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The Moderating Role of Personality Dimensions in the Relationship between Brain-Behavioral Systems and Multiple Sclerosis Severity

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Multiple Sclerosis (MS) is one of the neurological disorders that occur along with the degeneration of the myelin sheath. The aim of the present study was to investigate the moderating role of personality dimensions in the relationship between brain-behavioral systems and multiple sclerosis severity in individuals suffering from MS. This research was a correlational study in which 162 patients with MS were selected as statistical samples by the purposive sampling method in the City of Shiraz. Data were analyzed by Pearson's correlation coefficient and moderated regression. The findings revealed that brain-behavioral systems significantly predict MS severity ($P < .01$ and $F_{Change} = 5.66$) and only the neuroticism dimension as the moderator significantly increased the determined variance on MS severity ($P < .01$, $\beta = .77$, and $F_{Change} = 54.22$). Therefore, neuroticism was able to moderate these relationships and increase their amounts. The obtained results confirmed the moderating role of neuroticism in the relationship between reinforcement sensitivity and the severity of the extent of disability in MS.

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Multiple Sclerosis is the most prevalent autoimmune disease that disables the Central Nervous System (CNS), and emerges as a result of gliosis and axonal degeneration in the form of inflammation (Troster & Alexander, 2006); therefore, all the parts of the CNS are exposed to risk (Kikuchi, 2013). Inflammation and degeneration of the myelin sheath through astrocytes duplication not only affects the sensory and motor functions but also results in the incidence of psychopathological symptoms (Haussleiter, 2009). Lesions inside of or adjacent to the cortex bear significant impacts on the relationship between brain injury in MS patients and cognitive disorders; in addition, there is a relationship between cognitive disorders and psychological changes, such as apathy and depression, in this clinical population (Dennison, 2009). Although MS is rarely fatal in comparison to individuals suffering from other chronic diseases, it has a wide range of unpleasant and disabling symptoms (Harbige, 2007), and psychological problems are prevalent in MS patients (Haussleiter, 2009).

According to several evidences, patients with MS experience impairments in personality and affect (Charcot, 1889). It is assumed that these impairments may be the result of a psychological reaction to the stress of MS and/or brain pathology. Initial neurological studies have also distinguished between acute mood disorders and chronic disorders that are related to personality and emotional changes in MS (Benedict, Priore, Miller, Munschauer & Jacobs, 2001). Common personality and emotional changes in MS include disinhibition,

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apathy, instability, impulsivity (Bruce, 2011), high rate of depression and distress (Nocentini & Caltagirone, 2012), anxiety (Ožura, 2010), reduced quality of life (Hopman, 2007; Hopman, 2009) and trouble with social roles (Mohr, 2004).

Some theorists believed that there is a relationship between personality constructs and individual vulnerabilities to psychological disorders; in this regard, various theoretical approaches, as an instance of Gray's theory, have been proposed (Gray, 2000). In Gray's view there are three brain-behavioral systems which affect personality differences: the Fight-Flight-Freeze System (FFFS) is responsible for mediating reactions to all aversive, conditioned and unconditioned stimuli (Gray, 2000; Harnett, 2013), the Behavioral Activation System (BAS), which is sensitive to pleasant positive emotions such as pleasure and hope (Corr, 2004), and the Behavioral Inhibition System (BIS), in which the individual tends to respond to potential environmental punishments and shows sensitivity to internal disorders such as anxiety (Corr, 2008). BIS activity in solving conflicts is mentally experienced as worry or rumination (Alloy, 2008). This system results from the activity of afferent, noradrenergic, and serotoninergic paths (Corr, 2001). Jeffry Gray's Reinforcement Sensitivity Theory (RST) (Gray, 1970; Gray, 2000) can be used to comprehend the fundamental chain mechanisms between normal behavior in healthy individuals and psychological symptoms such as depression, anxiety, and impulsion control disorders (Johnson, 2003). Gray also illustrated that anxiety and impulsivity are the main personality dimensions (Corr, 2008). Some studies have shown that in an MS population, the prevalence of anxiety is greater than depression (by 25–46%), which if not treated, leads to a reduced

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quality of life, problems in pursuing treatment, and intensifying the MS symptoms (Garfield, 2012). Yet, the main factor that causes anxiety in this clinical population has not been determined so far (Iova & Popescu, 2014), and no study has been conducted to explain whether brain-behavioral systems can predict the psychological symptoms of MS patients or not. A part of the present study is devoted to this subject and may thus lead to significant findings.

On the other hand, studies conducted regarding the subject of personality, based on the Five-Factor Model, have shown that there is a significant relationship between psychopathology and personality pathology in MS patients (Bruce, 2011). Among the personality models, the Five-Factor Model (FFM) developed by McCrae and Costa (2004) can sufficiently describe personality trait changes (Matthews, 2003). In this model, the differences between individual personalities are explained by five personality dimensions; these are neuroticism, extroversion, openness to experience, conscientiousness, and agreeableness (McCrae & Allik, 2002). The majority of the findings showed that MS patients suffer from increased neuroticism (Bruce, 2011). In studies conducted by Benedict et al. (2008), and Bruce and Lynch (2011), higher neuroticism and lower extroversion, agreeableness, and conscientiousness were observed based on FFM in anxious / depressed MS patients in comparison to healthy individuals (Benedict et al. 2008; Bruce & Lynch, 2011). Farahani and A'lami (2006) also observed that these patients obtained higher scores in the neuroticism factor (Farahani & Alami, 2006). As described above, the base levels of neuroticism can be considered as a vulnerability indicator (Roberts, 1999). The conducted studies and the proposed

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theories also suggest that understanding the relationship between personality and health is considered highly important; each of these five factors has affected health levels (Jackson, 2009). Therefore, it is expected that these factors moderate the relationship between the personality construct and the health levels. According to Diana, Grosz, and Mancini (1985), investigating the psychological aspects of MS patients in comparison to healthy people revealed that some psychological aspects were associated with disease severity; it can thus be suggested that their bases goes back to early childhood as personality patterns (Diana, Grosz & Mancini, 1985). All in all, the research indicates that there is a complex relationship between personality features and mood disorders/anxiety (Bruce, 2011), and MS severity.

By referring to psychopathological theory based on Gray's theory and the FFM studies conducted, such as by Benedict et al. (2008), and Bruce and Lynch (2011), a question is proposed which enquires whether the dysregulation of brain-behavioral systems accompanied by the moderation of FFM personality dimensions are among the factors involved in the MS severity of symptoms? Considering the daily increase in the presented statistics of MS and its subsequent negative effects on the individual's performance in daily life, its consequences in society, the high levels of inability in social, vocational, and sensory functions in the progression of this disease, and the significant economic expenses of medical services, it seems that the results of this research can be used in etiology and can develop psychological interventional programs to improve MS in patients' psychological functions and their quality of life (Grech et al., 2015). Conducting such studies cannot only

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increase one's psychological knowledge about the predictive factors of MS severity but it also provides us with valuable information about preventive and psychological interventions. This research is attempting to answer the question of whether brain-behavioural systems contribute to the severity of MS symptoms and whether it is possible for personality dimensions to have mediating role?

Method

The research design of the present study is correlational in domain of fundamental-operational studies. The study population includes all the MS patients in the City of Shiraz; the statistical sample includes 162 MS patients who visited the MS Clinic and Association in Shiraz and these patients were selected through the purposive sampling method considering some inclusion and exclusion criteria.

NEO Five-Factor Personality Inventory

McCrae and Costa developed the NEO personality inventory in 1985; the shortened version of this inventory (NEO-FFI) was a 60-item questionnaire which was used to assess the five main factors of personality and its validity coefficients were obtained between .83–.75 (McCrae & Costa, 2004). In Iran, the Cronbach's alpha coefficients in each of major factors of neuroticism, extraversion, openness, agreeableness, and conscientiousness were achieved as .86, .73, .56, .68, and .87, respectively (Garousi Farshi, Mehryar & Ghazi Tabatabaei, 2001).

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Jackson-5 scales Questionnaire

Jackson (2009) developed this questionnaire in order to measure the Revised Reinforcement Sensitivity Theory (r-RST) properly. It includes the subscale of the Behavioral Activation System (BAS), the Fight-Flight-Freeze System (FFFS), and the Behavioral Inhibition System (BIS). For each r-RST sub-scales, six articles are considered. Using the exploratory and confirmatory factor analyses, Jackson attempted to develop and test the new scales (Jackson-5 scales). The validity of this test has been reported from .74 to .83 (Jackson, 2009). In Iran, the validity of this test using the Cronbach's alpha coefficient was between .72 and .88, and its retest coefficients were between .64 and .78 (Hasani, 2012).

Expanded Disability Status Scale

Expanded Disability Status Scale (EDSS) is a method of assessing the status of nervous disorder in MS. This scale, being developed by John F. Kurtzke, determines the quantity of disability in the EDSS in the eight functional systems and allows neurologists to check out the Functional System Score (FSS) (pyramidal, cerebellum, brainstem, sensory, intestine and bladder, visual system, brain functions, sensory, intestinal and bladder functions, and other systems) and assign each of them a score (Kurtzke, 1983). EDSS in MS patients is calculated from 0 to 10 so that the neurologist checks out the physical disabilities of the individual from different aspects and assigns a score between 0-to-10 for his physical disabilities. For example, an individual whose EDSS is 0 has not been physically disabled yet, an individual with EDSS = 6 needs to use a stick when

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walking, and an individual with EDSS = 7 moves using a wheelchair (Rasouli Fard et al., 2013).

Research Procedure and Data Analysis

After regarding ethical considerations such as informed consent and personal information privacy, the patients with MS were invited to participate in this research. After one neurologist was approved for the diagnosis of MS in participants and the severity of the disability was determined by the Expanded Disability Status Scale (EDSS), the subjects completed two questionnaires.

Data analysis was performed by using Pearson's correlation coefficient to investigate the relationship variables, and then the testing of the moderational role of personality factors in the relationship between the brain-behavioral systems and MS severity was determined using hierarchical regression analysis. Statistical analyses were conducted with the SPSS V.21 statistical software.

Results

In the present research, 162 MS patients were studied, the majority of whom were women (78%); the average age was 35 years. Most of the studied patients (74%) were married, and in terms of educational level, 11% (19 people) had elementary school degrees, 13% (22 people) had guidance school degrees, 32% (52 people) had diplomas, and 42% (69 people) had degrees higher than a diploma. Patients of this study suffered from MS for 6 years on average. Table 1 presents the descriptive statistics of the predictive and the criterion variables.

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Table 1
Descriptive Statistics (Mean and Standard Deviations) for the Variables of the Study (N=162)

Variables	Mean	Standard Deviations
Neuroticism	33.09	8.22
Extraversion	28.37	6.80
Openness	24.08	4.14
Agreeableness	28.54	5.58
Conscientiousness	35.28	6.29
Behavioural Inhibition System	21.17	3.11
Behavioural Approach System	26.71	2.19
Fight System	17.59	4.34
Flight System	19.99	4.69
Freeze System	20.45	5.33
EDSS	2.49	1.79

As showed in Table 1, among the components of brain-behavioral systems, the BIS, with an average of 26.71, and the Fight System (FS), with an average of 17.59, have the highest and the lowest averages, respectively. In addition, from the personality dimensions, conscientiousness, with an average of 35.28, and neuroticism, with an average of 33.09, have the two highest means and openness (O), with an average of 24.08, has the lowest mean.

In order to investigate the mediating role of personality dimensions in the relationship between brain-behavioral systems and the severity of MS symptoms, moderated regression based on hierarchical regression was used. Hierarchical regression results are presented in Table 2

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Table 2

Hierarchical Regression Analysis of the Reinforcement Sensitivity and Personality Dimensions on the Severity of MS Symptoms (N=162)

	Predictive Variables	Statistical Indicators			
		β	**Sig**		
First step	Behavioral Approach	-.23	.000		
	Behavioral Inhibition	.26	.000		
	Fight System	.09	NS		
	Flight System	-.01	NS		
	Freeze System	.15	.000		
	EDSS*RTS		.000	R^2 = .208	F_{Change} = 5.66
Second Step Moderators		**β**	**Sig**		
Neuroticism	Neuroticism	.77	.000	R^2 = .26	F_{Change} = 54.22
	Behavioral Approach	-.07	NS		
	Behavioral Inhibition	.15	.000		
	Fight System	.07	NS		
	Flight System	-.06	NS		
	Freeze System	-.06	NS		
	EDSS*RTS		.000	R^2 = .35	F_{change} = 3.18
Extroversion	Extroversion	-.13	NS	R^2 = .09	F_{change} = 1.49
	Behavioral Approach	-.2	NS		
	Behavioral Inhibition	.26	.000		
	Fight System	.08	NS		
	Flight System	.004	NS		
	Freeze System	.12	NS		

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	EDSS*RTS		.000	R^2 = .21	F_{Change} = 5.54
Openness	Openness	.16	NS	R^2 = . 000	F change = .03
	Behavioral Approach	-.25	NS		
	Behavioral Inhibition	.27	.000		
	Fight System	.07	NS		
	Flight System	.01	NS		
	Freeze System	.17	NS		
	EDSS*RTS		.000	R^2 = .22	F change = 5.88
Agreeableness	Agreeableness	-.23	23/0-	R^2 = .29	F change = 5.65
	Behavioral Approach	-.24	NS		
	Behavioral Inhibition	.24	NS		
	Fight System	.01	NS		
	Flight System	-.003	NS		
	Freeze System	.1	NS		
	EDSS*RTS		.000	R^2 = .22	F_{change} = 5.12
Conscientiousness	Conscientiousness	-.11	NS	R^2 = .01	F_{change} = 2.1
	Behavioral Approach	-.2	NS		
	Behavioral Inhibition	.26	0/000		
	Fight System	.08	NS		
	Flight System	.02	NS		
	Freeze System	.13	NS		
	EDSS*RTS		.000	R^2 =.21	F_{Change} = 5.38

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In order to analyze the data presented in this study, the predictive and criterion variables as well as the dimensions of the mediator were set into the equation in consecutive stages. In the first stage, the components of reinforcement sensitivity were inserted into the equation and it was observed that the components of reinforcement sensitivity variable significantly (20.8%) predicted the variance of MS symptoms severity scores ($P<.01$ and $F_{Change}=5.66$). In the next stage, each of the personality dimensions was set into the equation.

Neuroticism entered the analysis as the mediator and the determined variance rate in the criterion variable significantly increased to 35 percent ($P< .01$, $\beta= .77$, and $F_{Change}= 54.22$). Extroversion entered into analysis as the mediator and the results showed that the explanatory power of the prediction variable increased by .9 percent and had reached 21 percent ($P< .01$, $\beta=-.13$, and $F= 1.49$). Openness entered the analysis as the mediator and variance in the criterion variable was determined as 22 percent ($P< .86$, $\beta= .16$, and $F= .03$). Agreeableness entered the analysis as the mediator and variance in the criterion variable was determined as 22 percent ($P< .02$, $\beta= -.23$, and $F=5.56$). Conscientiousness entered the analysis as the mediator and variance in the criterion variable was determined as 21 percent ($P<.15$, $\beta= -.11$, and $F= 2.1$).

The results indicate that the explanatory power of the dimensions of extroversion, openness, and conscientiousness had not moderated the relationship between the brain-behavioral systems and the severity of MS symptoms. Therefore, the moderating effect of neuroticism in the relationship between brain-behavioral systems and the severity of MS symptoms is

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confirmed and the mediatory effect of this component is proved (F = 5.66; df = 7, 151).

Discussion

Based on the findings of the present research, there is a significant relationship between neuroticism and the severity of MS symptoms. In addition, there is a significant relationship between brain-behavioral systems and the severity of MS symptoms, in which the neuroticism dimension is able to moderate this relationship and has increased its values. Among the components of brain-behavioral systems, the behavioral inhibition component has shown the highest significance power; this structure increases impulsivity and attention, the recollection of emotional states of anxiety, behavioral inhibition, passive avoidance, silence, and the experience of negative affections (Caseras, 2003). Similar results are obtained in the studies of (Gray, 1970; Heym, 2008; Kimbrel, 2010; Harnett, 2013), s in which anxiety is investigated. As a result, the active behavioral inhibition system corresponds to feelings of anxiety, worry, and mental rumination (Caseras, 2003).

In explaining the moderating role of the neuroticism dimension in the relationship between brain-behavioral systems and the severity of disability in MS, one can refer to the personality character of neuroticism. The neuroticism index in the five-factor model is representative of the individuals' differences in terms of neuroticism, incompatibility, the dimension of emotional stability, and the comparison of compatibility and nervousness. Although this index as a transdiagnostic factor that measures the aspects of individuals' normal personality in this model, individuals who get a high

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score in this index may be exposed to the risk of being afflicted with some the psychiatric disorders. Usually these people have problems in planning, understanding, and feeling the real existence of the problem and the threat; they always feel negative emotions such as fear, anxiety, anger, sadness, and shame (Fathi Ashtiani, 2013). Two of the components of this index are anxiety and depression. Anxiety is defined as the sense of predicting future risks and anxious people are usually prone to worry and fear, and are nervous, terrified, and stressful. Individuals with depression are also prone to the feeling of sin, sorrow, hopelessness, and solitude; they are easily disappointed and helpless. Even those who obtain a low score in this component are not necessarily lively and happy (Diana et al., 1985). Symptoms of anxiety and depression are prevalent in MS patients, while it is not yet clear whether these symptoms reflect a mood disorder or whether they are physical manifestations of MS. Recent studies have shown that MS patients are at 50% risk of depression (Tröster Arnett, 2006). In addition, compared to many nervous disorders and other chronic diseases, this risk is much higher in the general population (Tröster & Arnett, 2006).

MS patients sometimes experience multiple psychological challenges such as the troubles with the treatment process, the unpredictability of disease attacks, reduction in previous abilities, and the need to ask for help from others. They may also face problems like losing their jobs and side effects might from receiving treatment, which may occupy their minds, and lead to stress and anxiety. Therefore, high levels of stress (Hopman, Coo, Edgar & McBride, 2007), and on the other hand, low levels of social support and the intensification of the disease/drug treatment will lead to increased depression and

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emotional distress (Vargas & Arnett, 2010). This is while anxiety and depression are considered as the components of the neuroticism index that affects health levels and are consistent with the findings of Benedict et al. (2001; 2008) and Bruce and Lynch (2011). Neurotic individuals are affected in a particular way with respect to their responses to the negative incidents in their lives. In addition, neurotic individuals have particular tendency toward developing a fear of new situations and they are prone to experiencing feelings such as helplessness and dependence (Bakker, Van Der Zee, Lewig, & Dollard, 2006). On the other hand, due to the unpredictability of disease attacks, the minds of MS patients are always involved with incidents and the uncontrollability of the attacks (Nocentini, Caltagirone & Tedeschi, 2012). These cases confirm the findings of the present research, which indicates that a lack of emotional stability has a correlation with the severity of disability in MS.

The findings of this research confirm that none of the indexes of extroversion, openness, agreeableness, and conscientiousness was able to have a mediatory effect on the relationship between brain-behavioral systems and the severity of disability in MS patients. In explaining these findings, one can suggest that the extroversion index refers to those individuals who are always sociable, interested in communication, participate in associations and parties, and are hopeful for the future. The openness trait refers to individuals who are curious, seeking pleasure in new issues, and have numerous positive and negative feelings. Agreeableness refers to those who, alike extrovert people, place emphasis on their personal desires; and the feeling of sympathy along with an enthusiasm for cooperation is one of the characteristics of this index. Finally, the conscientiousness

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index refers to those individuals who are characterized by a predetermined order, goals, and strong wishes (Esmaeili, Hosseini, Sadeghi et al., 2013).

The majority of patients suffering from MS are afraid of disability and are not assured in relation to this disease. Several psychological disorders including anxiety and depression emerge in the aftermath of this disease (Askey-Jones, 2013). Multiple Sclerosis is considered as a life threatening disease by some individuals and it demands high adjustment; considering this, the life of many individuals are altered in a way such that psychological problems are added to physical issues. Therefore, psychological problems can strengthen the individual suffering from Multiple Sclerosis during one's confrontation with stressful life events to some extent, although a noticeable number of individuals suffering from Multiple Sclerosis live with this disease through the employment of ample management and adaptation (Ožura, 2013). As a result, a wide range of various psychological experiences, inadvertent emotional experiences, memories, and thoughts relating to the other physical signs and other cases are reduced.

The participation of only a limited number of patients in this research, the EDSS value being lower than 4, the high number and variety of questions, and the paresis of sample members, which prolonged the answering time, were among the limitations of this study. In order to confirm data, a repetition of this study in other provinces is suggested, and the patients' psychological issues are to be considered. Therefore, psychology sessions should be planned for patients who are prone to anxiety and depression, which constitute their personal

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characteristics. The performance of similar studies is suggested in relation to other physical diseases.

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