Relationship between Behavioral Inhibition/Approach System and Perceived Stress: With White Blood Cell in Multiple Sclerosis Patients

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Abstract—Multiple sclerosis (MS) is a chronic, often disabling disease in which the immune system attacks the myelin sheath of neurons in the central nervous system. The purpose of this study was to explore the correlation between the Behavioral Inhibition/Approach System (BIS-BAS) and Perceived Stress (PS), while controlling for White Blood Cell (WBC) count. 60 MS patients (36.7% male, 63.3% female; aged 15-65 years) participated in this study. They completed a demographic questionnaire, underwent a complete blood cell (CBC) test, filled out the Behavioral Activation and Behavioral Inhibition Scale (BIS-BAS), and responded to the Perceived Stress Questionnaire (PSS-14). The results indicated a significant relationship between the BAS-Reward Responsiveness (BAS-RR) subscale and PS, particularly in a subset of MS patients with increased WBC counts.

Keywords—Behavioral inhibition/approach system, multiple sclerosis, perceived stress, white blood cell.

I. INTRODUCTION

MS is an autoimmune condition characterized by the migration of immune cells into the central nervous system, production of proinflammatory cytokines, demyelination, and neuronal damage. A neurodegenerative process may contribute to loss of neurologic function during later secondary progressive MS [1]. People with MS have long reported that psychological stress can worsen their symptoms, and studies show that chronic exposure to a wide range of challenging life events is correlated with worsening neurological symptoms in MS [1]-[5]. This process is highly personalized and influenced by inherent personality traits, early life experiences, and learned responses to stressful events [6]. Moreover, studies show that alterations in stress physiology may affect the stress response in MS [7], [8]. Given that the function of the body's major stress response system may be altered in MS, it is particularly important to understand specific factors that influence vulnerability to stress in people with MS [9]-[11].

Functional neurological disorder (FND) is now considered a neuropsychiatric condition [12]. The study confirms abnormal interceptive abilities in patients with motor FND under stress with a dissociation between perceived and objective stress. This study [12] also confirms that adverse life events play a role in FND as they are linked to a hyper arousal state, which is specific to motor FND. It does not, however, imply adverse events have a causal link, and future studies should aim to refine the role of life events as potential triggers or mediators of the disorder.

Finally, our study opens the door to future research aiming to understand why such stress hyper arousal occurs in FND [13]. Initially, severe stressors can lead to an increase in stress, which in turn reduces the brain's capacity to inhibit behavior, restrain negative emotions, and control impulsive behavior. These changes in impulsivity and the inability to regulate negative emotions [14] can have an impact on the immune system. Stress can act as a trigger, leading to the production of cytokines and inflammation [15]. While there is limited evidence of a genetic basis for FND, some familial cases have been reported [16]. Gene-environment interaction should also be studied and the recent development of epigenetics offers this possibility [17]. Hence, the attack on neurons may result from heightened emotional responses and misinterpretations in coping with problems. Considering the limited research findings regarding the role of mental health in the development and etiology of MS, the present study aims to investigate the relationship between the behavioral inhibition/approach system, perceived stress, and WBC count in MS patients.

II. METHODS

A. Patients

This was a cross-sectional study of a sample of the general population of Iranian MS patients. As part of this study, 60 MS patients were randomly recruited from the MS treatment clinic of Emamreza (Dr. S.I.) in Shiraz, Iran, between February and November 2022. These patients were selected based on specific criteria, including literacy, early diagnosis of MS, consent to participate in the research, and an age range of 15 to 65 years. A correlation study was conducted, employing the Pearson correlation coefficient for data analysis. The group of relapsing-remitting MS patients consisted of 22 males and 38 females, with a mean age of 33.53 (SD = 1.18). Among them, 28 had completed either a diploma or under diploma education, 43 were married, 21 were engaged in homemaker jobs, and most experienced MS onset between the ages of 27-32 years. The average disease duration was more than 6 months, and the age range of the participants was between 15 and 65 years (see Table I). All diagnostic criteria were determined by a subspecialist of neurology (Dr. S.I.). The MS patients included in the study had no prior or current history of psychiatric or

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mental retardation. Additionally, they had no previous or current history of psychiatric and neurological disorders, which was determined using the Structured Clinical Interview for DSM-IV-TR Axis I Disorder, Non-patient version (SCID-I/NP) [18]. Written informed consent was obtained from each subject, and the study was conducted in accordance with the 1989 revision of the Helsinki Declaration, as approved by the Code of Ethics of the MS treatment clinic of Dr. S.I.

B. .Instruments

Demographic questionnaire: Participant's demographic characteristics (gender, age, education, age at onset of MS, and duration of illness) were collected.

Count Blood Cell (CBC) test: The WBC count of participants was measured.

Behavioral Activation and Behavioral Inhibition Scale (BIS-BAS): The BIS/BAS scale [19] is a self-report measure consisting of 20 questions, with responses ranging from "Very True = 1" to "Very False = 4". Traditionally, this scale comprises four separate subscales: BIS, BAS-Drive (reflecting goal-directed motivation), BAS-Reward Responsiveness (related to response upon receiving rewards), and BAS-Fun Seeking (associated with the desire for novel rewards). The convergent and discriminant validity of the BIS/BAS scales has been previously supported [20]. In this study, we used Persian version of the BIS/BAS scale. In Iran, Mohammadi [21] confirmed the psychometric properties of the Persian version of BIS/BAS scale using test-retest reliability, Cronbach's alpha, and exploratory factor analysis. See Table II for the Cronbach's alpha coefficient of BIS/BAS in the present study.

Perceived Stress Questionnaire (PSS-14): Perceived stress was measured using the Perceived Stress Scale (PSS) [22], which comprised of 14 questions with responses varying from 0 to 4 for each item and ranging from never, almost never, sometimes, fairly often and very often, respectively, on the basis of their occurrence during one month prior to the survey. The PSS has an internal consistency of 0.85 (Cronbach's alpha co-efficient) and test-retest reliability during a short retest interval (several days) of 0.85 [22]. It assesses the degree to which participants evaluate their lives as being stressful during the past month. It does not tie to a particular situation; the scale is sensitive to the nonoccurrence of events as well as ongoing life circumstance. PSS-14 scores are obtained by reversing the scores on four positive items, for example 0 = 4, 1 = 3, 2 = 2, etc., and then summing across all 14 items. Items 4, 5, 6, 7 and 10 are the positively stated items. See Table II for the Cronbach's alpha coefficient of SPSS-16 in the present study.

C. Statistical Analysis

Demographic and research variables are presented as mean ± standard deviation or as percentages within a specific range. The relationship between the BAS-DR subscale and PS, as well as the BIS subscale with control WBC, was analyzed using zero-order correlation. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed by using SPSS@ version 16.0 for Windows (IBM Corporation, Armonk, NY, USA). The reliability of the applied

scales was assessed using Cronbach's alpha coefficient. The result of the Kolmogorov-Smirnov test revealed that the data were normal. Also, there were no missing values.

III. RESULTS

The demographic and clinical characteristics are presented in Table I. There were 60 MS patients in the study, consisting of 22 males and 38 females. The mean age was 3.53 years with a standard deviation of 1.18. Among the patients, 28 (46.7%) had an education level under diploma or diploma, 43 (71.7%) were married, and 21 (35.0%) had homemaker jobs. The majority of patients (31.7%) experienced MS onset between the ages of 27 and 32 years, and 34 (56.7%) had a disease duration of more than 6 months.

TABLE I
PARTICIPANTS' CHARACTERISTICS (N = 60)

Variable	N (%)
Gender, males–females	(22–38) (63.3%–36.7%)
Age - age of begin, no.	
15-20	1 (1.7%) - 5 (8.3%)
21-26	9 (15.0%) - 12 (20.0%)
27-32	22 (36.7%) - 19 (31.7%)
33-38	14 (23.3%) - 14 (23.3%)
39-44	10 (16.7%) - 9 (15.0%)
45+	4 (6.7%) - 1 (1.7%)
Level of education, no.	
Under diploma & diploma	28 (46.7%)
Associate degree & bachelor	25 (41.7%)
MA & PHD	7 (11.7%)
Marital status, no.	
Single	16 (26.7%)
Married	43 (71.7%)
Divorced	1 (1.7%)
Duration of the disease, no.	
Under 6 months	34 (56.7%)
6 month - under 2 years	6 (10.0%)
2-5 years	16 (26.7%)
6-9 years	1 (1.7%)
10+ years	3 (5.0%)
Job, no.	
Homemaker	21 (35.0%)
Student	3 (5.0%)
Self employed	11 (18.3%)
Employee	10 (16.7%)
University professor	3 (5.0%)
Unemployed	12 (20.0%)

The means, standard deviations, Cronbach's alpha, and correlations among the studied variables are reported in Table II. The results showed a positive relationship between the BAS-DR subscale and PS (r = 0.332, p < 0.05), indicating that higher scores on the BAS-DR subscale were associated with higher levels of perceived stress in MS patients. Additionally, there was a negative relationship between the BIS subscale and WBC (r = -0.271, p < 0.05), suggesting that higher scores on the BIS subscale were associated with lower WBC in MS patients. Please refer to Table II for more details.

TABLE II
MEAN, SD, CRONBACH'S ALPHA; ZERO-ORDER CORRELATIONS FOR THE BIS,
BAS-DR, BAS-RR, BAS-FS SUBSCALE AND PS AND WBC (N = 60)

	Variables	1	2	3	4	5	6
1	WBC	-					
2	BIS	-0.27*	-				
3	BAS-reward responsiveness	0.10	0.28*	-			
4	BAS-drive	-0.24	0.48**	0.39**	-		
5	BAS- fun seeking	-0.20	0.35**	0.29*	0.46**	-	
6	PS	0.14	-0.02	0.33*	-0.02	-0.15	-
7	Cronbach's a	-	0.21	0.30	0.45	0.46	0.41
8	M	-	20.16	10.31	17.41	11.48	43
9	SD	-	0.38	0.30	0.31	0.31	0.67

Notes: DAS = depression anxiety stress; BIS = behavioral inhibition system; BAS = behavioral approach system-reward; PS = perceived stress; * P < 0.05 (two tailed); ** P < 0.01 (two tailed).

IV. DISCUSSION

The main objective of this study was to investigate the relationship between behavioral brain functions, perceived stress, and psychological symptoms with control WBC count in MS patients. The data revealed a positive relationship between the BAS-DR subscale and perceived stress (PS) and a negative relationship between the BIS subscale and WBC count in MS patients. These results suggest that certain behavioral tendencies and stress levels may be associated with variations in WBC counts among individuals with MS, and were in accordance with previous findings [23]. Herbert and Cohen demonstrated substantial evidence supporting a relationship between stress and decreases in functional immune measures, such as the proliferative response to mitogens and natural killer cell activity [24]. Stress is also associated with the numbers and percentages of circulating WBCs, immunoglobulin levels, and antibody titers to herpes viruses. Subsequent analyses suggest that objective stressful events are related to larger immune changes than subjective self-reports of stress, and that immune response varies with stressor duration. Therefore, when emotions are not expressed, environmental stressors are more severe and can be exacerbated by behavioral inhibition. This, in turn, affects blood cells and neurons, which are identified as visible signs of fear and worry. To the extent that the immune system recognizes sensitized or damaged neurons as a result of oxidative stress caused by high perceived stress as invaders and attacks them, and the myelin sheath of these neurons is destroyed by the immune system, a person gets MS and this destruction continues as long as there is stress, but if the stress is long-term, it is possible that without the presence of stress, as a result of cellular conditioning, apoptosis genes are expressed, and for its non-progress, in addition to stress management for treatment, the sick person needs to receive love from his family or spouse. Also, one of the patients reported that when he was in a romantic relationship, all the chronic symptoms of the disease, such as movement problems, disappeared.

V. CONCLUSION

In conclusion, it can be inferred that a higher BIS subscale score is predictive of more WBCs in MS patients. This suggests that the BIS might amplify the count of WBC through the perception of stress, particularly catastrophizing, in MS patients. Thus, when emotions are not expressed, environmental stress is perceived more acutely, behavioral inhibition is reduced, and WBC are increased to counter the visible signs of fear and anxiety, such as highly active and stress-sensitive neurons, to the point that the immune system recognizes neurons with high perceived stress as invaders and attacks them. It seems that by performing coping skills that play a role in stopping the progress of psychosomatic disorders, it is possible to activate the neuropsychological system of the prefrontal lobe, which plays a role in controlling behavioral inhibition from top to bottom, in order to reduce the severe perception of stress and to express it was appropriate for the emotions to stop the progression of MS.

REFERENCES

[1] Frischer, JM., Bramow, S., Dal-Bianco, A., Lucchinetti, CF., Rauschka, H., Schmidbauer, M., Laursen, H., Sorensen, PS., Lassmann, H.,2009. The relation between inflammation and neurodegeneration in multiple sclerosis brains. Brain. 132(Pt 5):1175-89. DOI: 10.1093/brain/awp070

[2] Yamout, B., Itani, S., Hourany, R., Sibaii, AM., Yaghi, S., 2010. The effect of war stress on multiple sclerosis exacerbations and radiological disease activity. J. Neurol. Sci. 288(1-2), 4-42. doi: 10.1016/j.jns.2009.10.012

[3] Golan, D., Somer, E., Dishon, S., Cuzin-Disegni, L., Miller, A., 2008. Impac of exposure to war stress on exacerbations of multiple sclerosis. 64(2), 143-8. doi: 10.1002/ana.21409

[4] Li, J., Johansen, C., Bronnum-Hansen, H., Stenager, E.,Koch-Henriksen, N., Olsen, J., 2004. The risk of multiple sclerosis in bereaved parents: A nationwide cohort study in Denmark. Neurology. 62(5), 726-9.

[5] Mohr, DC., Goodkin, DE., Bacchetti, P., Boudewn, AC., Huang, L., Marrietta, P., Cheuk, W., Dee, B., 2000. Psychological stress and the subsequent appearance of new brain MRI lesions in MS. Neurology. 55(1), 55-61.

[6] Lecic-Tosevski, D., Vukovic, O., Stepanovic, J., 2011. Stress and personality. Psychiatriki . 22(4), 290-7.

[7] Heesen, C., Mohr, DC., Huiinga, I., Then Bergh, F., Gaab, J.,Otte, C., Gold,SM., 2007. Stress regulation in multiple sclerosis – current issues and concepts. Multiple Sclerosis Journal. 2(s), 143-148.

[8] Gold, SM., Mohr, DC, Huitinga, I., Flachenecker, P., Sternberg, EM., Heesen., C., 2005. The role of stress-response systems for the pathogenesis and progression of MS. Trends Immunol. 26(12), 644-652.

[9] Brown KW, Ryan RM., 2003. The benefits of being present: mindfulness and its role in psychological well-being. J Pers Soc Psychol. 84(4), 822-848.

[10] Bränström, R., Duncan, LG., Moskowitz, JT., 2011. The association between dispositional mindfulness, psychological well-being, and perceived health in a Swedish population-based sample: influence of dispositional mindfulness. Br J Health Psychol. 16(2), 300-316.

[11] Salmoirago-Blotcher, E., Crawford, S., Carmody, J., Rosenthal, L., Ockene, I., 2012. Characteristics of dispositional mindfulness in patients with severe cardiac Patient. J. Evid. Based. Complementary. Altern. Med. 16(3), 218-225.

[12] Carson, A, J., 2014. Introducing a 'neuropsychiatry' special issue: but what does that mean? J. Neurol. Neurosurg. Psychiatry. 85, 121-122.

[13] Apazoglou, K., Mazzola, V., Wegrzyk, J., Polara, GF., Aybek, S., 2017. Biological and perceived stress in motor functional neurological disorders. Psychoneuroendocrinology. 85, 142-150. doi: 10.1016/j.psyneuen

[14] Lazo, A., 2010. Integrating joiner's interpersonal psychological theory of suicide with the Rorschach, A dissertation submitted to the Wright Institute Graduate School of psychology, in partial fulfillment of the requirements for the degree of Doctor of psychology. Page 134.

[15] Lehrer, PM., Karavidaz, MK., Lu, SE., Feldman, J., Kranitz, L., Smarithy, A., Sanderson, W., Reynolds, R., 2008. Psychological treatment of co morbid asthma and panic disorder. J Anxiety Disorder. 22 (4), 83-671.

[16] Stamelou, M., Cossu, G., Edwards, M, J., Murgia, D., Parees, I., Melis, M., Bhatia, K, P., 2013. Familial psychogenic movement disorders.

Mov.Disord. 28, 1295-1298.

[17] Frodl, T., 2017. Recent advances in predicting responses to antidepressant treatment, F1000 Faculty. Rev. 619. doi: 10.12688/f1000research.10300.1

[18] First, M, B., Spitzer, R, L., Gibbon, M., Williams, J, B, W., 2002. Structured clinical interview for DSM-IV-TR axis I disorder, research version, non-patient edition (SCID-I/NP). New York: Biometrics Research Department, New psychiatric Institute.

[19] Carver, C. S., White, T.L., 1994. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS scales. Journal of Personality and social Psychology. 67, 319-333. doi:110.1037/0022-3514.67.2.319.

[20] Jorm, A, F., Christensen, H. H., Henderson, A. S., Jacomb, P. A., Rodgers, B.B., 1999. Using the BIS/BAS scales to measure behavioral inhibition and behavioral activation: Factor structure, validity and norms in a large community sample. Personality and individual Differences. 26, 49-58. Doi: 10.1016/S0191-8869(98) 00143-3.

[21] Mohammadi, N., 2008. The psychometric properties of the Behavioral Inhibition System (BIS) and Behavioral Activation System (BAS) scales among students of Shiraz University (Persian text). Clinical Psychology. 1 (28), 61-68. http://cpap.shahed.ac.ir/browse.php?a_code=A-10-1-250&slc_lang=en&Sid = 1

[22] Cohen, S., Kamarck, T., Mermelstein, R., 1983. A Global Measure of Perceived Stress. Journal of Health and Social Behavior. 24,385-396.

[23] Ghorbani, F., Khosravani, V., Jamaati Ardakani, R., Alvani, A., Akbari, H., 2017.The alexithymia, cognitive emotion regulation, and physical symptoms in Iranian asthmatic patients. Psychiatry Res, 247, 144-151. http://dx.doi.org/10.1016/j.psychres.2016.11.015

[24] Herbert, TB., Cohen, SH., 1993. Stress and Immunity in Humans: A Mea-Analytic Review. Psychosomatic medicine. 55, 364-379.