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RESEARCH ARTICLE

Associations between sleep quality, severity of dissociation, pathological worry, and functional impairment in multiple sclerosis: a case-control study

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ABSTRACT

Objective: The current study was designed to investigate differences between patients with multiple sclerosis (MS) and healthy controls regarding sleep quality, worry, and dissociative experiences. We also explored the potential correlates of functional impairment in this group.

Method: Eighty-eight patients with MS and 139 healthy adults participated in the study. The mean age was 30.96 (standard deviation=8.88) years. The Expanded Disability Status Scale, Dissociative Experiences Scale (DES), Penn State Worry Questionnaire (PSWQ), and Pittsburgh Sleep Quality Index (PSQI) were completed by clinical and nonclinical subjects. Binary logistic and multiple regression analyses were performed.

Results: Of the MS patients, 55.7% were identified as poor sleepers. However, total scores on the PSQI did not differ significantly between clinical and nonclinical subjects. Logistic regression analysis showed that patients with MS reported significantly lower levels of habitual sleep efficiency than healthy controls. Interestingly, healthy adults reported higher scores on pathological worry than patients with MS. Patients with MS and healthy adults did not differ in the DES scores. Duration of illness and worrisome thoughts were significant predictors of the functional impairment occurring during the course of the illness.

Conclusion: Patients with MS had poor habitual sleep efficiency, which may be a significant risk factor for management and improvement of the illness. Pathological worry seems to be associated with disability status. Cognitive behavioral interventions including sleep-informed instructions should be integrated into clinical practices to enhance positive outcomes during the course of the treatment in this group.

Keywords: Dissociative experiences, habitual sleep efficiency, post-traumatic growth, sleep disturbance

INTRODUCTION

Multiple sclerosis (MS) is a chronic demyelinating disease characterized by localized areas of inflammation, axonal loss, and gliosis in the brain and spinal cord that results in damage in the central nervous system (1). Specific symptoms of MS may be diplopia, weakness in the muscles, and problems with sensation or motor

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coordination. The illness may take several forms, including symptoms with isolated attacks or occurring gradually over time (2). According to the McDonald criteria, clinical and radiographic evidence is required for the diagnosis of MS (3). MS is a debilitating disease of the central nervous system resulting in a greater risk of sleep disorders for patients compared to the general population (4,5). In a national survey including 2.375 patients with MS, Brass et al. (6) found that 37.8% of the sample was screened positive for obstructive sleep apnea, 31.6% for moderate to severe insomnia, and 36.8% for restless legs syndrome. In a clinical survey, 47.5% of the patients were identified as having poor sleep quality measured on the Pittsburgh Sleep Quality Index (PSQI) (7).

Sleep is a crucial part of human existence, affecting cognitive and emotional regulation (8-16). The default of good sleep is a natural state, including both plasticity, a term referring to the 'absorb and readjust' capacity of the sleep-wake cycle in response to variability in personal and situational factors, and automaticity, a term referring to the involuntary nature of a well-adjusted schedule (17). Cognitive theory posits that dysregulation in cognitive processing is central in the formation and persistence of sleep problems (18).

Studies identified a typical profile for insomniacs marked by a pronounced tendency towards internalization that leads to heighted emotional activation and physiological hyper-arousal (19,20). Morin (21) proposed an integrated conceptualization, suggesting that cognitive, emotional, and physiological arousal interacting reciprocally with dysfunctional cognitions, maladaptive sleep habits, and arousal-generating consequences play a significant role in sleep problems. Accordingly, sleep problems at first originate from physiological reactivity which, in turn, generates intrusive thoughts related to hyper-aroused physiological and emotional states, particularly during the pre-sleep period. Catastrophizing and probability overestimation were two evident cognitive distortions highlighted in regard to insomnia (22-26). The maladaptive role of using sleep-related thought control strategies during bedtime have long been recognized (27-30). In a more recent study, core sleep-related thought control strategies were identified as 'aggressive suppression and worry', 'behavioral and cognitive distraction', and 'reappraisal' (31).

Dissociation is conceptualized as a disruption in the normal integration of consciousness, memory, identity, emotion, perception, body representation, and motor behavior (32). The phenomenon refers to a range of conceptualizations across different theoretical approaches (33-37), which can be best understood on a continuum from an adaptive coping strategy at milder levels to being akin to a form of severe experiential avoidance at pathological levels (38). Dissociative experiences represent a multifaceted construct for which factor-analytic investigations generally supported a three-dimensional factor structure of absorption/imaginative involvement, depersonalization/derealization, and dissociative amnesia (39-43).

A vast body of evidence has indicated robust links between dissociation and sleep (44-56). Although underpinning mechanisms of these phenomena may differ, interactions between sleep and dissociative symptomatology seem to be reciprocal. Scholars asserted that dream-like states arising from a labile sleep-wake cycle intrude into waking consciousness, producing memory failures and dissociative states (49,52,55,57). Mostly, dissociative experiences are imaginative in nature (58). On the other hand, worry is mainly verbal, more realistic, less voluntary, more distressing, and of longer duration relative to dissociative phenomena (59). Worry is experienced primarily as negative verbal activity in contrast to imaginal content (60,61) and seems no longer to allow imaginative processing due to excessive thought content (62). The worrying process, which is primarily verbal in nature, may keep accessibility to parallel-processed images at bay, particularly in cases of catastrophic images that become less vivid and intrusive through this processing (63-65). In keeping with the assertion of the avoidance hypothesis conjectured by Mowrer (66), Yildirim et al. (67) determined that dissociative experiences had significant indirect influences on deterioration of sleep quality through exacerbating worrisome thoughts.

Scholars have widely recognized that sleep problems are a hallmark in MS (68-70), playing a crucial role in more severe fatigue (71-73), poor quality of life (74,75), and impairment in cognitive function (76,77). Korostil and Feinstein (78) detected that lifetime prevalence of any anxiety disorder among patients with MS was as high as 35.7%, with generalized anxiety disorder (GAD) being one of the most common diagnoses. GAD is characterized by sleep disturbance, restlessness, fatigue, irritability, and/or muscle tension (32). More importantly, uncontrollable and excessive worry is an integral part of GAD. Despite the paucity of research in MS, Thornton et al. (79) outlined a specific pattern of worry among 40 patients with MS, including a decreased sense of being able to attend positive activities or effect positive outcomes. In a community-based sample of 50 patients with relapsing-remitting and

secondary progressive MS, Bruce and Arnett (80) found that patients reported greater levels of worry, depression, and trait anxiety compared to 45 healthy individuals. Correlational analyses indicated that patients' heightened level of worry was significantly associated with sleep problems, fatigue, problem-solving deficits, pain, and disability status. Nevertheless, relationships between sleep, worry, and dissociation still remain elusive in this group. The main aim of this study was to explore whether MS patients differ from healthy controls regarding sleep quality, dissociative symptomatology, and worry after controlling for demographic variables (age, sex, marital status, education, prior mental disorder, and familial loading). Additionally, associations of functional impairment as measured by the Expanded Disability Status Scale (EDSS) with dissociative experiences, worrisome thoughts, and sleep quality were investigated.

METHOD

Participants and procedure

Eighty-eight inpatients with MS being treated for at least 6 months and 139 healthy adults from the general population participated in the study. The mean age of the clinical and nonclinical subjects was 30.96 (standard deviation=8.88) years. Just over half of the overall sample were female (57.3%) and 51.1% of the participants were single. Twelve percent of clinical and nonclinical individuals reported at least one prior mental disorder and 3.1% reported the presence of a psychiatric disorder among their first-degree relatives. Sample characteristics are presented in Table 1.

Inclusion criteria for MS patients were a diagnosis of MS (3) and an EDSS score below 7.0 (81). Exclusion criteria were an age under 18 or over 65 years and any cognitive disability that could affect compliance with the study procedures. All participants were informed about the purposes and procedures of the study and provided written consent. The procedures of the study received ethical approval from the Ethics Committee of Van Yuzuncu Yil University.

Measures

Expanded Disability Status Scale (EDSS): The EDSS is a method of quantifying disability in MS through assessing disability in eight functional systems: pyramidal, cerebellar, brainstem, sensory, bowel and

Table 1: Sample characteristics and comparisons between control and patient groups

	Overall sample n=227		Controls n=139		Multiple sclerosis patients n=88			
	n	%	n	%	n	%		p
Age (mean, SD)	30.96	8.88	28.86	7.99	34.27	9.26	t (225)=-4.678	<0.001
Sex								
Female	130	57.27	73	52.52	57	64.77	LR (1)=3.336	0.068
Male	97	42.73	66	47.48	31	35.23		
Marital status								
Single	111	48.90	84	60.43	27	30.68	LR (1)=19.469	<0.001
Married	116	51.10	55	39.57	61	69.32		
Education								
Uneducated	13	5.73	0	0.00	13	14.77	LR (4)=94.174	<0.001
Primary school	26	11.45	2	1.44	24	27.27		
Secondary school	16	7.05	6	4.32	10	11.36		
High school	46	20.26	25	17.99	21	23.86		
University	126	55.51	106	76.26	20	22.73		
Prior mental disorders	27	11.95	7	5.04	20	22.73	LR (1)=15.815	<0.001
Familial loading	7	3.10	3	2.16	4	4.55	LR (1)=0.995	0.319
Pittsburgh Sleep Quality Index								
PSQI≥5	140	61.67	91	65.47	49	55.68	LR (1)=2.172	0.141
Duration of multiple sclerosis (mean, SD)	-	-	-	-	7.99	5.85		
Expanded Disability Status Scale (mean, SD)	-	-	-	-	2.30	1.66		

LR: Likelihood ratio test, PSQI: Pittsburgh Sleep Quality Index, SD: Standard deviation

bladder, visual, cerebral, and other. The severity of disability is rated on a scale ranging from 0 to 10, where higher scores indicate a greater impairment of the eight functional systems (81). The Turkish version of the instrument was reliably used among patients with MS (82).

Dissociative Experiences Scale (DES): The DES originally measures dissociation on a continuum ranging from normal dissociative experiences to pathological forms of dissociation (83,84). The instrument consists of 28 self-report items that are rated on a scale ranging from 0 to 100, which are tapping into three dimensions: absorption/imaginative involvement, amnesia, and depersonalization/derealization (85). A DES score of 30 and above is indicative of pathological dissociation (38,86). The DES has good validity and reliability and good overall psychometric properties (85). The Turkish version of the scale has good reliability and validity, with Cronbach's α=0.91 and a test-retest correlation coefficient r=0.78 (87).

Penn State Worry Questionnaire (PSWQ): The PSWQ is a widely used measure of excessive and uncontrollable worry (88). It consists of 16 items that are rated on a five-point scale. The measure yields a total score ranging from 16 to 90. Evidence from various clinical and nonclinical groups supports the reliability, unidimensional structure, and convergent and discriminant validity of the PSWQ (89-92). The Turkish version was demonstrated to have good reliability and validity (93).

Pittsburgh Sleep Quality Index (PSQI): The PSQI is a reliable and valid instrument assessing sleep quality and disturbances over a 1-month time interval (94). The measure consists of 19 self-report questions. The instrument yields seven components of sleep quality: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The screening tool discriminates well between good and poor sleepers (PSQI≥5) and is an excellent general screening measure of sleep disturbances (95). The Turkish version of the PSQI was adapted by Agargun et al. (96).

Statistical Analysis

We began with computing descriptive statistics for clinical and nonclinical samples. Demographic characteristics of patients with MS were compared with healthy controls using nonparametric likelihood-ratio test (LR) and Student's t-test. Demographic characteristics (age, sex, marital status, education, prior mental disorders, and familial loading), scores on the PSWQ, subscales of the DES (depersonalization/derealization, absorption, and amnesia) and seven components of the PSQI (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction) were regressed on to patient status using binary multiple logistic regression analysis. Beta coefficient (β), odds ratio (OR), and 95% confidence interval (CI) were computed for each independent variable. To explore potential correlates of functional impairment in MS, multiple regression analysis was conducted with socio-demographic characteristics, pathological worry, dissociation, and sleep quality as independent variables and the EDSS score as the dependent variable.

RESULTS

Sample Characteristics

Using Student's t-test, we found that the age in the patient group was higher than in the healthy adult group (t [225]=-4.678, p<0.001). The majority of patients with MS were married, whereas most of the individuals from general population were single (LR [1]=19.469, p<0.001). MS patients had lower levels of education than healthy adults (LR [4]=94.174, p<0.001). The patient group reported more prior mental health problems than controls (LR [1]=15.815, p<0.001). Clinical and nonclinical groups did not differ significantly by sex, familial loading of psychiatric disorders, and frequency of poor sleep quality (p>0.05).

Multiple Logistic Regression Analysis

Using binary multiple logistic regression analysis, we explored whether MS patients significantly differed from healthy controls on the PSWQ, subscales of the DES (depersonalization/derealization, absorption, and amnesia) and the seven components of the PSQI (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction) after controlling for demographic characteristics (age, sex, marital status, education, prior mental disorders, and familial loading). Multiple logistic regression analysis showed that MS patients had significantly lower levels of education (OR=0.30, 95% CI=0.197-0.466, p<0.001), greater frequency of prior mental disorders (OR=6.50, 95% CI=1.607-26.278, p=0.006), lower levels of worrisome thoughts (OR=0.95, 95% CI=0.914-0.989, p=0.012) and better habitual sleep (OR=2.01, 95%

CI=1.078-3.759, p=0.028) than healthy controls. Findings are presented in Table 2.

Multiple Regression Analysis on Functional Impairment

We performed multiple regression analysis to investigate the relationship of functional impairment in MS with demographic characteristics (age, sex, marital status, education, prior mental disorders, and familial loading), scores on the PSWQ, subscales of the DES (depersonalization/derealization, absorption, and amnesia) and the seven components of the PSQI (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction). Higher functional impairment was significant associated with lower levels of education (β=-0.27, t=-2.118, p<0.05), positively associated with the duration of the illness (β=0.33, t=2.567, p<0.05), and positively associated with worrisome thought (β=0.29, t=2.071, p<0.05). Findings are presented in Table 3.

DISCUSSION

Main aim of this study was to explore differences in sleep quality, worry, and dissociative experiences between patients with MS and healthy controls. We found that, in comparison to the control group, MS patients had significantly poorer habitual sleep efficiency but lower levels of pathological worry than control subjects. On the other hand, patient and control groups did not differ significantly in dissociative symptomatology. More intriguingly, inpatients with MS reported significantly lower worrisome thoughts as measured by the PSWQ than did healthy controls. Nevertheless, heightened level of worry was significantly associated with more functional impairment among patients with MS. As far as we can tell, the current findings relative to lower levels of pathological worry and unsubstantial dissociative symptomatology among MS patients compared to healthy controls can be best understood in the context of post-traumatic growth, where people faced with chronic conditions may show positive changes in their understanding of life, their own self, and interpersonal relationships (97-99). Despite the paucity of research, Aflakseir and Manafi (100) indicated that appreciation of life through spiritual change and personal strength was significantly associated with positive changes in response to debilitating conditions in MS. Further studies addressing the positive psychological changes in chronic neurological conditions are needed, particularly among MS patients.

Table 2: Multiple logistic regression on patient status

	OR	p	95% CI
Age	1.021	0.448	0.967-1.079
Sex	1.006	0.988	0.456-2.222
Marital status	2.370	0.057	0.973-5.771
Education	0.303	<0.001	0.197-0.466
Prior mental disorders	6.499	0.009	1.607-26.278
Familial loading	1.268	0.836	0.133-12.115
Penn State Worry Questionnaire	0.951	0.012	0.914-0.989
Dissociative Experiences Scale (DES)			
DES-Depersonalization/derealization	1.005	0.834	0.960-1.052
DES- Absorption/imaginative involvement	0.993	0.738	0.950-1.037
DES-Amnesia	1.009	0.719	0.961-1.059
Pittsburgh Sleep Quality Index (PSQI)			
PSQI-Subjective sleep quality	1.159	0.593	0.675-1.990
PSQI-Sleep latency	1.442	0.144	0.883-2.357
PSQI-Sleep duration	0.586	0.051	0.342-1.003
PSQI-Habitual sleep efficiency	2.013	0.028	1.078-3.759
PSQI-Sleep disturbances	1.222	0.643	0.524-2.853
PSQI-Use of sleeping medication	0.645	0.485	0.188-2.211
PSQI-Daytime dysfunction	0.863	0.564	0.524-1.423

OR: Odds ratio, CI: Confidence interval

Table 3: Multiple regression on EDSS scores among MS patients

	β	t	p
Age	0.217	1.449	0.152
Sex	0.052	0.441	0.660
Marital status	-0.146	-1.305	0.196
Education	-0.269	-2.118	0.038
Previous mental disorder	0.031	0.242	0.810
Familial loading	-0.012	-0.119	0.906
Duration of MS illness	0.332	2.567	0.013
Penn State Worry Questionnaire	0.293	2.071	0.042
Dissociative Experiences Scale (DES)			
DES-Depersonalization/Derealization	0.221	1.245	0.218
DES-Absorption/ Imaginative involvement	-0.206	-0.885	0.380
DES-Amnesia	-0.024	-0.133	0.895
Pittsburgh Sleep Quality Index (PSQI)			
PSQI-Subjective sleep quality	0.089	0.676	0.502
PSQI-Sleep latency	-0.199	-1.560	0.123
PSQI-Sleep duration	0.210	1.640	0.106
PSQI-Habitual sleep efficiency	0.052	0.442	0.660
PSQI-Sleep disturbances	0.059	0.414	0.681
PSQI-Use of sleeping medication	-0.232	-1.999	0.050
PSQI-Daytime dysfunction	-0.014	-0.116	0.908

EDSS: Expanded Disability Status Scale; β: Standardized beta coefficients, MS: Multiple sclerosis

MS is a demyelinating disease of the central nervous system, and a sizable proportion of MS patients, approximately 40-70%, experience cognitive difficulties (101,102). Perceived planning/organization impairment and perceived retrospective memory impairment were significant predictors for quality of life (103). Training processing speed and working memory was demonstrated to be beneficial to produce moderate improvement in cognitive functioning (104). In a sample of 79 MS patients, self-reported memory problems were significantly associated with higher levels of normative dissociation, which was also significantly correlated with depression, anxiety, and neuroticism (105). However, we could not replicate these findings with regard to dissociative symptomatology, given that MS patients and healthy controls did not differ in dissociative symptomatology as assessed by the DES. Moreover, dissociative experiences were not associated with functional impairment in MS.

Subjective sleep complaints are common among MS patients; surveys identified a significant minority, ranging from 30.0 to 31.6%, with clinical insomnia (4,6). Almost half of the patients with MS reported poor sleep quality (7). Even though our findings were in line with the literature in that more than half of the MS patients reported poor sleep quality on the PSQI (55.7%), frequency of sleep problems in the patient group did not differ significantly from healthy controls (65.5%). However, considering the components of the PSQI, we observed that MS patients had significantly lower levels of habitual sleep efficiency than control subjects. Additionally, the frequency of poor sleepers among MS patients was not low in our sample, given the relations between sleep and poor prognosis in this group. Despite a considerable variation in the results depending on the assessment methodology, objective measures of sleep disturbance were generally found to be significantly associated with cognitive processing speed and attention among patients with MS (106). The significance of associations between sleep disturbance, fatigue and quality of life has long been established in this group (5,68,73,107-109). In a prospective study of sleep quality in MS, Kotterba et al. (110) found that patients with poor sleep had significantly poorer physical health, greater fatigue, and more severe depression and anxiety. Sleep abnormalities in patients with MS are a multifactorial issue, with circadian

rhythm disorders and increased levels of pro-inflammatory cytokines apparently affecting sleep homeostasis (111). Therefore, sleep-improving practices are proposed to be integrated into the treatment procedures in MS (112).

Poor sleep in MS was found to be significantly associated with greater disability measured by scores on the EDSS (7,113); however, functional impairment related to sleep is not conclusive (114,115). Vitkova et al. (116) suggested that sleep-related disability can be best understood by untangling indirect associations with depression, pain, and physical fatigue. We explored the direct relationship between sleep and disability status but could not find a substantial link between these two variables in our patient group. On the other hand, duration of the ailment and worrisome thoughts were significant predictors of higher scores for disability. These results were consistent with the previous literature: Bruce and Arnett (80) identified significant links of patients' pathological worry with fatigue, sleep disturbances, problem solving deficits, pain, and disability. More specifically, worrisome thoughts about being able to afford health care, which were significantly associated with depression, anxiety, fatigue, sleep disturbance, pain interference, social function, and perceived cognitive functioning, were prominent among MS patients (117). These results show that clinicians should regularly monitor and treat worry in order to obtain more positive treatment outcomes in MS.

This study had certain limitations that should be mentioned. First, our clinical and nonclinical samples were not large, limiting the generalizability of the current data. Second, instead of applying objective measures of sleep such as polysomnography, subjective measures in the form of psychological variables were used. Third, our results should be treated with caution because MS subtypes and treatment modalities were not included and controlled in the statistical analyses. More importantly, neurological and psychiatric comorbidity, which might be accompanied by severe impairment in sleep, was not assessed in the patient group. Fourth, MS patients and healthy controls were not matched in their socio-demographic characteristics (e.g., age, marital status, education, and history of past mental disorders). Further case-control studies with matching demographic features of patients with MS and healthy controls are needed to understand the interplay of sleep, worry, and dissociation in MS more fully. Finally, this study had a cross-sectional design, whereas a longitudinal study could have provided more reliable relationships among variables of interest.

Contribution Categories		Author Initials
Category 1	Concept/Design	A.Y., M.B., V.C.
	Data acquisition	A.Y., M.B., V.C.
	Data analysis/Interpretation	A.Y., M.B., V.C.
Category 2	Drafting manuscript	A.Y., M.B., V.C.
	Critical revision of manuscript	A.Y., M.B., V.C.
Category 3	Final approval and accountability	A.Y., M.B., V.C.
Other	Technical or material support	A.Y., M.B., V.C.
	Supervision	A.Y., M.B., V.C.

Ethics Committee Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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