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

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

Abstract

Objective: The current study was set out to investigate differences between patients with multiple sclerosis (MS) and healthy controls in 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 a hundred and thirty-nine healthy adults participated in the study. The mean age was 30.96 (SD ± 8.88). The Expanded Disability Status Scale (EDSS), 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: 55.7% of MS patients 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 greater scores on pathological worry than patients with MS. Patients with MS and healthy adults did not differ on the DES scores. Duration of the illness and worrisome thoughts were significant antecedents 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: Sleep disturbance, Dissociative experiences, Habitual sleep efficiency, Post-traumatic growth

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 the MS may be diplopia, weakness in muscles, troubles with sensation or motor coordination. The illness may take several forms, including symptoms with isolated attacks or occurring gradually over time (2). Clinical and radiographic evidence is required for the diagnosis of MS according to the McDonald criteria (3). MS is a debilitating disease of central nervous system that, in comparison to general population, patients are at greater risk of sleep disorders (4, 5). In a national survey including 2,375 patients with MS, Brass, Li and Auerbach (6) found that 37.8% of the sample were 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 on the Pittsburgh Sleep Quality Index (PSQI) (7).

Sleep is a crucial part of human existence as well as cognitive and emotional regulation (8-16). Sleep is default to good sleep as a natural state, including both *plasticity*, a term referring to the 'absorb and readjust' capacity of sleep-wake cycle in response to variability in personal and situational factors, and *automaticity*, a term referring to involuntary nature of 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 to internalization that leads to heighted emotional activation and physiological hyper-arousal (19, 20). Morin (21) proposed an integrated conceptualization that cognitive, emotional and physiological arousal which are reciprocally interacting with dysfunctional cognitions,

maladaptive sleep habits, and arousal generating consequences play 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 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 that 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 differentiate, interactions between sleep and dissociative symptomatology seem to be reciprocal. Scholars asserted that dream-like states arising from a labile-sleep-wake cycle intrudes into waking consciousness that produces memory failures and dissociative states (49, 52, 55, 57). Most and foremost, 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 phenomenon (59). Worry is experienced primarily as negative verbal activity in contrast to imaginal content (60, 61) and seems to no longer allow imaginative processing due to excessive thought content (62). Worrying process which is primarily verbal in nature may keep accessibility to parallel-processed images at bay, particularly in cases of catastrophic images in which they become less vivid and intrusive (63-65). In keeping with the assertion of the avoidance hypothesis conjectured by Mowrer (66), Yıldırım, Boysan and Yılmaz (67) identified that dissociative experiences had significant indirect influences on deterioration of sleep quality through exacerbating the worrisome thoughts.

Scholars have widely recognized that sleep problems are hallmark in MS (68-70), which play 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 much as 35.7%, with generalized anxiety disorder (GAD) was 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, Tedman, Rigby, Bashforth and Young (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 levels 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. In this vein, the main aim of this study was to explore whether MS patients differentiate from healthy controls on 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 a hundred and thirty-nine healthy adults from general population participated in the study. The mean age of the clinical and nonclinical subjects was 30.96 (SD ± 8.88). Almost half of the overall sample were female (57.3%) and 51.1 % of the participants were single. 12.0% of clinical and nonclinical individuals reported at least one prior mental disorder and 3.1% reported 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 the Expanded Disability Status Scale (EDSS) score less than 7.0 (81). Exclusion criteria were age less than 18 years or greater than 65 years and cognitive disability that could intervene 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 Ethical Committee of the Van Yüzüncü Yıl University.

Instruments

Expanded Disability Status Scale (EDSS)

The EDSS is a method of quantifying disability in multiple sclerosis through assessing disability in eight functional systems: pyramidal, cerebellar, brainstem, sensory, bowel and

bladder, visual, cerebral, and other. The severity of disability is rated on a scale ranging from 0 to 10, in which higher scores indicate a greater impairment on 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 onto three dimensions: absorption /imaginative involvement, amnesia, and depersonalization / derealization (85). A DES score of 30 and higher 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 a Cronbach's alpha of α=0.91 and test-re-test correlation coefficient of 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, which are rated on 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 Pittsburgh Sleep Quality Index (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, Kara and Anlar (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 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 onto 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, a multiple regression analysis was conducted. In the multiple regression analysis socio-demographic characteristics, pathological worry, dissociation, and sleep quality were independent variables and the EDSS scores was the dependent variable.

RESULTS

Sample characteristics

Using student t-test, we found that patients were older than healthy adults ($t(225) = -4.678$, $p < 0.001$). Majority of the 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). Patient group reported more prior mental health problems than controls (LR (1) = 15.815, p <0.001). Clinical and nonclinical groups did not significantly differ in sex, familial loading of psychiatric disorders and frequency of poor sleep quality (p > 0.05).

Table 1 about here

Multiple logistic regression analysis

Using binary multiple logistic regression analysis, we explored whether MS patients significantly differentiated from healthy controls 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) 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.

Table 2 about here

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 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 ($\beta = -0.27$, $t = -2.118$, $p < 0.05$), was positively associated with the duration of the illness ($\beta = 0.33$, $t = 2.567$, $p < 0.05$) and was positively associated with worrisome thought ($\beta = 0.29$, $t = 2.071$, $p < 0.05$). Findings are presented in Table 3.

Table 3 about here

DISCUSSION

The 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 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 significantly differentiate in dissociative symptomatology. More intriguingly, inpatients with MS reported significantly lower worrisome thoughts as measured by the PSWQ than did healthy controls. Nevertheless, heightened levels of worry was significantly associated with more functional impairment among patients with MS. To the best of our opinion, the current findings relevant to lower levels of pathological worry and unsubstantial dissociative symptomatology among MS patients than healthy controls can be best understood in the conjecture of post-traumatic growth that 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 following by 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.

MS is a demyelinating disease of the central nervous system and a sizable proportion, approximately 40-70%, of MS patients experience cognitive difficulties (101, 102). Perceived planning/organization impairment and perceived retrospective memory impairment were significant antecedents of quality of life (103). Processing speed and working memory training 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 significant correlate of depression, anxiety, and neuroticism (105). However, we could not replicate these findings with regard to dissociative symptomatology that MS patients and healthy controls did not differ in dissociative symptomatology as indexed by the DES. Moreover, dissociative experiences were not associated with functional impairment in MS.

Subjective sleep complaints are common among MS patients that surveys identified a significant minority, ranging from 30.0 to 31.6%, had 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 that more than half of the MS patients reported poor sleep quality on the PSQI (55.7%), frequency of sleep problems among patient group did not differ significantly from heath controls (65.5%). However, considering 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 the considerable variation on 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 significant associations between sleep disturbance, fatigue and quality of life have long been established in this group (5, 68, 73, 107-109). In a prospective study of sleep quality in MS, Kotterba, Neusser, Norenberg, Bussfeld, Glaser, Dorner and Schurks (110) identified 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 that circadian rhythm disorders and increased levels of pro-inflammatory cytokines seem to be 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 as measured by the scores on the EDSS (7, 113); however, functional impairment related to sleep is not conclusive (114, 115). Vitkova, Gdovinova, Rosenberger, Szilasiova, Mikula, Stewart, Groothoff and van Dijk (116) identified that sleep related disability can be best understood through untangling the indirect associations with depression, pain and physical fatigue. We explored direct relationship between sleep and disability status that we could not find a substantial link between these two variables of interest in our patient group. On the other hand, duration of the ailment and worrisome thoughts were significant antecedents of greater scores on disability. These results were consistent with previous literature that Bruce and Arnett (80) identified significant linkages of patient's pathological worry with fatigue, sleep disturbances, problem solving deficits, pain and disability. More specifically, worrisome thoughts about affording 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 suffered certain limitations that must be mentioned. First, our clinical and nonclinical samples were not large enough, limiting the generalizability of the current data. Second, instead of objective measures of sleep such as polysomnography subjective measures of psychological variables were used. Third, our results should be treated with caution because of that 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 among the patient group that our findings should be interpreted with caution. 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 in which the demographic features of patients with MS and healthy controls were matched are needed to more fully understand the interplay of sleep, worry and dissociation in MS. Finally, this study had a cross-sectional design that a longitudinal study could have provided more reliable relationships among variables of interest.

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Ethical 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.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Conflict of Interest: The authors declare no conflict of interest.

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

			Overall sample n = 227		Controls n = 139		Multiple sclerosis patients n = 88			P
Age		Mean, SD	30.96	8.88	28.86	7.99	34.27	9.26	*t* (225) = -4.678	<0.001
Sex	Female	n, %	130	57.27%	73	52.52%	57	64.77%	LR (1) = 3.336	0.068
	Male	n, %	97	42.73%	66	47.48%	31	35.23%		
Marital status	Single	n, %	111	48.90%	84	60.43%	27	30.68%	LR (1) = 19.469	<0.001
	Married	n, %	116	51.10%	55	39.57%	61	69.32%		
Education	No diploma	n, %	13	5.73%	0	.00%	13	14.77%	LR (4) = 94.174	<0.001
	Primary school	n, %	26	11.45%	2	1.44%	24	27.27%		
	Secondary school	n, %	16	7.05%	6	4.32%	10	11.36%		
	High school	n, %	46	20.26%	25	17.99%	21	23.86%		
	University	n, %	126	55.51%	106	76.26%	20	22.73%		
Prior mental disorders		n, %	27	11.95%	7	5.04%	20	22.73%	LR (1) = 15.815	<0.001
Familial loading		n, %	7	3.10%	3	2.16%	4	4.55%	LR (1) = 0.995	0.319
Pittsburgh Sleep Quality Index	PSQI ≥ 5	n, %	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

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

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.