



Research Article

A SCITECHNOL JOURNAL

Sleep Changes in Multiple Sclerosis: from the Individual's Perspective

Lauren B Strober^{1,2*} and Peter A Arnett³

Abstract

Sleep difficulties are common in multiple sclerosis (MS), with prevalence rates ranging from 36% to 62%. Sleep problems have been shown to have a grave impact on individuals in the general population and to contribute to reports of fatigue and reduced quality of life in MS. However, despite these high rates and overall impact, sleep problems in MS frequently go unrecognized. The present investigation sought to examine sleep changes among a sample of 97 individuals with MS and to gain a better appreciation as to what individuals with MS report as contributing to their change in sleep. Approximately 58% of participants complained of changes in their sleep. Among these 56 participants, bladder incontinence, muscle stiffness and leg spasms were most often endorsed as a contributor, with rates ranging from 57% to 63%. When asked about the primary attribution of their sleep change, the majority of individuals (43%) described problems with bladder incontinence. Following this, 17% and 15% reported worry and problems with leg spasms as the primary contributors, respectively. Furthermore, those who rated worry as their primary reason for change in their sleep also endorsed greater symptomatology of depression and anxiety. These findings suggest that sleep difficulties in MS may be a result of many physical and/or psychological symptoms. Proper identification of the etiology of sleep changes in MS is warranted in order to treat these problems and hopefully ameliorate individuals' difficulty with sleep and fatigue.

Keywords

Multiple sclerosis; Sleep disturbance; Fatigue

Introduction

Sleep problems in multiple sclerosis (MS) have seen relatively little study devoted to them until recently, despite contentions dating to the mid-1990's that sleep difficulties in MS would be an important area for future research [1-5]. The majority of investigations of sleep disturbance in MS have, for the most part, been prompted by its relevance to fatigue in MS. Given the known severe impact of fatigue, nearly all studies examining sleep problems in MS have been an attempt to understand its relationship to fatigue and potential mediating effects, with a few exceptions. In particular, a number of studies in the MS literature have focused on sleep disturbance as a significant contributor to fatigue in MS [6-13]. However, as investigations pertaining to sleep problems in MS have emerged,

many have begun to recognize the importance of sleep problems as its own entity and the strikingly high prevalence among MS study samples. In fact, Attarian's 2009 editorial titled, "Importance of sleep in the quality of life of multiple sclerosis patients: a long under-recognized issue" reiterated the contention that sleep disturbance is a significant problem in MS and worthy of further investigation [14]. Fortunately, some investigators have responded to these suggestions and the literature has witnessed an increased interest in sleep disturbance among individuals with MS. In particular, several studies have been published in the past five years that have examined the nature, prevalence, and relationship of sleep disturbance to fatigue and quality of life in MS.

Available research suggests that, compared to healthy controls, a sample of MS participants with mild disability was three times more likely to experience sleep difficulties [15]. Other investigations have found rates ranging from 36% to 62% [16-21] and reports as high as 80% when describing the incidence of obstructive sleep apnea in a clinical sample [22]. Restless leg syndrome (RLS) [20,23], periodic limb movement (PLM) [24], narcolepsy-cataplexy syndrome, rapid eye movement behavior disorder [24], and obstructive sleep apnea [25] have all been reported. Sleep disturbance in MS may have a neurological etiology. For instance, RLS, which has been found to occur in 19% to 37% of MS samples, has been found to be associated with cervical lesions [23,26] and PLM, which was found in 36%, has been shown to be associated with higher lesion load in the infratentorial regions [2] and lesions in the right and left frontal supraventricular white matter, and the deep white matter of the right insula [15]. However, some researchers contend that sleep disturbance in MS may be a result of cascading symptoms such as bladder incontinence, muscle stiffness and spasms, underlying depression [4] and pain [19]. In fact, a review of the literature shows that individuals with MS display more nocturnal awakenings due to such causes as opposed to direct neurological factors such as nocturnal respiratory involvement or circadian rhythm abnormalities [3-5,8,21].

Given the high rate and amenability to treatment of some of these symptoms (e.g., nocturnal spasms), clinical trials aimed at addressing these concerns [27] are likely to increase; thus, proper identification of the nature of sleep difficulty in MS is paramount. Obtaining in depth knowledge concerning an individual's change in sleep is important for treatment and whether intervention is necessary at the physiological or psychological level, or both. The present investigation sought to examine the nature of sleep changes in MS.

Methods

Participants

Multiple sclerosis participants were recruited through an advertisement in a newsletter distributed to individuals in Western Pennsylvania, the local chapter of the Multiple Sclerosis Society and support group meetings, and flyers distributed in the State College, Pennsylvania region. Exclusion criteria included history of alcohol/drug abuse; history or current diagnosis of a neurological disorder besides MS; severe visual or motor impairment that would impede cognitive testing that was conducted for purposes outside the scope of the present investigation; evidence of a premorbid learning disability;

*Corresponding author: Lauren B. Strober, 300 Executive Drive, West Orange NJ 07052, USA, Tel: 973.324.8459; Fax: 973.324.8373; Email: lstrober@kesslerfoundation.org

Received: July 19, 2013 Accepted: November 06, 2013 Published: November 08, 2013

and severe physical or neurological impairment that would have made evaluation impractical.

Procedures

Participants underwent a neuropsychological evaluation as part of an ongoing study examining the contributors to and consequences of depression in MS. The results of the investigation presented here were solely based on the administration of a modified Beck Depression Inventory that was administered during the testing session.

Measures

Modified Beck Depression Inventory (MBDI): The MBDI takes into account research in MS and clinical observations in adding follow-up questions to certain BDI [28] items thought to be confounded with MS symptomatology. These questions are intended to ascertain whether and how much ones' endorsement of particular BDI items is due to MS or depression, per se. Follow up questions were provided on items hypothesized to be related to the experience of MS. Upon endorsement of these items, participants were asked to make attributions regarding the extent to which their physical or cognitive symptoms of MS contributed to their response. For some questions, more specific follow-up questions were asked. The MBDI, like the BDI, consists of 21 items and asks individuals to pick the statement that best describes how they have been feeling for the past week, including the present day. The sleep disturbance item, in particular, asks individuals if their sleep changes are due to their MS. If so, they are subsequently asked to endorse and rank order the greatest contributors from a list provided. This list included physical complaints (bladder incontinence, muscle stiffness, chronic pain, leg spasms), psychological complaints (worrying about your MS or worrying in general), medications, as well as a place to describe other factors not listed. This modified BDI was developed by the present authors and designed to explore attributions individuals make for their endorsements on self-report depression questionnaires.

Expanded Disability Status Scale (EDSS): The EDSS [29] measures disability based on ambulation and neurologic symptoms. Scores range from "0" to "10", with "0" being no impairment or disability and "10" being death due to MS. Scores ranging from 1.0 to 4.5 refer to individuals with MS who are fully ambulatory. Scores between 5.0 and 7.5 are indicative of some impairment in ambulation that requires some aid (cane, walker, wheelchair). Scores above 7.5 indicate that the individual can only be propelled by others in a wheelchair or are essentially restricted to a bed or chair. A self-report measure used in other studies conducted by our lab was administered. Self-report measures have been found to have intraclass correlations comparable to independent ratings made by neurologists [30]. An experienced neuropsychologist with expertise in MS (P.A.) made the EDSS ratings based on the self-report of participants on a questionnaire after receiving instruction from a neurologist specializing in MS.

Depression was assessed by the Chicago Multiscale Depression Inventory (CMDI) [31], a self-report measure that was specifically designed to assess depression in MS and other medically-ill groups. It consists of three subscales: Evaluative, Mood, and Vegetative. Each subscale contains 14 items and patients are asked to rate themselves on a 5-point Likert scale the extent to which each word/phrase describes them during the past week, including today with "1" being "Not at All" and "5" being "Extremely."

Anxiety was assessed by the State Trait Anxiety Inventory (STAI)

[32]. The STAI is a 40-item measure divided into two, 20-item scales to assess both present (state) and longstanding (trait) anxiety. Ratings are based on a 4-point Likert scale. Participants are asked to describe how they feel at the present moment (state) as well as how they generally feel (trait).

Results

All statistical analyses were conducted using SPSS 18.0 computer software. Participants were primarily women (79%) and had a mean age of 47.3 (S.D. 8.9) and mean disease duration of 11.6 (S.D. 8.3). Mean Expanded Disability Status Scale (EDSS) was 4.6 (S.D. 1.6). Frequency analyses were conducted to determine the incidence of sleep changes among the sample and their initial rating (e.g., 0,1,2,3) on the modified BDI. Subsequent frequency analyses were conducted to examine the percentage of individuals who endorsed each attribution and the relevant rankings of their attributions. Fifty six participants (58%) endorsed some degree of change in sleep. The majority (77%) endorsed a ranking of "1", which is described as "I do not sleep as well as I used to." Thirteen (23%) endorsed a score of "2" or "3", which refer to early morning awakening. Of these 56, seven participants (13%) did not endorse any symptoms as contributing to their change in sleep, resulting in a sample of 49 of which endorsements were evaluated. An additional three participants endorsed symptoms as contributing to their sleep changes, but did not supply ratings for their endorsement. The remaining 46 participants supplied ratings to the attributions they made for their present change in sleep (Table 1). As can be seen, bladder incontinence, leg spasms, and muscle stiffness were most often reported as contributing to participants' reports of sleep change, with 57% to 63% endorsing these symptoms.

With regard to what participants rated as their primary reason for changes in sleep, similar findings were found. In particular, approximately 43% reported that bladder incontinence was the primary contributor to their change in sleep and 15% attributed it to leg spasms. Seventeen percent reported that worrying in general was the primary contributor of their change in sleep (Table 2). Muscle stiffness, chronic pain, medication side effects and worrying about ones' MS were less likely to be ranked as the primary reason participants were not sleeping well.

Table 1: Contributing factors to sleep problems in multiple sclerosis.

Contributing Factor	Percentage
Bladder Incontinence	63% (31/49)
Muscle Stiffness	59% (29/49)
Leg Spasms	57% (28/49)
Chronic Pain	45% (22/49)
Worrying in General	43% (21/49)
Medications	24% (12/49)
Worrying about MS	16% (8/49)
Other	10% (5/49)

Table 2: Primary contributor to sleep problems in multiple sclerosis.

Contributing Factor	Percentage
Bladder Incontinence	43% (20/46)
Worrying in General	17% (8/46)
Leg Spasms	15% (7/46)
Muscle Stiffness	7% (3/46)
Chronic Pain	7% (3/46)
Medications	4% (2/46)
Worrying about MS	4% (2/46)
Other	2% (1/46)

To further examine the causes of the participants' attributions and their relationship to other factors, groups were divided based on the primary contributors. More specifically, they were categorized into two groups: "primary worry" (those that endorsed worrying about MS or worrying in general as their number one contributor) and "primary physical" (those that endorsed bladder incontinence, muscle stiffness, leg spasms or chronic pain as their number one contributor). This resulted in a group of 10 "worriers" and 31 "physical" as 3 chose "other" and 2 chose "medications" as their primary contributor. The groups were then compared on disease variables (severity and duration), depression, and anxiety in hopes of illuminating what may contribute to one reporting more physical versus psychological symptoms and vice versa. Individuals who reported worry as their primary contributor were in fact found to be experiencing significantly greater anxiety and depression. There were no differences with regard to disease variables to suggest that those who complained of more physical symptoms had a greater level of disease severity (Table 3).

Discussion

The purpose of this investigation was to explore sleep changes in an MS sample and more importantly, to explore the attributions individuals with MS make with regard to their change in sleep. Similar to recent reports, the frequency of sleep problems in our sample was approximately 58%. Participants were most likely to endorse bladder incontinence, muscle stiffness, and leg spasms as contributors to their change in sleep. Participants also endorsed chronic pain and worry at relatively high rates (43% to 45%). Medication side effects and worrying about ones' MS were less likely contributors, 24% and 16%, respectively. When given the opportunity to rank order their contributing symptoms, the majority of individuals with MS reported that bladder incontinence was the greatest culprit of their change in sleep. This is not surprising given the rate of bladder incontinence is upwards of 70% to 80% in MS [33] and is consistent with previous findings that have found nocturia to be a significant cause of disturbed sleep in MS. Nocturnal spasms have also been reported to be a primary cause of sleep complaints in MS [27] and findings of the present investigation confirmed this, with 59% describing leg spasms as a problem and 15% reporting leg spasms as the primary contributor. Pain, which has previously been shown to be a contributing factor to poor sleep in MS was also frequently reported as a contributor (45%), but not often found to be a primary contributor (7%) in this sample.

Given that such symptoms can be treated, proper identification and subsequent effective interventions are likely to result in a decrease in sleep complaints among individuals with MS. Moreover, given that sleep disturbance has been shown to be a significant predictor of fatigue [9] and that pain and depression are linked to fatigue [34],

effective treatment of these symptoms may have both direct and indirect effects on ameliorating fatigue in MS.

Beyond these physical complaints, a relatively large proportion (43%) of participants also reported that general worry contributed to their poor sleep. Twenty-one percent reported worrying about their MS or worrying in general as their primary reason. When further examined, these individuals were found to report greater symptomatology of depression and anxiety than those who reported primarily physical symptoms as contributing to their sleep difficulties. Given the high prevalence of depression and anxiety in MS, these findings further suggest that close attention be given to reports of psychological symptoms (e.g., worry, anhedonia) in MS and that consideration be given to the multifaceted effects such symptoms are likely to have on individuals' overall physical and mental functioning. Moreover, the high rates of both physical and psychological symptoms as contributors to poor sleep further underscores the importance of thorough interviews and clinical assessment when assessing individuals with MS. It has been strongly recommended in the past that all individuals complaining of fatigue be questioned about their sleep patterns (as well as pain and mood) in order to better inform treatment (e.g., treating nocturnal spasms or nocturia or addressing concomitant depressive disorder) [35]. Present findings provide support for such intervention. Lastly, effective treatment of sleep problems has been shown to result in reduced depression [36] and should be considered and assessed as an outcome associated with improved sleep as much as fatigue is studied.

Although our study expands our understanding of sleep changes in MS, it had limitations. For one, we used a single item on a self-report measure of sleep complaints, particularly the use of one item on the modified BDI. Given the use of self-report as opposed to a clinical interview, this also resulted in a small percentage of individuals not responding to the follow-up item in which they were asked to endorse what most contributed to their sleep difficulty. However, this approach was novel and provided meaningful information with regard to individuals' attributions on a self-report depression measure for the majority of the sample. Further studies are warranted in which objective sleep measures are used to develop a better appreciation for the problems commonly seen in MS. Additionally, given that certain endorsed symptoms such as leg spasms may be a result of a diagnosable sleep disorder such as PLS, greater attention to specific diagnostic criteria is warranted. Finally, further studies encompassing a larger sample size are warranted to better determine the incidence of sleep complaints and their etiology in MS. Related to this, given that this study was part of a larger investigation examining depression and cognitive functioning in MS, individuals were excluded who had severe physical or neurological impairment. Thus, findings

Table 3: Comparisons of primarily physical group and primarily psychological group on disease variables, depression, and anxiety.

	Primary Worry Mean (SD)	Primary Physical Mean (SD)	t-test, sig.
EDSS	4.9 (1.3)	4.9 (1.3)	t = .042, ns
Disease Duration	11.9 (10.8)	12.6 (8.0)	t = .235, ns
BDI-II	18.5 (6.9)	13.0 (7.1)	t = -2.15, p = .038
CMDI Mood	29.4 (12.2)	22.2 (8.8)	t = -2.04, p = .048
CMDI Evaluative	24.5 (13.0)	19.1 (7.5)	t = -1.65, ns
CMDI Vegetative	38.2 (7.4)	38.5 (9.9)	t = .074, ns
STAI State	34.0 (9.5)	34.1 (9.1)	t = .039, ns
STAI Trait	48.4 (8.6)	39.6 (9.6)	t = -2.57, p = .014

Note. EDSS = Expanded Disability Status Scale; BDI-II = Beck Depression Inventory-Second Edition; CMDI = Chicago Multiscale Depression Inventory; STAI = State Trait Anxiety Inventory

may not be most generalizable to the entire MS population given this exclusion. Further studies with a broader range of neurological impairment and disease severity are warranted to examine the host of sleep problems endured across varying levels of impairment and disease involvement.

Despite its limitations, the present study expands our understanding of sleep changes in MS. In particular, findings confirm that sleep problems in MS are commonly attributed to nocturia, muscle stiffness, leg spasms, and pain; with nocturia being the greatest culprit. However, there were also a high number of individuals in our study who reported worry as a primary cause. These individuals were found to, in fact, report more depressive symptoms. This suggests that simply asking generally about one's sleep is not sufficient. Obtaining more specific information as to the direct perceived cause is likely to result in better assessment and treatment of the problem. Given the increased awareness of sleep problems in MS and their impact, it is expected that more research will be conducted aimed at assessing and treating sleep disturbances in MS. Such research should improve our understanding of the impact of MS on this most basic function, and also provide important suggestions for treatment that will likely improve quality of life of individuals with MS.

References

- Devins GM, Edworthy SM, Paul LC, Mandin H, Seland TP, et al. (1993) Restless sleep, illness intrusiveness, and depressive symptoms in three chronic illness conditions: rheumatoid arthritis, end-stage renal failure, and multiple sclerosis. *J Psychosom Res* 37:163-170.
- Ferini-Strambi L, Filippi M, Martinelli V, Oldani A, Rovaris M, et al. (1994) Nocturnal sleep study in multiple sclerosis: correlations with clinical and brain magnetic resonance imaging findings. *J Neurol Sci* 125: 194-197.
- Leo G J, Rao SM, Bernardin L (1991) Sleep disturbance in multiple sclerosis (abstract). *Neurology* 41:320.
- Saunders J, Whitman R, Schaumann B (1991) Sleep disturbance, fatigue, and depression in multiple sclerosis (abstract). *Neurology* 41:320.
- Taphoorn MJ, van Someren E, Snoek FJ, Strijers RL, Swaab DF, et al. (1993) Fatigue, sleep disturbances and circadian rhythm in multiple sclerosis. *J Neurol* 240: 446-448.
- Attarian HP, Brown KM, Duntley SP, Carter JD, Cross AH (2004) The relationship of sleep disturbances and fatigue in multiple sclerosis. *Arch Neurol* 61: 525-528.
- Kaynak H, Altintas A, Kaynak D, Uyanik O, Saip S, et al. (2006) Fatigue and sleep disturbance in multiple sclerosis. *Eur J Neurol* 13: 1333-1339.
- Stanton BR, Barnes F, Silber E (2006) Sleep and fatigue in multiple sclerosis. *Mult Scler* 12: 481-486.
- Strober LB, Arnett PA (2005) An examination of four models predicting fatigue in multiple sclerosis. *Arch Clin Neuropsychol* 20: 631-646.
- Veauthier C, Gaede G, Radbruch H, Gottschalk S, Wernecke KD, et al. (2013) Treatment of sleep disorders may improve fatigue in multiple sclerosis. *Clin Neurol Neurosurg* 115: 1826-1830.
- Côté I, Trojan DA, Kaminska M, Cardoso M, Benedetti A, et al. (2013) Impact of sleep disorder treatment on fatigue in multiple sclerosis. *Mult Scler* 19: 480-489.
- Kaminska M, Kimoff RJ, Benedetti A, Robinson A, Bar-Or A, et al. (2012) Obstructive sleep apnea is associated with fatigue in multiple sclerosis. *Mult Scler* 18: 1159-1169.
- Veauthier C, Radbruch H, Gaede G, Pfueller CF, Dörr J, et al. (2011) Fatigue in multiple sclerosis is closely related to sleep disorders: a polysomnographic cross-sectional study. *Mult Scler* 17: 613-622.
- Attarian H (2009) Importance of sleep in the quality of life of multiple sclerosis patients: a long under-recognized issue. *Sleep Med* 10: 7-8.
- Clark CM, Fleming JA, Li D, Oger J, Klonoff H, et al. (1992) Sleep disturbance, depression, and lesion site in patients with multiple sclerosis. *Arch Neurol* 49: 641-643.
- Alarcia R, Ara JR, Martín J, López A, Bestué M, et al. (2004) [Sleep disorders in multiple sclerosis]. *Neurologia* 19: 704-709.
- Bamer AM, Johnson KL, Kraft GH, Amtmann D (2007) Sleep problems in multiple sclerosis: assessing prevalence and the association with depression. *Mult Scler* 13:7-273.
- Lobentanz IS, Asenbaum S, Vass K, Sauter C, Klösch G, et al. (2004) Factors influencing quality of life in multiple sclerosis patients: disability, depressive mood, fatigue and sleep quality. *Acta Neurol Scand* 110: 6-13.
- Merlino G, Fratticci L, Lenchig C, Valente M, Cargnelutti D, et al. (2009) Prevalence of 'poor sleep' among patients with multiple sclerosis: an independent predictor of mental and physical status. *Sleep Med* 10: 26-34.
- Moreira NC, Damasceno RS, Medeiros CA, Bruin PF, Teixeira CA, et al. (2008) Restless leg syndrome, sleep quality and fatigue in multiple sclerosis patients. *Braz J Med Biol Res* 41: 932-937.
- Tachibana N, Howard RS, Hirsch NP, Miller DH, Moseley IF, et al. (1994) Sleep problems in multiple sclerosis. *Eur Neurol* 34: 320-323.
- Braley TJ, Chervin RD, Segal BM (2012) Fatigue, tiredness, lack of energy, and sleepiness in multiple sclerosis patients referred for clinical polysomnography. *Mult Scler Int* 2012: 673936.
- Manconi M, Rocca MA, Ferini-Strambi L, Tortorella P, Agosta F, et al. (2008) Restless legs syndrome is a common finding in multiple sclerosis and correlates with cervical cord damage. *Mult Scler* 14: 86-93.
- Italian REMS Study Group, Manconi M, Ferini-Strambi L, Filippi M, Bonanni E, et al. (2008) Multicenter case-control study on restless legs syndrome in multiple sclerosis: the REMS study. *Sleep* 31: 944-952.
- Fleming WE, Pollak CP (2005) Sleep disorders in multiple sclerosis. *Semin Neurol* 25: 64-68.
- Kaminska M, Kimoff RJ, Benedetti A, Robinson A, Bar-Or A, et al. (2012) Obstructive sleep apnea is associated with fatigue in multiple sclerosis. *Mult Scler* 18: 1159-1169.
- Solaro C, Uccelli MM, Guglieri P, Uccelli A, Mancardi GL (2000) Gabapentin is effective in treating nocturnal painful spasms in multiple sclerosis. *Mult Scler* 6: 192-193.
- Beck AT, Steer RA (1987) BDI: Beck depression inventory manual. Psychological Corporation. New York.
- Kurtzke JF (1983) Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 33: 1444-1452.
- Solari A, Amato MP, Bergamaschi R, Logroscino G, Citterio A, et al. (1993) Accuracy of self-assessment of the minimal record of disability in patients with multiple sclerosis. *Acta Neurol Scand* 87: 43-46.
- Nyenhuis DL, Luchetta T, Yamamoto C, Terrien A, Bernardin L, et al. (1998) The development, standardization, and initial validation of the Chicago Multiscale Depression Inventory. *J Pers Assess* 70: 386-401.
- Spielberger CD, Gorsuch RL (1983) Manual for the State-trait anxiety inventory (form Y) ("self-evaluation questionnaire"). Consulting Psychologists Press: Palo Alto, CA.
- Amarenco G, Kerdran J, Denys P (1995) [Bladder and sphincter disorders in multiple sclerosis. Clinical, urodynamic and neurophysiological study of 225 cases]. *Rev Neurol (Paris)* 151: 722-730.
- Patrick E, Christodoulou C, Krupp LB; New York State MS Consortium (2009) Longitudinal correlates of fatigue in multiple sclerosis. *Mult Scler* 15: 258-261.
- Krupp LB (2003) Fatigue in multiple sclerosis: definition, pathophysiology and treatment. *CNS Drugs* 17: 225-234.
- Schwartz DJ, Karatinos G (2007) For individuals with obstructive sleep apnea, institution of CPAP therapy is associated with an amelioration of symptoms of depression which is sustained long term. *J Clin Sleep Med* 3: 631-635.

Author Affiliations

Top

¹Kessler Foundation Research Center, West Orange, NJ, USA

²Department of Physical Medicine and Rehabilitation, New Jersey Medical School, the State University of New Jersey, NJ, USA

³Department of Psychology, The Pennsylvania State University, University Park, PA, USA