Levels of salivary immunoglobulin A under psychological stress and its relationship with rumination and five personality traits in medical students

Reza Afrisham[a,b]
Mohammad Aberomand[b]
Omid SoliemaniFar[c]
Wesam Kooti[d]
Damoon Ashtary-Larky[a,b]
Fatima Alamiri[e]
Sedigheh Najjar-Asl[f]
Ali Khaneh-Keshi[f]
Sahar Sadegh-Nejadi[a,b,*]

[a] Student Research Committee, Ahvaz
   Jundishapour University of Medical
   Sciences, Ahvaz

[b] Department of Clinical Biochemistry,
   Faculty of Medicine, Ahvaz Jundishapur
   University of Medical Sciences, Ahvaz

[c] Department of Psychology, Abdanan
   Payame Noor University, Abdanan

[d] Student Research Committee, Kurdistan
   University of Medical Sciences, Sanandaj

[e] Sophmore/Health and Medical Studies,
   Henry Ford Early College at Henry Ford
   College, Dearborn, Michigan

[f] Department of Psychology, Psychology
   Faculty, Behbahan Branch, Islamic Azad
   University, Behbahan

IRAN
USA

ABSTRACT – *Background and Objectives:* The measurement of salivary immunoglobulin
A is a useful and non-invasive method for measuring stress. Personality traits and rumination
act as possible mediators in the relationship between psychological stressors and the im-
mune system. This study was aimed to evaluate the levels of salivary IgA under psychologi-
cal stress and its relationship with rumination and five personality traits in medical students.

Methods: In this cross- sectional study, 45 medical students who intended to participate in
the final exam were selected by simple random sampling. Two months before the exam, in the

basal conditions, the NEO Personality Inventory-Short Form and Emotional Control Question-naire (ECQ) were completed. Saliva samples were taken from students in both the basal conditions and exam stress conditions. Salivary IgA was measured by an ELISA test. Data was analyzed using paired samples T-test, Pearson correlation analysis, and stepwise regression.

Results: A significant reduction of salivary IgA levels was found in exam stress conditions. Also, a significant negative correlation was found between traits of neuroticism and rumination with salivary IgA, as well as a significant positive correlation between of openness to experience and emotional inhibition with salivary IgA. Openness to experience and emotional inhibition may predict a substantial variance (34%) of salivary IgA under exam stress.

Conclusions: Salivary IgA is reduced in response to exam stress. In addition, the rumination and personality traits may reduce or increase stress effects on the immune system, particularly the salivary IgA.

Introduction

Stress is an environmental and psychological stimulus that creates mental or physiological responses and this may lead to disease in individuals. Mild stress can be useful for tasks and cognitive performance, while constant and high stress leads to anxiety and depression[1]. Studies show that acute stress can reduce the performance of the immune system and suppress the production of immunoglobulin[2]. The effects of stress and negative emotions on the levels of IgA are one of the major issues in the field of psychoneuroimmunology studies[3]. Recently, the measurement of salivary immunoglobulin A (sIgA) is another potential non-invasive method for the measurement of stress. The IgA is the most frequent class of antibodies in mucous membrane, which is a very important factor in the protection against infectious agents, allergy, and external proteins and has a concentration that can be affected by stress[4]. It is reported that salivary IgA level changes in response to psychological factors, such as desirable or undesirable daily events, daily hassles, positive and negative mood, short-term stressful cognitive tasks and presentation[5]. Even studies conducted on animals (such as mature dogs) showed that IgA levels following prolonged stress and acute stress is reduced[4]. In the present study, we focused on stressful situations by experienced medical students. Exams are one of the important academic stressful situations.

Academic exams are considered as one of psychological stressors, because success in exams is related to future professional life of students[6]. Exams (a psychological stress factor) play an important role in the assessment of learning outcomes and competence of students. In particular, medical students experience a high level of anxiety during exams. Previous studies showed that exam stress can increase anxiety, salivary cortisol levels and blood pressure[7]. It is known that stress from academic exams has a significant impact on the well-being of individuals and it is associated with mental and physical health changes such as increased anxiety, negative mental state, and changes in immune function[8]. Various studies have examined the effects of educational and exam stress as psychological stressors on the immune system, particularly IgA levels[9]. However, there are conflicting findings. For example, the long-term peri-

ods of exam stress[10,11], as well as an oral examination[12] are associated with a significant reduction in salivary IgA levels. On the other hand, increased levels of salivary IgA in the days before and during their academic exams[13,14] and lower levels during the days between exams[13] and after the announcement of the scores (Associated with academic success) have been observed[14]. In addition, the daily changes in salivary IgA concentration sometimes seem to be disturbed due to the academic stress[13]. Given the above background, it seems the association between examination stresses with IgA levels is not known reliably, yet. Thus, in the present study, we examined the effect of exam stress on salivary IgA levels in medical students. Additionally, the student reaction to exam stress may be influenced by psychological factors and personality traits. Accordingly, the relationship between rumination and personality traits with salivary IgA under exam stress has been studied.

Rumination, as a psychological construct associated with stress, can cause and maintain physiological activities associated with stress factors[15]. Rumination is important to maintain and increases the severity of depression and stress, and its increase is associated with rise stress levels[16]. Research findings show the association between rumination with cortisol responses[15] and salivary alpha amylase[17] to psychological stress. The question arises as to whether changes in salivary IgA levels can be influenced by traits of persons rumination. We have tried to study the relationship between the rumination and salivary IgA under psychological stress.

In the initial reports about the relationship between stress and disease, there was an assumption that the stress factors similarly affect everyone. However, since the relationship between stress and disease in general was low, the researchers were more interes-

ted in adjusted variables or psychological characteristics of individuals that may increase or reduce the effects of stress variables[3]. The hypothesized relationship between the personality and the immune system has been prevalent for a minimum of 25 years and therefore recognizing the relationship can help us to understand the effects of personality on the extent and period of chronic diseases, including cancer and heart disease. A number of aspects of personality, such as suppression, hostility, attribution style, and extraversion-introversion have been associated with parameters of the immune system[18]. But in particular, psychological characteristics associated with personality, such as a sense of humor, internal locus of control, hardiness and inhibited and stressed power motivation have been reported in association with the concentration and level of salivary IgA secretion. However, there are other studies that show conflicting findings on the relationship between the personality traits and salivary IgA levels[3]. Using the Five Factor model, previous studies have reported the relationship between neuroticism trait with cortisol[19] and salivary alpha-amylase[17,20], as well as a negative[20] and positive[17] correlation between agreeableness and salivary alpha-amylase. Nevertheless, some findings showed that the conscientiousness affects parameters of the immune system such as delayed type hypersensitivity (DTH)[21]. In one study, individuals with low levels of extraversion characteristics had higher basic natural killer cell activity, but the number of their natural killer cells was stable[22]. Based on the information stated in the background, we assume that the five major personality traits could be predictive key factors in relation to the parameters of the immune system, particularly the salivary IgA.

The main objective of the present study was to investigate the salivary IgA levels under psychological stress and its relationship with five personality traits and rumination.

Methods

Participants

This was a cross-sectional study. The study population consisted of medical students in Ahvaz Jundishapur University of Medical Sciences (AJUMS), entered on October 2014, who had to attend a final exam. A sample size of 45 participant (22 females, 23 males) was selected using Cochran formula and simple random sampling method from the prepared list (the statistical population = 73 people) from Medical School. Written consent was obtained from all the students and the purpose and method was explained to them. Because academic examinations stress were reported to have a significant impact on the student's well-being, and are associated with changes in the mental and physical health such as increasing anxiety, increasing negative mood and changes in the immune functioning[23]. Furthermore, due to the students being freshmen, the first exam was considered as a stressful situation. The natural conditions did not change the normal level of biochemical factors significantly, however in exam stress conditions or mental pressure, changes are obvious[17,24]. Thus, the exam was considered as psychological stressful situation.

Measures

In this study, data collection tools included a shortened version of the NEO Five-Factor Inventory (NEO-FFI), and Emotional Control Questionnaire (ECQ). Two months before the exam (basal conditions) all participants filled the NEO- Short Form and the ECQ.

1. A shortened version of the NEO-FFI: In this study, McCrae and Costa's 60-statement questionnaire (1992) was used. This scale measures the five major personality traits, which include: Neuroticism (N), Extraversion (E), Agreeableness (A), Openness to Experience (O), and conscientiousness (C). Each of these traits can be measured with 12 questions. The answer to the questionnaire is set based on the Likert scale, completely disagree (0); disagree (1); indifferent (2); agree (3); and completely agree (4). Based on Cronbach's alpha coefficients by Costa and McCrae the internal consistency of this scale for the traits of the N, E, O, A, and C was 0.66, 0.77, 0.73, 0.68 and 0.81, respectively[25]. In this study, using Cronbach's alpha the coefficient of reliability of the questionnaire calculated for the traits of the N, E, O, A, and C was 0.76, 0.68, 0.77, 0.72, and 0.81, respectively.

2. Emotional Control Questionnaire (ECQ): The questionnaire has been developed by Roger and Nesshoever (1987) and has been renewed by Roger and Najarian (1989). The ECQ measures four scales of emotional inhibition, aggression control, rumination, or rehearsing and benign control measures and has 56 items. Each sub-scale has 14 questions. The score of a person in each sub-scale is ranging from 0 to 14 and in the total scale is ranging from 0 to 56. High scores indicate greater emotional control[26]. The validity of the questionnaire using internal consistency, and Cronbach's alpha coefficient calculated by Rafineya *et al*. (2006) for each sub-scale of emotional inhibition, aggression control, rumination, and benign control were 0.70, 0.76, 0.77, and 0.58, respectively and its total validity was 0.68[27]. In the present study, the reliability coefficient obtained using Cronbach's alpha coefficient for the total scale was 0.78 and for each of the sub-scales of emotional inhibition, aggression control, rumination, and benign control was 0.59, 0.63, 0.68 and 0.73, respectively.

Sampling and analyses of saliva

To conduct this research in the first phase, two months before the exam (basal conditions) and two days after the filling out of the questionnaires by the participants, saliva samples were taken to measure salivary IgA in the basal conditions. Then, in the second phase, to measure salivary IgA during the exam stress condition, the subjects' saliva samples were taken at the start of the exam. In both phases of sampling, the subjects were told not to have caffeine from the night before taking the saliva samples until the taking of the samples, and they were not permitted the intake of any food one hour prior to exam to prevent any interference in the process of sample collection and measurement of salivary IgA[26]. To take salivary samples, the subjects were asked to collect their secreted saliva for five minutes in the tubes determined by passive methods[28]. Both times, sampling from saliva was performed in identical circumstances at one particular time (10 am). Saliva samples taken in two steps immediately were sent to the laboratory of Biochemistry Department of AJUMS for analysis. First, the samples were centrifuged with a round of 3000g for 15 minutes and for the evaluation of IgA the supernatant was frozen at -70 °C. When measuring salivary IgA, at first the saliva samples were melted and then centrifuged again with the previous conditions, and measured by a Kit (Diametra, Italy) by ELISA method using an ELISA reader (BIOTEK, model ELX800, USA).

Statistical analyses

To analyze the data, descriptive statistical methods, including mean, standard deviation, minimum and maximum scores were used, and Pearson correlation coefficient was used for measuring the strength of the association between the two variables. In addition, to determine the best predictor of IgA under psychological stress the stepwise regression analysis was used and paired sample t-test was utilized to compare differences in levels of IgA under the exam stress with the basal conditions of the participants; SPSS version 15 was used for this purpose.

Results

Table 1 shows descriptive statistics (mean, standard deviation, minimum and maximum scores) of the variables of the study in the medical students.

Then, to compare the level of salivary IgA under basal condition and in the exam condition the paired samples t-test was used. Table 2 shows a comparison of means of salivary IgA levels (µg / ml) in the conditions of before the exam and under the exam.

As reflected by Table 2, there are significant differences in the means of salivary IgA levels (µg/ml) of students in the basal conditions and exam conditions (P = 0.004, T = 3.054). In other words, the levels of salivary IgA of students under exam stress are significantly less than the basal conditions. Then, to investigate the association between rumination and personality traits with salivary IgA levels in the exam conditions, the stepwise regression analysis was used. Table 3 shows the correlation matrix between the studied variables.

According to the results of Table 3, there was a significant correlation between the traits of neuroticism (r = - 0.36) and openness to experience (r = 0.38) with salivary IgA at the level of 0.05, as well as a significant correlation between the rumination (r = -0.34) and emotional inhibition (r = 0.39) with salivary IgA at the levels of 0.05 and 0.01, respectively.

Table 1
The mean, standard deviation, minimum and maximum scores of variables

Variables	Mean	SD	Minimum score	Maximum score	N
Neuroticism	20.56	4.80	13	35	
Extraversion	25.40	5.08	16	35	
Openness to experience	25.54	4.21	11	33	
Agreeableness	27.11	4.00	16	38	
Consciousness	31.04	5.58	15	42	
Rumination	7.63	2.28	4	12	
Emotional inhibition	8.06	1.87	3	11	45
Aggression control	7.09	1.65	4	10	
Benign control	6.45	2.13	3	11	

Table 2
A comparison between means of salivary IgA levels (µg / ml) in basal conditions and under the exam conditions

Groups	Mean	A 95% confidence interval of the difference		T	df	p-value
		Minimum	Maximum			
Basal conditions	98.51	13.72	67.06	3.054	45	0.004
Exam conditions	58.12					

Table 3
The correlation matrix between the variables under study

Variables	1	2	3	4	5	6	7	8	9	10
1. Neuroticism	1									
2. Extraversion	-0.041	1								
3. Openness to experience	0.077	-0.12	1							
4. Agreeableness	0.16	0.029	0.10	1						
5. Consciousness	0.15	-0.17	0.43**	0.13	1					
6. Rumination	0.091	0.012	-0.062	0.061	-0.30*	1				
7. Emotional inhibition	-0.13	0.043	-0.25	-0.32*	-0.37*	0.073	1			
8. Aggression control	0.090	0.22	-0.25	-0.19	-0.26	-0.075	0.11	1		
9. Benign control	0.014	0.13	-0.18	-0.39**	-0.34*	0.30*	0.21	0.23	1	
10. Salivary IgA (exam conditions)	-0.36*	0.10	0.38*	0.00	-0.23	-0.34*	0.39**	0.075	0.044	1

$*P < 0.05$; $**P < 0.01$.

Table 4 shows the results of stepwise regression analysis to predict salivary IgA (μg / ml) under exam stress. According to the results of Table 4, the regression analysis suggests that emotional inhibition and openness respectively, with the beta coefficients of 0.39 and 0.31, may predict salivary IgA levels in the stressful exam conditions, and predicted 34% of its variance.

Table 4
Results of stepwise regression analysis to predict salivary IgA (μg / ml) in the exam conditions

Criterion variable	Predictor variable	MR	R2	F	β	p-value
Salivary IgA	Emotional inhibition	0.394	0.15	7.71	0.39	0.008
	Openness to experience	0.496	0.24	6.70	0.31	0.031

Discussion

The purpose of this study was to evaluate levels of salivary IgA under psychological stress and its relationship with rumination and personality traits in the medical students. As the results displayed, there was a significant difference between salivary IgA of students in the basal condition (two months ago) and under exam stress conditions (Table 2). This means that the exam circumstances are stressful conditions that cause changes in functions of the immune system, particularly in the salivary IgA. In addition, the correlation results indicated that among the five personality traits, only neuroticism and openness to experience had significant negative and positive correlations with salivary IgA, respectively. Additionally, a significant positive and negative correlation between the rumination and emotional inhibition traits with salivary IgA was found (Table 3), respectively. The regression analysis suggested that emotional inhibition and openness may predict salivary IgA in the stressful exam condition (Table 4).

Limitations of the present includes the nation the subjects represented by this study were only medical students in Ahvaz, thus, the results cannot be generalized to other levels of education, cities, cultures and other universities. Also, studies on the relationship between the five personality traits, particularly rumination with IgA at the country and abroad, were minimal. In this context, there is little research to compare the results. Furthermore, the effect of possible external factors (such as academic stress or prolonged academic pressures associated with exam periods, stressful life events, etc.) has not been evaluated that simultaneously may have an impact on students' exam stress. Other limitations of this study that may have influenced the results include the sample size of the research. Because, using a larger sample might reveal more meaningfulness in of relationships between the variables. For example, the considerable results of the present study found a negative correlation between conscientiousness trait and salivary IgA (r = -0.23), but it was not statistically significant.

In terms of methodology, we took samples of the salivary IgA two months after assessment of the personality of the subjects. the big five personality traits may predict the levels of salivary IgA in the future stressful conditions and previous pathological studies have evaluated the use of the Big Five Factor Model of

personality in the diagnosis and prognosis of psychiatric diseases such as mood, depressive and anxiety disorders[29,30] and multiple sclerosis[31]. A strength of this study was the use of saliva samples. Salivary IgA has a important role in mucosal immunity and is proved as a sensitive and objective indicator of stress in humans. Saliva samples are easily collected and without inconvenience to individuals, with only a small sample volume being required. Even in animals[32] salivary IgA is a useful marker of stress. Use of the Medical students that are frequently exposed to heavy examination stress and academic rumination was also a strength of the research sample.

Salivary IgA levels under exam stress

This result is specifically consistent with previous studies of the effects of exam stress on reduction in salivary IgA levels[10-12]. Similarly, the laboratory studies have shown that examination stress in healthy medical students could lead to decrease parameters of immune system such as a decrease in NK cell activity, a decrease in the response of peripheral blood lymphocytes (PBLs) to mitogens, a decrease in production of IFN- by PBLs in response to stimulation by Con A, a decrease in the antibody and virus-specific T-cell response to a hepatitis B vaccination, and changes in the ability of the immune system to control the expression of latent herpesviruses such as Epstein-Barr virus (EBV) and herpes simplex virus type 1 (HSV-1)[33]. A study on medical students showed that stress causes a decrease in IgE levels (parameter of immune system) and an increase in cortisol levels at the same time[23]. In another study, the levels of salivary cortisol and sIgA both significantly increased after the acute examination stress (mental arithmetic challenge). However, the increase of sIgA was transient;

the sIgA fall was significantly correlated with the cortisol rise during the 20 minutes after stress[34]. Previous studies have shown the relationship between cortisol and levels of sIgA after the stressful situation in animals[4]. It is reported that basal sIgA (an index of mucosal immunity) and cortisol levels could predict stress-related health outcomes. Participants with low basal sIgA levels and high basal cortisol levels had poorer health outcomes during the examination session than did participants with high basal sIgA levels and low basal cortisol levels[35]. In a study on first-year medical students, in order to assess the stress-reducing effects of MBMS (Mind Body Medicine Skills Program), changes in levels of cortisol, DHEA-S, testosterone, and IgA were measured in both groups [(T2p)-post-intervention and (T2c)-control] during the period of final examinations. The results, after implementation of the intervention program (MBMS) showed that cortisol, DHEA-S, testosterone levels at T2p were significantly lower than T2c, whereas sIgA levels were not statistically different[36]. Releasing too much cortisol can suppress aspects of immune function and negative effects on health[37]. Overall, the results show that it is possible that there is a correlation between the increase of cortisol activity and mucosal immune function.

In contrast, some studies have reported an increase in the concentration or an increase in the secretion of salivary IgA in response to the exam stress[13,14,38]. While present results showed lower levels of salivary IgA in exam conditions. some studies observed higher cortisol levels before than after the exam, whereas no significant differences were noted between the pre- and post-test saliva samples for salivary IgA and chromogranin A (CgA) levels. Also, students' perceived stress scores before the exam were associated with raised salivary cortisol, but not IgA or CgA[39]. In contrast to these findings, another research

found that both IgA and CgA concentrations statistically increased immediately after the examination and decreased two hours after the examination. No significant differences were observed between, before, and after the examination in the salivary cortisol concentration[40]. Results of a meta-analytical study also showed that brief naturalistic stressors (such as exams) tended to suppress cellular immunity while preserving humoral immunity[37]. In general, studies are classified[9] on a basis of whether samples were taken close to (i.e., during, or minutes before or after) a single exam, or were taken sometime during the extended exam period. Studies[38,41-46] whose samples were collected close to an examination were found increased in salivary IgA levels, whereas lower levels of S-IgA have been reported in Studies[10,11,47-50] in which samples were taken during the extended exam period, and one study[51] showed no change. Thus, according to this classification, saliva samples taken during, minutes before or after the exam or during an extended examination may see different effects of examination stress on levels of IgA.

Relationship personality traits and psychological variables with IgA

In addition to psychological stressors, psychological characteristics and personality of individuals could also play a mediating role in the intensity of the impact of stress on biological responses, in particular the immune system. Specifically, it has been found that subjects with higher scores in neuroticism and anxiety are defined by lower levels of the basal salivary IgA and more significant reduction IgA in certain stress conditions[52]. Previous studies have identified the relationship between personality traits with cortisol and alpha amylase activity. For example, cor-

tisol secretions positively increase with neuroticism traits[19,26]. Also, a negative correlation between openness to experience and salivary cortisol has been observed[53]. Similarly, some studies have reported a negative correlation[17,20] between neuroticism with salivary alpha amylase, and also a negative[20] and positive[17] correlation between agreeableness and salivary alpha-amylase under psychological stress.

In the present study, rumination and emotional inhibition were statistically correlated with salivary IgA under psychological stress. A few studies in this field were found. However, evidence suggests that rumination affects the physiological system and makes longer stress-related stimulation of the hypothalamic-pituitary-adrenal (HPA) axis; the effect was also observed by cortisol reaction to the stressor[54]. Studies indicated that rumination is related to other salivary biomarkers such as cortisol[15] and alpha amylase[17]. Furthermore, emotional inhibition is defined as a desire to inhibition and suppression of the experienced emotions[26]. Its role is delaying the physiological activation and improving the delayed muscle tension following stress[55]. Researches that show salivary IgA levels under examinations stress influenced by the emotional inhibition were not found. However, previous studies about effects of the expression of negative emotions on the immune system showed that subjects who are clearly crying during a tragic movie, compared with those who inhibit the expression of weeping openly, had salivary IgA concentration levels lowered significantly after watching the movie[56]; an increase in salivary IgA levels in individuals who do not cry clearly during the movie has been reported[57]. Nevertheless, positive or negative effects of emotional inhibition on the immune system, specifically the salivary IgA are unknown, because of conflicting findings. For example, increased salivary IgA levels with an increase in negative emotions, have been observed[58].

The present study showed that salivary IgA can be used both as a marker of the immune system and may a marker of the autonomic nervous system, whereas other biomarkers such as alpha amylase and cortisol are only markers of the autonomic nervous system. As the results indicated, the mean salivary IgA in the exam stress was less than the basal conditions. So, measurement of salivary IgA could be a useful and non-invasive method to measure the effects of stress on the immune system. It seems that personality traits determine not only a specific form of emotional and behavioral responsiveness, but possibly a certain form of physiological responsiveness to specific stressful situations. Traditionally the Five-Factor Model is applied in the diagnosis and pathology of mental disorders. Nevertheless, more psychoneuro-immunological research using the Five Factor Model is required to determine psychological and physiological effects associated with the personality traits on the immune system. Furthermore, psychological variables such as rumination and emotional inhibition may be considered to identify vulnerability of individuals to stressful situations. We suggest that in future studies appropriate experimental designs be used to control some of the factors that influence the results, such as time patterns of salivary sampling and the type of stress (short or long, psychological or actual) in order to clarify the real impact of psychological factors (rumination and emotional inhibition) and personality traits on the immune system under stress.

Acknowledgments

Author's contribution

All authors contributed to the study design. RA and SS were Leader of the research. WK and D AL conducting the statistical analysis and MA, EE and S NA prepared the Manuscript. A KK and OS read and editing the manuscript. All authors read and approved the final version of the manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding/Support

References

1. Joshi RM, Sanghavi SJ, Upadhyaya DP, Chauhan A, Halvadia S. Effect of examination stress on the plasma cortisol level. National Journal of Medical Research. 2012; 2(4): 435-8.

2. Cohen S, Miller GE, Rabin BS. Psychological stress and antibody response to immunization: a critical review of the human literature. Psychosom Med. 2001; 63(1): 7-18.

3. Valdimarsdottir HB, Stone AA. Psychosocial factors and secretory immunoglobulin A. Crit Rev Oral Biol Med. 1997; 8(4): 461-74.

4. Svobodová I, Chaloupková H, Kon el R, Bartoš L, Hradecká L, Jebavý L. Cortisol and Secretory Immunoglobulin A Response to Stress in German Shepherd Dogs. PLoS One. 2014; 9(3): e90820.

5. Nomura S, Handri S, Honda H. Development of a bionanodevice for detecting stress levels. IOP Conference Series: Materials Science and Engineering. 2011; 21(1): 012029.

6. Singh R, Goyal M, Tiwari S, Ghildiyal A, Nattu SM, Das S. Effect of examination stress on mood, performance and cortisol levels in medical students. Indian J Physiol Pharmacol. 2012; 56(1): 48-55.

7. Choi J, Chung M, Lee Y. Modulation of pain sensation by stress related testosterone and cortisol. Anaesthesia. 2012; 67(10): 1146-51.

8. Shamsdin SA, Anvar M, Mehrabani D. The Effect of Exam Stress on Serum IL-6, Cortisol, CRP and IgE Levels. Iranian Red Crescent Medical Journal. 2010; 2010(4): 484-8.

9. Bosch JA, Ring C, Amerongen AVN. Academic examinations and immunity: academic stress or examination stress? Psychosom Med. 2004; 66(4): 625-6.

10. Deinzer R, Kleineidam C, Stiller-Winkler R, Idel H, Bachg D. Prolonged reduction of salivary immunoglobulin A (sIgA) after a major academic exam. Int J Psychophysiol. 2000; 37(3): 219-32.

11. Jemmott JB, Magloire K. Academic stress, social support, and secretory immunoglobulin A. J Pers Soc Psychol. 1988; 55(5): 803.

12. Lowe G, Urquhart J, Greenman J, Lowe G. Academic stress and secretory immunoglobulin A. Psychol Rep. 2000; 87(3): 721-2.

13. Otsuki T, Sakaguchi H, Hatayama T, Takata A, Hyodoh F, Tsujita S, et al. Secretory Ig A in saliva and academic stress. International journal of immunopathology and pharmacology. 2004; 17(2 suppl): 45-8.

14. Sarid O, Anson O, Yaari A, Margalith M. Academic stress, immunological reaction, and academic performance among students of nursing and physiotherapy. Res Nurs Health. 2004; 27(5): 370-7.

15. Zoccola PM, Dickerson SS. Assessing the relationship between rumination and cortisol: A review. J Psychosom Res. 2012; 73(1): 1-9.

16. Hu E, Koucky EM, Brown WJ, Bruce SE, Sheline YI. The role of rumination in elevating perceived stress in posttraumatic stress disorder. Journal of interpersonal violence. 2013: 0886260513511697.

17. Afrisham R, Sadegh-Nejadi S, SoliemaniFar O, Abromand M, Kooti W, Najjar Asl S, et al. Evaluating the Salivary Alpha-amylase Level under Psychological Stress and its Relationship with Rumination and the Five Personality Traits. Journal of Mazandaran University of Medical Sciences. 2015; 25(126): 22-33.

18. Segerstrom SC. Personality and the immune system: Models, methods, and mechanisms. Ann Behav Med. 2000; 22(3): 180-90.

19. Nater UM, Hoppmann C, Klumb PL. Neuroticism and conscientiousness are associated with cortisol diurnal profiles in adults-role of positive and negative affect. Psychoneuroendocrinology. 2010; 35(10): 1573-7.

20. Inukai K, Shinada M, Tanida S, Takahashi C, Mifune N, Takagishi H, et al. Salivary alpha-amylase levels and big five personality factors in adults. Neuro Endocrinol Lett. 2009; 31(6): 771-4.

21. Segerstrom SC, Castañeda JO, Spencer TE. Optimism effects on cellular immunity: testing the affective and persistence models. Pers Individ Dif. 2003; 35(7): 1615-24.

22. Miller GE, Cohen S, Rabin BS, Skoner DP, Doyle WJ. Personality and tonic cardiovascular, neuroendocrine, and immune parameters. Brain Behav Immun. 1999; 13(2): 109-23.

23. Shamsdin S, Anvar M, Mehrabani D. The Effect of Exam Stress on Serum IL-6, Cortisol, CRP and IgE Levels. Iranian Red Crescent Medical Journal. 2010; 12(4): 484-8.

24. Ghafourian-Boroujerdnia M SZ HN, Hemmati AA, Kooti W. The Relationship of Hardiness and Immune System Cells. J Isfahan Med Sch. 2014; 31(260): 1812-20.

25. Costa PT, McCrae RR. Reply to Eysenck. Pers Individ Dif. 1992; 13(8): 861-5.

26. Roger D, Najarian B. The relationship between emotional rumination and cortisol secretion under stress. Personality and Individual Differences. 1998; 24(4): 531-8.

27. Rafineya P RTSK AFP. The relation between emotional expression and mental health in students. J Psychol. 2006; 10(1): 85-104[persian].

28. Susman EJ, Dockray S, Granger DA, Blades KT, Randazzo W, Heaton JA, et al. Cortisol and alpha amylase reactivity and timing of puberty: Vulnerabilities for antisocial behaviour in young adolescents. Psychoneuroendocrinology. 2010; 35(4): 557-69.

29. Bienvenu OJ, Nestadt G, Samuels JF, Costa PT, Howard WT, Eaton WW. Phobic, panic, and major depressive disorders and the five-factor model of personality. The Journal of nervous and mental disease. 2001; 189(3): 154-61.

30. Kotov R, Gamez W, Schmidt F, Watson D. Linking "big" personality traits to anxiety, depressive, and substance use disorders: a meta-analysis. Psychol Bull. 2010; 136(5): 768.

31. Khodarahimi S, Rasti A. The roles of fatigue, depression, and Big Five Personality traits in males with and without multiple sclerosis disease. Clínica y Salud. 2015; 26(2): 91-6.

32. Takahashi A, Uchiyama S, Kato Y, Yuhi T, Ushijima H, Takezaki M, et al. Immunochromatographic assay using gold nanoparticles for measuring salivary secretory IgA in dogs as a stress marker. Science and Technology of Advanced Materials. 2009; 10(3): 034604.

33. Yang E, Glaser R. Stress-induced immunomodulation: impact on immune defenses against infectious disease. Biomed Pharmacother. 2000; 54(5): 245-50.

34. Fan Y, Tang Y, Lu Q, Feng S, Yu Q, Sui D, et al. Dynamic changes in salivary cortisol and secretory immunoglobulin A response to acute stress. Stress and Health. 2009; 25(2): 189-94.

35. Volkmann ER, Weekes NY. Basal SIgA and cortisol levels predict stress-related health outcomes. Stress and Health. 2006; 22(1): 11-23.

36. MacLaughlin BW, Wang D, Noone A-M, Liu N, Harazduk N, Lumpkin M, et al. Stress biomarkers in medical students participating in a mind body medicine skills program. Evid Based Complement Alternat Med. 2011; 2011.

37. Segerstrom SC, Miller GE. Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. Psychol Bull. 2004; 130(4): 601.

38. Evans P, Bristow M, Hucklebridge F, Clow A, Pang FY. Stress, arousal, cortisol and secretory immunoglobulin A in students undergoing assessment. Br J Clin Psychol. 1994; 33(4): 575-6.

39. Ng V, Koh D, Mok B, Chia S-E, Lim L-P. Salivary biomarkers associated with academic assessment stress among dental undergraduates. J Dent Educ. 2003; 67(10): 1091-4.

40. Takatsuji K, Sugimoto Y, Ishizaki S, Ozaki Y, Matsuyama E, Yamaguchi Y. The effects of examination stress on salivary cortisol, immunoglobulin A, and chromogranin A in nursing students. Biomed Res. 2008; 29(4): 221-4.

41. McClelland DC, Ross G, Patel V. The effect of an academic examination on salivary norepinephrine and immunoglobulin levels. J Human Stress. 1985; 11(2): 52-9.

42. Bosch J, Brand H, Ligtenberg A, Bermond B, Hoogstraten J, Nieuw-Amgerongen A. The response of salivary protein levels and S-IgA to an academic examination are associated with daily stress. Journal of Psychophysiology. 1998; 12(4): 384-91.

43. Bosch JA, Brand HS, Ligtenberg TJ, Bermond B, Hoogstraten J, Amerongen AVN. Psychological stress as a determinant of protein levels and salivary-induced aggregation of Streptococcus gordonii in human whole saliva. Psychosom Med. 1996; 58(4): 374-82.

44. Bristow M, Hucklebridge F, Clow A, Evans PD. Modulation of secretory immunoglobulin A in saliva in relation to an acute episode of stress and arousal. Journal of Psychophysiology. 1997; 11(3): 248-55.

45. Spangler G. Psychological and physiological responses during an exam and their relation to personality characteristics. Psychoneuroendocrinology. 1997; 22(6): 423-41.

46. Huwe S, Hennig J, Netter P. Biological, emotional, behavioral, and coping reactions to examination stress in high and low state anxious subjects. Anxiety, stress, and coping. 1998; 11(1): 47-65.

47. Jemmott J, Borysenko M, Chapman R, Borysenko J, Mcclelland D, Meyer D, et al. Academic stress, power motivation, and decrease in secretion rate of salivary secretory immunoglobulin A. The Lancet. 1983; 321(8339): 1400-2.

48. Mouton C, Fillion L, Tawadros É, Tessier R. Salivary IgA is a weak stress marker. Behav Med. 1989; 15(4): 179-85.

49. Li S, Xiu B, Qian Z, Tang P. Changes in salivary cortisol and S-IgA in response to test stress. Chinese Mental Health J. 1997; 11: 336-8.

50. Deinzer R, Schüller N. Dynamics of stress-related decrease of salivary immunoglobulin A (sIgA): relationship to symptoms of the common cold and studying behavior. Behav Med. 1998; 23(4): 161-9.

51. Kiecolt-Glaser JK, Garner W, Speicher C, Penn GM, Holliday J, Glaser R. Psychosocial modifiers of immunocompetence in medical students. Psychosom Med. 1984; 46(1): 7-14.

52. Rohrmann S, Hennig J, Netter P. Trait anxiety–possible consequences for health. German Journal of Psychiatry. 2000; 3(3): 19-25.

53. Wirtz PH, Elsenbruch S, Emini L, Rüdisüli K, Groessbauer S, Ehlert U. Perfectionism and the cortisol response to psychosocial stress in men. Psychosom Med. 2007; 69(3): 249-55.

54. Zoccola PM, Dickerson SS, Zaldivar FP. Rumination and cortisol responses to laboratory stressors. Psychosom Med. 2008; 70(6): 661-7.

55. Kaiser J, Hinton JW, Krohne HW, Stewart R, Burton R. Coping dispositions and physiological recovery from a speech preparation stressor. Pers Individ Dif. 1995; 19(1): 1-11.

56. Labott SM, Ahleman S, Wolever ME, Martin RB. The physiological and psychological effects of the expression and inhibition of emotion. Behav Med. 1990; 16(4): 182-9.

57. Martin RB, Guthrie CA, Pitts CG. Emotional crying, depressed mood, and secretory immunoglobulin A. Behav Med. 1993; 19(3): 111-4.

58. Evans P, Bristow M, Hucklebridge F, Clow A, Walters N. The relationship between secretory immunity, mood and life events. Br J Clin Psychol. 1993; 32(2): 227-36.

* Corresponding author:
Sahar Sadegh-Nejadi
Department of Clinical Biochemistry,
Faculty of Medicine, Ahvaz Jundishapur
University of Medical Sciences, Ahvaz
Iran
Tel. 00989339772675
Fax 00986134457684
E-mail: s_laboratory87@yahoo.com