

Effectiveness of Cognitive Behavioral Therapy for Multiple Sclerosis (MS) Fatigue

Neda Nazarboland¹, Maryam Tehranizadeh², Farzaneh Mozaffarinejad³

¹ Assistant Professor, Faculty of Education and Psychology, Shahid Beheshti University, Tehran, Iran

² Assistant Professor, Payam e Noor University, Tehran, Iran ³Allameh Tabatabai University, Tehran, Iran

³Clinical Psychologist

Submitted: 26 December 2016

Accepted: 19 February 2017

Int J Behav Sci. 2017; 10(4): 156-161

Corresponding Author:

Neda Nazarboland,
Assistant Professor,
Faculty of Education and Psychology,
Shahid Beheshti University,
Tehran, Iran
E-mail: nnazarboland@gmail.com

Abstract

Introduction: Multiple sclerosis (MS) has a wide range of physiological and neuropsychological symptoms. Over 75% of MS patients complain about fatigue, which for many is one of their most debilitating symptoms, having a substantial impact on their quality of life and ability to carry out day-to-day tasks. Previous investigations on the effectiveness of different types of psychotherapy on MS fatigue are extremely limited. The aim of this study was to investigate the efficacy of Cognitive Behavioral Therapy (CBT) as a therapy for MS fatigue.

Method: By using convenient sampling, 22 patients with fatigue symptoms (score of ≥ 5 on Fatigue Scale) were randomly assigned into experimental (n=11) and control (n=11) groups. The subjects in the experimental group attended eight 50-minute sessions of weekly CBT based on van Kessel's model, whereas the patients in the control group attended in eight 50-minute weekly sessions of relaxation training. All the subjects completed the fatigue scale at the end of the therapy and 12 weeks follow-up.

Results: Analysis of Covariance (ANCOVA) data indicated that the CBT group reported greater reductions in fatigue symptoms. This is while the fatigue scores of both groups were decreased. Fatigue scores of the experimental group were significantly reduced in the follow-up assessment.

Conclusion: Results indicated that cognitive behavioral therapy appears to be a clinically effective treatment for fatigue in MS patients and could be implemented as a complementary therapy for MS patients in order to promote their quality of life.

Keywords: Multiple Sclerosis (MS), Cognitive Behavioral Therapy (CBT), Fatigue

Introduction

Multiple Sclerosis (MS) is a chronic demyelinating disease of the central nervous system and is broadly known as a common neurologic complication in humans [1]. It is estimated that over 2.5 million people are suffering from this ailment all around the world [2] and it has been reported that at least 20,000 sufferers live in Iran [3]. It is more prevalent among females, especially within the ages of 20 to 40 [4, 5]. The cause has not yet been detected and no definite treatment has been found; however, pharmacological treatments exhibited some success in the reduction of intensity and recurrence of this disease [6, 7].

MS represents a wide range of symptoms such as muscle pain and cramp, insentience, sensory problems, vision complications, cognitive disorders, excretory problems, speech disabilities, pain, and fatigue [8, 9]. Actually, 76-97% of the sufferers complain about fatigue [10-13]. What causes fatigue, as one of the most unbearable symptoms, in MS-sufferers has remained a question [14]. Approximately 65% of sufferers mentioned fatigue-related symptoms as one of the three most harassing aspects of their case [15] with a profound

side effect on their life quality and daily performance [11,16,17]. Fatigue interferes with the patients' daily activities, causing numerous troubles in occupational, educational, economic, recreational, and family areas, which ultimately narrows down their communications and threatens their mental health [18, 19].

Clinical endeavors have experimented with various treatments for the fatigue caused by MS. Some success has been reported on pharmacological treatments, which were most optimistically partly effective [20-27]. In contrast, there were reports on ineffectiveness of medication on MS-caused fatigue [22, 28]. Given the ineffectiveness or partial success of medical treatments, very few studies have been performed on the adoption of non-pharmacological treatments to ameliorate MS fatigue [29]. Some studies indicate the integrating effect of medication and exercise [30] or energy management [31] to successfully reduce MS fatigue symptoms. In this regard, the treatments based upon physical activity and exercise have yielded rather promising results [32, 33]. However, these findings are extremely limited and very few follow-up studies have been conducted. Moreover, sparse data exist on the effectiveness of psychotherapies to reduce MS fatigue. Some studies reported that psychotherapies such as relaxation and cognitive behavioral therapy may exert positive and rather consistent influence to decrease the level of fatigue in MS sufferers [34-36]. Nonetheless, these studies mostly focused on behavioral aspects such as energy storage and exercise and neglected cognitive dimensions, leading to appearance of controversial results [37].

Cognitive Behavioral Therapy (CBT) was originally outlined as a therapy for mood and affective disorders such as depression and anxiety [38]. It has been, however, considered recently as a method of curing symptoms (e.g. pain) of chronic diseases [39-40] and improving the mental status and social functions of sufferers [41].

CBT is based upon the principle that physical, behavioral, cognitive, and affective responses and functions interact with one another with mutual effects. Therefore, any change in each of these aspects might bring about variations in functions and responses of ones. A cognitive behavioral therapist makes a client aware of how body is influenced by contents of beliefs and cognition and helps them make some changes in other systems (e.g. affective and physical responses) through management of cognitions and behaviors [42]. Previously reported studies confirmed the effectiveness of CBT on amelioration of complications conjugated with MS such as depression [43-46], anxiety [47,48], adjustment disorders [49,50], and severity of symptoms [44].

Given the wide prevalence and numerous complications caused by MS, it is very important to adopt therapies capable of consistently controlling the symptoms. Development of non-pharmacological treatments, e.g. psychotherapy, is unquestionably important due to extensive complaints about MS-caused fatigue and contradictory findings on the effectiveness of pharmacological-based treatments. In this regard, van Kessel et al. [35] developed individual CBT in which clients

are taught how to recognize negative thoughts and incorrect cognitions exacerbating physical symptoms rather than focusing on symptoms caused by the disease. The model investigates primary physical symptoms of MS to cause fatigue. How a patient determines these symptoms from a cognitive approach may lead to affective and behavioral responses, which can in turn exacerbate fatigue-related symptoms. Therapy process in this model, thus, aids patients to manage fatigue-related anxiety and physical symptoms by incorporating assisting thoughts and managing cognitions [51].

Since very limited investigations have been devoted to scrutinize the effectiveness of cognitive/behavioral interventions on MS fatigue and also the given results are rudimentary, contradictory, and without follow-up studies [51-54], the present study aimed to explore the effectiveness of CBT in the amelioration of MS fatigue by using the model proposed by van Kessel [51]. The results of this study may greatly contribute to improve the physical status, mental health, and personal-social efficiency of MS sufferers.

Method

The present study is a quasi-experimental, pretest-posttest, and control group investigation. Statistical population consists of all MS sufferers of Tehran. The study sample (n=22) were selected among the clients of private offices through convenient sampling. The subjects met the following criteria:

1. Diagnosis of MS by a neurologist which incorporate clinical features with magnetic resonance scanning.
2. Being within normal or average dysfunction and excluding those scoring ≤ 6 in the Expanded Disability Status Scale (EDSS);
3. Being identified as a case level of fatigue; fatigue score of 4 or greater on the Fatigue Scale (FS); and
4. Willingness to abstain from any new psychological or pharmacological treatment during the duration of the study; Patients established on beta-interferon treatments for longer than 3 months were included in this study.
5. Patients with any serious psychological disorders (including psychotic disorders or active substance abuse), or those with any chronic illness that may be contributing to fatigue were excluded.

Following in person explanations regarding the purpose of the study and obtaining their consent, the subjects were randomly assigned into experimental (n=11, 3 males and 8 females) and control (n=11, 4 males and 7 females) groups. The experimental group was subjected to weekly CBT sessions for 8 weeks. The control group attended relaxation sessions with identical duration and structure in order to control the influence of therapist's support on the experimental group.

CBT was designed on the basis of van Kessel's model [51]. The main objective of this treatment was challenging all external factors (e.g. behavioral, cognitive, and affective factors) envisioned to play a role in the development and persistence of fatigue in MS patients. The treatment

sessions were directed individually. Table 1 presents a summary of the sessions. In the first and second sessions, participants learned about fatigue-related symptoms as well as CBT and its effectiveness. The third and fourth sessions were devoted on the introduction of behavioral strategies. The fifth session introduced cognitive strategies to decrease fatigue. The last three sessions were about how to adopt the proposed strategies consistently.

The structure of sessions in terms of duration and order were identical for the control group. The subjects of control group attended eight sessions focusing on treatment based on relaxation (adoption of diaphragm muscles, progressive muscle relaxation, visualization, symptom-based relaxation, and fast relaxation). In order to evoke cooperation and motivation to continue the treatment, the first session was devoted to the logic of relaxation-based treatment and its effectiveness on MS fatigue; the control subjects were told that stress may exacerbate and prolong the symptoms of MS fatigue and

relaxation-based treatment based on stress management provides a basis to neutralize adverse effects of MS fatigue. During the sessions on relaxation-based treatment, no advice regarding how to control fatigue symptoms, sleep and rest timing, daily activity scheduling, and adoption of fatigue-reducing cognitive strategies were given to the subjects. Following the first session on presenting the logic of treatment and teaching how to use diaphragm breathing, the educated techniques were reviewed and new procedures were taught on how to use relaxation methods in the remaining sessions. After each session, the clients were asked to practice using already taught technique(s).

In order to measure the effectiveness of treatment, the subjects of both groups completed FS after the eight sessions again. Furthermore, the subjects recompleted FS twelve weeks after the termination of intervention course in order to determine the persistence of the given treatment.

Table 1. Summary of CBT sessions [51]

No.	Subject	Description
First session	MS fatigue explained	Overview of what causes MS fatigue. Explanation of cognitive behavioral model for MS fatigue. Assessment of individual symptoms, behavior, cognitive, emotional responses, and external factors
Second session	CBT for MS fatigue	Introduction of treatment rationale, which includes an explanation of CBT and how it relates to MS fatigue Participants are asked to keep daily diaries of their levels of activity, rest, and fatigue
Third session	Activity scheduling	Levels of activity, rest, and fatigue are reviewed. Information is given of how patterns of rest and activity or over-activity affect the body and fatigue. Importance of consistency in activity and rest is outlined, and benefits of moderate physical exercise is discussed. Participants are encouraged to set goals to improve levels of resting, activity, and exercise
Fourth session	Sleep improvement	Information is provided on how sleeping too much or too little can impact on fatigue, and behavioral techniques (basic sleep hygiene) which can help change this are discussed, e.g., having a set bed/ waking times, avoiding caffeine before bedtime, getting up if lying awake in bed for longer than 20 min. Participants are encouraged to set goals for improving sleep.
Fifth session	Understanding MS symptoms	The concepts of symptom focusing and symptom attribution are introduced, and how these can have an impact on MS fatigue. Alternative explanations of somatic symptoms are discussed, and participants are encouraged to keep a record of somatic symptoms and to try and come up with alternative explanations
Sixth session	Changing the way of thinking	The concept of negative thoughts is introduced, and how this can impact on fatigue and mood. Participants are asked to keep daily thought records of unhelpful thoughts and to try and come up with alternative thoughts.
Seventh session	Stress management, controlling emotions, and adaptation	Managing stress, determining a sense of control and coping with emotions. Basic stress management and coping with emotions is discussed. Participants are encouraged to set goals for stress management and practicing alternative ways to manage their emotions
Eighth session	Social support and preparing for the future	The importance of social support for MS patients is discussed, and participants' personal support systems are reviewed. Participants are encouraged to continue to employ the skills they have learnt throughout the manual to manage their fatigue

Results

The demographic data including gender, marital status, and type of disease related to both experimental and control groups are summarized in Table 2.

According to Table 2, the majority of the participants in the present study suffer from Relapsing-Remitting MS

(RRMS), with female subjects being slightly more than male subjects. Table 3 represents descriptive data related to age of the subjects, duration of being affected, EDSS scores, and FS scores in pretest, posttest, and follow-up test in experimental and control groups.

Table 2. Demographic data of experimental and control groups.

		Experimental group		Control group		Total	
		Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Gender	Female	8	72.72	7	63.63	15	68.19
	Male	3	27.28	4	36.37	7	31.81
Marital status	Married	8	72.72	9	81.81	17	72.28
	Unmarried	3	27.28	2	18.19	5	27.72
Disease	Relapsing-remitting	9	81.81	8	72.72	16	72.72
	Progressing	2	18.19	2	18.19	5	22.73
	Minor symptoms	0	0	1	9.09	1	4.55

Table 3. Descriptive data of experimental and control groups.

		Experimental group		Control group	
		Average	SD	Average	SD
Age (years old)		43	9.45	48.50	9.29
Duration of being affected (years)		5.98	4.08	6.33	4.42
EDSS score		3.01	1.54	3.12	1.70
FS score	Pretest	20.90	3.17	20.54	3.58
	Posttest	8.54	2.42	11.45	4.00
	Follow-up	10.09	3.41	14.90	3.78

As it can be seen in Table 3, the control group scored slightly higher than the experimental group in the duration of being affected ($t=0.25$) and EDSS ($t=0.19$) although the differences were found to be insignificant ($p>0.05$). Therefore, these two groups are homogenous in terms of these two factors.

In addition, according to Table 2, FS scores in both groups decreased after CBT and relaxation; however, in the follow-up study, the average scores of both groups increased compared to the scores of posttest.

In order to determine the effectiveness of CBT on

amelioration of MS fatigue in the subjects, Analysis of Covariance (ANCOVA) was adopted. Before running the ANCOVA, the required preconditions were controlled. Normal distribution of data regarding dependent variables (posttest and follow-up) and equality of variances were confirmed by Kolmogorov-Smirnov test and Levene's test, respectively. Table 4 presents the results obtained from ANCOVA to determine the effectiveness of CBT on amelioration of MS fatigue in the subjects of the present study.

Table 4. The results of Analysis of Covariance (ANCOVA) to determine the effectiveness of CBT on amelioration of MS fatigue after adjusting the effect of pretest scores

Source	Sum of squares	df	Mean square	F	Sig.	Partial Eta Squared
Pretest	140.80	1	140.80	34.01	0.000	0.642
Group	55.92	1	55.92	13.51	0.002	0.416
Error	78.64	19	4.13			
Total	2466	22				

The results revealed that after eliminating the effect of pretest, there is significant difference between experimental and control groups ($F=13.51$; $p<0.01$) and the effect of intervention was found to be high ($\eta^2=0.416$) [55]. Therefore, it can be concluded that CBT had a favorable effect to reduce MS fatigue symptoms.

Afterwards, ANCOVA was adopted in order to determine the persistence of effectiveness of CBT on amelioration of MS fatigue. After eliminating the effect of posttest, FS scores were compared between experimental and control groups (Table 5).

Table 5. The results of Analysis of Covariance (ANCOVA) to determine the effectiveness of CBT on amelioration of MS fatigue after adjusting the effect of posttest scores

Source	Sum of squares	df	Mean square	F	Sig.	Partial Eta Squared
Pretest	173.10	1	173.10	37.93	0.000	0.666
Group	22.65	1	22.65	4.96	0.038	0.207
Error	92.28	19	4.85			
Total	3982	22				

According to Table 5, the results obtained from ANCOVA confirm the significant difference in follow-up scores between experimental and control groups ($F=4.96$; $p<0.05$). Also, the effect of its persistence was found to be moderate ($\eta^2=0.207$) [55]. It can, therefore, be concluded that CBT had a persistent effect on the amelioration of MS fatigue.

Discussion

The present study was formulated in order to determine the effectiveness of Cognitive Behavioral Therapy (CBT) in the amelioration of MS fatigue. Results revealed that this treatment had a considerably higher effect compared to relaxation on amelioration of MS fatigue. However, it should be noted that both methods resulted in significant reductions in MS fatigue. In addition, follow-up evaluations revealed that amelioration of MS fatigue will persist over time due to the application of CBT.

The results of this study are coherent with the investigations which found various dimensions of CBT influential in MS fatigue management; these methods include individual CBT [51], group CBT [52] and Internet-based CBT self-management programs [53].

Despite the hypothesis, the results indicated that control group (just receiving relaxation treatment) experienced significant improvement in the reduction of MS fatigue. This could be due to side attributes such as adjustment to treatment process and structure, support and attention from therapist, convincing the client on the logic of treatment, and treatment expectations by the client in both types of treatment. In other words, although in the relaxation-based treatment, the main principles of CBT such as focus on cognitions, fatigue-reducing cognitive circumstances, focus on fatigue symptoms, were not provided for the control group, side attributes of treatment were persistent in both methods of treatment. Furthermore, although relaxation-based treatment was considered as a neutral treatment in the control group, it can be regarded as an exclusive treatment in the amelioration of MS fatigue. Actually, relaxation techniques might have a positive influence on stress reduction and sleep improvement, which may effectively reduce fatigue symptoms.

Moreover, the use of a single therapist for both interventions may have limited the results since it can have an influence on the other results. Therefore, it is recommended that future studies adopt other controlling methods such as waiting lists.

In spite of the mentioned limitations, the present study can be regarded as a positive step toward finding and adopting non-pharmacological treatments in order to ameliorate fatigue levels in MS patients. MS fatigue consists of several symptoms which severely influences the efficiency of sufferers [11,16,17,18,19]. Investigations into psychotherapy-based treatment can be fruitful in the improvement of life quality and amelioration of pains in MS patients.

Acknowledgements

The authors would like to thank the neurologists for their precious cooperation in introducing target patients. We are also grateful to the Iranian MS Community for their collaboration. Last but not least, we appreciate the priceless cooperation of the patients in this study.

References

1. Werring DJ, Thompson AJ. Improving the quality of life of patients with multiple sclerosis: diagnosis. *Drugs of today* (Barcelona, Spain: 1998). 1998; 34(2):145-56.
2. Dennison L, Moss-Morris R. Cognitive-behavioral therapy: what benefits can it offer people with multiple sclerosis? *Expert review of neurotherapeutics*. 2010; 10(9):1383-90.
3. Nabavi M, Poorfarzam S, Ghasemi H. Epidemiology, clinical course and prognosis of Multiple sclerosis in 203 patients referred to MS clinic of Shahid Mostafa Khomeini hospital of Tehran in 2002. *J Med Fac of Med Sci of Tehran Univ*. 2006; 67(4):90-7. [Persian].
4. Neild C. What is MS? In: *Society MS*, editor. 3rd ed. UK2008.
5. Compston A, Coles A. Multiple sclerosis. *The Lancet*. 2002; 359(9313):1221-31.
6. Goodin DS. Disease-modifying therapy in multiple sclerosis: update and clinical implications. *Neurology*. 2008; 71(24 Suppl 3):S8-13.
7. Rudick RA. Disease-modifying drugs for relapsing-remitting multiple sclerosis and future directions for multiple sclerosis therapeutics. *Archives of neurology*. 1999; 56(9):1079-84.
8. Guinness M, Peters S. The diagnosis of multiple sclerosis: peplau's international relations model in practice. *Rehabil Nurs*. 1999; 24: 30-6.
9. Taggart HM. Multiple sclerosis update. *Orthopedic nursing*. 1998; 17(2):23-7; quiz 8-9.
10. Schwartz JE, Jandorf L, Krupp LB. The measurement of fatigue: a new instrument. *Journal of psychosomatic research*. 1993; 37(7):753-62.
11. Freal JE, Kraft GH, Coryell JK. Symptomatic fatigue in multiple sclerosis. *Archives of physical medicine and rehabilitation*. 1984; 65(3):135-8.
12. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Archives of neurology*. 1989; 46(10):1121-3.
13. Schwartz CE, Coulthard-Morris L, Zeng Q. Psychosocial correlates of fatigue in multiple sclerosis. *Archives of physical medicine and rehabilitation*. 1996; 77(2):165-70.
14. Giovannoni G. Multiple sclerosis related fatigue. *Journal of neurology, neurosurgery, and psychiatry*. 2006; 77(1):2-3.
15. Branas P, Jordan R, Fry-Smith A, Burls A, Hyde C. Treatments for fatigue in multiple sclerosis: a rapid and systematic review. *Health technology assessment* (Winchester, England). 2000; 4(27):1-61.
16. Fisk JD, Pontefract A, Ritvo PG, Archibald CJ, Murray TJ. The impact of fatigue on patients with multiple sclerosis. *The Canadian journal of neurological sciences*. 1994; 21(1):9-14.
17. Metz L. Multiple sclerosis: symptomatic therapies. *Seminars in neurology*. 1998; 18(3):389-95.
18. Monks J. Experiencing symptoms in chronic illness: fatigue in multiple sclerosis. *International disability studies*. 1989; 11(2):78-83.
19. Edgley K, M S, E D. A survey of multiple sclerosis: Part 2. Determinants of employment status. *Can J Rehabil*. 1991; 4:127-32.
20. Cohen RA, Fisher M. Amantadine treatment of fatigue associated with multiple sclerosis. *Archives of neurology*. 1989; 46(6):676-80.
21. Group TCMR. A randomized controlled trial of amantadine in fatigue associated with multiple sclerosis. *The Canadian MS Research Group. The Canadian journal of neurological sciences Le journal canadien des sciences neurologiques*. 1987; 14(3):273-8.
22. Krupp LB, Coyle PK, Doscher C, Miller A, Cross AH, Jandorf L, et al. Fatigue therapy in multiple sclerosis: results of a double-

- blind, randomized, parallel trial of amantadine, pemoline, and placebo. *Neurology*. 1995; 45(11):1956-61.
23. Murray TJ. Amantadine therapy for fatigue in multiple sclerosis. *The Canadian journal of neurological sciences*. 1985; 12(3):251-4.
 24. Rosenberg GA, Appenzeller O. Amantadine, fatigue, and multiple sclerosis. *Archives of neurology*. 1988; 45(10):1104-6.
 25. Weinshenker BG, Penman M, Bass B, Ebers GC, Rice GP. A double-blind, randomized, crossover trial of pemoline in fatigue associated with multiple sclerosis. *Neurology*. 1992; 42(8):1468-71.
 26. Tomassini V, Pozzilli C, Onesti E, Pasqualetti P, Marinelli F, Pisani A, et al. Comparison of the effects of acetyl L-carnitine and amantadine for the treatment of fatigue in multiple sclerosis: results of a pilot, randomised, double-blind, crossover trial. *Journal of the neurological sciences*. 2004; 218(1-2):103-8.
 27. Wingerchuk DM, Benarroch EE, O'Brien PC, Keegan BM, Lucchinetti CF, Noseworthy JH, et al. A randomized controlled crossover trial of aspirin for fatigue in multiple sclerosis. *Neurology*. 2005; 64(7):1267-9.
 28. Stankoff B, Waubant E, Confavreux C, Edan G, Debouverie M, Rumbach L, et al. Modafinil for fatigue in MS: a randomized placebo-controlled double-blind study. *Neurology*. 2005; 64(7):1139-43.
 29. Asano M, Finlayson ML. Meta-analysis of three different types of fatigue management interventions for people with multiple sclerosis: exercise, education, and medication. *Multiple sclerosis international*. 2014; 2014:798285.
 30. Pilutti LA, Greenlee TA, Motl RW, Nickrent MS, Petruzzello SJ. Effects of exercise training on fatigue in multiple sclerosis: a meta-analysis. *Psychosomatic medicine*. 2013; 75(6):575-80.
 31. Blikman LJ, Huisstede BM, Kooijmans H, Stam HJ, Bussmann JB, van Meeteren J. Effectiveness of energy conservation treatment in reducing fatigue in multiple sclerosis: a systematic review and meta-analysis. *Archives of physical medicine and rehabilitation*. 2013; 94(7):1360-76.
 32. Petajan JH, Gappmaier E, White AT, Spencer MK, Mino L, Hicks RW. Impact of aerobic training on fitness and quality of life in multiple sclerosis. *Annals of neurology*. 1996; 39(4):432-41.
 33. 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 (Houndmills, Basingstoke, England)*. 2002; 8(2):161-8.
 34. Kohli IS, Kataria A, Singla S, Kaushik P, Jindal R, Aggarwal A. Effect of cognitive behavioural therapy on multiple sclerosis fatigue: a systematic review of randomised control trials. *Value in Health*. 2012; 15(7):A545-A6.
 35. van Kessel K, Moss-Morris R. Understanding multiple sclerosis fatigue: a synthesis of biological and psychological factors. *Journal of psychosomatic research*. 2006; 61(5):583-5.
 36. Branas P, Jordan R, Fry-Smith A, Burls A, Hyde C. Treatments for fatigue in multiple sclerosis: a rapid and systematic review. *Health technology assessment (Winchester, England)*. 2000; 4(27):1-61.
 37. Krupp LB, Serafin DJ, Christodoulou C. Multiple sclerosis-associated fatigue. *Expert review of neurotherapeutics*. 2010; 10(9):1437-47.
 38. Beck AT. *Cognitive therapy and the emotional disorders*. In: Penguin Books. UK: 1976.
 39. Morley S, Eccleston C, Williams A. Systematic review and meta-analysis of randomized controlled trials of cognitive behaviour therapy and behaviour therapy for chronic pain in adults, excluding headache. *Pain*. 1999; 80(1-2):1-13.
 40. Malouff JM, Thorsteinsson EB, Rooke SE, Bhullar N, Schutte NS. Efficacy of cognitive behavioral therapy for chronic fatigue syndrome: a meta-analysis. *Clinical psychology review*. 2008; 28(5):736-45.
 41. Moorey S, Cort E, Kapari M, Monroe B, Hansford P, Mannix K, et al. A cluster randomized controlled trial of cognitive behaviour therapy for common mental disorders in patients with advanced cancer. *Psychological medicine*. 2009; 39(5):713-23.
 42. Beck AT. Cognitive therapy. A 30-year retrospective. *The American psychologist*. 1991; 46(4):368-75.
 43. Mohr DC, Boudewyn AC, Goodkin DE, Bostrom A, Epstein L. Comparative outcomes for individual cognitive-behavior therapy, supportive-expressive group psychotherapy, and sertraline for the treatment of depression in multiple sclerosis. *Journal of consulting and clinical psychology*. 2001; 69(6):942-9.
 44. Mohr DC, Likosky W, Bertagnolli A, Goodkin DE, Van Der Wende J, Dwyer P, et al. Telephone-administered cognitive-behavioral therapy for the treatment of depressive symptoms in multiple sclerosis. *Journal of consulting and clinical psychology*. 2000; 68(2):356-61.
 45. Mohr DC, Hart SL, Julian L, Catledge C, Honos-Webb L, Vella L, et al. Telephone-administered psychotherapy for depression. *Archives of general psychiatry*. 2005; 62(9):1007-14.
 46. Hind D, O' Cathain A, Cooper CL, Parry GD, Isaac CL, Rose A, et al. The acceptability of computerised cognitive behavioural therapy for the treatment of depression in people with chronic physical disease: a qualitative study of people with multiple sclerosis. *Psychology & health*. 2010; 25(6):699-712.
 47. Mohr DC, Cox D, Epstein L, Boudewyn A. Teaching patients to self-inject: pilot study of a treatment for injection anxiety and phobia in multiple sclerosis patients prescribed injectable medications. *Journal of behavior therapy and experimental psychiatry*. 2002; 33(1):39-47.
 48. Mohr DC, Cox D, Merluzzi N. Self-injection anxiety training: a treatment for patients unable to self-inject injectable medications. *Multiple sclerosis (Houndmills, Basingstoke, England)*. 2005; 11(2):182-5.
 49. Malcomson KS, Dunwoody L, Lowe-Strong AS. Psychosocial interventions in people with multiple sclerosis: a review. *Journal of neurology*. 2007; 254(1):1-13.
 50. Thomas PW, Thomas S, Hillier C, Galvin K, Baker R. Psychological interventions for multiple sclerosis. *The Cochrane database of systematic reviews*. 2006(1):Cd004431.
 51. van Kessel K, Moss-Morris R, Willoughby E, Chalder T, Johnson MH, Robinson E. A randomized controlled trial of cognitive behavior therapy for multiple sclerosis fatigue. *Psychosomatic medicine*. 2008; 70(2):205-13.
 52. Thomas S, Thomas PW, Nock A, Slingsby V, Galvin K, Baker R, et al. Development and preliminary evaluation of a cognitive behavioural approach to fatigue management in people with multiple sclerosis. *Patient education and counseling*. 2010; 78(2):240-9.
 53. Moss-Morris R, McCrone P, Yardley L, van Kessel K, Wills G, Dennison L. A pilot randomised controlled trial of an Internet-based cognitive behavioural therapy self-management programme (MS Invigor8) for multiple sclerosis fatigue. *Behaviour research and therapy*. 2012; 50(6):415-21.
 54. Nordin L, Rorsman I. Cognitive behavioural therapy in multiple sclerosis: a randomized controlled pilot study of acceptance and commitment therapy. *Journal of rehabilitation medicine*. 2012; 44(1):87-90.
 55. Cohen J. A power primer. *Psychological bulletin*. 1992; 112(1):155-9.