



Brain-Behavioral Systems and Psychological Distress in Patients with Diabetes Mellitus; A Comparative Study

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ABSTRACT

Background: Diabetes mellitus is a common metabolic disorder worldwide. It imposes excessive psychological stress on patients which negatively affect the course of the disease. The brain-behavioral systems have a role in dealing with stressful events such as chronic disorders.

Objective: Comparison the brain-behavioral systems and psychological distress in diabetic patients and non-diabetics.

Materials and Methods: This causal-comparative study was conducted on patients with diabetes type II and controls that were selected by simple sampling method from January to March 2015 in Tehran, Iran. A demographic questionnaire and also Behavioral Inhibition/Activation systems scale (BIS/BAS) and Depression, Anxiety, Stress Scale (DASS) were used to assess subjects.

The data were analysed in SPSS 18 software using descriptive statistics and multi-variate analysis of variance (MANOVA).

Results: A total of forty-three subjects (22 female and 21 male) were included in each group of diabetic and control subjects with mean age of 41.77 ± 5.34 and 40.21 ± 6.47 years respectively ($p > 0.01$).

The groups had a significant difference in terms of brain-behavioral systems activity [$F_{(5, 80)} = 22.33, p < 0.001$] with significant differences in BAS and its subscales of drive and pleasure seeking, while no significant difference was observed between the two groups in BIS activity or BAS subscale of reply to reward. Also results demonstrated significant differences as the matter of psychological distress [$F_{(3, 82)} = 26.26, p < 0.001$] with difference in all of its dimensions.

Conclusion: People with diabetes are prone to psychological distress, also strong behavioral activation system can be considered as factors in the persistence and exacerbation diabetes.

Keywords: Diabetes Mellitus, Psychological Distress, Brain-Behavioral Systems

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Introduction

D iabetes Mellitus is a common metabolic disorder among adults and one of the most common endocrine

disorders in the world. It has so many long-term complications that adversely affect cardiovascular system, kidneys, retina, and

nervous system as the time passes. Currently, it is highly prevalent in the Middle East. Also in Iran, almost 7.7% of the population is estimated to suffer from diabetes (1). Because of its complexity and etiology, diabetes ought to be studied through a biological-psychosocial model (1). Diabetes was responsible for 4 million deaths in 2011 and also six years reduction in life expectancy compared with fifty years ago (2). Diabetes imposes excessive psychological stress on the affected individuals which can negatively affect the course of the disease. Psychological distress is a multidimensional construct which includes experiencing the unpleasant emotions resulted in lowering quality of life. It is one of the most important debilitating risk factors in diabetic patients. In a study Hamer et al. showed an association between psychological distresses and some limitations in daily life, self-care and also social and familial functions (3). Jimenez-Garcia et al. also demonstrated greater psychological distress in diabetic patients compared to normal people. Anxiety and depression are two dimensions of psychological distress in these patients, which are greatly related to treatment outcomes and exacerbation of disease and have been considered as both risk factors and also consequences of diabetes mellitus. Depression symptoms are significantly related to disabilities in diabetic patients (4). Anxiety and depression are highly prevalent in diabetics and are related to negative treatment results (5,6). Anxiety is one of the less studied comorbid disorders with diabetes, sixty percent prevalence which has among diabetic patients. It is associated with disabilities and poorer treatment outcomes. Also have shown by research results that diabetes increases the odds of anxiety disorders and symptoms (7,8). So

there is a reciprocal association between diabetes and anxiety disorders, and the same relationship exists with depression (9). In a study conducted by Eriksson et al. which measured baseline level of glucose tolerance and psychological distress, diabetic patients were found to have high levels of glucose tolerance, as well as greater psychological distress, and this relationship persisted even in the period of four months follow-up (10).

Researchers are interested in the role of individual differences including personality in psychosomatic disorders. Personality and personality traits are among major risk factors for diabetes (11). In their study, Goodwin et al. identified neuroticism as a predictive and also risk factor for diabetic complications (12). Several studies have identified the relationship between diabetic patients' personality and their psychological and behavioral characters. Neuroticism is found to be related to obesity, hypertriglyceridemia, metabolic syndrome, and high level of blood glucose (13). Personality is considered as a risk factor for metabolic disorders, and this vulnerability emerges in some ways such as lifestyle, seeking internal and external stimuli, vulnerability against symptoms of anxiety and depression, and order and organization in personal life. In these patients, personality plays an effective role in self-care and treatment outcomes (14). Studies on the effect of psychological factors on psychosomatic disorders have identified personal differences as psychological factor that affects the course of the disease (15).

Gray's theory of personality is one of the theories that deal with personal differences, proposed in the form of personality traits that affect medical illnesses and psychological distress (16). Gray used his theory to explain biological sensitivity as the basis for

development of disorders (17). By reviewing studies on animals in Reinforced Sensitivity Theory (RST), Gray presented a biological model of personality, which explains personal differences at biological level. Each of these brain-behavioral systems calls for a different emotional reaction, such as fear and anxiety. Behavioral Inhibitory System (BIS) responds to conditional stimuli of punishment and lack of reward, and also to intrinsic new and frightening stimuli. This system is also associated to negative emotions such as anxiety, disappointment, and sadness. Anatomically the related structures are located in hippocampal septal area which includes three main parts of hippocampus, septal area (consisting of medial and lateral septal areas) and the Papez Circuit (18). BIS produces inhibitory and avoidance responses by means of activity of noradrenergic and serotonergic neurotransmitters (19). Behavioral Activation System (BAS) also responds to conditional stimuli of reward and lack of punishment. BAS activity is associated with positive emotions such as hope, peace of mind, and happiness, and is divided into 3 subsets of seeking pleasure, and responding to reward and drive (20). Key neurological components of BAS including basal ganglia (ventral and dorsal striatum, ventral and dorsal pallidum), the ascending dopaminergic nerve fibers from mesencephalon (Substantia-Nigra and A10 core) supplying the basal ganglia and thalamic nuclei that are closely related to basal ganglia (21). These brain-behavioral systems are associated with negative emotions (20,23), depression (24), and anxiety disorders (25), all of which are risk factors of diabetes mellitus (26).

Considering substantial effects of psychological distress on diabetic patients,

the role of brain-behavioral systems in dealing with stressful events, and considering the little amount of studies in this field, the present study aimed to investigate the brain-behavioral systems and psychological distress in patients with type II diabetes.

Materials and Methods

This causal-comparative study was conducted on two groups of patients with type II diabetes and controls from January to March 2015. Patients with diabetes mellitus were selected from Diabetes Centers and Endocrinology Clinics in Tehran State, Iran. The inclusion criteria were: minimum of reading and writing literacy, at least 18 years of age, no other physical illnesses. All patients had been diagnosed with type II diabetes for at least one year and been receiving treatment. Control group was so selected from normal population and was matched with the case group in terms of age, education, marital status, gender, and occupation as much as possible. Both groups were selected by simple sampling method. An explanation about study was given to participants and they fulfilled a written informed consent before making contribution in study.

The questionnaires used are listed as following:

- *Demographic questionnaire*: A researcher-designed questionnaire used to collect data such as age, gender, family history, past medical and psychological history, drug history, education (years of education), marital status, and other social history and etc.

- *Behavioral Inhibition/Activation systems scale (BIS/BAS)*: This questionnaire contains 24 items, of which 7 belong to BIS and 13 to BAS. BAS scale consists of 3 subscales of

drive (4 items), seeking pleasure (4 items), and responding to reward (5 items), and 4 items as diversion items (not scored). Cronbach's alpha for BIS scale was reported 0.77, and for above subscales 0.76, 0.71, and 0.73, respectively (20).

- *Depression, Anxiety, and Stress Scale (DASS)*: This scale has been designed to measure negative emotions such as depression, anxiety, and stress over the past 3 weeks. Factor analysis has confirmed 3 subscales of depression, anxiety, and stress, with Eigenvalues of 2.89, 1.23, and 9.07, and Cronbach's alpha of 0.92, 0.95, and 0.97, respectively (27). In the Persian version, test-retest reliability was reported for depression, anxiety, and stress as 0.8, 0.76, and 0.77, and Cronbach's alpha was reported as 0.81, 0.74, 0.78, respectively (28).

The researcher was actively present when participants were filling out questionnaires to prevent random answers and to answer any question participants may have had. Collected data were analysed in SPSS-18 software using descriptive statistics and multi-variate analysis of variance (MANOVA).

Results

A total of forty-three (22 female and 21 male) were included in each group of diabetic and control subjects. In diabetic group, thirty four patients and in control group thirty five subjects were married. The patients demonstrated the mean age of 41.77 ± 5.34 years and the control subjects as $40.21 \pm (6.47)$ years. The means level of education were also 12.77 ± 3.53 and 12.23 ± 3.81 years respectively in two mentioned groups.

Independent t-test showed no significant difference between two groups regarding of age [$t(84) = 0.56, p > 0.01$], or education [$t(84) = 0.68, p > 0.01$], which confirms two groups were matched in those variables.

Multivariate analysis was used to compare the two groups in terms of brain-behavioral systems activity and psychological distress. To this end, at first the miscellaneous data were converted into standard (Z) scores and Z scores outside the range of +1.5 and -1.5 were eliminated.

In comparing the brain-behavioral activity, the range of Levene's test [$F_{(1, 84)} = 0.88-1.79; p > 0.01$] and Kolmogorov-Smirnov (0.55-1.6) tests indicated equality of variances and normal distribution of data. Also, the results of Box M test [$F_{(15, 28409.68)} = 1.33, p > 0.01$] showed covariance matrix of dependent variable are equal across groups, so the multivariate analysis could be used. Wilks' Lambda multivariate test result was significant [$F_{(5, 80)} = 22.33, p < 0.001$], which confirmed significant differences between two groups in terms of brain-behavioral systems activity, but did not show in which component of brain-behavioral systems activity the two groups differed. To find this, one-way variance analysis was used. Table 1 presents the values of F, one-way variance analysis, mean and standard deviation of brain-behavioral systems activity.

Table 1 shows significant differences between the two groups in BAS and its subscales of drive and pleasure seeking, with higher mean scores in diabetic patients compared to controls, while no significant difference was observed between the two groups in BIS activity or BAS subscale of reply to reward.

Table 1: The mean, standard deviation of scores and the results of uni-variate analysis for comparison the activity of brain / behavioral systems in diabetic and control subjects

Brain/ behavioral systems	Group	Number	The Mean \pm (SD*)	F df=(1, 84)	η^2
BAS**	Diabetic	43	43.63 \pm (12.18)	11.12	0.12
	control	43	37.07 \pm (4.23)		
Drives	Diabetic	43	14.47 \pm (5.57)	25.85	0.23
	control	43	10.00 \pm (1.45)		
Reply to reward	Diabetic	43	15.67 \pm (4.43)	0.31	0.004
	control	43	16.09 \pm (2.19)		
Pleasure seeking	Diabetic	43	13.49 \pm (3.21)	22.45	0.21
	control	43	10.81 \pm (1.84)		
BIS***	Diabetic	43	20.05 \pm (5.44)	0.11	0.001
	control	43	19.74 \pm (2.49)		

* Standard Deviation
** Behavioral Activation System
*** Behavioral Inhibition System

In comparison of the two groups as the points of psychological distress, range of Levene's test [$F_{(1, 84)} = 0.58-1.46, p > 0.01$] and Kolmogorov-Smirnov (0.39-1.28) tests showed the equality of variances and normal distribution of data. Box M test results [$F_{(6, 51122.72)} = 1.02; p > 0.01$] showed covariance's matrix of dependent variables in the two groups are equal, and so multivariate analysis could be used. Wilks' Lambda multivariate test result was significant [$F_{(3, 82)} = 26.26, p < 0.001$], which demonstrated significant differences between the two groups as a

matter of psychological distress, but did not show in which dimensions of psychological distress the two groups differed. To this end, one-way variance analysis was used. Table 2 represents mean and standard deviation, and results of one-way variance analysis of the dimensions of psychological distress. The results presented in table 2 show significant differences between the two groups in all dimensions of psychological distress, and depression, anxiety, and stress are more observed in patients with diabetes.

Table 2: The mean, standard deviation of scores and the results of one-way variance analysis for comparison of the dimensions of psychological distress in diabetic and control subjects

Dimensions of Psychological Distress	Group	Number	The Mean \pm (SD*)	F df=(1, 84)	η^2
Depression	Diabetic	43	17.77 \pm (5.94)	63.99	0.43
	control	43	9.88 \pm (2.54)		
Anxiety	Diabetic	43	19.42 \pm (6.85)	76.35	0.48
	control	43	9.67 \pm (2.55)		
Stress	Diabetic	43	20.88 \pm (8.52)	54.01	0.39
	control	43	10.91 \pm (2.58)		

* Standard Deviation

Discussion

The present study showed greater psychological distress in diabetic patients compared with controls, which is in agreement with the results found in studies by

Standberg et al. (28), Bystritsky et al.(29), and Lipscombe et al. (30) regarding greater amount of anxiety symptoms in diabetic patients compared with healthy people. Also it is in agreement with the results of studies by Hessler et al. (31), Rodríguez et al. (32),

and Davis et al. (33) regarding more depression symptoms in diabetic patients in comparison with normal individuals. Besides it is concurred with the results of researches by Dabhi & Mistery (34), and Shallcross et al. (35) regarding high level of stress in diabetic patients compared to healthy people.

Diabetes mellitus plays a key role in presentation of somatoform symptoms and exacerbation of psychological distress. Association between depression and diabetes is the best example for explaining the bidirectional relationship between mind and body. Diabetes causes suffering of individual from a variety of psychological disorders such as anxiety, depression, and mental preoccupation with illness (36). Evidence shows negative effect of metabolic disorders (such as diabetes) on the central nervous system and it has been shown that diabetes causes cognitive and mood dysfunction, predisposing people to mood disorders and mental regression such as Alzheimer's disease (37,38). A quarter of diabetics show symptoms of depression (39) and diabetes is a risk factor for depression (40). Diabetic women are twice as likely to suffer postpartum depression compared with normal women. Association between depression and diabetes leads to more frequent complaints related to diabetes, poorer self-care, more deaths, and higher expenses of caring for these patients (41). Depression and stressful life events can lead to pituitary gland dysfunction, and by complex hormonal interactions resulted in pathogenesis of metabolic disorders (42). Given association between these two disorders, treatment of each one can affect the other. Many studies have cited metabolic results of psychotherapy and vice versa (9). Demonstrated biological, psychological and sociological mechanisms

in pathogenesis of depression and diabetes can accelerate mental and metabolic processes of both disorders (39). Increased symptoms of diabetes are associated with psychological stresses, and lead to reduced coping ability of individual (which is a factor for depression per se). Fatigue caused by treatment of diabetes such as insulin injection and glucose check can lead to negative emotions and maladaptive behaviors, consequently leading to the individual toward disinterest, lack of energy, unhealthy diet, and sleep disturbance (10). Expressed feelings at the time of diabetes diagnosis include stress, depression, and reduced sense of well-being, and some emotional changes can lead to conflict among family members, friends and colleagues (43).

According to studies, about 20% of diabetics suffer symptoms of anxiety (44). Several longitudinal studies have confirmed association of anxiety disorders and symptoms with diabetes (45). Anxiety symptoms in diabetics are associated with increased complaints about disease (46), greater pain, increased glucose (47), reduced quality of life (48), increased depression (49), and higher BMI (50), and more disabilities. In new treatment methods, anxiety therapy techniques are used to reduce symptoms of diabetic patients, which show the effects of anxiety on diabetes. Since anxiety takes longer to be diagnosed compared rather than depression, it will become chronic and so requires greater attention (51). Diabetes also causes increased stress and anxiety as the results of hormonal and metabolic activities in diabetic patients (45).

Other findings of the present study include significant differences between the two groups in BAS activity and its subscales of drive and pleasure seeking, and mean scores

were greater in diabetics compared to normal people, and this agrees with previous studies (52).

One of the theories used as the basis to explain the interpersonal differences in psychopathology of disorders is Reinforced Sensitivity Theory (RST) proposed by Jeffery Gray (53). According to this theory, personality cannot be considered independent of brain-behavioral systems, and is definable according to these systems. RST believes people are born with genetically determined various levels of cerebral systems sensitivity and then affected by environmental and learning factors in the course of life. In his initial theory, Gray proposed three systems having roles in behavioral motivations: 1- fight/flight system that is sensitive to unconditioned aversive stimuli (such as inner painful stimuli), and provides some emotions such as anger and fear. 2-Behavioral Activation System (BAS), with sensitivity to conditioned appealing stimuli and activation in presence of reward or lack/termination of punishment. It is also associated with impulsiveness. [Carver & White (20) believed this system to include 3 subsets: A) Response to drive (rapidly and powerfully peruses the target), B) Response to reward (seeks reward), and C) Pleasure seeking (seeks new and rewarding experiences)] 3- Behavioral Inhibition System (BIS), which is sensitive to non-rewarding stimuli (such as punishment and lack/termination of reward), and is associated with anxiety (54).

Making clear the strong behavioral activation system among diabetic persons, this system's relationship with eating disorders and obesity can be addressed. BAS has potential for some harmful behaviors, such as a notable appetite for high fat and sugar containing diet that is very enjoyable

for consumer. Davis et al. found a positive relationship between BAS and BMI because of relationship with overeating and high-fat diet (55). People with strong BAS are more interested in unhealthy foods which predispose them to obesity (52). Furthermore, obesity and overeating are considered as risk factors for diabetes type II (56). In fact, diabetes is a presentation of a broader disorder called metabolic syndrome, which consists of several disorders (abdominal obesity, arterial hypertension, insulin resistance, and glucose abnormality). Obesity increases the risk of diabetes by tenfold (57). As a subscale of BAS, drive is directly related to high-fat diet and partiality to high-caloric foods (58). BAS is directly related to eating disorders (59). Strong BAS leads to vulnerability to obesity and overweight (60).

Dopaminergic system is another factor involved in strong BAS in these people. Dopaminergic neurotransmitters are also supposed as the affective etiologic factors in diabetes (61). Previous studies have found that diabetics are faced with reduced secretion of dopamine (62), which is associated with high levels of BAS in these patients (63).

The limitations of this study included lack of control of variable of gender in diabetic patients, low sample size, data collection tool and simple sampling method that could have caused bias in sample selection and their non-homogeneity, which may have caused limitations in generalization of results and interpretation of variables.

Conclusion

People with diabetes are prone to psychological distress, as well as strong behavioral activation system can be considered as factors in the persistence and

exacerbation diabetes. It seems that BAS is associated with behaviors that lead to persistence of a disorder such as tendency to overeat and unhealthy diets, which subsequently lead to increased anxiety and depression seeking psychological interventions in these patients.

Conflict of Interest

No Conflict of Interest

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