compared using stastical t-tests of the two independent groups and Pearson's correlation (Software SPSS 20). The results showed that there exists a significant difference between the mean levels of serotonin, testosterone and cortisol in the normal and aggressive subjects, and the in the aggressive subjects, a drop in serotonin, an increase in testosterone and also a reduction in cortisol could be observed in comparison to the normal subjects.

Key words: Aggressiveness; Hormone; Serotonin, Cortisol, Testosterone

INTRODUCTION

In line with the development of industry and science and transformation of human life, human relationships have become more complex than ever before. In this regard, a lot of psychological problems in human societies have been occurred which this situation is indicative of necessity to perform an extensive and careful review of psychological issues such as aggression. So that today dealing with the issue of aggression is not limited to psychological books and it has been broadly analyzed in other scientific fields such as psychology, psychiatry, physiology, psychopathology, social psychology and even criminology as one of the branches of criminal law[1].

It appears that provide a definition for the term aggression that can be accepted by the majority is not possible because there are different replies on the question that: whether we have to define the term "aggression" based on the tangible and objective results or based on objective intentions. As a result, different definitions of "aggression" have been emerged. Some psychologists consider aggression as a behavior

that could potentially harm others. This damage can be physical, such as hitting, kicking and biting, or as verbally such as insult and yell, or be legal such as seize something forcefully from somebody[1].

Another definition provided for aggression relies on the intention of aggressive person, and aggression is recognized as a behavior conducted by the child with the intention to damage or harm. Some have criticized this definition and said that the intention is not objective and tangible, and is subject to various interpretations. Many researchers have adopted a combination of the definitions, and they recognize the behavior as aggressive that lead to harm others, particularly when the perpetrator knows that his act will entail another person's harm[2].

Aggression is one important reason for people's referral to counseling and psychotherapy centers. The main case that has drawn the attention of researchers to aggressive behaviors is negative effect of aggressive acts on interpersonal behavior and also their traumatic effect on internal mental states[3].

In examining the causes of aggressive behavior, different issues shave been proposed such as hereditary and natural factors, function of sex hormones, social reasons, family reasons, failure, benchmarking, and so forth. In the area of biology, in examining the causes of aggression, some factors including nervous-hormonal systems and relevant disorders have been taken into account. Central nervous system, especially in the areas located in the depth of the temporal part and limbic system, plays important roles in stimulating and controlling aggressive behavior[4].

The influence of some hormones and neurotransmitters on aggression has been substantiated as well[5]. In this regard, researchers suggest that the hormones secreted by the endocrine glands undoubtedly exert a decisive impact on the incidence of such behaviors. For instance, it is possible to refer to the effects of adrenaline, serotonin, cortisol, thyroxine and sex hormones.

Serotonin or 5-hydroxytryptamine is a monoamine neurotransmitter which synthesized in the central nervous system and enterochromaffin cells of digestive system. Platelets and leukocytes contain large amounts of serotonin and histamine. Serotonin and histamine released by intestinal mast cells and chromaffin cells are taken and then packaged by this set of blood cells, and they flow through the whole body by blood circulation[6].

Serotonin in pain transmission pathways to the nerve centers acts as an inhibitor. Other actions of serotonin include establish a sleep mode, adjust the feeding behavior, and mood variations[7].

In terms of function, serotonin is a nervous intermediary which plays fundamental roles in regulating some moods such as a sense of hope, enjoyment of life, regulation of sleep, love of work and a number of other positive features. The importance of serotonin in the body is not less than insulin. Serotonin is the master key of natural ecstatic and mood disorders in the body[6]. Researchers reinstate that serotonin is a chemical matter in the brain that is associated with mood, and plays an important role in regulation of emotions such as aggression. Normal amount of human blood serotonin is 101-283 ng/ml [8].

Another hormone that has been linked with aggression is testosterone which is recognized as a very effective male hormone in the growth and development of sex organs and the emergence of secondary sex characteristics such as facial hair, deepening of the voice, male hair loss and anabolic properties such as growth of muscle and bone mass. This hormone causes growth spurt in adolescence and the cessation of height growth by blocking the growth plates at the ends of the bones. The main site of synthesis and secretion of testosterone in men is testicular Leydig cells, even though a small amount is also in the adrenal glands. Therefore, removal of the testicles (eunuch) gives rise to the reduction of secondary sexual characteristics. In women, this hormone is synthesized in the ovary and adrenal glands[6]. It seems that there is a direct association between testosterone and aggressive behaviors[5]. Decreased testosterone levels in men cause insomnia, irritability and loss of sexual desire; and the increased testosterone in the body can cause behavioral problems like anger and aggression[9]. Many believe that this hormone is a

major factor in people's willingness to aggression. Even some of the women consider the hormone as the main cause of manly stereotypical behaviors ranging from extreme interest in some sports to tendency to disobedience. It is believed that high levels of testosterone are directly associated with aggression (10). The natural amount of release of testosterone in adult men is approximately 4 to 9 mg per day. Its existing normal rate in plasma is about 22 nanomoles per liter, which its maximal amount establishes a link with plasma and a limited part of it is converted into estrogen[11]. The natural level of testosterone in adult men is 3-10 ng/ml and in older women is 0.2 to 0.8 ng/ml[12].

Cortisol or hydrocortisone is the best known glucocorticoid in the body which is secreted from adrenal gland. Corticosteroids are steroids that are made in the cortical section of adrenal glands. Steroids are fat compounds with four carbon rings. Corticosteroids are divided into two main groups including mineralocorticoids such as aldosterone and glucocorticoids such as cortisol (21 carbons)[6].

This hormone is involved in activities such as blood pressure regulation, proper sugar metabolism, secretion of insulin for maintaining blood sugar levels, the immune system, irritation, and inflammation reactions. Cortisol is normally high in the morning, and it is at the lowest levels in the body at night. Although stress is not the single cause of the secretion of cortisol into the blood stream, as the secretion of cortisol in the body's response to stress is raised to a high level and also as cortisol is responsible for several changes in the body, so it is called "stress hormone[13]. Secretion of cortisol, corticosterone and androgens of adrenal gland are regulated by adrenocorticotropic hormone that is a stimulator of adrenal cortex and is secreted from the anterior pituitary. Adrenocorticotropic hormone secretion, in turn, is regulated by corticotropin releasing factor. Neural and psychological pain and distresses by acting on the hypothalamus give rise to an increase in the secretion of corticotropin releasing factor, which in turn, the secretion of corticosteroids is increased[5]. The secretion of cortisol hormones and releasing factor of corticotropin and adrenocorticotropic occur in a fluctuating mode during a day, so that it is high at the early hours of morning and it is low at evening time. The normal amount of cortisol in adults at 8 am is 5-23 ìg /dl and at 4 pm is 3-13 ìg/dl[14].

In the area of the relationship between serotonergic and dopaminergic systems with behavioral traits such as aggression, emotions, love, sexual desires, and self-confidence, extensive research has been performed that the majority done on mice and monkeys[15, 16, 17, 18,19]. In the research conducted on the aggressive monkey by Mon et al. reduction in the concentration of serotonin was observed both in plasma and monkeys' brain[21]. Also, in the study conducted by Mcdougle et al. (1998), Schreuder (1990), Yudofsky et al. (1984), the most common cause of aggression was impairment in serotonergic systems[22,19, 18]. Chiavegatto and Nelson in 2011 stated that there is an inverse correlation between serotonin and aggressive behavior[19].The study performed by Connor et al (2003) also proves the claim[23]. Research conducted by Miczek et al. (2002) and Sowan (2003) suggests that serotonin reuptake inhibitors and also dopaminergic activity reduction drugs can decrease aggression[17]. Winstanley et al (2005) also underlines an interactive relationship between serotonergic and dopaminergic systems and aggressive behaviors[17]. The research carried out on humans and non-human primates show that low levels of brain serotonin are associated with aggressive behaviors and anti-social personality. However, in the area of monkey research, more information has been attained about the relationship between neurotransmitters with aggression[24]. Almeida and colleagues have also investigated the role of neurotransmitters in the incidence of aggression, and have concluded that a lack of serotonin in the brain cause a critical, destructive and violent character (25, 16). A research conducted by Abby and colleagues suggests the role of serotonergic system in the incidence of aggression[15, 16]. In addition, some evidence exists on the role of testosterone on aggressive behavior. In an interventional study, participants showed more aggression after administration of testosterone (26). Also, in a study conducted on 32 patients, there was a time lag between testosterone and emotional behavior[27]. Testosterone plays a major role in the behavior of

individuals and is associated with violent or competitive reactions[17]. In an interventional study, out of 91 men, 46 received testosterone by injection and the rest were given a placebo. The result was that in men who received testosterone, sense of pride was increased, and in the face of stressful situations they exhibited more aggressive behavior[28].

In addition, any changes in cortisol levels affect individual behavior. In a study conducted by Gustavo and Martinez, it is stated that low cortisol levels are strongly correlated with aggressive behavior. In this study, the cortisol in saliva samples of adolescents in response to stimulation and stress was measured[29]. On the other hand, the results of a meta-analysis shows that, so far, the relationship between cortisol levels and aggression has not been confirmed empirically but there is evidence that confirm high cortisol levels and more resultant aggression in children and adolescents. In this research, children who were exposed to stress showed more aggression[30]. The current article mainly aims to investigate the blood level of the hormones such as serotonin, cortisol, and testosterone in the blood of people with aggressive behavior and compare it with normal people. In this direction, the research methodology will be described further.

Research Methodology

This study is an interventional one in which 70 male subjects in the age range of 20 to 40 years with no history of addiction, depression and cardiovascular disease, thyroid, intestinal obstruction were divided into two groups including ordinary and aggressive subjects. To examine aggressive behavior, two methods including Aggression Questionnaire developed by Arnold H. Buss and Mark Perry, and interview Technique were used. The results relevant to the Aggression Questionnaire presented to individuals were scored from 29 to 145 that the higher the score, the greater the likelihood of aggressive behavior. According to the questionnaire or interview, people who attained the score more than 85 were ranked as aggressive. The lowest score was 38 and the highest score was 105. Therefore, the questionnaire was distributed among the subjects from different ranges, and after a review and validation of the questionnaires, the blood samples were taken from the subjects. To do so, half of the people had to account for high aggression scores. Therefore, among those referred to Boukan Hospital ICU, some were targeted who were mainly the saboteurs of the city, and had a record of conflict, misuse by knives, machetes and many other abnormalities. Some of the subjects had medical record in prison, and the same record was used to do scoring. Of each of the sample under examination, after approval of the psychiatrist, 5 cc of blood were collected from vein in the arm. The samples obtained were refrigerated, and were transferred to the laboratory in the quickest time possible. It should be noted that the formal consent of all subjects for blood taking and information were obtained.

Cortisol levels of blood serum were measured by ELISA kit (Enzyme-linked immunosorbent assay (ELISA)) produced by German company DIASORIN. To measure testosterone, ELISA kit was developed based on competitive enzyme immonulogical assays, and also the device used is DIASORIN made in Germany. Finally, to measure serotonin, serum based on ELIZA made in German company IBL and also UNO HUMAN ELIZA device were utilized.

For data analysis, the software SPSS-20 was used; data were analyzed in two levels of descriptive and inferential. In the latter, the measures of central tendency (mean, median and exponent) and dispersion measures (standard deviation and variance) were utilized. In the former, independent t-test and Pearson's correlation coefficient were used.

Findings

Table 1 presents the average level of serotonin, testosterone and cortisol for the normal and aggressive subjects. In addition, the significance of differences in the mean of the groups is addressed.

In Table 1, the average levels of serotonin, testosterone and cortisol in normal and aggressive groups are offered; also, the results from

independent t-test showed that significant level obtained from t-test is less than 0.01, and so with 99% confidence, it could be said that there is a significant difference between the average amount of serotonin, testosterone and cortisol in normal and aggressive individuals. In fact, the results showed that the amount of cortisol and serotonin in aggressive subjects is lower compared to ordinary people, and testosterone is at a higher level. In Table 2 shows the results from the relationship between serotonin, testosterone and cortisol with the extent of aggression.

Based on the results from Pearson correlation analysis (Table 2), the correlation of aggressive behavior with serotonin level is -0.664, with testosterone is 0.646, and with cortisol level is -0.691, and all three are significant at the level of 99%. In other words, the negative sign in the relationship between aggression and cortisol levels shows that with by an increase in serotonin and cortisol, the aggression will be reduced.

DISCUSSION AND CONCLUSION

Given the important role of hormones in behavior, in the current research, three hormones including serotonin, testosterone and cortisol were studied in normal and aggressive subjects. The variations of these three hormones in the body play particular roles in the incidence of behaviors. For this reason, out of 70 individuals selected by using questionnaire or interview, two groups (including normal and aggressive subjects) were categorized based on the criteria outlined in the area of psychology, and serum levels of each of the two groups were examined. The results obtained in this study are indicative of the effective role of these hormones, such that increase or decrease in serum levels of these hormones can cause changes in behavior. The results from the current research in the experimental group compared with the control group showed that decrease in serum serotonin causes aggressive behaviors in people. This research is consistent with those of Chiavegatto and Nelson (2011) and Connor et al. (2003)[19, 23]. Studies on humans and non-human primates show that lower levels of serotonin either in the brain or in serum are associated with the incidence of aggressive behaviors and antisocial personality. However, more information has been achieved about the relationship between neurotransmitters and aggression in monkeys[24]. Almeida and colleagues have investigated the role of neurotransmitters in the incidence of aggression

Table 1: A comparison of the amount of serotonin, testosterone (ng/ml), cortisol (µg/dl), in aggressive and normal people (n=35)

Hormone	Sample	Mean	Standard Error	Significance obtained from t-test
Serotonin	Normal	283.8123	15.87	<0.01
	Aggressive	138.1098	10.540	
Testosterone	Normal	2.6806	0.200	<0.01
	Aggressive	7.0486	0.461	
Cortisol	Normal	12.63	1.267	<0.01
	Aggressive	3.2149	1.171	

Table 2: Pearson correlation analysis to examine the relationship between hormone levels and aggressive behavior

Type of Hormone	Correlation Coefficient	Significance Level
Serotonin	-0.664	<0.01
Testosterone	0.646	<0.01
Cortisol	-0.691	<0.01

and have concluded that a lack of serotonin in the brain cause a critical, destructive and violent character[25, 16]. Abby et al.'s study () also indicated the role of the serotonergic system in the development of aggression[16, 15]. Another study conducted by Pozity et al. showed the relationship between behavioral disorders and interactions between serotonergic and dopaminergic systems[17, 10] and Dally also reviewed and approved it[15]. Furthermore, it is shown that serotonin has an inhibitory action in the brain and plays effective roles in the regulation of behavior and emotions[47]. In addition, any disruption in serotonergic and dopaminergic systems will cause aggressive behavior[10]. Then, serotonin is a hormone affecting the behavior that its reduction will lead to hostile and aggressive behaviors in men, and because it can cross the blood brain barrier, any reduction in serotonin in serum and plasma can affect the levels of the hormone in the brain. The results from the present study, in the experimental group compared with the control group, suggest that the higher serum testosterone, the more likely to perform aggression behaviors. Testosterone receptors are located in the hypothalamus, where testosterone is aromatized and converted into estrogen and the final result is aggression. Testosterone also increases vasopressin in the central amygdala and the lateral hypothalamus which are involved in violent behaviors[32, 31]. In an interventional study, participants showed more aggression after administration of testosterone[26]. Testosterone plays a major role in the behavior of individuals and is related to violent or competitive reactions[17]. In another interventional study, researchers injected testosterone to a group of men, and observed that in the men who received testosterone, sense of pride was increased, and they were more aggressive in the face of stressful situations[28]. Men are more aggressive compared with women in various situations, especially in stressful situations and this is due to the male hormone testosterone. However, the amount of this hormone also varies between men, so we can see men who in similar situations become more aggressive quicker than other, and demonstrate more aggressive behaviors.

Also, based on the results, there was a significant relationship between cortisol and aggressive behavior, such that decreased cortisol could lead to aggressive behavior. There is evidence that high cortisol levels can lead to aggression in children and adolescents. In this study, the children who were exposed to stress showed more aggression[30]. Cortisol levels and its secretion in the body normally elevate when people undergo a stressful situation. It also helps people regulate their emotions, particularly anger and aggression[29]. Various studies on hypothalamic-pituitary-adrenal system have confirmed the relationship between the reduction in cortisol and anti-social behavior[33]. By a reduction in cortisol levels, in case of the presence of the person in stressful situations, man is not able to create a series of changes associated with stress and as a result the man cannot be compatible with the conditions incurred. Failure to comply with the critical conditions makes a person lose control of emotions and this leads to anger or aggressive behavior shown by him.Therefore, the findings of this study showed that decrease in serotonin, increase in testosterone and decrease in cortisol are three effective physiological factors affecting aggressive behavior, and in case of changes in these hormones, it is necessary to first apply non- pharmaceutical methods and then pharmaceutical techniques to regulate them in the aggressive individuals.

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