Reviews/Short communication

Fatigue in Progressive Neurological Conditions: A literature Review

Setareh Ghahari
School of Rehabilitation Therapy, Queen's University, Kingston, Canada
University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

Shahriar Parvaneh*
University of Social Welfare and Rehabilitation Sciences, Tehran, Iran
School of Occupational Therapy and Social Work, Curtin University, Perth, Australia

Tanya L. Packer
School of Occupational Therapy, Dalhousie University, Halifax, Canada

This paper reviews the current literature examining the pervasive symptom of fatigue experienced in three of the most common degenerative neurological conditions: multiple sclerosis (MS), Parkinson's disease (PD) and post-polio syndrome (PPS). The existing literature can be considered under four headings; definition and prevalence, type, cause, impact of fatigue. Fatigue is a common symptom in degenerative conditions and has physical, cognitive and psychosocial manifestations. Although the causes of fatigue seem to differ between conditions, its pattern, with few exceptions, is very similar regardless of diagnosis. The literature consistently shows that the impact of fatigue on the person's physical and mental performance considerably increasing the risk of unemployment and reduced quality of life. Fatigue is one of the most disabling symptoms in degenerative neurological conditions. With few pharmacological solutions, non-pharmacological solutions for fatigue management should be considered when determining rehabilitation interventions for this group of people.

Keywords: fatigue, neurological conditions, multiple sclerosis, Parkinson's disease, post-polio syndrome

Submitted: 20 September 2013
Accepted: 10 November 2013

Introduction

Fatigue is a common symptom experienced by virtually everyone at some time during life. It is possibly the most common symptom to be found across all medical conditions (1). Fatigue is a particularly common and debilitating symptom in chronic neurological conditions often with profound impact on the person's day to day life. People with extreme fatigue have lower quality of life, restricted occupational performance and higher rates of unemployment (2-7). Therefore it is important for health care professionals, especially the rehabilitation team, to understand fatigue, its causes, types and how it impacts on persons' lives in order to better serve clients with neurological conditions.

There is a vast amount of research on fatigue in different conditions however studies on progressive neurological conditions report both similarities and differences with respect to prevalence rates, causes, types and impact on life. Hence this paper is a review of the current literature with a focus on multiple sclerosis (MS), Parkinson's disease (PD) and post-polio syndrome (PPS) as three of the most common progressive neurological conditions.

1- Fatigue - Definition, Prevalence and Patterns

Fatigue secondary to chronic conditions is different from fatigue experienced by people without chronic conditions (8,9). Fatigue secondary to chronic conditions is associated with physiological and psychological manifestations which are not relieved by rest, sleep or positioning (10,11). Acute or 'normal' fatigue because of physical or mental efforts can be relieved in these ways (12). In chronic conditions fatigue is defined as "an overwhelming sustained sense of exhaustion and deceased capacity for physical and mental work at usual level" (13 [p.3]).

Between 75 and 95% of individuals with MS report fatigue, with 50 to 60% naming it as their worst or one of their worst symptoms (14-16). Fatigue also occurs in 59-89% of individuals with PPS, which is probably the major and most disabling symptom in this chronic

* All correspondances to Shahriar Parvaneh, Email: <sh_parvaneh@yahoo.com>

condition (17-19). Two national surveys in the US have shown that 91% of polio survivors report post-polio syndrome (PPS), a delayed syndrome characterized by excessive fatigue, with 41% reporting fatigue as significantly interfering with performing or completing tasks, and 25% reporting fatigue as interfering with their activities of daily living (20). People with PD frequently report fatigue as well. A prevalence study by Friedman & Friedman (21) using the modified version of the Fatigue Severity Scale (FSS) showed that 67% of 58 people with PD rated their fatigue as different to the fatigue experiences before the onset of the disease. The people with PD were more fatigued than age-matched controls. More than 50% of participants with PD claimed that fatigue constituted one of the three most disabling symptoms of the disease. The authors followed up 26 of the participants for nine years. The results showed that 50% of the participants still were affected by fatigue, explaining it as one of the most disabling symptoms of their condition (22). In another prevalence study of 245 people with PD, only 43% of the participants were experiencing fatigue; however, the reliability and validity of the fatigue scale used for the study was not discussed (23). When compared to the prevalence of 7-45% in people without chronic conditions, these figures show a very high rate of fatigue in people with chronic conditions (24).

The pattern of fatigue is very similar across these three diagnoses; it can be easily triggered and is not relieved by rest, sleep, or positioning (10,25). It occurs daily, worsens as the day progresses, can last up to 24 hours per day and has a lengthy recovery time (14,23). This pattern can be seen in most neurological conditions including MS, PD and PPS (26-29). The only distinctive feature of fatigue related to MS seems to be heat sensitivity; ninety percent of people with MS report that their fatigue worsens in warmer environmental temperatures (30,31). Although evidence suggests that MS fatigue may pre-date the onset of other symptoms (32,33), qualitative studies of the experience of fatigue report a close relationship between fatigue and exacerbation of other symptoms (34,35) including physical, cognitive, and emotional symptoms.

2- Types of Fatigue

The literature categorises fatigue in different ways; by its origin, cause, and length of time. Fatigue, based on its origin, is categorized as a primary symptom or as secondary symptom in a chronic condition. Primary fatigue may result from centrally mediated processes characterized by the disease, such as demyelination and axonal loss in the central nervous system or immune reactions. Secondary fatigue results from medications or disease-related manifestations. Both primary and secondary types of fatigue may occur simultaneously with each impacting on the other. Fatigue and depression also interact. Depression as a result of primary fatigue may cause decrease in activity level. This lower level of activity may in turn increase secondary fatigability as a result of deconditioning (31). The clinical approach, based on the anatomical cause of fatigue, is to categorize it as either central or peripheral fatigue. Peripheral fatigue is a sense of exhaustion caused by repeated use of muscles. It can be due to disorders in muscle and neuromuscular junction and is frequently observed in neurological diseases such as myasthenia gravis or Guilain-Barre syndrome (36) as well as immunological diseases such as rheumatoid arthritis (25). This objective reduction in motor power is measureable by testing the rate of decline in peak force generated during maximum voluntary muscle contraction. Peripheral fatigue is a distinctive topographic pattern of myopathic weakness. Central or cortical fatigue is characterized by a feeling of constant exhaustion. People with central fatigue have difficulty with initiating or maintaining any voluntary physical or even mental activity (37). This subjective sense of fatigue is essentially perceived at the level of the central nervous system (CNS) (1). Both central and peripheral fatigue occur in PD, MS and PPS (27,38,39). Fatigue can also be categorized as acute fatigue or chronic fatigue based on the length of time with the symptom. Acute fatigue is fatigue that exists for 6 weeks or less and chronic fatigue presents more than 50% of the time for more than 6 weeks (40).

In addition to categories of fatigue, it is often described based on its dimensions: physical and mental (psychological and cognitive) fatigue. Physical fatigue may happen after minimal physical effort and, in neurological conditions, worsens as the day progresses. Mental fatigue is frequently reported in people with MS specifically in the cognitive domains of memory, learning, attention, and information processing (39). While impairments in verbal memory nor enhanced cortical function have not been reported by people with PPS they too report deficits in attention and memory (41). Word-finding difficulty and anomia are examples of task-specific mental fatigue seen in persons with PPS (42). Physical and mental fatigue are also considered to be two independent symptoms in PD (43). Physical effort is reported after physical exertion and mental fatigue is reported after mental effort. Apathy is a characteristic symptom of people with PD (44). Therefore, although there are differences in fatigue dimensions between diagnoses, the overall pattern is similar in neurological conditions.

3- Causes of fatigue

Despite its prevalence and pervasive nature, the cause or causes (etiology and pathology) of fatigue is unclear. Most researchers believe it is a complex interaction between biological, psychological and behavioral processes (25). There are several hypotheses for the origin of fatigue in MS: 1) an increased number and volume of lesions in the white matter 2) diffused axonal damage 3) lesion load and fatigue and 4) progression in brain atrophy (45).

The first two hypotheses have largely been rejected by research. Bakshi et al. assessed fatigue in 71 individuals with MS and categorised them into MS-fatigue and MS-non-fatigue groups. The results of the study did not show significant correlation between fatigue severity and regional or global MRI plaque load or atrophy assessed by conventional sequences. No significant differences were noted in any MRI measures between MS-fatigue and MS non-fatigue groups. (32,46). Another study investigated whether the extent of cerebral grey matter (GM) pathology was associated with the presence and severity of MS-fatigue. Fatigued and non-fatigued participants (14 participants in each group) did not differ in terms of grey matter pathology of the cerebral cortex of the frontal lobe and basal ganglia. The authors concluded that structural grey matter pathology is not a major contributing factor to the development of fatigue in persons with MS.

Evidence supports the third hypothesis: the correlation of lesion load in brain and fatigue. In a mixed method study (47), fatigue was assessed by an interview and scored by the Fatigue Severity Scale (FSS). Two groups of MS participants, those with (n = 15) and those without (n = 15) fatigue, were matched for sex, age, disease duration, and scores on the Expanded Disability Status Scale score, Pyramidal Functional System score, and depression score. A significant association was found between scores on the FSS and the burden of MRI lesions ($r = .5$; $p < .005$). Significantly higher parietal lobe ($p < .05$), internal capsule ($p < .05$), and periventricular trigone ($p < .05$) lesion loads were found in persons with fatigue compared with the group without fatigue. This study also supported the fourth theory of a central nervous system origin of fatigue in people with MS (45). The study showed that in non-disabled non-depressed persons with MS, pathophysiological process of demyelination and axonal loss caused higher fatigue levels (45). A longitudinal study including 134 people with MS suggested that fatigue predicts brain atrophy as opposed to being a consequence of the demyelination process (48).

Several hypotheses have been proposed for cause of fatigue in PD: 1) altered activation of the hypothalamic-pituitary-adrenal system due to prolonged stress; 2) inflammatory processes; and 3) dysfunction in the basal ganglia and striato-thalamo-cortical loop caused by change in neurotransmitters (49). Degeneration of the axon sprouts can explain the new muscle weakness and fatigue in polio survivors, but what causes the degeneration in the first place remains a mystery (50). In PPS, it seems that poliovirus-induced damage to the brain activating system is responsible for decreasing cortical activation, impairing attention and generating the symptoms of post-polio fatigue (51).

While both primary pathological mechanisms and secondary contributory factors are extensively explored, research suggests that the etiology of fatigue is multi-factorial (52) and the nature of fatigue in MS, at least, appears to be more complex than other conditions (52).

4- Impact of Fatigue on Daily Life

There is evidence for reduced levels of activity participation and negative emotional consequences as a result of fatigue in chronic neurological conditions. The impact of fatigue was mostly studied in the 1980-1990s with limited new research since that time. Krupp et al. (53) interviewed 32 people with MS and compared them with 33 healthy adults matched by age and sex. The MS participants suggested that MS fatigue was more severe and had a more disabling impact on activities of daily living than fatigue experienced by the comparison group (53). Their results were consistent with the results from Freal et al.'s (30) study in which 309 individuals with MS were evaluated. Results of this study revealed that fatigue interfered with activities of daily living. Fatigue was worse for 83% after 'vigorous exercise' and for 64% after 'moderate exercise' although 15% reported that moderate exercise helped to reduce fatigue. But another study shows that the fatigue perceived during a physical or cognitive activity does not correlate with an objective reduction of observed performance (54).

Packer, Sauriol and Brouwer (18) used the Fatigue Severity Scale and the Human Activity Profile (HAP) to assess fatigue and activity level in people with and without chronic neurological conditions in comparison with a control group. Their study included 28 people with PPS, 13 people with chronic fatigue syndrome, 9 people with MS and 11 healthy participants. The participants with chronic conditions had significantly higher scores on the FSS and lower scores on the HAP compared to healthy participants. Their results support this hypothesis that higher fatigue may be correlated with decreased activity (or energy) levels. Packer, Foster and Bouwer (55) continued their research evaluating activity patterns of people with and without chronic fatigue syndrome. The results showed significant difference between the percentage of time spent by the two groups with respect to the variable of rests, work and productivity (work and household). The study also found that the participants with chronic fatigue syndrome spent less time on productivity and greater time in rest than the controls.

Similar results are seen in studies on PD. People with PD who experience fatigue report that their fatigue prevents sustained physical activity (56). Fatigue was reported to be negatively correlated with self-report activities of daily living among people with PD with FSS scores greater than 4 (57). Garber and Friedman (58) found a significant inverse relationship between fatigue severity and leisure activity level, the frequency of vigorous physical activity and time spent performing daily tasks in people with PD. The results also showed that fatigue was correlated with more sedentary behaviour, lessened functional capacity for exercise and worse physical conditioning. In contrast, a study on individuals with PD showed that the physical activity level of people with fatigue was not different from those without fatigue when it was measured objectively by waste-worn activity monitor (56).

On the other hand, evidence supports the idea that a higher level of activity can decrease fatigue levels. One study reported that a 4-week aerobic exercise intervention resulted in improvement on quality of life and a tendency toward reduction in fatigue among people with MS (59). Training consisted of 5×30 minute sessions per week of bicycle exercise with individualized intensity. Another, study by Oken et al. (60) also demonstrated similar effects. Participants with MS and Expanded Disability Status Score less than or equal to 6.0 were randomly assigned to one of three groups lasting 6 months: weekly Iyengar yoga classes along with home practice, weekly exercise classes using a stationary bicycle along with home exercise, or a waiting-list control group. The participants in both active groups showed improvement on the Multi-Dimensional Fatigue Inventory, and the Short Form (SF)-36 health-related quality of life scores compared to the control group. This is while a cross-sectional study showed no relationship was between fatigue impact and spiroergometric parameters (61). However these studies only focused on structured activity rather than lifestyle activity.

Morris et al. (62) tested the relationship of observed fatigue and motor performance. It was expected that higher fatigue scores in the afternoon would accompany reduced motor performance as the day progressed. In their study 14 individuals with MS and a similar number of matched controls were compared; no differences in gait pattern were found between morning and afternoon assessment, whereas fatigue scores increased in the afternoon. They concluded that the mechanisms for motor control and the subjective experience of fatigue were dissimilar.

In addition to physical and activity participation limitations as a result of fatigue, emotional consequences are also reported in the literature on fatigue. Flenser, Ek and Soderhamn (63) provided a thorough description of persons' experience of fatigue in a qualitative study. A lowered sense of self-worth, feelings of shame, sorrow, and anger related to the perception of fatigue were experienced by persons with MS.

The debilitating nature of MS fatigue has a known impact on quality of life and health status (3-6,34,64). Fatigue not only limits performance in daily life and at home but also it has a negative impact on work (65). Changes in employment are increasingly associated specifically with the symptom of fatigue (66,67). Fatigue is also reported as a central cause of persons with MS being unable to maintain full-time employment (68). Chaudhuri and Behan (1) reported that people with fatigue may be inactive and overstressed because of not being able to return to the same job. Financial pressure is another outcome of living with extreme fatigue. A study of 113 adults with MS who lived in urban and rural regions of Australia showed that fatigue was the major health variable that predicted cost of MS and its economic pressure (69).

Conclusion

Fatigue is a very common symptom in degenerative neurological conditions with unknown and multifactorial cause(s). The impact of fatigue upon the everyday lives of people with neurological conditions, who already struggle with several other symptoms, constitutes a problem deserving significant attention.

References

1. Chaudhuri A, Behan PO. Fatigue in neurological disorders. The Lancet. 2004; 363(9413):978-989.
2. Amato MP, Ponziani G, Rossi F, Liedl CL, Stefanile C, Rossi L. Quality of life in multiple sclerosis: the impact of depression, fatigue and disability. Multiple Sclerosis 2001;7(5):340-4.
3. Benedict RH, Wahlig E, Bakshi R, Fishman I, Munschauer F, Zivadinov R, et al. Predicting quality of life in multiple sclerosis: accounting for physical disability, fatigue, cognition, mood disorder, personality, and behavior change. J Neurol Sci 2005;15;231(1-2):29-34.
4. Di Fabio RP, Choi T, Soderberg J, Hansen CR. Health-related quality of life for patients with progressive multiple sclerosis: influence of rehabilitation. Phys Ther 1997;77(12):1704-16.
5. Lobentanz IS, Asenbaum S, Vass K, Sauter C, Klosch G, Kollegger H, et al. Factors influencing quality of life in multiple sclerosis patients: disability, depressive mood, fatigue and sleep quality. Acta Neurol Scand 2004;110(1):6-13.
6. Pittion-Vouyovitch S, Debouveriea M, Guilleminb F, Vandenberghea N, Anxionnatc R, Vespignania H. Fatigue in multiple sclerosis is related to disability, depression and quality of life. J Neurol Sci 2006; 243(1-2):39-45.
7. Stuifbergen AK, Rogers S. The experience of fatigue and strategies of self-care among persons with multiple sclerosis. Applied Nursing Research 1997; 10(1):2-10.
8. Aaronson LS, Teel CS, Cassmeyer V, Neuberger GB, Pallikkathayil L, Pierce J, et al. Defining and measuring fatigue. Image--the journal of nursing scholarship 1999;31(1):45-50.
9. Hammell KW, Miller WC, Forwell SJ, Forman BE, Jacobsen BA. Fatigue and spinal cord injury: a qualitative analysis. Spinal Cord 2009; 47(1):44-49.
10. Dittner A, Wessely S, Brown R. The assessment of fatigue: A practical guide for clinicians and researchers. J Psychosom Res 2004; 56(2):157-170.
11. 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):21-25.
12. Ream E, Richardson A. Fatigue: A concept analysis. International journal of nursing studies 1996;33(5):519-29.
13. North American Nursing Diagnosis Association. NANDA nursing diagnosis: Definitions and classification 2001-2002.
14. Fisk JD, Pontefract A, Ritvo PG, Archibald CJ, Murray TJ. The impact of fatigue on patients with multiple sclerosis. Canadian Journal of Neurological Science 1994;21(1):9-14.
15. Kraft GH, Freal JE, Coryell J. Disability, disease duration and rehabilitation service needs in multiple sclerosis: Patient perspectives. Arch Phys Med Rehabil 1986;67:164-168.
16. Krupp LB, LaRocca NG, Muir J, Steinberg AD. A study of fatigue in systemic lupus erythematosus. J Rheumatol 1990;17(11):1450-2.
17. Berlly MH, Strauser WW, Hall KM. Fatigue in postpolio syndrome. Archives of physical medicine and rehabilitation 1991;72(2):115-8.
18. Packer TL, Sauriol A, Brouwer B. Fatigue secondary to chronic illness: Postpolio syndrome, chronic fatigue syndrome, and multiple sclerosis. Arch Phys Med Rehabil 1994;75(10):1122-6.
19. Schanke A, Stanghelle J, Andersson S, Opheim A, V S, Solbakk A. Mild versus severe fatigue in polio survivors: Special characteristics. J Rehabil Med 2002;34(3):134-140.
20. Parsons P. Data on polio survivors from the National Health Interview Survey, 1989.
21. Friedman EH. Fatigue in multiple sclerosis. Can J Neurol Sci 1995;22(1):75.
22. Friedman JH, Friedman HH. Fatigue in Parkinson's disease: A nine-year follow-up. Movement Disorders 2001;16(6):1120-2.
23. Karlsen K, Larsen JP, Tandberg E, Jørgensen K. Fatigue in patients with Parkinson's disease. Movement Disorders 1999;14(2):237-41.
24. Lewis G, Wessely S. The epidemiology of fatigue: more questions than answers. Journal of epidemiology and community health 1992;46(2):92-7.
25. Swain M. Fatigue in chronic disease. Clin Sci 2000;99(1):1-8.
26. Bruno RL, Creange SJ, Frick NM. Parallels between post-polio fatigue and chronic fatigue syndrome: a common pathophysiology? Am J Med 1998;105(3, Supplement 1):66-73.
27. Friedman JH, Friedman HH. Fatigue in Parkinson's disease. Neurology 1993;43(10):2016-2018.
28. Abe K, Takanashi M, Yanagihara T. Fatigue in patients with Parkinson's disease. Behavioural Neurology 2000;12(3):103-106.
29. Packer TL, Martins I, Krefting L, Brouwer B. Activity and post-polio fatigue. Orthopedics 1991;14(11):1223-6.
30. Freal JE, Kraft GH, Coryell JK. Symptomatic fatigue in multiple sclerosis. Arch Phys Med Rehabil 1984;65(3):135-138.
31. Kos D, Kerckhofs E, Nagels G, D'Hooghe MB, Ilsbroukx S. Origin of fatigue in multiple sclerosis: review of the literature. Neurorehabilitation and neural repair 2008;22(1):91-100.
32. Bakshi R, Miletich RS, Henschel K, Shaikh ZA, Janardhan V, Wasay M, et al. Fatigue in multiple sclerosis: Cross-sectional correlation with brain MRI findings in 71 patients. Neurology 1999; 22;53(5):1151-3.
33. Bakshi R. Fatigue associated with multiple sclerosis: diagnosis, impact and management. Multiple Sclerosis 2003;9(3):219-27.
34. Stuifbergen AK. Physical activity and perceived health status in persons with multiple sclerosis. J Neurosci Nurs 1997;29(4):238-243.
35. Yorkston K, Klasner E, Swanson K. Communication in context: A qualitative study of the experiences in individuals with multiple sclerosis. American Journal of Speech-Language Pathology 2001;10(2):126-137.
36. Merkies IS, Schmitz PI, Samijn JP, van der Meche FG, van Doorn PA. Fatigue in immune-mediated polyneuropathies. European Inflammatory Neuropathy Cause and Treatment (INCAT) Group. Neurology 1999;10;53(8):1648-54.
37. Chaudhuri A, Behan PO. Fatigue and basal ganglia. J Neurol Sci 2000;179(1-2):34-42.
38. Bruno RL. The neuropsychology of post-polio fatigue. Arch Phys Med Rehabil 1993;74(10):1061.
39. Krupp LB, Pollina DA. Mechanisms and management of fatigue in progressive neurological disorders. Current Opinions in Neurology 1996;9(6):456-60.
40. Bethoux F. Fatigue and multiple sclerosis. Annales de Réadaptation et de Médecine Physique 2006;49(6):355-60.
41. Hazendonk KM, Crowe SF. A neuropsychologica l study of the postpolio syndrome: support for depression without neuropsychological impairment. Neuropsychiatry Neuropsycho l Behav Neurol 2000;13:112-8.
42. Bruno RL. Word finding difficulty as a post-polio sequelae. American Journal of Physical Medicine & Rehabilitation 2000;79(4):343-348.
43. Lou JS, Kearns G, Oken B, Sexton G, Nutt J. Exacerbated physical fatigue and mental fatigue in Parkinson's disease. Movement Disorders 2001;16(2):190-196.
44. Isella V, Melzi P, Grimaldi M, Iurlaro S, Piolti R, Ferrarese C, et al. Clinical, neuropsychological, and morphometric correlates of apathy in Parkinson's disease. Movement Disorders 2002;17(2):366-371.
45. Colombo B, Martinelli Boneschi F, Rossi P, Rovaris M, Maderna L, Filippi M, et al. MRI and motor evoked potential findings in nondisabled multiple sclerosis patients with and without symptoms of fatigue. J Neurol

2000;247(7):506-9.
46. Codella M, Rocca MA, Colombo B, Martinelli-Boneschi F, Comi G, Filippi M. Cerebral grey matter pathology and fatigue in patients with multiple sclerosis: a preliminary study. J Neurol Sci 2002;15;194(1):71-4.
47. Codella M, Rocca MA, Colombo B, Rossi P, Comi G, Filippi M. A preliminary study of magnetization transfer and diffusion tensor MRI of multiple sclerosis patients with fatigue. J Neurol 2002;249(5):535-7.
48. Marrie RA, Fisher E, Miller DM, Lee JC, Rudick RA. Association of fatigue and brain atrophy in multiple sclerosis. J Neurol Sci 2005 ; 15;228(2):161-6.
49. Fumihito YoshiiHirohide TakahashiRyuya KumazawaSatoko K. Parkinson's disease and fatigue. J Neurol 2006;253-248.
50. Halstead LS. Post-polio syndrome. Sci Am 1998;278(4):42-7.
51. Bruno RL. Pathophysiology of a central cause of post-polio fatigue. Ann N Y Acad Sci 1995;753(1):257-275.
52. Smith C, Hale L. The unique nature of fatigue in multiple sclerosis: prevalence, pathophysiology, contributing factors and subjective experience. Physical Therapy Reviews 2007;12(1):43-51.
53. Krupp LB, Alvarez LA, LaRocca NG, Scheinberg LC. Fatigue in multiple sclerosis. Arch Neurol 1988;45(4):435-437.
54. Parmenter BA, Denney DR, Lynch SG. The cognitive performance of patients with multiple sclerosis during periods of high and low fatigue. Multiple Sclerosis 2003;9(2):111-8.
55. Packer T, Foster D, Brouwer B. Fatigue and activity patterns of people with chronic fatigue syndrome. The Occupational Journal of Research 1997;17(3):186-199.
56. Hoff JI, Van Hilten JJ, Middelkoop HAM, Roos RAC. Fatigue in Parkinson's disease is not associated with reduced physical activity. Parkinsonism Relat Disord 1997;3(1):51-54.
57. Shulman L, Taback R, Bean J, Weiner W. Comorbidity of the nonmotor symptoms of Parkinson's disease. Movement Disorders 2001;16(3):507-510.
58. Garber CW, Friedman JH. Effects of fatigue on physical activity and function in patients with Parkinson's disease. Neurology 2003;60(1119-1124).
59. Mostert S, Kesselring J. Effects of a short-term exercise training program on aerobic fitness, fatigue, health perception and activity level of subjects with multiple sclerosis. Multiple Sclerosis 2002;8(2):161-8.
60. Oken BS, Kishiyama S, Zajdel D, Bourdette D, Carlsen J, Haas M, et al. Randomized controlled trial of yoga and exercise in multiple sclerosis. Neurology 2004;62(11):2058-2064.
61. Rasova K, Brandejsky P, Havrdova E, Zalisova M, Rexova P. Spiroergometric and spirometric parameters in patients with multiple sclerosis: are there any links between these parameters and fatigue, depression, neurological impairment, disability, handicap and quality of life in multiple sclerosis? Multiple Sclerosis 2005;11(2):213-21.
62. Morris ME, Cantwell C, Vowels L, Dodd K. Changes in gait and fatigue from morning to afternoon in people with multiple sclerosis. J Neurol Neurosurg Psychiatr 2002;72(3):361-5.
63. Flensner G, Ek AC, Soderhamn O. Lived experience of MS-related fatigue: A phenomenological interview study. International journal of nursing studies 2003;40(7):707-17.
64. Amato MP, Ponziani G, Siracusa G, Sorbi S. Cognitive dysfunction in early-onset multiple sclerosis: a reappraisal after 10 years. Archives of neurology 2001;58(10):1602-6.
65. Vercoulen JH, Hommes OR, Swanink CM, Jongen PJ, Fennis JF, Galama JM, et al. The measurement of fatigue in patients with multiple sclerosis. A multidimensional comparison with patients with chronic fatigue syndrome and healthy subjects. Arch Neurol 1996;53(7):642-9.
66. Black D, Grant C, Lapsley H, Rawson G. The services and social needs of people with multiple sclerosis in New South Wales, Australia. The Journal of Rehabilitation 1994;60(4):6-10.
67. National Health Priority Action Council. National chronic disease strategy. 2006.
68. Jongbloed L. Disability incomes: The experience of women with multiple sclerosis. Canadian Journal of Occupational Therapy 1998;65:193-201.
69. McCabe MP. Multiple sclerosis and economic well-being: Role of health, age, and duration of illness. Journal of Clinical Psychology in Medical Settings 2003;10(3):139-147.