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Chronotype and the Big-Five personality traits as predictors of chronic fatigue among patients with sarcoidosis. A cross-sectional study

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Abstract. *Background.* Sarcoidosis may seriously hamper patients' quality of life despite fairly good prognosis. *Objectives.* To assess the relationship between the Big Five personality traits, chronotype and severity of fatigue symptoms, in the context of selected clinical variables and general mental health among patients with sarcoidosis. *Methods.* The study group comprised 60 patients with a confirmed diagnosis of sarcoidosis. They were asked to share relevant clinical data and complete a set of questionnaires: Fatigue Asessment Scale (FAS), General Health Questionnaire (GHQ-28), the NEO Five Factor Inventory and Composite Scale of Morningness. *Results.* In linear regression analysis, FAS score was predicted by female sex, active sarcoidosis status, Morning Affect and Conscientiousness. In principal component analysis, FAS score and all GHQ-28 subscale scores (somatic symptoms, anxiety/insomnia, social dysfunction and depressive symptoms) formed a single component explaining 60% of variance. The factor loading for each variable exceeded 0.6. *Conclusions.* The psychological burden appeared to rise with the severity of the fatigue, regardless the inactive/active phase of sarcoidosis. The severity of fatigue may be linked to patient's poor morning affect. The profile of psychological burden presented by the patients may be associated with their personality and clinical presentation of sarcoidosis.

Introduction

Sarcoidosis can be defined as a chronic inflammatory granulomatous disease of unknown etiology. It involves predominantly lungs and intrathoracic lymph nodes, but other organs can be involved as well, e.g. heart, liver or brain. Despite fairly good prognosis, with low mortality and a spontaneous remission rate of around 60%, the disease may hamper patients' quality of life thus causing a negative impact on their well-being in general (1,2). This may take form of chronic fatigue syndrome (i.e. sarcoidosis-associated fatigue), which may prevail beyond the active phase of sarcoidosis (post-sarcoidosis fatigue syndrome) (3–5).

Sarcoidosis is also linked to mental health sequelae. Up to one third of patients with sarcoidois may suffer from an overlap of clinically significant anxiety and mood disorder(6). Those concerns appear to be of particular importance since psychological burden was associated with poor clinical outcome among patients with sarcoidosis (7). Thus, it is of

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utter importance to recognize general and disease-specific risk factors for psychiatric comorbidities and fatigue syndrome.

Little is known about the link between personality dispositions and the course of sarcoidosis. Type D Personality features (i.e. negative emotionality and proneness to social inhibition) was found in 25% of sarcoidosis patients and was related to the intensity of fatigue symptoms, but not severity of the disease itself (8). Korenromp et al. found that high harm avoidance increased a risk of post-sarcoidosis fatigue syndrome (9).

Up to date there is no published data regarding the possible link between the Big Five Personality traits and the course of sarcoidosis. The possible association between neuroticism and fatigue symptoms in sarcoidosis has previously been suggested (7–9).

Chronotype can be defined as a personal disposition towards an optimal pattern of circadian functioning. In a classic approach a single dimension of the construct is delineated, i.e. morningness-eveningness, which considers the preferable time of day for peak activity and mood (10). Exemplary recent studies revealed a second aspect of the chronotype, i.e. morning affect (11,12). Eveningness has been repeatedly reported as a risk factor for depression (13). Less is known about clinical significance of morning affect, however its transcultural relevance has been recognized and it has been found to be associated with increased indices of fatigue among patients with irritable bowel syndrome 12,14). No direct data regarding chronotype among patients with sarcoidosis has been published so far.

The aim of hereby research was to assess the relationship between the Big Five personality traits, chronotype and severity of fatigue symptoms, in the context of selected clinical variables, general mental health indices, somatic comorbidities among patients with sarcoidosis.

Materials and methods

Study sample and design

The study was conducted from June 2018 to August 2019 among patients of Lung Disease Outpatient Clinic and Clinical Ward of Pneumonology and Allergy in Barlicki Memorial University Hospital in Lodz, Poland. The inclusion criteria were: confirmed diagnosis of sarcoidosis and informed consent for participation in the study. Patients in both active and inactive phase of sarcoidosis were included. The sarcoidosis diagnosis was verified by lung disease specialists and internal medicine specialists (JMD, ŁG, WP). in accordance with the practice guidelines(15). Disease activity was assessed and defined according to available standards (15,16). Active disease was diagnosed, when the patient presented with new sarcoidosis symptoms, experienced progression on imaging examinations (conventional chest X-ray or computer tomography), worsening of lung function tests results, presented signs of new extrapulmonary involvement, or laboratory abnormalities suggestive of sarcoidosis. Inactive disease was diagnosed when complete or partial regression of radiological signs of disease was noted, extrapulmonary disease was excluded, lung function tests results were normal or stable, there were no symptoms related to any particular organ involvement, and laboratory tests results were also normal. Positron emission tomography or scintigraphy were not used for the assessment of sarcoidosis activity. The exclusion criteria comprised: lack of informed consent, diagnosis of major neurocognitive disorder, diagnosis of other interstitial lung disease, diagnosis of cancer, serious and unstable heart disease, a severe psychological trauma within six months preceding the study, serious mental illness (e.g. schizophrenia or bipolar affective disorder or other psychotic disorder) or psychopharmacological treatment. The exclusion criteria regarding the aforementioned possible psychiatric comorbidities were verified by psychiatrists and psychologists (ŁM and TP).

In total, 78 sets of questionnaires were distributed. After signing the informed consent, the participants were asked to complete a set of questionnaires. The clinical data regarding the course of sarcoidosis and comorbidities were completed based on the previous medical history, accessed by the physicians (JMD, ŁG, ŁM). Upon completion of the questionnaires and clinical data, the patients were once again verified regarding the exclusion/inclusion criteria. At this point, N=18 patients were excluded, mostly due to missing data in variables of interest or inability to define the activity status of the disease. The final sample comprised N=60 patients.

Questionnaires

The variables of interest were operationalized based on recognized psychometric tools, with satisfactory validity and reliability for the purposes of scientific research (17).

Fatigue Assessment Scale (FAS) was utilized to assess the sarcoidosis-associated fatigue. The questionnaire was developed by de Vries et al. (18). It consists of ten items, which target both mental and physical symptoms of fatigue. The test-retest reliability of FAS was 0.89 in the original study. The questionnaire was translated to Polish by A. Dubaniewicz and is available online(19). © FAS (Fatigue Assessment Scale): ild care foundation (www.ildcare.nl).

The Big-Five personality traits were measured with *NEO Five Factor Inventory* (NEO-FFI) developed by Costa and McRae. The Polish adaptation was prepared by Zawadzki, Strelau, Szczepaniak and Śliwińska. The tool comprises five 15-item scales, i.e. Neuroticism, Extraversion, Openness, Agreeableness and Conscientiousness, each scored from 0 to 48. Cronbach's alpha coefficients for the Polish version of the scales in Polish adaptation span from 0.68 (for Openness and Agreeableness) to 0.82 (for Conscientiousness)(20).

Chronotype was assessed with the *Composite Scale of Morningness* (CSM), created by Smith et al. and adapted to Polish by Jankowski. It comprises 13 items divided into two scales: Circadian Preference (or Clock Timing, CT, the cognitive-functional component, seven items, scores range from 7 to 31) and Morning Affect (MA, the emotional-motivational domain of the chronotype, six items, scores range from 6 to 24). The two-factor structure of the CSM was proven to be transculturally valid(12). A higher score indicates a morning type. Cronbach's alpha for the Polish version of the CSM was 0.835. (21,22).

The *General Health Questionnaire, 28-item version (GHQ-28)* is a screening tool designed to screen for mental health issues in non-psychiatric samples in four dimensions, i.e. somatic symptoms (A), anxiety/insomnia (B), social dysfunction (C) and depressive symptoms (D). It was developed by Goldberg and adapted to Polish by Makowska and Merecz. Each scale comprises seven items, with answers representing the frequency of the named symptoms being arranged on a four-point Likert-like scale. As the answers were appointed 0-1-2-3, the scores ranged from 0 to 21 in each scale (23,24).

The *Functional Comorbidity Index* was used to quantify the comorbidities of the patients. The scale was originally developed by Groll et al. for the purposes of prediction of functional outcome in chronic diseases (25).

Ethical considerations

This study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Bioethical Committee of the Medical University of Łódź, resolution no RNN/09/20/KE. Ethical matters of the study concern mainly the selection and use of psychometric tools and the interpretation of their results; these are discussed in a more detailed manner in the literature (17,26).

Statistical analysis

The statistical analysis was conducted in STATISTICA 13 (Dell, USA). Continuous variables were described as mean values with standard deviations. The normality of distribution of the continuous variables was verified with the analysis of the histograms and Shapiro-Wilk's W test. The heterogeneity of variance between the subgroups was confirmed with Levene's test. Intergroup comparisons were conducted by analysis of variance: the Snedecor's F test or Welch's test, depending on the Levene's test result. The Chi-square test was performed to assess contingencies in 2x2 tables: i.e. comparison of categorical variables of interest between faculties. If the expected value in any of the cells of the 2x2 tables was below ten, a two-tailed Fisher's exact test was used instead of Chi-square test. The Pearson's correlation quotient was used to assess the relationship between two continuous variables. The Benjamini-Hochberg correction (with an assumed false discovery rate of 0.25) was applied to p-values of correlation quotients, to avoid type 1 error due to multiple testing. Linear regression models were created by means of stepwise elimination to predict the FAS score and each of the GHQ-28 subscales scores (five models in total). The variables of interest are shown in Table 1.

Sigma-restricted coding was used to represent the effects for categorical predictor variables. An analysis of residuals was performed to assess the validity of assumptions of normality, homoscedasticity and independence between observations (with the Durbin–Watson test). Tolerance indices were analyzed to track possible multicollinearities. The predictive value of the whole model was verified by means of 10-fold cross-validation.

On the second level of analysis, the interrelationship between FAS and GHQ-28 subscales was assessed by means of principal component analysis (PCA). The number of the respondents was sufficient for the purposes of the PCA as a low number of items was maintained (i.e. five: FAS score and four GHQ-28 subscales scores) (27). Kaiser-Meyer-Olkin measure and Bartlett's test were used to assess whether data was fit for the detection of a structure.

Table 1. Descriptive statistics for the variables of interest in the studied group of patients with sarcoidosis – comparison between patients with active and non-active disease. Continuous variables are presented as mean±*standard deviation; dichotomous variables are shown as number of observations with percentage of prevalence in each subgroup.*

		Active (N=31)	Non-active (N=27)	p
Sex (female)		13 (41%)	13 (48%)	0.190
Age		40.61 ± 9.33	46.67 ± 12.81	0.052
Tobacco smoking		5 (16%)	3 (11%)	0.181
Body Mass Index (kg/m2)		28.15 ± 4.02	27.51 ± 4.69	0.155
Years since diagnosis		1.45 ± 1.76	8.90 ± 9.58	0.017
Number of organs currently involved		1.68 ± 0.65	0.89 ± 0.93	0.026
Current treatment with corticosteroids		5 (16%)	5 (18%)	0.138
Loefgren syndrome currently		8 (25%)	2 (7%)	0.069
History of Loefgren syndrome		10 (32%)	3 (11%)	0.086
Involved organs	Lymph nodes	30 (96%)	11 (42%)	0.009
	Lungs	18 (58%)	13 (48%)	0.172
	Heart	2 (6%)	0 (0%)	0.121
	Spleen	2 (6%)	0 (0%)	0.129
	Liver	1 (3%)	0 (0%)	0.241
	Skin	1 (3%)	0 (0%)	0.250
Functional Comorbidity Index		0.58 ± 0.85	0.59 ± 0.84	0.216
Arterial hypertension		6 (19%)	3 (11%)	0.112
CSM	Clock Times	25.83 ± 4.8	25.77 ± 4.76	0.224
	Morning Affect	18.33 ± 3.38	19.46 ± 3.8	0.103
NEO FFI	Neuroticism	19.77 ± 8.71	19.81 ± 8.98	0.233
	Extraversion	24.74 ± 5.69	24.56 ± 5.51	0.198
	Opennes	25.32 ± 7.26	24.3 ± 5.46	0.147
	Agreeableness	30.32 ± 6.25	30.19 ± 4.86	0.207
	Conscientiousness	33.97 ± 5.23	31.44 ± 6.27	0.078
Fatigue Assessment Scale score		31.87 ± 8.09	28.54 ± 8.72	0.095
GHQ-28	Somatic symptoms	10.48 ± 4.33	7.96 ± 3.61	0.043
	Anxiety and Insomnia	9.52 ± 5.29	6.33 ± 4.1	0.034
	Social dysfuction	10.26 ± 3.66	8.48 ± 3.09	0.060
	Depressive symptoms	2.74 ± 4.06	2.26 ± 2.98	0.164

CSM– Composite Scale of Morningness, GHQ-28 – General Health Quality, 28-item version, NEO-FFI – The Big Five Personality Inventory, , M – mean value, SD – standard deviation

Indices with a common variance of at least 0.3 were considered as a significant association.

Effect sizes, in statistical terms, were assessed in three manners: for a linear regression model as a whole (coefficient of determination R^2), for each parameter in the model (semipartial correlation sR) and for each variable as factor loading in PCA. The level of significance was adopted for $\alpha = 0.05$.

Results

Active vs non-active sarcoidosis – intergroup comparison

Descriptive statistics for the variables of interest are shown in Table 1. Patients with active sarcoidosis had on average shorter time since diagnosis of the disease, had a greater number of organs involved, had higher GHQ-28 somatic symptoms and anxiety/insomnia scores compared to those with remitted disease. The differences in terms of the remaining variables of interest were not statistically significant.

Correlations

There was a moderate negative correlation between FAS score and Morning Affect score. FAS score also correlated positively with Neuroticism and negatively with Conscientiousness. Significant and moderate correlations were found between FAS score and GHQ-28 Somatic symptoms, Anxiety and Insomnia and Social dysfunction, but not Depressive symptoms, after application of Benjamini Hochberg correction. Chosen significant correlation quotients are shown in Table 2. Detailed correlation matrix is shown in Supplementary Table 1.

Linear regression models of prediction

FAS score was predicted by female sex (sR=0.352, p=0.001), active sarcoidosis status (sR=0.248, p=0.021), a fall in Morning Affect (sR=-0.272, p=0.012) and a fall in Conscientiousness score (sR=-0.334, p=0.002). Somatic symptoms severity was predicted by female sex (sR=0.277, p=0.012), active status of the disease (sR=0.313, p=0.009) and a fall in Morning Affect (sR=-0.310, p=0.010). .The severity of Anxiety and Insomnia was predicted by: female sex (sR=0.369, p<0.001), active disease status (sR=0.368, p<0.001) and Neuroticism (sR=0.559, p<0.001). An increase in Social dysfunction score was associated with a fall in years since diagnosis (sR=-0.246, p=0.020), female sex (sR=0.379, p<0.001), currently presented Loefgren syndrome (sR=0.283, p=0.008), fall in Conscientiousness (sR=-0.242, p=0.022) and rise in Neuroticism (sR=0.247, p=0.019). A rise in depressive symptoms severity was predicted by history of tobacco smoking (sR=0.295, p=0.004) and an increase in Neuroticism (sR=0.606, p<0.001) (Supplementary Table 2).

Principal component analysis

A single factor was elucidated, comprising all five included scores, i.e. FAS, GHQ-28 Somatic symptoms, Anxiety and insomnia, Social dysfunction, Depressive symptoms. Thus, the factor was named "Fatigue-associated mental health". The

Table 2. A shortened matrix of the Pearson correlation quotients between the continuous variables of interest in the studied group of patients with sarcoidosis. The full matrix is placed in Supplementary Material.

		FAS	GHQ A	GHQ B	GHQ C	GHQ D
CSM	Clock Times	-0.145	-0.033	0.100	-0.097	0.107
	Morning Affect	-0.484*	-0.387*	-0.475*	-0.368*	-0.287
NEO FFI	Neuroticism	0.352*	0.176	0.596*	0.376*	0.623**
	Extraversion	-0.258	0.029	-0.287	-0.122	-0.186
	Openness	0.239	0.210	0.131	0.341*	-0.031
	Agreeableness	0.127	0.164	0.144	0.070	0.011
	Conscientiousness	-0.258	-0.081	-0.059	-0.302	-0.162

*p<0.05, **p<0.001 (two-way, after Benjamini-Hochberg correction); BMI – Body Mass Index, FAS – Fatigue Assessment Scale, CSM – Composite Scale of Morningness, GHQ – General Health Quality questionnaire, 28-item version: A – somatic symptoms scale, B – anxiety/insomnia scale, C – social dysfunction scale, D – depression scale; NEO-FFI – The Big Five Personality Inventor

detected structure, i.e. the single factor, explained 61% of variance in the analysis. The lowest factor loading (0.6) was observed for GHQ-28 Depressive symptoms. The remainder factor loadings oscillated around 0.8 (Figure 1).

Discussion

In hereby study, a surge in the severity of fatigue symptoms was predicted by low conscientiousness. There was a positive correlation between FAS score and the Big-Five Neuroticism score, but this association was not confirmed in a regression model. The relationship between low conscientiousness and high fatigue indices stay in line with previous data regarding the trait being the risk factor of poor physical health and mental wellbeing in chronic diseases (28). Also, similar relationships was previously reported in different samples, e.g. Fernandez-Munoz et al. found conscientiousness to be associated with fatigue among patients with multiple sclerosis, while Tanaka et al. concluded that low self-directedness (a trait similar to conscientiousness) predicted increased fatigue among medical students (29,30).The link between fatigue and conscientiousness may be explained by their mutual relation to anti-health behaviours, e.g. physical inactivity, which was generally reported to be prevalent among patients with sarcoidosis (31,32). The possible role of the personality in prediction of fatigue in sarcoidosis should be further studied, since previous researches indicate neuroticism, agreeableness and extraversion could also be of importance (28–30).

Morning affect, but not circadian preference (i.e. morning-to-evening orientation), was found to be associated with fatigue symptoms in the studied sample of patients with sarcoidosis. A poor morning affect was linked to increased indices of fatigue. The second hypothesis was partially confirmed and the results are partially in line with previous findings. In a sample of patients with inflammatory bowel diseases, Chrobak et al. found both eveningness and morning affect to be associated with general fatigue among patients with inflammatory bowel disease (14). It may raise concern that the link between evening circadian preference and fatigue severity was found insignificant, since previous research delineate such relationship(14,33). Patients with late chronotype are prone to experience circadian rhythm

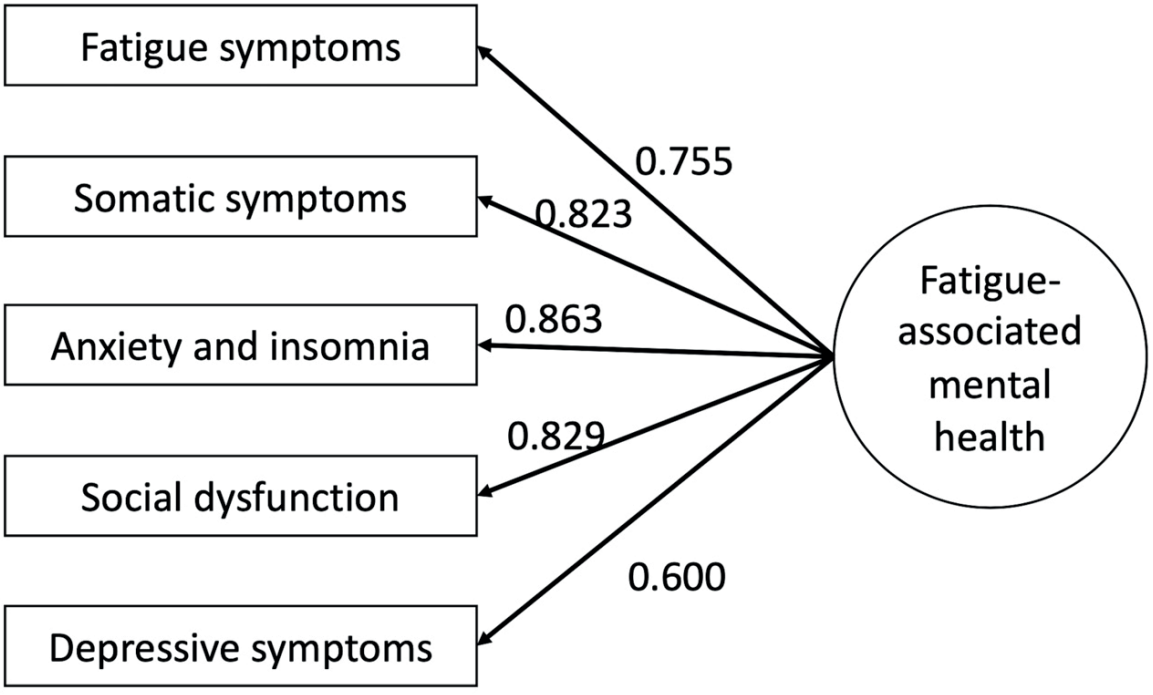

Figure 1. Graphic presentation of detected structure (named Fatigue-associated mental health) in principal component analysis based on scores of Fatigue Assessment Scale and General Health Questionnaire in the studied group of patients with diagnosed sarcoidosis.

dysregulation, which may be considered a chronic stressor and thus contribute to increased psychological burden or sense of fatigue (34,35). In turn, sense of fatigue (or tiredness) after waking up or in the morning may contribute to a decrease in mood and thus result in poor morning affect(36). However, the topic has not been studied extensively in general population, let alone in patients with granulomatous lung diseases. A link between fatigue and morning affect but not circadian preference, may be a specific observation for sarcoidosis-associated fatigue, but a confirmation on a larger sample, with at least case-control setting, is required.

A principal component analysis resulted in finding a common factor to fatigue symptoms, anxiety and insomnia, social dysfunction and depressive symptoms, explaining 60% of variance. The hypothetical factor was named "fatigue-associated mental health". This subanalysis confirmed that there is a close relationship between fatigue and general mental health indices among patients with sarcoidosis. Holas et al. reported that distress and physical concerns (as dimensions of anxiety sensitivity) predicted the severity of fatigue in sarcoidosis patients (37). In a study by Bosse-Henck et al. fatigue was associated with high score in Pittsburgh Sleep Quality Index, which contains questions concerning insomnia symptoms(38). Hendriks et al found fatigue to be associated with reduced work ability (which is a measure of social dysfunction)(39). The relationship between depression and fatigue symptoms is particularly supported by the previous research, including a prospective follow-up study (40,41). However, it should be noted that in a setting of anxiety, social dysfunction and somatic symptoms – the factor loading of depressive symptoms in relation to fatigue was relatively the smallest one. It should be remembered that the symptomatology of depression goes beyond mere fatigue and include lack of drive, poor mood, lack of pleasure or poor concentration as well (42,43). On the other hand, previous studies by Bunevicius et al. and Corfield et al. indicate that the relationship between depression and fatigue may be independent of their overlapping symptoms(44,45). The coexistence of depression and fatigue raise a concern and warrants additional treatment, both in general population and among patients with sarcoidosis (40,45).

One other important thing was an observed association between selected clinical variables and the mental health indices. Active phase of the sarcoidosis predicted an increase in fatigue, somatic symptoms and anxiety/insomnia. This observation may be explained by an increased inflammation (characteristic for active phase of sarcoidosis), which was previously linked to poor mental health, psychological burden and fatigue in different populations, for example in healthy persons, older adults, bereaved ones and among patients with post-traumatic stress disorder (46–49).

Another interesting observation was that presence of Loefgren syndrome predicted an increase in Social dysfunction. This phenotype of sarcoidosis is associated with fairly good prognosis, e.g. low probability of chronic trend(50). Yet, it appears that it may hamper one's functioning on its presentation. This may be contributed to the link between Loefgren syndrome and involvement of the joints and thus impairing movement(50). This is the first study indicating such association.

A relationship between depression severity and number of involved organs, observed by Hinz et al., was not confirmed in hereby study(51). This may be contributed to either too small sample size or utilization of different clinical scales assessing severity of depression, yet the association require further verification.

Interestingly, time since diagnosis was associated negatively with social dysfunction, i.e. longer duration of the disease was linked to an improvement in social functioning. The association was independent of the active status of the disease and personality factors. There is no comparable research to back the observed relationship. Yet, it may be explained in the light of adaptation to the chronic disease. Consequently, patients learn over years to function in society despite the fact of the diagnosis and presence of its symptoms(52,53). However, future studies deepening the understanding of this association are warranted.

It was also investigated whether the current use of corticosteroids may contribute to the fatigue and mental state of the patients with sarcoidosis, but the variable was eliminated from the models due to statistically non-significant association with the variables of interest. It has been previously recognized that use of glucocorticosteroids may be associated with psychiatric complications(54). Yet, the current study does not provide any evidence for the association between use of glucocorticosteroids, fatigue and mental health status among patients with sarcoidosis

The verification of this association is required on a larger multi-center group.

Despite the novelty of the results, several drawbacks should be enlisted regarding the current study. The research was conducted on a relatively small, non-random sample of a single center. However, it should be noted that sarcoidosis remain a rare disease and a limited number of clinical centers take care of patients with this disease. Thus, the studied sample came from the whole country to the aforementioned outpatient clinic. The single-point measurement and observational character of the study unables to conclude about possible causalities. Therefore, a need of a longitudinal, multicenter, randomized, controlled study should be emphasized in order to further investigate the interplay between chronotype, personality, fatigue and mental health among patients with sarcoidosis.

Conclusions

The psychological burden appeared to rise with the severity of the fatigue, independently of the activity of sarcoidosis. The severity of fatigue may be linked to patient's poor morning affect. Presentation of Loefgren's syndrome may be linked to perceived social dysfunction. The profile of psychological burden presented by the patients may be associated with their personality and clinical presentation of sarcoidosis. Thus, we confirm and provide further data that there is a need of a complex, multidisciplinary therapeutic care, with regards to individual differences (personality and chronotype) for patients with sarcoidosis.

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Data availability statement. The database, used to support the findings of this study, may be released upon application to the corresponding author.

Declaration of interest. The authors have no conflict of interest to report.

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Supplementary Table 1. A detailed matrix of the Pearson correlation quotients between the continuous variables of interest in the studied group of patients with sarcoidosis.

			Age	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1		Years since diagnosis		0.513*														
2		Functional Comorbidity Index	0.390*	0.394*														
3		BMI (kg/m2)	0.188	0.211	0.569*													
4		No of organs involved	0.022	0.013	0.192	-0.079												
5	CSM	Clock Times	0.065	0.073	-0.004	-0.078	0.075											
6	CSM	Morning Affect	0.161	0.160	0.068	0.053	-0.038	0.475*										
7	NEO FFI	Neuroticism	-0.207	-0.203	-0.046	-0.170	0.021	0.148	-0.428*									
8	NEO FFI	Extraversion	-0.136	-0.149	0.097	0.020	-0.053	-0.160	0.066	-0.340								
9	NEO FFI	Openness	-0.038	-0.040	-0.134	-0.015	-0.136	-0.266	-0.166	-0.050	0.211							
10	NEO FFI	Agreeableness	0.319	0.318	0.391*	0.234	-0.018	0.233	0.060	-0.179	-0.050	0.080						
11	NEO FFI	Conscientiousness	0.251	0.250	0.227	0.053	0.212	0.220	0.318	-0.331	0.148	-0.046	0.234					
12		FAS score	-0.073	-0.063	-0.015	0.124	-0.067	-0.145	-0.484*	0.352*	-0.258	0.239	0.127	-0.382*				
13	GHQ-28	Somatic symptoms	-0.002	0.002	0.071	0.159	-0.058	-0.033	-0.387*	0.176	0.029	0.210	0.164	-0.081	0.574*			
14	GHQ-28	Anxiety and Insomnia	-0.022	-0.016	0.069	0.056	0.037	0.100	-0.475*	0.596*	-0.287	0.131	0.144	-0.059	0.552*	0.601**		
15	GHQ-28	Social dysfuction	-0.010	-0.014	-0.067	0.020	-0.150	-0.097	-0.368*	0.376*	-0.122	0.341*	0.070	-0.302	0.519*	0.630**	0.665**	
16	GHQ-28	Depressive symptoms	-0.284	-0.282	-0.151	-0.041	0.022	0.107	-0.287	0.623**	-0.186	-0.031	0.011	-0.162	0.338	0.342	0.486*	0.341

*p<0.05, **p<0.001 (two-way, after Benjamini-Hochberg correction); BMI – Body Mass Index, FAS – Fatigue Assessment Scale, CSM – Composite Scale of Morningness, GHQ-28 – General Health Quality, 28-item version, NEO-FFI – The Big Five Personality Inventory

Supplementary Table 2. Parameters (B) with 95% Confidence Intervals (CI) identified for the prediction of Fatigue Assessment Score and General Health Questionnaire (GHQ-28) dimensions in the studied group of patients with sarcoidosis; effect sizes are given as semi-partial correlations (sR) of linear regression models.

Fatigue Assessment Scale score prediction						
R^2=0.414; F= 10.550. df=4. p<0.001						
	B	**B 95% CI**		**sR**	**t**	**p**
Intercept	61.689	49.665	73.713		10.305	<0.001
Sex (female)	3.009	1.220	4.798	0.352	3.378	0.001
Active disease status	2.185	0.345	4.026	0.248	2.385	0.021
Morning Affect	-0.702	-1.241	-0.162	-0.272	-2.612	0.012
Conscientiousness	-0.539	-0.877	-0.201	-0.334	-3.204	0.002
GHQ-28 Somatic symptoms score prediction						
R^2=0.281; F= 8.044, df=3, p<0.001						
	B	**B 95% CI**		**sR**	**t**	**p**
Intercept	15.886	10.798	20.975		6.268	<0.001
Sex (female)	1.218	0.277	2.159	0.300	2.599	0.012
Active disease status	1.272	0.330	2.213	0.313	2.712	0.009
Morning Affect	-0.357	-0.624	-0.091	-0.310	-2.689	0.010
GHQ-28 Anxiety and Insomnia score prediction						
R^2=0.584; F=26.247, df=3, p<0.001						
	B	**B 95% CI**		**sR**	**t**	**p**
Intercept	1.778	-0.375	3.930		1.658	0.103
Sex (female)	1.815	0.949	2.682	0.369	4.207	<0.001
Active disease status	1.791	0.933	2.649	0.368	4.188	<0.001
Neuroticism	0.309	0.212	0.407	0.559	6.365	<0.001
GHQ-28 Social Dysfunction score prediction						
R^2=0.441; F=9.384, df=5, p<0.001						
	B	**B 95% CI**		**sR**	**t**	**p**
Intercept	14.381	8.881	19.880		5.259	<0.001
Years since diagnosis	-0.159	-0.268	-0.0.24	-0.246	-2.405	0.020
Sex (female)	1.445	0.658	2.232	0.379	3.692	<0.001
Loefgren syndrome currently	1.449	0.393	2.505	0.283	2.759	0.008
Conscientiousness	-0.159	-0.294	-0.023	-0.242	-2.357	0.022
Neuroticism	0.109	0.018	0.200	0.247	2.408	0.019
GHQ-28 Depressive symptoms score prediction						
R^2=0.545; F=11.789, df=6, p<0.001						
	B	**B 95% CI**		**sR**	**t**	**p**
Intercept	-1.223	-3.213	0.767		-1.233	0.223
Smoking	1.599	0.524	2.675	0.295	2.982	0.004
Neuroticism	0.247	0.166	0.329	0.606	6.118	<0.001

R2 – coefficient of determination, F – statistics in the F test, *df* – degrees of freedom, t – statistics in the Wald test, p – probability in the statistical test