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Relationship of serum serotonin and salivary cortisol with sensation seeking

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ABSTRACT

The present study was conducted to investigate the possible relationship of serum serotonin and salivary cortisol with the sensation seeking (SS) trait. Blood and saliva samples were taken from 57 male volunteers (mean age 23 ± 5 years) to measure serum serotonin and salivary cortisol concentrations. Zuckerman's Sensation Seeking Scale (SSS-V) was used to assess SS. Pearson's correlation coefficient revealed that high serum serotonin levels did not correlate significantly with low SS scores ($r = 0.12$). However, a negative correlation between SS scores and salivary cortisol levels ($r = -0.34$, $p < 0.01$) was significant, suggesting that high SS scores are related to low concentrations of salivary cortisol. The negative correlation between salivary cortisol and SS is clearly compatible with the optimal level of Catecholamine system activity (CSA), component of SS theory, indicating that high sensation seekers (HSSers) tend to seek excitement and novelty to compensate for the shortage of CSA achieving optimal arousal. Further investigation is needed before conclusions can be drawn regarding the relationship of serum serotonin and SS.

1. Introduction

In the early 1970s, Marvin Zuckerman described the personality trait of sensation seeking (SS) as "a trait defined by the seeking of varied, novel, complex and intense sensations and experiences, and the willingness to take physical, social, legal and financial risks for the sake of such experiences" (Zuckerman, 1994, P. 27). Much research has been performed to explain this highly heritable trait (Fulker et al., 1980) more efficiently. Previous studies described a wide variety of risky behaviors associated with this trait (e.g. a tendency to smoke, Ripa et al., 2001; Urban, 2010; drug and alcohol abuse, Martins et al., 2008; risky and drunken driving habits, Richer and Bergeron, 2009; Zakletskaia et al., 2009; risky activities, Jack and Ronan, 1998; Steinberg et al., 2008; and pathological gambling, Zuckerman, 2005a; Myrseth et al., 2009; high sexual SS, Gullette and Lyons, 2005; Perry et al., 2007).

The Sensation Seeking Scale (SSS) is related to the scale of novelty seeking (Zuckerman, 2005b) although they are not argued as identical (Zuckerman, 2007a). Investigators have shown that total SSS scores correlate significantly with total novelty seeking scores from Cloninger's Tridimensional Personality Questionnaire (McCourt et al., 1993). In addition The Barratt Impulsiveness Scale, the Eysenck Impulsiveness Scale, and the Behavioral Constraint factor of the Multidimensional Personality Questionnaire (Roberti, 2004) all measure traits that are correlated with SSS.

It is well documented by research that novelty seeking scores are associated with high levels of the dopamine neurotransmitter (Wiesbeck et al., 1995) and low platelet monoamine oxidase type B (MAO_B) activity (Sadock and Sadock, 2005); also a positive relationship has been found between the activities of dopamine system and SS scores (Campbell et al., 2010; Netter et al., 1996; Wiesbeck et al., 1996). Investigators have suggested that there is a positive relationship between MAO_B and serotonin turnover based on similar distribution in brain areas (Oreland et al., 1981). Because serotonin and norepinephrine preferentially are oxidized by MAO_A, and the serotonin system is mostly involved in avoidance behavior (Zuckerman, 2005b), HSSers are expected to have lower serotonin system activity. Overall, high SS is a function of a strong approach and weak inhibition and arousal systems. Dopamine is positively associated with approach, serotonin with inhibition, and norepinephrine with arousal (Zuckerman, 2007a).

Netter et al. (1996) conducted a three-part study investigating the effects of a neurotransmitter challenge (ipsapirone) on the serotonergic system by hormonal response (cortisol and prolactin) to the challenge. This study reported that activity in dopamine and serotonin systems is associated with particular subscales of SSS. A negative relationship between Disinhibition (DIS) and Experience Seeking (ES) factors of SSS with serotonergic systems activity has been reported. In the light of previous findings regarding MAO_A and activity in serotonin systems, hypoactive serotonergic system in HSSers is expected.

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The model of optimal level of CSA suggests that in an unstimulated state and low basal level of CSA, dopamine and norepinephrine are low in HSSers and are much below their optimal levels of CSA. This produces a state of boredom, which in turn, compels the individual to seek novel and risky experiences (Zuckerman, 2007a). Several studies show that cortisol, an arousal hormone which increases under stress, is associated with SS due to noradrenergic system activity:

Ruegg et al. (1997) examined the relationship between the cortisol response to a serotonergic challenge and three elemental dimensions of personality. Cortisol response correlated with harm avoidance, but not with novelty seeking or reward dependence; but Tyrka et al. (2006, 2007) reported that novelty seeking was negatively associated with plasma cortisol concentrations in the Dexamethasone/Corticotropin Releasing Hormone (Dex/CRH) test.

In the field of SS studies, Gerra et al. (1999) found no relationship between SS scores and cortisol. However, when Rosenblitt et al. (2001) examined the relationship between SS behaviors and cortisol in male and female college students, the results revealed a significant negative relationship between salivary cortisol and SS in men, but not in women. White et al. (2006) suggested that the Thrill and Adventure Seeking (TAS) subscale of SSS is negatively related to the cortisol response to D-amphetamine, and finally, Couture et al. (2008) reported that hypothalamic–pituitary–adrenal (HPA) axis dysregulation is positively associated with engagement in high-risk behaviors, including alcohol consumption, SS, and cigarette smoking. Croissant et al. (2008) investigated the stress-response dampening effects of SS in the neuroendocrine domain of 86 healthy men and women. They found a negative association between SS and serum cortisol of both genders, and also a negative relationship between SS and alcohol-induced stress-response dampening effects in serum cortisol of females.

The central nervous system (CNS) contains less than 2% of the serotonin in the body. Peripheral serotonin is located in platelets, mast cells and enterochromaffin cells of the gastrointestinal system (Sadock and Sadock, 2005). Because CNS serotonin concentrations cannot be measured directly, Anderson et al. (2006) compared whole blood serotonin levels between autistic and healthy subjects and found that serotonin was significantly higher in autistic subjects. In this study, we similarly investigated the relationship between the SS trait and peripheral serotonin level in blood serum using a static method. To our knowledge, this study is the first of its kind. Also we considered the relationship between SS scores and salivary cortisol as a noradrenergic system activity. Thus we hypothesized that both serum serotonin and salivary cortisol levels negatively correlate with SS scores.

2. Materials and methods

2.1. Participants

The protocol of this study was ethically and scientifically approved by the Research Committee of Science and Research Branch of Islamic Azad University. Because the method of study was not experimental, the protocol was not considered by the Declaration of Helsinki for human subjects.

All participants were male students at a large university in Tehran and were selected randomly from various classes on campus. Participation was unremunerated and voluntary. Screening forms were used to select suitable participants for the study. Participants were excluded if reported acute stress (n = 7) (defined as experiencing stressors totaling greater than 45 marks in "Holms and Rahe's Life Schedule of Recent Events"), recent surgery (n = 3), severe bleeding (n = 1), drug abuse and addiction (n = 3), or medical treatment by tranquilizing or serotonin axes-affecting drugs (n = 11). Hematophobic volunteers (n = 4) were excluded to avoid the possible influence of stress caused by blood donation on the cortisol response. Overall, 29 participants were excluded from sample group. The 57 remaining participants were between 18 and 29 years old (mean age of 22.80 years, SD = 3.06). Participants received an instruction form noting the specimen conditions, and were asked to attend the laboratory at 0800 h without having had breakfast. To control the acute effects of nicotine on serotonin (Launay et al., 2008; Rausch et al., 1989) and cortisol levels (Winternitz and Quillen, 1977), participants were requested to not smoke after awakening, nor to brush their teeth within half an hour of sampling.

2.2. Procedure

Upon arrival at the laboratory, subjects were asked to wash their mouths and hands with tap water, put on disposable plastic gloves, and collect 1 ml of saliva samples (without stimulation) through straws into 2 ml polypropylene microtubes. To avoid arbitrary results, five saliva samples were collected from each subject every half hour at 0, 30, 60, 90, and 120 min between 0800 h and 1000 h daily. At the end of sample collection (at 1000 h), all saliva samples were frozen (−24 °C). Samples were later thawed, mixed and centrifuged for mucin separation. During the intervals between the saliva sampling, subjects were asked to complete the Zuckerman's SSS. After saliva sampling at 1000 h, blood samples were collected (one sample per subject). Because serotonin is stable for only 2 h at room temperature, blood samples were centrifuged immediately after clotting (at room temperature), and frozen in microtubes at −24 °C, extending their stability for three months.

At the end of the study, each participant received the results of his own SSS score, serum serotonin and salivary cortisol levels, accompanied by a brief explanation of the research.

2.3. Measures

2.3.1. Sensation seeking

The Sensation Seeking Scale (SSS-V) developed by Zuckerman has shown good reliability and validity (Roberti et al., 2003; Zuckerman, 1984, 2007b). This scale consists of 40 items and four subscales: Thrill and Adventure Seeking (TAS), Disinhibition (DIS), Experience Seeking (ES), and Boredom Susceptibility (BS) subscales. With this scale, scores of 0 to 40 can be obtained with higher scores indicating more severe SS traits. The present study used a standardized Persian translation of Zuckerman's SSS-V. The reliability of the Persian version is reported as acceptable with alpha coefficient of 0.78 (Mahvi Shirazi, 1997).

2.3.2. Serum serotonin

To measure levels of serum serotonin, a commercial Enzyme Linked Immunosorbent Assay (ELISA) kit (Immuno Biological Laboratories' serotonin kit, Cat number: RE59121, Homburg, Germany) was used. The kit uses the indirect competitive ELISA method for assaying serotonin in human serum, plasma, platelets and urine. The kit includes a mouse monoclonal antibody with sensitivity for serum samples of 6.2 ng/ml from 2SD ± zero standards; the correlation of its data with other methods was 98% and no cross-reactivity with other typically tested substances is known. The assay's normal range is 30–200 ng/ml. To eliminate the possibility of foods high in hydroxyindole affecting plasma 5-HIAA results (Burtis et al., 2005), only fasting blood samples were collected for serotonin. In this research, serum sample serotonin had an intra-assay Coefficient of Variations percent (%CV) of 6.2% (replication number = 6, mean = 230.45, SD = 14.32) which was acceptable.

2.3.3. Salivary cortisol

Salivary cortisol levels were measured (which enabled us to measure the free fraction of the hormone with high sensitivity), using an ELISA kit (Demeditec free cortisol in saliva kit, Cat number: DESLV2930, Demeditec Diagnostics, Germany). The kit was measured free cortisol using the