Feature article

Prevalence of depression, fatigue, and sleep disturbances in patients with myelopathy: Their relation with functional and neurological recovery

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Objectives: To observe the prevalence of fatigue, depression, and sleep disturbance in patients with myelopathy and their correlation with neurological and functional recovery.
Patients and methods: Study conducted in a university tertiary research hospital with 127 patients with myelopathy (92 males) admitted to neurorehabilitation unit between January 2010 and December 2013. Mean age was 32.71 ± 13.08 years (range 15–65 years), and mean duration of injury was 76.22 ± 82.5 days (range 14–365 days). Functional status and impairments were assessed using Barthel Index and Spinal Cord Independence Measures. Depression, fatigue, and sleep disturbances were assessed using Hospital Anxiety and Depression Scale, Fatigue Severity Scale, and Pittsburgh Sleep Quality Index scales, respectively. Neurological recovery was assessed using American Spinal Injury Association's impairment scale.
Results: Forty-four out of 104 (42%) patients had borderline or confirmed depression, 36/108 (33%) had significant fatigue, and 62/106 (58%) had significant sleep disturbances at admission. Significant correlation was observed between change in fatigue and depression scores with change in functional status scores ($P < 0.05$) but no correlation ($P > 0.05$) between change in sleep disturbance scores and functional status score and neurological recovery ($P > 0.05$). Similarly, change in fatigue and depression scores had no correlation with neurological status improvement. Fatigue, depression, and sleep disturbance scores showed significant improvement, that is, admission vs. discharge scores ($P < 0.05$) with significant correlation between improvement in all three variables ($P < 0.05$).
Conclusions: Study variables showed significant improvement in the present study with myelopathy patients but not necessarily correlating with functional and neurological recovery.

Keywords: Myelopathy, Fatigue, Depression, Sleep disturbance, Neurological and functional recovery

Introduction

Depression is a mood disorder characterized by a sense of inadequacy, despondency, decreased activity, pessimism, anhedonia, and sadness where these symptoms severely disrupt and adversely affect the person's life.[1] It is prevalent in about 25% of patients with myelopathy and impairment and disability associated with depression is equal to that attributed to cardiovascular disease, and greater than that caused by other chronic physical disorders such as hypertension, diabetes mellitus, and arthritis.[2,3]

"Fatigue is a total body feeling and experience, encompassing physical, cognitive and emotional dimensions; an odious and unpleasant experience which causes distress; a chronic and unrelenting phenomenon and a subjective experience dependent upon an individual's perceptions."[4] In contrast to 4–9% of the general population, fatigue is present in up to 57% of patients

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with myelopathies and is more common in patients with incomplete injuries.[5]

Patients with myelopathies commonly have excessive daytime sleepiness and disturbed sleep, including reduced rapid eye movement (REM) sleep, increased need for sleep medications, snoring, and sleep-apnea syndrome.[6–8] Sleep disturbances such as sleep disordered breathing or obstructive sleep-apnea syndrome occur in 40–45% of patients.[9]

With increasing survival of myelopathy patients due to better medical and surgical management in the initial stages, prevalence of these conditions is set to increase. Identification and management of secondary complications and comorbidities assume an important role in this scenario. All three conditions—depression, fatigue, and sleep disturbances—can be considered as significant comorbidities affecting patients with myelopathies to a large extent and tend to interfere with the subsequent lifestyle, quality of life, and well-being. Fatigue and depression are among those comorbidities, which are identified as research priorities by people with myelopathy themselves.[10] The objective of this study is to observe the prevalence of these conditions in patients with myelopathies who are admitted to rehabilitation department in various stages (acute, subacute, and chronic) and their correlation with neurological and functional recovery in these patients during hospital stay. We also wanted to observe if any correlation exists between these conditions with each other.

Patients and methods

This prospective descriptive study included patients with myelopathy admitted to neurological rehabilitation department between January 2010 and December 2013 in a tertiary university research hospital in India. Prior approval for the study was taken from the institute's ethics committee. Informed consent was obtained from all the patients to participate in the study. Patients with confirmed myelopathy (who had undergone CT or MRI scan imaging) of traumatic and nontraumatic origin with monophasic insult were included. Patients medically fit to participate in rehabilitation program were included in the study. Patients with multiple sclerosis, having cardiovascular illness, unstable vertebral injuries, requiring ventilatory support were excluded. There were three sources of patient recruitment: (1) patients reporting in outpatient department of neurological rehabilitation department, (2) patients admitted and referred from department of neurology, and (3) patients admitted and referred from the department of neurosurgery. All the patients meeting the inclusion criteria were recruited in the study. Their functional status and impairments were assessed using Barthel Index (BI) and Spinal Cord Independence Measures (SCIM). Depression, fatigue, and sleep disturbances in the patients were assessed using Hospital Anxiety and Depression Scale (HADS), Fatigue Severity Scale (FSS), and Pittsburgh Sleep Quality Index (PSQI) scales, respectively. All scales were used both at admission and discharge. Other details regarding diagnosis, duration of injury, and neurological level of injury (using American Spinal Injury Association (ASIA) impairment scores) were also recorded.

Outcome measures

The BI is a 10-item ordinal scale (range: 0–100) with ratings for feeding, moving from wheelchair to bed and return, grooming, transferring to and from a toilet, bathing, walking on a level surface, going up and down stairs, dressing, and continence of the bowels and bladder. BI has adequate inter-rater agreement, internal consistency, and constructs validity in myelopathy patients.[11]

The SCIM is the only comprehensive ability rating scale that has been designed specifically for patients with spinal cord lesions. The instrument focuses on performing everyday tasks, and captures the economic burden of disability as well as the impact of disability on the patient's overall medical condition and comfort with validity and reliability.[12]

The HADS was developed by Zigmond and Snaith in 1983 to identify "caseness" (possible and probable) of anxiety disorders and depression among patients in nonpsychiatric hospital clinics. It is divided into an anxiety subscale (HADS-A) and a depression subscale (HADS-D), both containing seven intermingled items. Patients scoring up to 7 points are considered to be not having any anxiety or depression, scores between 8 and 10 suggestive of borderline illness whereas scores of 11 or more suggestive of moderate to severe anxiety and depression.[13]

The FSS is a 9-item measure of the severity of fatigue. It requires the participant to choose the degree of agreement on a 7-point ordinal scale ranging from 1 (strongly disagree) to 7 (strongly agree). Scores are calculated by deriving an arithmetic mean. Cutoff scores of over 4 are indicative of significant fatigue. The FSS has acceptable reliability with regard to internal consistency, test–retest reliability, and validity for use in persons with SCI.[14]

The PSQI consists of 19 self-rated questions, which assess a wide variety of factors relating to sleep quality, including estimates of sleep duration and latency and of the frequency and severity of specific sleep-related problems. These 19 items are grouped into 7-component scores, each weighted equally on a 0–3 scale. The 7-component scores are then summed to yield a global PSQI score, which has a range 0–21 with higher scores indicating worse sleep quality. A score of >5 indicates impaired sleep quality.[15]

ASIA impairment scale (AIS) was used to assess the neurological status/recovery in all cases. Patients were assessed by the senior residents in the unit well acquainted and trained in using AIS.

Rehabilitation program

It included medical treatment, management of complications along with physical therapy, occupational therapy, providing orthoses for upper and lower limbs, counseling for psychological issues such as low mood, aggression, coping strategies for nociceptive and neuropathic pain, insomnia, and fatigue. Medications for sleep disturbance were not routine but if other measures such as activity scheduling and progressive muscle relaxation would fail, patients were given medications such as benzodiazepines and zolpidem. Physical therapy consisted of a range of motion exercises, strengthening exercises for limbs and trunk, gait training in the form of conventional gait training, and body weight support treadmill training (as and when indicated), balance assessment and training (Biodex Balance Master), and electrotherapy. Occupational therapy included activity of daily living training, functional ability training, fine motor hand skills training, coordination exercises, sensory, and proprioceptive reeducation. Assistive adaptive devices, barrier-free environment at home and working place, and modification orientation training were provided to the patients. Quadriplegic patients showing distal upper limb and hand recovery were trained with hand robot (Amadeo). Orthotic management included providing patients with limb orthoses. The majority of patients required short lower limb orthoses (ankle foot orthoses). Knee gaiter, wrist cock-up splints, resting splints, and tenodesis splints were also provided to patients for prevention/correction of limb deformities.

Statistical analysis

Data were collected and managed with SPSS version 15 (SPSS Inc., Chicago, IL, USA), and analysis was also done on the same software. Data were tested for normal distribution, and suitable parametric or nonparametric tests were used. For comparison of BI and SCIM at admission and discharge, paired *t*-test was used, and for comparison of nonparametric data such as FSS, PSQI, and HADS, Wilcoxon rank-sum was used. For finding correlation between the change in HADS, FSS, and PSQI scores and functional improvement, Spearman's rho was used. For testing the change between admission and discharge in ASIA scores, McNemar–Bowker test was used and for comparing ASIA improvement and improvement in functional scores and study variables, Mann–Whitney test was used. Statistical significance was considered at P-value < 0.05.

Results

A total of 127 patients meeting the criteria were included in the study. The mean age was 32.71 ± 13.08 years (range 15–65 years). Ninety-two patients were males (72.4%) and 35 were females (27.6%). Patients stayed in the rehabilitation for a mean of 39.91 ± 25.43 days (range 14–130 days). Mean duration of lesion was 76.22 ± 82.5 days (range 14–365 days). Most common neurological level of lesion was lumbosacral seen in 45 patients (35.4%) followed by lower dorsal level (D7–D12 level) in 41 patients (32.3%), cervical level in 23 patients (18.1%), and upper dorsal (D1–D6 level) in 17 patients (13.4%).

Sixty-three patients (49.6%) had traumatic etiology and 64 patients (50.4%) had a variety of nontraumatic myelopathies. Among the nontraumatic myelopathies group, 29 patients had acute transverse myelitis (22.8%), 5 had spinal tuberculosis (3.5%), 13 had primary spinal tumors (10.2%), 7 had ossified posterior longitudinal ligament/ligamentum flavum (5.5%), 8 had prolapsed intervertebral disc (6.3%), and 2 patients had spinal vascular disease (1.6%).

All the patients were assessed within 24–48 hours of admission in the rehabilitation unit by a senior resident in-charge of the respective wards using the outcome measures. Similar outcome measures were used to assess patients within 24 hours of discharge. Changes were noted down in the scores for comparison and analysis later on.

The mean scores for BI, SCIM, HADS, FSS, and PSQI at admission and discharge are given in Table 1. There was a significant difference at admission and discharge for all these variables indicating an improvement in functional status, fall in levels of depression and fatigue, and better sleep quality in these patients' admission vs. discharge. Though the average HADS (depression) score was 6.93 at admission, 44 out of 104 (42%) at admission had scores of 8 or more on the HAD scale indicating borderline or confirmed depression. Similarly, 36 out of 108 (33%) at admission had FSS scores of 4 or more indicating significant fatigue. Poor sleep quality defined as scores higher

Table 1 Mean scores of functional indices and study variables at admission and discharge

	Mean scores (at admission)	Mean scores (at discharge)	P-value
Barthel Index	29.88 ± 18.89	55.45 ± 23.1	<0.001
Spinal Cord Independence Measures	29.27 ± 15.11	53.51 ± 21.42	<0.001
Hospital Anxiety and Depression Scale (depression)	6.87 ± 4.28	4.54 ± 3.72	<0.001
Fatigue Severity Scale	3.12 ± 1.51	2.17 ± 1.22	<0.001
Pittsburgh Sleep Quality Index	6.75 ± 4.5	4.89 ± 3.75	<0.001

Table 2 ASIA scores at admission and discharge

	ASIA at discharge				
	ASIA at admission				
	A	B	C	D	Total
A	47	6	4	1	58 (47.1%)
B	0	10	2	6	18 (14.6%)
C	0	0	20	16	36 (29.2%)
D	0	0	0	11	11 (8.9%)
Total	47 (38.2%)	16 (13%)	26 (21.1%)	34 (27.6%)	123

than 5 was seen in 62 out of 106 patients (58%) at admission.

The ASIA scores at admission and discharge are provided in Table 2. There was a significant change in the ASIA scores at admission and discharge ($P < 0.001$), showing significant neurological recovery during stay in the rehabilitation unit.

Spearman correlation coefficients were calculated to determine the strength of the associations between continuous variables, because the study variables were not normally distributed. (Kolmogorov–Smirnov test).

Correlation between study variables and functional improvement is given in Table 3.

Improvement in fatigue, sleep, and depression scores was compared with each other. We observed significant correlation between fatigue and depression ($P = 0.003$), fatigue, and sleep disturbance ($P = 0.009$). Similarly, significant correlation between sleep disturbance and depression was observed ($P = 0.001$).

We tried to observe the correlation between neurological recovery (ASIA scores) with fatigue, depression, and sleep disturbances statistically. There was no significant correlation between neurological recovery with fatigue ($P = 0.997$), sleep disturbances ($P = 0.694$), and depression ($P = 0.242$).

Table 3 Correlation of change in study variables with functional improvement

	Change in BI	Change in SCIM
Change in FSS	ρ = 0.166 P = 0.085	ρ = 0.283 **P = 0.031**
Change in PSQI	ρ = 0.187 P = 0.055	ρ = 0.247 P = 0.062
Change in HADS (depression)	ρ = 0.221 **P = 0.024**	ρ = 0.290 **P = 0.027**

ρ = Spearman's rho.
* Bold value indicates statistical significance.

Discussion

The results show that there was significant improvement in functional status of patients during the period of inpatient rehabilitation. Improvement in functional status did not correlate significantly with improvement in sleep but correlated with decrease in fatigue and depression. An earlier study in the same setup reported no significant correlation between functional recovery and depression in myelopathy patients.[16] These different observations could be attributed to the fact that the current study has relatively larger sample size and more patients had incomplete injuries. Previous studies have reported prevalence of depression over the first year after myelopathies between 23 and 38%.[17–19] A recent study has reported much higher prevalence of depression (63.9%) within the first 6 months following SCI.[20] Another recent study has reported 15% of patients with SCI of less than 1 year having major depressive disorder.[21] Kennedy and Rogers[22] demonstrated that in the acute phase of injury, depression scores initially decrease followed by an increase at around 18 weeks, which peaks at around 48 weeks and the longer stay of subjects in the hospital setting, the more likely they are to become depressed. In the current study, we did not try to observe the correlation between prevalence of depression and duration of illness and length of stay in hospital as this was not the objective of the study. The same study showed that functional improvement peaked at 1–3 months postadmission in hospital. The authors reported that functional independence was negatively correlated with depression unlike our study. The positive correlation between functional recovery and depression observed in our study could be attributed to the fact that most of these patients had "reactive depression" occurring as a result of myelopathy and ensuing disability. With patients becoming more and more independent for their activities of daily living following rehabilitation, their depression scores improved. Counseling including coping strategies and antidepressant medications (in some patients) would have played some role in improvement in depression.

A large study with 4976 subjects at 1-year post-spinal cord injury reported that functional improvement was negatively correlated to somatic symptoms of depression.[23] One other study with small sample size reported that functional status indicators significantly improved at discharge as did depression scores, but not significantly.[24] A study of 244 people with spinal cord injury revealed that only ASIA D group had higher scores on depression scales,[25] whereas our study showed insignificant correlation between neurological recovery and depression scores.

Fatigue following myelopathies is said to be of two types: (i) physical fatigue that occurs in muscles partially or totally paralyzed below the level of weakness and (ii) chronic fatigue, which is a debilitation condition with physical, psychological, and age-related components.[26] Less exercise, poor diet, intake of pain medications, and alcohol intake are some of the factors reported to be associated with more severe fatigue scores in myelopathy patients.[27] In a study of 41 patients with SCI, Wijesuriya *et al.*[28] found no correlation between fatigue and age, level of injury, and completeness of lesion. Only duration of injury negatively correlated with fatigue scores. Present study also found no correlation between improvement in neurological status and change in fatigue scores, although significant correlation was observed between fatigue and functional abilities. We hypothesize that this correlation could be because of the psychological component as well as improvement in the activity of daily living with various rehabilitation strategies adopted. Depression, pain, effect of medications, poor sleep quality, posture, diet, and effort required to accomplish tasks are factors most consistently associated with fatigue in spinal cord injured patients.[29] Nearly one-third patients in the present study reported significant fatigue (FSS ≥ 4), which is lower as compared with some earlier studies, which have reported fatigue prevalence to be more than 50% in this patient population.[30,31] It has to be mentioned though these studies used different outcome measures for fatigue assessment and prevalence when compared with our study. Jensen *et al.*[32] reported fatigue in more than two-third SCI patients with a healthy sample size. Authors observed that fatigue was negatively correlated with social integration and psychological functioning.

DiPiro *et al.*[33] observed disabling fatigue in 10.3% and moderate to severe depression in 21.2% in a study with 652 myelopathy patients. Disabling fatigue and use of support of other people for ambulation were found to increase the odds of having depression in this group. Lidal *et al.*[34] reported that prevalence of fatigue was 25% among patients who had lived with SCI for more than 20 years. Same study reported direct correlation between high depression scores with high fatigue scores, which is in agreement with our study. Anton *et al.*[35] reported high prevalence of fatigue in ASIA complete and motor-complete myelopathy patients, 1-year post-lesion. They also observed significant correlation between fatigue and depression. Another study with myelopathy patients with a two and a half-year duration of lesion observed significant correlation between fatigue and depression.[36] Interestingly, myelopathy patients indulging in heavy physical activity report lesser fatigue.[37] In other words, individuals who are at a higher level of functioning have lesser fatigue. Same study also reported that individuals who were even mildly active had lesser depression scores. Similar observations have been made in our study. Some other studies have reported fatigue correlates not only with depression but also with pain in individuals with myelopathy.[38,39]

Higher prevalence of poor sleep quality has been demonstrated in myelopathy patients.[40] Sleep disturbances are reported to be due to the injury itself *per se*, decreased melatonin levels after the injury, more common in tetraplegics and incomplete injuries, due to pain and spasm and in patients with bladder incontinence.[41] Difficulty in falling asleep, night-time awakenings, sleep apnea, snoring, daytime sleepiness, and using prescription pills for inducing sleep are all common in this population.[42] Periodic limb movements and restless leg syndrome have also been observed in these patients, particularly ASIA A individuals.[43] Older patients tend to have fewer sleep dysfunctions when compared with younger group and duration of lesion and age at onset are not related with sleep dysfunctions.[44] Patients with sleep disturbance/insomnia (28.2%) and depressive symptoms (25.2%) tend to have disturbing lesion-related neuropathic pain.[45] A study of 100 patients who had completed more than a year after SCI showed that poor sleep quality was present in about 38% of the patients, and there was no correlation between sleep quality and level of injury, which agrees with our data.[46]

We believe that our study is unique in bringing out correlation between improvement in sleep quality, fatigue, and depression scores during in-patient rehabilitation. Our patients significantly improved in all three parameters, and improvement in fatigue scores was significantly correlated with improvement in sleep quality and depression scores. Similarly, improvement in sleep quality scores was significantly correlated to improvement in depression scores in these patients. We hypothesize that there is correlation between all three variables in myelopathy patients, and it is impossible to pin point which variable triggers or exacerbates the other. Strategies including physical and psychosocial rehabilitation are complimentary and contribute to the improvement in depression, fatigue, and sleep disturbances individually and collectively. This study did not assess the effect of improvement in depression or fatigue (with intervention in the form of counseling or pharmacological treatment) on better and positive functional outcome. Further study is recommended to observe this causal relationship between the study variables.

Limitations of the study

The study had relatively smaller sample size considering multiple variables. The study was conducted with heterogeneous group of myelopathy patients in terms of etiopathology and duration of illness.

The data cannot be generalized as it was a single-center study. The study could have been more informative in terms of sociodemographic information such as education, marital, and vocational status of the patients.

Conclusions

High prevalence of fatigue, depression, and sleep disturbance was observed in the myelopathy patients. But these variables showed significant recovery in the present study when admission and discharges scores were compared. All patients showed significant neurological and functional recovery at the time of discharge. Each of these variables was found to be statistically insignificantly correlated with neurological recovery, but improvement in fatigue and depression significantly correlated with functional improvement. Improvement in all three variables significantly correlated with each other.

Disclaimer statements

Contributors All authors/co-authors have contributed to this research and the preparation of the manuscript.

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Conflicts of interest None.

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References

1 Eby GA, Eby KL. Rapid recovery from major depression using magnesium treatment. Med Hypotheses 2006;67(2):362–70.
2 Hoffman JM, Bombardier CH, Graves DE, Kalpakjian CZ, Krause JS. A longitudinal study of depression from 1 to 5 years after spinal cord injury. Arch Phys Med Rehabil 2011;92(3):411–8.
3 Elliott TR, Frank RG. Depression following spinal cord injury. Arch Phys Med Rehabil 1996;77(8):816–23.
4 Ream E, Richardson A. Fatigue: a concept analysis. Int J Nurs Stud 1996;33(5):519–29.
5 Fawkes-Kirby TM, Wheeler MA, Anton HA, Miller WC, Townson AF, Weeks CA. Clinical correlates of fatigue in spinal cord injury. Spinal Cord 2008;46(1):21–5.
6 Scheer FA, Zeitzer JM, Ayas NT, Brown R, Czeisler CA, Shea SA. Reduced sleep efficiency in cervical spinal cord injury; association with abolished night time melatonin secretion. Spinal Cord 2006; 44(2):78–81.
7 NorrbrinkBudh C, Hultling C, Lundeberg T. Quality of sleep in individuals with spinal cord injury: a comparison between patients with and without pain. Spinal Cord 2005;43(2):85–95.
8 Burns SP, Little JW, Hussey JD, Lyman P, Lakshminarayanan S. Sleep apnea syndrome in chronic spinal cord injury: associated factors and treatment. Arch Phys Med Rehabil 2000;81(10): 1334–39.
9 Biering-Sørensen F, Jennum P, Laub M. Sleep disordered breathing following spinal cord injury. Respir Physiol Neurobiol 2009; 169(2):165–70.
10 Hammell KR. Spinal cord injury rehabilitation research: patient priorities, current deficiencies and potential directions. Disabil Rehabil 2010;32(14):1209–18.
11 Furlan JC, Noonan V, Singh A, Fehlings MG. Assessment of disability in patients with acute traumatic spinal cord injury: a systematic review of the literature. J Neurotrauma 2011;28(8): 1413–30.
12 Catz A, Itzkovich M, Tesio L, Biering-Sorensen F, Weeks C, Laramee MT, *et al.* A multicenter international study on the Spinal Cord Independence Measure, version III: Rasch psychometric validation. Spinal Cord 2007;45(4):275–91.
13 Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res 2002;52(2):69–77.
14 Anton HA, Miller WC, Townson AF. Measuring fatigue in persons with spinal cord injury. Arch Phys Med Rehabil 2008; 89(3):538–42.
15 Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28(2):193–213.
16 Gupta A, Deepika S, Taly AB, Srivastava A, Surender V, Thyloth M. Quality of life and psychological problems in patients undergoing neurological rehabilitation. Ann Indian Acad Neurol 2008;11: 225–30.
17 Hancock KM, Craig AR, Dickson HG, Chang E, Martin J. Anxiety and depression over the first year of spinal cord injury: a longitudinal study. Paraplegia 1993;31(6):349–57.
18 Fann JR, Bombardier CH, Richards JS, Tate DG, Wilson CS, Temkin N, PRISMS Investigators. Depression after spinal cord injury: comorbidities, mental health service use, and adequacy of treatment. Arch Phys Med Rehabil 2011;92(3):352–60.
19 Nair KPS, Taly AB, Maheshwarappa BM, Kumar J, Murali T, Rao S. Nontraumatic spinal cord lesions: a prospective study of medical complications during in-patient rehabilitation. Spinal Cord 2005;43:558–64.

20 Shin JC, Goo HR, Yu SJ, Kim DH, Yoon SY. Depression and quality of life in patients with the first 6 months after the spinal cord injury. Ann Rehabil Med 2012;36(1):119–25.
21 Williamson ML, Elliott TR. Major depressive disorder and factorial dimensions among individuals with recent onset spinal cord injury. Rehabil Psychol 2013;58(1):10–7.
22 Kennedy P, Rogers BA. Anxiety and depression after spinal cord injury: a longitudinal analysis. Arch Phys Med Rehabil 2000; 81(7):932–7.
23 Hartoonian N, Hoffman JM, Kalpakjian CZ, Taylor HB, Krause JK, Bombardier CH. Evaluating a spinal cord injury-specific model of depression and quality of life. Arch Phys Med Rehabil 2014;95(3):455–65.
24 Hu X, Zhang X, Gosney JE, Reinhardt JD, Chen S, Jin H, *et al.* Analysis of functional status, quality of life and community integration in earthquake survivors with spinal cord injury at hospital discharge and one-year follow-up in the community. J Rehabil Med 2012;44(3):200–5.
25 Bombardier CH, Fann JR, Tate DG, Richards JS, Wilson CS, Warren AM, *et al.* An exploration of modifiable risk factors for depression after spinal cord injury: which factors should we target? Arch Phys Med Rehabil 2012;93(5):775–81.
26 Barat M, Dehail P, de Seze M. Fatigue after spinal cord injury. Ann Readapt Med Phys 2006;49(6):277–82, 365–9.
27 Saunders LL, Krause JS. Behavioral factors related to fatigue among persons with spinal cord injury. Arch Phys Med Rehabil 2012;93(2):313–8.
28 Wijesuriya N, Tran Y, Middleton J, Craig A. Impact of fatigue on the health-related quality of life in persons with spinal cord injury. Arch Phys Med Rehabil 2012;93(2):319–24.
29 Hammell KW, Miller WC, Forwell SJ, Forman BE, Jacobsen BA. Fatigue and spinal cord injury: a qualitative analysis. Spinal Cord 2009;47(1):44–9.
30 Saunders LL, Krause JS. Behavioral factors related to fatigue among persons with spinal cord injury. Arch Phys Med Rehabil 2012;93(2):313–8.
31 Craig A, Tran Y, Wijesuriya N, Middleton J. Fatigue and tiredness in people with spinal cord injury. J Psychosom Res 2012;73(3):205–10.
32 Jensen MP, Kuehn CM, Amtmann D, Cardenas DD. Symptom burden in persons with spinal cord injury. Arch Phys Med Rehabil 2007;88(5):638–45.
33 DiPiro ND, Saunders LL, Brotherton S, Kraft S, Krause JS. Pain and fatigue as mediators of the relationship between mobility aid usage and depressive symptomatology in ambulatory individuals with SCI. Spinal Cord 2014;52(4):316–21.
34 Lidal IB, Jensen AE, Larsen TW, Stanghelle JK. Fatigue in persons who have lived with spinal cord injury for >20 years. Spinal Cord 2013;51(2):103–8.
35 Anton HA, Miller WC, Townson AF. Measuring fatigue in persons with spinal cord injury. Arch Phys Med Rehabil 2008; 89(3):538–42.
36 Freixes O, Rivas ME, Agrati PE, Bochkezanian V, Waldman SV, Olmos LE. Fatigue level in spinal cord injury AIS D community ambulatory subjects. Spinal Cord 2012;50(6):422–5.
37 Tawashy A, Eng JJ, Lin KH, Tang PF, Hung C. Physical activity is related to lower levels of pain, fatigue and depression in individuals with spinal cord injury: a correlational study. Spinal Cord 2009; 47(4):301–6.
38 Craig A, Tran Y, Siddall P, Wijesuriya N, Lovas J, Bartrop R, *et al.* Developing a model of associations between chronic pain, depressive mood, chronic fatigue, and self-efficacy in people with spinal cord injury. J Pain 2013;14(9):911–20.
39 Alschuler KN, Jensen MP, Sullivan-Singh SJ, Borson S, Smith AE, Molton IR. The association of age, pain, and fatigue with physical functioning and depressive symptoms in persons with spinal cord injury. J Spinal Cord Med 2013;36(5):483–91.
40 Verheggen RJ, Jones H, Nyakayiru J, Thompson A, Groothuis JT, Atkinson G, *et al.* Complete absence of evening melatonin increase in tetraplegics. FASEB J 2012;26(7):3059–64.
41 Giannoccaro MP, Moghadam KK, Pizza F, Boriani S, Maraldi NM, Avoni P, *et al.* Sleep disorders in patients with spinal cord injury. Sleep Med Rev 2013;17(6):399–409.
42 Biering-Sørensen F, Biering-Sørensen M. Sleep disturbances in the spinal cord injured: an epidemiological questionnaire investigation, including a normal population. Spinal Cord 2001;39(10): 505–13.
43 Telles SC, Alves RC, Chadi G. Periodic limb movements during sleep and restless legs syndrome in patients with ASIA A spinal cord injury. J Neurol Sci 2011;303(1–2):119–23.
44 Jensen MP, Hirsh AT, Molton IR, Bamer AM. Sleep problems in individuals with spinal cord injury: frequency and age effects. Rehabil Psychol 2009;54(3):323–31.
45 Mann R, Schaefer C, Sadosky A, Bergstrom F, Baik R, Parsons B, *et al.* Burden of spinal cord injury-related neuropathic pain in the United States: retrospective chart review and cross-sectional survey. Spinal Cord 2013;51(7):564–70.
46 Matin M, Taheri Otaghsara SM, Latifi S, Javidan AN, Koushki D, Abedi F, *et al.* Subjective sleep quality in Iranian patients with spinal cord injury: results of Pittsburgh Sleep Quality Index in a referral center. J Neurol Psychol 2014;2(1):4.