Contents lists available at ScienceDirect



Neurology, Psychiatry and Brain Research

journal homepage: www.elsevier.com/locate/npbr

## Peculiarities of sleep problems in multiple sclerosis

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#### ARTICLE INFO

Article history: Received 1 March 2015 Received in revised form 6 September 2015 Accepted 11 September 2015 Available online 28 September 2015

Keywords: Sleep problems Bladder/sexual dysfunction Pain Multiple sclerosis Depression Anxiety

#### ABSTRACT

*Background and objective:* Recent research indicates that sleep problems are common in persons with relapsing-remitting multiple sclerosis (RRMS), however, the relation between sleep problems and socio-demographic and clinical characteristics of patients with RRMS has not yet been investigated systematically. The objective of our study was to investigate the relations between sleep problems and social and clinical peculiarities in RRMS patients.

*Material and methods:* 18–74 years old individuals with RRMS (N = 101) involved in an ongoing self-report survey study were asked to complete the Medical Outcomes Study Sleep (MOSS) Scale, Fatigue Severity Scale (FSS), Numerical Rating Scale (NRS) for pain, Visual Analoque Scale (VAS) for bladder/sexual dysfunction, and Hospital Anxiety and Depression scale. Multiple regression was used to evaluate relations between sleep problems and socio-demographic and clinical characteristics of study participants.

*Results*: The mean sleep problems score on the MOSS scale was 39.22 and 54.5% of the sample had sleep problems. In a regression model variables statistically significantly related with sleep problems included female sex, older age, higher level of disability, fatique, pain, bladder/sexual dysfunction, depression and anxiety.

*Conclusion:* The sleep problems were highly prevalent in RRMS patients and related with some of the socio-demographic and clinical characteristics.

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#### 1. Introduction

Individuals with multiple sclerosis (MS), a chronic disease of the central nervous system, are at risk of increased co-morbidity associated with sleep problems. Current studies suggest that persons with MS may have significantly more sleep problems than the general population, though prevalence estimates range from 25 to 54% (Neau et al., 2012; Pokryszko-Dragan et al., 2013; Leonavicius & Adomaitiene, 2014). The relations between sleep problems and fatigue, pain, bladder/sexual dysfunction, depression, anxiety, as well as other socio-demographic and clinical characteristics in patients with MS has not yet been investigated systematically. To our knowledge, this is the first study that has examined these conditions in Latvian MS patients. The objective of this study is to determine the prevalence of sleep problems in individuals with relapsing-remitting (RR) MS and its relationship with socio-demographic and clinical characteristics.

#### 2. Material and methods

A total of 101 RRMS outpatients were consecutively recruited, including outpatients attending the Latvian Maritime Medicine Center between January 2012 and January 2013. The local Bioethical Committee approved the study protocol and all patients who agreed to participate gave informed consent. For inclusion, subjects had to be from 18 to 74 years old, diagnosed with definite MS according to McDonald's criteria (McDonald et al., 2001), a RR course of the disease, a stable clinical condition for at least one month, and having an Expanded Disability Status Scale (EDSS) score of between 0 and 7. Exclusion criteria were severe medical comorbidities (decompensated cardiopulmonary disease, cancer, decompensated renal failure, etc.), drug and alcohol abuse, pregnancy, difficult mental conditions, and nursing.

The following socio-demographic and clinical data were collected: gender, age, residence, education level, marital status, professional activity, duration of RRMS, EDSS score assigned by a blinded clinical neurologist (Kurtzke, 1983), disease-modifying therapy (IFN beta or glatiramer acetate), sleep problems, fatigue, pain, bladder/sexual dysfunction, and symptoms of depression and anxiety.

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Sleep problems were measured using the 12-item Medical Outcomes Study Sleep (MOSS) scale (Hays & Stewart, 1992), which scored to yield six different sleep subscales and an overall sleep problems index (Sleep Problems Index II). Subscales were standardized to yield scores from 0 to 100, with higher scores on the Sleep Problems Index II and sleep disturbance subscales indicating more sleep problems or more sleep disturbances. The MOSS scale has been validated in large samples and a comparison of this sample with normative scores was completed previously by Bamer, Johnson, Amtmann and Kraft (2008). A single indicator of mild, moderate, or severe sleep problems was calculated from item 12 of the MOSS scale based on the recommendations of Manocchia, Keller and Ware, (2001). The sum of these scores was calculated as a total result (named sleep problems present/absent) and used in the further analysis.

Fatigue was assessed using the Fatigue Severity Scale (FSS). As recommended, we used a score of 4 or more in the FSS as a cut-off for the presence of fatigue (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989).

Participants rated their average pain intensity during the past week on a 0–10 numerical rating scale (NRS), with 0 indicating "no pain" and 10 indicating "pain as bad as it could be". A large body of research supports the reliability and validity of the NRS for assessing pain intensity (Jensen & Karoly, 2011). NRS is commonly used in pain research in persons with MS. Moreover, 0–10 NRS have demonstrated their validity as measures of pain intensity in persons with MS through their significant and positive associations with measures of pain interference and pain-related disability. Zero to ten NRS has also demonstrated validity via its responsivity to pain treatments in persons with MS (Alschuler, Jensen, & Ehde, 2012; Leonavicius & Kalnina, 2015). Coding of prevalence of pain for further analysis was dichotomous—it was coded as present or absent.

To assess bladder/sexual dysfunction, participants were asked a single yes or no question, "do you have bladder or sexual dysfunction". For purposes of the regression, individuals who answered positively (yes) were considered as having bladder/ sexual dysfunction. Level of bladder/sexual dysfunction was measured using the Visual Analogue Scale (VAS)—a self-reported scale, where "0" indicates "no bladder/sexual dysfunction" and "10" indicates "severe bladder/sexual dysfunction" for the past seven days.

The presence or absence of depression and anxiety symptoms was assessed using the Hospital Anxiety and Depression Scale (HADS)—a self-assessment screening questionnaire for anxiety and

#### Table 1

Study participant characteristics (n = 101).

depression. The patients were asked to choose one answer from the four given per question. The questions relating to anxiety, marked "A" (7 questions), and to depression, marked "D" (7 questions), were given alternately. The separate scores (from 0 to 3) for each question in "A" and "D" were added together to obtain two results: for anxiety and depression. A total score of 0–7 indicates no abnormality, 8–10 is borderline, and 11 and above suggests anxiety or depression (Zigmond & Snaith, 1983; Leonavicius, Adomaitiene, & Leskauskas, 2011; Leonavicius and Adomaitiene, 2012 Leonavicius & Adomaitiene, 2012). In complying with the literature we used the cut-point of >10 to define prevalent anxiety or depression (Suh, Motl, & Mohr, 2010; Knippenberg, Bol, Damoiseaux, Hupperts, & Smolders, 2011; Leonavicius & Adomaitiene, 2013).

#### 2.1. All data was analysed using SPSS software version 18.0.

Continuous variables, compared by means of independent sample *t* test or ANOVA tests and Fisher's exact test, were used to compare categorical variables. A correlation coefficient (Pearson or Spearman) was applied to assess the relationship between variables. According to analysis, partial correlations were performed, *p* value <0.05 was considered as significant. Multiple linear regression modelling was completed to identify factors associated with sleep problems in this sample.

#### 3. Results

The large majority of participants were female (73.3%). The mean age of participants (N = 101) was 53.7 years and most were urban residents (76.2%), educated >12 years (63.4%), married or living with a partner (59.4%), and professionally inactive (77.2%). Additional sample clinical characteristics can be found in Table 1.

Mild, moderate and severe sleep problems were indicated by 54.5% of the study participants.

When using the MOSS single indicator of sleep problems, as defined by Manocchia et al. (2001), 9.9% of the MS population had mild sleep problems, 14.9% moderate, and 29.7% severe sleep problems.

The overall prevalence of fatigue assessed within the past month was 56.4% on FSS ( $\geq$ 36), which indicated severe fatigue or the need for further evaluation. Pain symptoms were experienced by 60.4% of participants, with mean current pain of 4.5 on the NRS (0–10), which is moderate pain intensity in persons with RRMS (Osborne, Jensen, Ehde, Hanley, & Kraft, 2007). Almost two thirds

Variable	Mean $\pm$ SD, range, or N (%)
Gender, female	74 (73.3%)
Age, years	$53.7 \pm 13.9,  18{-}74$
Residence, urban	77 (76.2%)
Education (>12 years)	64 (63.4%)
Marital status (living with a partner)	60 (59.4%)
Professional activity (active)	23 (22.8%)
Disease duration, years	$13.6 \pm 9.7, 0.5 - 27.5$
EDSS	$3.7\pm2.2,0.5-6.5$
Disease-modifying therapy	79 (78.2%)
Sleep problems (MOSS Sleep Problems index II)	$36.9\pm22.2$
Sleep disturbance (MOSS Sleep Disturbance subscale)	$34.7\pm26.8$
FSS global score	$5.18 \pm 2.44$
Pain	$4.5 \pm 3.1$
Bladder/sexual dysfunction	$6.6\pm2.2$
HADS-D	$7.6 \pm 4.8$
HADS-A	$8.5\pm4.6$

Abbreviations: EDSS—Expanded Disability Status Scale; MOSS— Medical Outcomes Study Sleep; FSS— Fatique Severity Scale; HADS-D—Hospital Anxiety and Depression Scale-Depression; HADS-A— Hospital Anxiety and Depression Scale-Anxiety; SD—Standard Deviation; N—Number of Participants.

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