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Vildan Altunayoglu Cakmak, MD

Karadeniz Technical University

E-mail valtunayoglu@yahoo.com

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Department of Neurology,

61080 Trabzon, Turkey **Tel** +90 462 377 1124

Fax +90 462 325 3205

Correspondence

Medical School,

Evaluation of Temperament and Character Features as Risk Factors for Depressive Symptoms in Patients with Restless Legs Syndrome

Vildan Altunayoglu Cakmak,^a Sibel Gazioglu,^a Nuray Can Usta,^a Evrim Ozkorumak,^b Ahmet Ayar,^c Murat Topbas,^d Cavit Boz^a

^aDepartments of Neurology, ^bPsychiatry, ^cPhysiology, and ^dPublic Health, Karadeniz Technical University Medical Faculty, Trabzon, Turkey

Background and Purpose Restless legs syndrome (RLS) is a common sleep-related movement disorder that is frequently associated with psychological disturbances. Personality traits are of considerable importance with respect to coping with chronic illness and disease vulnerability. This study assessed the temperament and character traits of RLS patients using an approach that involves the psychobiological model of personality.

Methods The personality features of 65 newly diagnosed and untreated RLS patients with no neurological or psychiatric diseases and 109 healthy controls were determined using the Temperament and Character Inventory and compared using covariance analyses. The International RLS Study Group Severity Scale was used to assess the severity of the RLS symptoms, and the Beck Depression Inventory was used to assess the presence and severity of depressive symptoms.

Results RLS patients scored significantly higher than healthy controls on the temperament dimension of harm avoidance (HA, p=0.02) and significantly lower on self-directedness (SD, p=0.001). No significant difference was observed in terms of the temperament dimension of novelty seeking (p=0.435). HA scores were significantly correlated with the BDI score but not with the RLS severity or duration.

Conclusions High HA and low SD scores are the main characterizing personality features of RLS patients. These personality dimensions may be among the factors predisposing patients to development of the depressive symptoms that are frequently associated with RLS.

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Key Words restless legs syndrome, Temperament and Character Inventory, personality, harm avoidance, serotonin, dopamine.

Introduction

Personality is defined as a dynamic and organized set of behavioral, mental, and emotional response patterns that make each person unique. It is becoming increasingly clear that personality features are important not only for social interactions but also for general medical health and vulnerability to various diseases processes.¹ Numerous studies have demonstrated a relationship between dimensions of personality and various psychiatric diseases^{2,3} and some neurological diseases, including Parkinson's disease (PD),⁴ migraine,⁵ chronic pain,⁶ and epilepsy.⁷ Personality is also known to be related to well-being.⁸ Together these findings suggest that knowledge about personality and its interaction with diseases can facilitate the understanding of clinical features and help to identify the pathophysiological mechanisms underlying neuropsychiatric diseases, and may have an impact on disease management.^{6,9}

Restless legs syndrome (RLS) is a sleep-related movement disorder with a worldwide reported prevalence of 0.013–15%

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in the general population.¹⁰ It is suspected that the pathogenesis of RLS involves dopaminergic dysfunction and iron deficiency in the brain, although the exact underlying mechanism remains to be established. RLS is characterized by an urge to move in response to unusual and uncomfortable sensations experienced in the limbs, and particularly in the legs. Symptoms worsen during rest and in the evenings or at night, and are relieved by movement. The most important consequences of this syndrome are insomnia and associated problems (e.g., fragmented sleep and excessive daytime sleepiness), and an impaired quality of life.¹¹ Ongoing symptoms and their progression can also lead to psychological disturbances.^{12,13}

The personality features of RLS patients and their impact on RLS-related factors have received little attention. In a recent study, Kalaydjian et al.¹⁴ examined the potential role of personality characteristics in the association between RLS syndrome and psychiatric disorders, and proposed that the personality of RLS patients could play a critical role in the development of mood disorders in RLS. Although that pioneering study identified the proposed association, confirmation is needed using other inventories to assess personality characteristics from different perspectives.

The Temperament and Character Inventory (TCI) is a personality questionnaire that is used widely in the literature, and is based on Cloninger's seven-dimension psychobiological model.¹⁵ Personality is evaluated using this model by dividing it into temperament and character dimensions according to evidence derived from family studies, studies of longitudinal development, psychometric studies of personality structure, and neuropharmacological and neuroanatomical studies of behavioral conditioning and learning.^{16,17} Cloninger suggested that temperament comprises the heritable part of personality, which is stable throughout life and is associated with neurotransmitters in the brain.¹⁶ The four derived temperament dimensions are novelty seeking (NS), harm avoidance (HA), reward dependence (RD), and persistence (P); it has been hypothesized that these four derived dimensions are linked to dopaminergic, serotonergic, noradrenergic, and glutaminergic activity, respectively.16 The external aspect of personality, which is composed of character dimensions with low heritability, is determined predominantly by environmental factors, and matures gradually throughout life. The three character dimensions of the TCI-self-directedness (SD), cooperativeness (C), and selftranscendence (ST)-are the main factors determining one's ability to cope with social-life experiences. They also individually influence vulnerability to emotional and behavioral disorders.2,15

Due to its psychobiological background and separate character dimensions that help to explain the self-adaptive behaviors of individuals, the TCI is highly suitable for assessing personality features. Therefore, in the present study the possible relationship between personality features and RLS-related symptoms was evaluated using the TCI to assess the temperament and character features of RLS patients, with a view to providing further information regarding the personality features of RLS patients.

Methods

Participants

This case-control study was conducted at the sleep disorders outpatient clinic of our Neurology Department in a university hospital setting between June 2012 and December 2012. The study protocol was approved by the local ethical committee. The investigation was carried out in accordance with the latest version of the Helsinki Declaration. Newly diagnosed, untreated RLS patients without any known neurological, psychiatric, or any other sleep disorders were considered for inclusion. Control subjects were selected from age-, gender-, and educational-level-matched subjects among relatives and neighbors of hospital staff without a history of neurological, psychiatric, or sleep disorders. Informed consent was obtained from the participants after they were provided with a full explanation of the study and its procedures. Before enrollment, a psychiatric interview was performed by a psychiatrist (E.O.) to rule out any current Axis-I mental disorders according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fourth edition. All patients and control subjects were examined by a neurologist (V.A.C.) with experience of sleep disorders. The demographic features of the subjects were recorded, detailed medical histories were taken, and physical and neurological examinations were conducted. Subjects with any chronic diseases including renal failure, hepatic diseases, rheumatologic diseases, or malignancy were not considered any further. Subjects unwilling to complete the TCI or who participated with incomplete data were also excluded.

The Beck Depression Inventory (BDI) was used to evaluate depressive symptoms in both the patients and controls.^{18,19} The BDI is a questionnaire that measures symptoms of depression in psychiatric patients and the general population. The following guidelines have been suggested for interpreting BDI scores: 0–13, minimal depression; 14–19, mild depression; 20–28, moderate depression; and 29–63, severe depression.

Evaluation of RLS

Diagnosis of RLS was based on the following four diagnostic criteria of RLS according to the revised International RLS Study Group guidelines:²⁰ 1) feeling an urge to move the legs usually accompanied or caused by uncomfortable or unpleasant sensations in the legs, 2) symptoms worsening during peri-

ods of rest or inactivity, 3) symptoms improving with movement, and 4) symptoms worsening in the evening or at night. All face-to-face interviews were carried out by a neurologist with experience of sleep disorders, and only those patients meeting all four criteria were assigned to the RLS population. In addition to neurological examination, laboratory investigations including the following laboratory examinations were performed to rule out secondary RLS: complete blood count, ferritin, vitamin B₁₂, folic acid, and creatinine. Disease severity was determined using the International Restless Legs Syndrome Severity Scale (IRLS).²¹ The IRLS consists of ten items for measuring symptom severity (items 1-3 and 6), impact on sleep (items 4 and 5), symptoms intensity and frequency (items 7 and 8), and impact on daily functions and mood (items 9 and 10). Each item has five response options graded from 0 (no symptoms) to 4 (very severe symptoms).

Personality assessment

Personality was assessed by using a self-administered questionnaire, the TCI, which was developed by Cloninger for clinical and research use.15 As mentioned above, the TCI has the advantage of evaluating four temperament dimensions (NS, HA, RD, and P) and three character dimensions (SD, C, and ST). Each dimension has between three and five subdimensions, except for P, which has no subdimensions. NS is regarded as having a heritable bias toward behavioral activation for innovation, active avoidance of punishment or disappointment, and extravagance in approach to cues for potential rewards. NS consists of NS1 (exploratory excitability vs. stoic rigidity), NS2 (impulsiveness vs. reflection), NS3 (extravagance vs. reserve), and NS4 (disorderliness vs. regimentation). HA is regarded as having a heritable bias toward the inhibition of behaviors such as pessimistic worry, passive avoidant behaviors such as fear of uncertainty and shyness with strangers, and rapid fatigability. HA consists of HA1 (anticipatory worry vs. uninhibited optimism), HA2 (fear of uncertainty vs. detachment), HA3 (shyness with strangers vs. gregariousness), and HA4 (fatigability vs. vigor). RD reflects a heritable tendency toward the maintenance of behavior in response to cues of social reward. RD has three subdimensions: RD1 (sentimentality vs. insensitivity), RD3 (attachment vs. detachment), and RD4 (dependence vs. independence). P is a hereditary tendency toward perseverance despite frustration and fatigue. SD refers to willpower and self-determination, and reflects the ability to identify behaviors that are appropriate for achieving individually chosen goals and values. SD consists of SD1 (responsibility vs. blaming), SD2 (purposefulness vs. lack of goal direction), SD3 (resourcefulness vs. ineffective), SD4 (self-acceptance vs. self-striving), and SD5 (congruent second nature vs. bad habits). C reflects the difference in identification of oneself with other people or the difference in acceptance of others, and has five subdimensions: C1 (social acceptance vs. intolerance), C2 (empathy vs. disinterest), C3 (helpfulness vs. unhelpfulness), C4 (compassion vs. revengefulness), and C5 (principled and purehearted vs. self-serving). ST expresses the extent to which an individual identifies him-/herself as an integral part of the universe, and consists of ST1 (self-forgetfulness vs. self-consciousness), ST2 (transpersonal vs. personal identification), and ST3 (spiritual acceptance vs. rational materialism).¹⁵

The TCI is composed of 240 items that require true or false answers. All participants were instructed to complete the questionnaire, and were allowed adequate time to achieve this. The items were then scored using a standard key, and scores were calculated according to the guidelines. Each of the TCI dimensions (except for P) was assessed as the sum of scores for the three to five subdimensions measuring more specific traits (e.g., HA is represented by the sum of the total scores of HA1, HA2, HA3, and HA4). There are also 14 items that are not scored according to the guidelines. The Turkish-language version of the TCI has been shown to have good reliability and validity.²²

Analysis

All data were analyzed using SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). The demographic variables of the RLS patients and controls were compared using Student's *t* test for continuous variables and the chi-square test for categorical variables. Since TCI scores are influenced by age²³ and the BDI scores differed significantly between the RLS and control groups, adjusted mean TCI scores were calculated, and TCI dimension scores were compared using analysis of covariance (ANCOVA) using age and BDI as covariates. Pearson correlation analyses were used to examine possible correlations between TCI scores, and items of the IRLS. The cut-off for statistical significance was set at *p*<0.05.

Results

Ninety RLS patients and 180 control subjects were considered for enrollment in the study. Seventeen RLS patients and 25 control subjects were excluded due to a diagnosis of current psychiatric disease (depression and panic disorder), 46 control subjects were excluded due to missing TCI data, and 8 RLS patients were excluded due to a diagnosis of secondary RLS. Therefore, 65 RLS patients (40 females, 15 males) and 109 control subjects (75 females, 34 males) were finally enrolled. The ages of the RLS patients and controls were 49.9±9.9 years (mean±standard deviation; range, 24–70 years) and 47.9±10.8 years (range, 21–76 years), respectively. The mean age, sex, and education level did not differ significantly between the two groups (p=0.236, 0.380, and 0.435, respectively). The mean RLS severity based on the IRLS scale was 23, and RLS duration was 8.0 ± 7.5 years. The mean BDI score was significantly higher for the RLS patients than for the controls (p=0.013). The demographic features of patients and controls are summarized in Table 1.

ANCOVA analysis of temperament dimensions revealed that RLS patients had significantly higher HA scores for the main dimensions (p=0.02). Subdimension analysis revealed that H4 and RD1 scores were also significantly higher in the RLS group than in the control group (p=0.005 and 0.011, respectively). The only significant differences in NS between the groups (p=0.435) were lower scores for the NS1 subdimension (p=0.041) and higher scores for the N2 subdimension (p=0.013)in the RLS group. Analysis of character dimensions revealed significantly lower scores for SD (p=0.001) as well as for four of the SD subdimensions (SD1, SD2, SD3, and SD5) in the RLS group (p=0.011, 0.005, 0.007, and 0.015, respectively). The only other character dimensions that differed significantly between the groups were the C5 and ST3 subdimensions (p=0.009 and 0.004, respectively). The results of the TCI analyses are summarized in Table 2.

Correlation analyses revealed that the severity of RLS was negatively correlated with SD (p=0.015) and positively correlated with ST (p=0.012), but was not correlated with any of the temperament dimensions, including HA. Duration of RLS was also not significantly correlated with any of the main dimensions. No significant correlation was detected between BDI score and the severity or duration of RLS. BDI in RLS patients was positively correlated with HA (p=0.015) and negatively correlated with RD (p=0.043, respectively), and in the control group it was positively correlated with HA (p=0.025) and negatively correlated with SD (p=0.000) and C (p=0.019). The results of correlation analyses of the clinical demographic features and TCI dimensions are summarized in Table 3.

Detailed correlation analysis of IRLS scale items with scores of the BDI and the main dimensions of the TCI main dimensions revealed that BDI score was not correlated with the scores for any of the IRLS items. In terms of TCI dimensions, SD was negatively correlated with scores for items 2 (the need to move the extremities; p=0.022) and 4 (sleep disturbances; p=0.002). ST was positively correlated with items 5 (fatigue and daytime sleepiness; p=0.002), 8 (duration of RLS symptoms over 24 hours; p=0.006), 9 (effect on daily activities; p=0.009), and 10 (effect on mood disturbances; p=0.020). The results of correlation analysis of scores for IRLS items with BDI and TCI dimensions are summarized in Table 4.

Discussion

This is the first study to document the temperament and character features of RLS patients using the TCI. The results from this cross-sectional, case-control study indicate that patients with RLS have higher HA temperament and lower SD character scores than control subjects. To the best of our knowledge, the first and only study of personality features of RLS patients was conducted by Kalaydjian et al.,14 who assessed personality by using the Neuroticism-Extraversion-Openness (NEO) Personality Inventory and reported that individuals with RLS had higher neuroticism scores than the controls. It is well documented that neuroticism is strongly and positively correlated with HA and negatively correlated with SD, although these are clinically and etiologically different entities.24 Our findings of high HA and low SD scores in RLS patients are therefore consistent with the finding of high neuroticism scores in RLS patients. We also found that RLS patients had high scores for the NS2 (impulsiveness) subdimension, which is included in neuroticism in the NEO Personality Inventory.

As noted by Cloninger et al.¹⁵ individuals with a high HA temperament score exhibit avoidant behavior toward negative signals and punishments, and tend to be cautious, apprehensive, passive, and pessimistic, even in situations that do not normally worry most people. Individuals with a low SD character are typically unable to control aversive situations and overcome obstacles in the absence of direction by a leader, easily lose their goals, and tend to blame others and the environment for their problems.¹⁵ In the literature, high HA tem-

Table 1. Clinical and demographic features of the participants
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	Control group (n=109)	RLS group (n=65)	p					
Age (years)	47.9±10.8	49.9±9.9	0.236					
Sex (females/males)	74/35	49/16	0.380					
Education (years)	10.6±2.9	10.4±3.0	0.435					
BDI score	9.2±7.8	12.4±9.0	0.013*					
IRLS score	-	22.9±7.8						
RLS duration (years)	-	8.0±7.5						

The data are presented as mean±standard deviation values.

*Significant difference across groups, p<0.05.

BDI: Beck Depression Inventory, IRLS: International Restless Legs Syndrome Severity Scale, RLS: restless legs syndrome.

perament scores and low SD character scores have consistently been reported in psychiatric patients, and especially those with depressive disorders.²⁵ The results of many studies have led to HA being regarded as a marker of emotional vulnerability to depression and SD as a marker of executive function that protects a person from depression.³ Epidemiological and case-control studies have found a high prevalence and co-occurrence of depressive disorders in RLS.^{13,26,27} Although the nature of this association remains unclear, various authors have suggested that clinical RLS symptoms such as pain, restlessness, and insomnia induce the development of depression. Alternatively, a shared underlying pathology such as dopamine deficiency may be another possible explanation.¹³ Gupta et al.²⁸ very recently examined the prevalence of depression in RLS and reported a high current prevalence of depression without any significant impact on associated depression of RLS-related factors including duration and disease severity. They suggested that RLS causes distress but is not able to induce clinical depression, or that it induces depression in biologically predisposed subjects in particular. Although the present study excluded subjects with current psychiatric disorders including depression, the BDI scores were significantly higher

Table 2. Results of ANCOVA with covariates (age and BDI score) comparing RLS patients and controls with respect to	all TCI scales

	Control group (n=109)	RLS group (n=65)	р
Temperament			
NS	15.6±0.4	16.0±0.5	0.435
NS1 (exploratory excitability vs. stoic rigidity)	5.6±0.1	5.0±0.2	0.041*
NS2 (impulsiveness vs. reflection)	3.3±0.1	3.8±0.2	0.013*
NS3 (extravagance vs. reserve)	3.5±0.1	3.5±0.2	0.871
NS4 (disorderliness vs. regimentation)	3.0±0.1	3.6±0.1	0.068
НА	16.6±0.5	20.0±0.6	0.020*
HA1 (anticipatory worry vs. uninhibited optimism)	5.5±0.1	6.3±0.2	0.210
HA2 (fear of uncertainty vs. detachment)	4.4±0.1	5.1±0.1	0.412
HA3 (shyness with strangers vs. gregariousness)	3.0±0.2	4.0±0.2	0.130
HA4 (fatigability vs. vigor)	3.5±0.1	4.5±0.2	0.005*
RD	14.36±0.2	15.2±0.3	0.092
RD1 (sentimentality vs. insensitivity)	7.5±0.1	7.8±0.1	0.011*
RD3 (attachment vs. detachment)	4.1±0.1	4.5±0.1	0.759
RD4 (dependence vs. independence)	2.6±0.1	2.8±0.1	0.568
P	5.3±0.1	5.5±0.2	0.333
Character			
SD	30.3±0.5	28.3±0.6	0.001*
SD1 (responsibility vs. blaming)	5.1±0.1	4.7±0.2	0.011*
SD2 (purposefulness vs. lack of goal direction)	6.3±0.1	5.8±0.1	0.005*
SD3 (resourcefulness vs. ineffective)	3.5±0.1	3.2±0.1	0.007*
SD4 (self-acceptance vs. self-striving)	6.1±0.2	5.7±0.3	0.118
SD5 (congruent second nature vs. bad habits)	9.1±0.1	8.8±0.1	0.015*
С	30.6±0.4	30.2±0.6	0.616
C1 (social acceptance vs. intolerance)	6.2±0.1	6.1±0.1	0.389
C2 (empathy vs. disinterest)	4.1±0.1	3.9±0.1	0.890
C3 (helpfulness vs. unhelpfulness)	5.1±0.1	5.1±0.1	0.171
C4 (compassion vs. revengefulness)	7.9±0.2	7.8±0.2	0.600
C5 (principled and pure-hearted vs. self-serving)	7.4±0.1	7.2±0.1	0.009*
ST	19.4±0.4	18.4±0.5	0.966
ST1 (self-forgetfulness vs. self-consciousness)	5.5±0.2	5.7±0.2	0.112
ST2 (transpersonal vs. personal identification)	5.7±0.2	5.5±0.2	0.250
ST3 (spiritual acceptance vs. rational materialism)	8.1±0.1	7.1±0.2	0.004*

The data are presented as mean±standard deviation values.

*Significant difference across groups, p<0.05.

ANCOVA: analysis of covariance, BDI: Beck Depression Inventory, C: cooperativeness, HA: harm avoidance, NS: novelty seeking, P: persistence, RD: reward dependence, RLS: restless legs syndrome, SD: self-directedness, ST: self-transcendence, TCI: Temperament and Character Inventory.

in the RLS patients than in the controls. The correlation analysis revealed that the BDI score was not correlated with any of the RLS-related factors such as severity, duration, and symptoms on the IRLS, but was positively correlated with HA. Our results concur with the conclusion drawn by Gupta et al.²⁸ that RLS patients have depressive symptoms that are probably due to shared neurobiological mechanisms, rather than being primarily due to the severity and duration of RLS. Explaining the association between HA and RLS with "neurobiological data" obtained from the TCI appears to be difficult since HA is thought to be related to dysfunction of serotonergic activity, while dopaminergic dysfunction is the main reported mechanism underlying RLS. However, there is still no common consensus in the literature regarding the relationship between serotonin and HA.^{29,32} Recent neuroimaging studies have indicated that the relationship between serotonin and

		RLS duration	RLSSS	Age	BDI	NS	HA	RD	Р	SD	С
RLS group	RLS duration										
	RLSSS	0.072									
	Age	0.171	0.098								
BDI NS HA	BDI	0.012	0.108	0.062							
	NS	0.081	0.066	-0.331*	0.117						
	HA	-0.086	0.026	0.024	0.299*	-0.115					
	RD	-0.139	-0.077	-0.167	-0.251*	-0.098	-0.159				
	Р	0.034	0.122	0.011	-0.032	-0.150	-0.201	0.117			
	SD	-0.080	-0.301*	-0.077	-0.157	-0.085	-0.237	-0.018	0.144		
	С	-0.084	-0.239	-0.076	-0.237	-0.020	-0.242	0.380*	0.026	0.393*	
	ST	-0.071	0.309*	0.081	0.056	0.173	-0.057	0.290*	0.138	-0.192	0.062
Control group	Age										
	BDI			0.111							
	NS			-0.193*	0.060						
	HA			0.088	0.215*	-0.422*					
	RD			-0.137	-0.068	0.109	-0.055				
	Р			-0.081	-0.214	0.166	-0.200*	0.100			
	SD			-0.093	-0.518*	-0.059	-0.417*	0.200*	0.210*		
	С			0.172	-0.224*	-0.123	-0.155	0.343*	0.143	0.385*	
	ST			0.294*	0.169	0.055	-0.045	0.117	0.257*	-0.257*	0.233*

*Significant difference across groups, p<0.05.

BDI: Beck Depression Inventory, C: cooperativeness, HA: harm avoidance, NS: novelty seeking, P: persistence, RD: reward dependence, RLS: restless legs syndrome, RLSSS: RLS symptom severity, SD: self-directedness, ST: self-transcendence, TCI: Temperament and Character Inventory.

Table 4. Results of correlation analysis between scores for items on the IRLS, and scores for the BDI and the TCI dimensions in RLS patients

	BDI	NS	HA	RD	Р	SD	С	ST
IRLS item								
Q1: discomfort in extremities	0.056	0.128	-0.010	-0.020	0.192	-0.243	-0.195	0.222
Q2: need to move the extremities	0.055	0.129	-0.111	-0.062	0.159	-0.285*	-0.159	0.240
Q3: relieved by movement	-0.020	-0.058	0.011	0.001	0.054	0.002	0.157	-0.051
Q4: sleep disturbances	-0.013	-0.068	0.101	-0.011	0.200	-0.375*	-0.174	-0.199
Q5: fatigue and daytime sleepiness	-0.193	0.007	0.019	0.197	0.055	-0.012	0.039	0.380*
Q6: severity as a whole	-0.031	0.178	-0.053	-0.042	0.233	-0.147	-0.088	0.211
Q7: frequency of symptoms	-0.010	0.089	0.105	-0.066	0.076	-0.114	-0.191	0.214
Q8: duration over 24 hours	-0.003	0.108	0.044	-0.053	0.052	-0.220	-0.239	0.336*
Q9: effect on daily activities	0.048	0.158	0.092	0.018	0.031	-0.235	-0.123	0.322*
Q10: effect on mood disturbances	0.056	0.124	0.239	-0.028	0.030	-0.071	-0.164	0.289*

*Significant difference across groups, p<0.05.

BDI: Beck Depression Inventory, C: cooperativeness, HA: harm avoidance, IRLS: International Restless Legs Syndrome Severity Scale, NS: novelty seeking, p: persistence, RD: reward dependence, RLS: Restless legs syndrome, SD: self-directedness, ST: self-transcendence, TCI: Temperament and Character Inventory.

HA is not direct, as originally thought by Cloninger,¹⁶ and that the HA dimension may be correlated with the balance of a complex neurotransmitter network including dopamine.33,34 There is also little information available about serotonergic activity in RLS. It has been suggested that serotonin acts through several serotonin receptor subtypes in the brain, to either facilitate or inhibit dopaminergic activity.35 Furthermore, evidence from population and case-control studies and from case reports indicates that serotonin reuptake inhibitors may induce and aggravate RLS symptoms, or in contrast may relieve such symptoms.³⁶ Jhoo et al.³⁷ recently investigated the availability of serotonin transporters in the pons and the medulla of patients with RLS and healthy controls, and found no difference between these two groups except for a negative correlation between serotonin transporters availability and the severity of RLS symptoms. Therefore, considering the current level of evidence in the literature, possible direct or indirect involvement of serotonergic dysfunction in RLS cannot be ruled out.

Correlation analysis also revealed that character dimensions were correlated with the severity of RLS. Detailed analysis of the IRLS findings revealed that the correlation between SD and RLS was restricted to certain symptoms due to RLS such as "need to move extremities" and "sleep disturbances due to RLS." We interpreted these results as a state effect of some RLS symptoms on SD. An alternative explanation is that being less self-directed may predispose the RLS patients to a more severe disease state. A correlation between ST and many of the items on the IRLS scale and RLS severity was a particularly interesting finding of the present study, since a high level of ST was not a prominent characteristic in RLS patients. ST scores are well known to be high in debilitating chronic diseases.38 It is assumed that ST represents the way in which individuals adapt to disease to achieve psychological well-being, although the disease itself is not actually relieved.³⁹ This may also apply to RLS patients who cope better with severe RLS symptoms.

Using the TCI to assess the personality features of RLS patients also allowed us to compare the personality features of two dopamine-related diseases: PD and RLS. Although the pathophysiology of RLS is unclear, the finding that RLS symptoms can be relieved by dopamine agonists and exacerbated by dopamine antagonists suggests that dopaminergic dysfunction plays a central role in the pathophysiology of RLS.⁴⁰ It is well documented that dopamine also occupies a central role in the pathogenesis of PD, which is characterized by dopaminergic neuron loss in various brain regions. Cloninger's personality model and its links to psychobiology have been extensively investigated in PD, with most studies finding lower NS scores and higher HA scores in PD patients than in healthy controls.^{4,41} We conclude from the findings of our study that the personality features of RLS are quite different from Parkinsonian personality features since the NS scores of our RLS patients did not differ significantly from those of the controls. The lower NS1 score in RLS patients compared to scores in controls may be associated with reduced dopaminergic activity. On the contrary, the higher NS2 scores in RLS patients compared to the controls were highly significant, and may indicate increased dopaminergic activity rather than dopaminergic deficiency. This controversy is also found in pathogenesis of RLS. As recently reviewed by Salas et al.⁴² unlike PD, RLS may be a hyperdopaminergic condition with an apparent postsynaptic desensitization. Differences in the personality features of RLS and PD patients can be considered as further evidence for a difference in pathophysiologies, despite the presence of shared dopaminergic insufficiency.

This study was subject to two main limitations. One that might directly interfere with the main outcome of the study is the exclusion of RLS patients with psychiatric disorders, including depression. It may have been possible to obtain more direct data about the association between these two entities if RLS patients experiencing current depression had not been excluded from the study, and it might then have been possible to better evaluate their intercorrelations. The second limitation is the cross-sectional design, which makes it difficult to draw conclusions concerning the causal relationships between personality features, RLS, and depressive symptoms. However, the current design did allow us to investigate the personality features of RLS patients and to identify the impact of HA temperament on RLS.

In conclusion, this is the first study to demonstrate the temperament and character profiles of RLS patients using the TCI. High HA and low SD scores were the prominent personality features of patients with RLS. The present results highlight the importance of awareness of the personality features of RLS patients, a dimension that has rarely been considered to date, but that is potentially important for understanding the pathophysiology and management of this clinical entity. These results also have the potential to contribute new evidence to the knowledge regarding the possible developmental mechanisms underlying the depressive disorders commonly associated with RLS. The neurobiological bases of the TCI may help to clarify the possible pathophysiological links between RLS, specific personality features, and depressive disturbances.

Conflicts of Interest .

The authors have no financial conflicts of interest.

REFERENCES

- 1. Smith TW, MacKenzie J. Personality and risk of physical illness. *Annu Rev Clin Psychol* 2006;2:435-467.
- 2. Bagby RM, Ryder AG. Personality and the affective disorders: past

efforts, current models, and future directions. Curr Psychiatry Rep 2000;2:465-472.

- Cloninger CR, Svrakic DM, Przybeck TR. Can personality assessment predict future depression? A twelve-month follow-up of 631 subjects. J Affect Disord 2006;92:35-44.
- Poletti M, Bonuccelli U. Personality traits in patients with Parkinson's disease: assessment and clinical implications. *J Neurol* 2012; 259:1029-1038.
- Boz C, Velioglu S, Ozmenoglu M, Sayar K, Alioglu Z, Yalman B, et al. Temperament and character profiles of patients with tension-type headache and migraine. *Psychiatry Clin Neurosci* 2004;58:536-543.
- Conrad R, Schilling G, Bausch C, Nadstawek J, Wartenberg HC, Wegener I, et al. Temperament and character personality profiles and personality disorders in chronic pain patients. *Pain* 2007;133:197-209.
- Yazici E, Yazici AB, Aydin N, Orhan A, Kirpinar I, Acemoglu H. Temperament and character traits in patients with epilepsy: epileptic personality. *J Nerv Ment Dis* 2013;201:365-370.
- Cloninger CR. The science of well-being: an integrated approach to mental health and its disorders. *World Psychiatry* 2006;5:71-76.
- Kampman O, Poutanen O, Illi A, Setälä-Soikkeli E, Viikki M, Nuolivirta T, et al. Temperament profiles, major depression, and response to treatment with SSRIs in psychiatric outpatients. *Eur Psychiatry* 2012;27:245-249.
- Ohayon MM, O'Hara R, Vitiello MV. Epidemiology of restless legs syndrome: a synthesis of the literature. *Sleep Med Rev* 2012;16:283-295.
- Allen RP, Walters AS, Montplaisir J, Hening W, Myers A, Bell TJ, et al. Restless legs syndrome prevalence and impact: REST general population study. *Arch Intern Med* 2005;165:1286-1292.
- Sevim S, Dogu O, Kaleagasi H, Aral M, Metin O, Camdeviren H. Correlation of anxiety and depression symptoms in patients with restless legs syndrome: a population based survey. *J Neurol Neuro*surg Psychiatry 2004;75:226-230.
- Lee HB, Hening WA, Allen RP, Kalaydjian AE, Earley CJ, Eaton WW, et al. Restless legs syndrome is associated with DSM-IV major depressive disorder and panic disorder in the community. *J Neuropsychiatry Clin Neurosci* 2008;20:101-105.
- Kalaydjian A, Bienvenu OJ, Hening WA, Allen RP, Eaton WW, Lee HB. Restless Legs Syndrome and the five-factor model of personality: results from a community sample. *Sleep Med* 2009;10:672-675.
- Cloninger CR, Svrakic DM, Przybeck TR. A psychobiological model of temperament and character. *Arch Gen Psychiatry* 1993;50:975-990.
- Cloninger CR. A systematic method for clinical description and classification of personality variants. A proposal. *Arch Gen Psychiatry* 1987;44:573-588.
- Gillespie NA, Cloninger CR, Heath AC, Martina NG. The genetic and environmental relationship between Cloninger's dimensions of temperament and character. *Pers Individ Dif* 2003;35:1931-1946.
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561-571.
- Hisli N. Beck Depresyon Envanteri'nin üniversite öğrencileri için geçerliği, güvenirliği. *Psikoloji Dergisi* 1989;7:3-13.
- 20. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisi J, et al. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med* 2003;4:101-119.
- Walters AS, LeBrocq C, Dhar A, Hening W, Rosen R, Allen RP, et al. Validation of the International Restless Legs Syndrome Study Group rating scale for restless legs syndrome. *Sleep Med* 2003;4:121-132.
- 22. Kose S, Sayar K, Kalelioglu U, Aydin N, Celikel FC, Gulec H, et al. Normative data and factorial structure of the Turkish version of the

Temperament and Character Inventory. *Compr Psychiatry* 2009;50: 361-368.

- Trouillet R, Gana K. Age differences in temperament, character and depressive mood: a cross-sectional study. *Clin Psychol Psychother* 2008;15:266-275.
- De Fruyt F, Van De Wiele L, Van Heeringen C. Cloninger's psychobiological model of temperament and character and the five-factor model of personality. *Pers Individ Dif* 2000;29:441-452.
- Mochcovitch MD, Nardi AE, Cardoso A. Temperament and character dimensions and their relationship to major depression and panic disorder. *Rev Bras Psiquiatr* 2012;34:342-351.
- 26. Kim WH, Kim BS, Kim SK, Chang SM, Lee DW, Cho MJ, et al. Restless legs syndrome in older people: a community-based study on its prevalence and association with major depressive disorder in older Korean adults. *Int J Geriatr Psychiatry* 2012;27:565-572.
- Li Y, Mirzaei F, O'Reilly EJ, Winkelman J, Malhotra A, Okereke OI, et al. Prospective study of restless legs syndrome and risk of depression in women. *Am J Epidemiol* 2012;176:279-288.
- Gupta R, Lahan V, Goel D. A study examining depression in restless legs syndrome. *Asian J Psychiatr* 2013;6:308-312.
- Sugiura M, Kawashima R, Nakagawa M, Okada K, Sato T, Goto R, et al. Correlation between human personality and neural activity in cerebral cortex. *Neuroimage* 2000;11(5 Pt 1):541-546.
- Moresco FM, Dieci M, Vita A, Messa C, Gobbo C, Galli L, et al. In vivo serotonin 5HT(2A) receptor binding and personality traits in healthy subjects: a positron emission tomography study. *Neuroimage* 2002;17:1470-1478.
- Karlsson H, Hirvonen J, Salminen JK, Hietala J. No association between serotonin 5-HT 1A receptors and spirituality among patients with major depressive disorders or healthy volunteers. *Mol Psychiatry* 2011;16:282-285.
- 32. Tuominen L, Salo J, Hirvonen J, Någren K, Laine P, Melartin T, et al. Temperament, character and serotonin activity in the human brain: a positron emission tomography study based on a general population cohort. *Psychol Med* 2013;43:881-894.
- Yasuno F, Suhara T, Sudo Y, Yamamoto M, Inoue M, Okubo Y, et al. Relation among dopamine D(2) receptor binding, obesity and personality in normal human subjects. *Neurosci Lett* 2001;300:59-61.
- 34. Kim JH, Son YD, Kim HK, Lee SY, Cho SE, Kim YB, et al. Association of harm avoidance with dopamine D2/3 receptor availability in striatal subdivisions: a high resolution PET study. *Biol Psychol* 2011; 87:164-167.
- Alex KD, Pehek EA. Pharmacologic mechanisms of serotonergic regulation of dopamine neurotransmission. *Pharmacol Ther* 2007;113: 296-320.
- Bayard M, Bailey B, Acharya D, Ambreen F, Duggal S, Kaur T, et al. Bupropion and restless legs syndrome: a randomized controlled trial. *J Am Board Fam Med* 2011;24:422-428.
- Jhoo JH, Yoon IY, Kim YK, Chung S, Kim JM, Lee SB, et al. Availability of brain serotonin transporters in patients with restless legs syndrome. *Neurology* 2010;74:513-518.
- Iwamoto R, Yamawaki N, Sato T. Increased self-transcendence in patients with intractable diseases. *Psychiatry Clin Neurosci* 2011;65: 638-647.
- Cloninger CR, Zohar AH. Personality and the perception of health and happiness. J Affect Disord 2011;128:24-32.
- Winkelman JW. Considering the causes of RLS. *Eur J Neurol* 2006;13 Suppl 3:8-14.
- Tomer R, Aharon-Peretz J. Novelty seeking and harm avoidance in Parkinson's disease: effects of asymmetric dopamine deficiency. J Neurol Neurosurg Psychiatry 2004;75:972-975.
- 42. Salas RE, Gamaldo CE, Allen RP. Update in restless legs syndrome. *Curr Opin Neurol* 2010;23:401-406.