The Concept of Fatigue in Multiple Sclerosis

Susan L. Johnson

Abstract: Fatigue is one of the most common symptoms of multiple sclerosis (MS), and it can have a major impact on health-related quality of life. Therefore, it is imperative that healthcare practitioners regularly assess fatigue in their patients with MS. Fatigue can be caused either by the disease process (primary fatigue) or by other problems such as insomnia, infections, or depression (secondary fatigue). Because the causes of secondary fatigue are generally amenable to treatment, it is important that healthcare practitioners distinguish between the two types of fatigue when assessing and treating fatigue. Because fatigue is a subjective experience, it can be difficult to measure. Tools such as the Fatigue Impact Scale and the Fatigue Severity Scale can be used to help clinicians and researchers measure fatigue. The Symptom Management Model can be used to guide healthcare practitioners in the assessment and treatment of fatigue. A variety of treatment options are available for MS-related fatigue, and it is important that patients and their support systems are made aware that fatigue can be managed.

The majority of people with multiple sclerosis (MS) will experience severe, debilitating fatigue at some point during the course of their illness (Egner, Phillips, Vora, & Wiggers, 2003; Mathiowetz, 2003). Fatigue impacts a person's health-related quality of life and ability to work (Bakshi, 2003; Forbes, While, Mathes, & Griffiths, 2006). Healthcare professionals need to include assessments of fatigue in their routine care of patients with MS and should be able to offer strategies to help them deal with any fatigue they might experience (Bakshi).

This article explores fatigue in the population with MS. The starting point is the definition of fatigue. The scope of the problem, the risk factors for developing fatigue, and the consequences of fatigue in persons with MS are examined. Depression as it relates to fatigue is discussed. A description of the manifestations of fatigue in the patient with MS is offered, as well as a tool that can be used to evaluate fatigue. Several evidence-based management strategies for dealing with fatigue in the patient with MS are presented. Finally, the Symptom Management Model is explored as a useful model that can be used for future studies on fatigue in this population.

Definition

Most people have probably experienced fatigue at some point in their lives. It is one of the most common symptoms of both acute infections and chronic illnesses (Aaronson et al., 1999; Ream & Richardson, 1996). Aaronson et al. proposed the following definition of *fatigue*: "The awareness of a decreased capacity for physical and/or mental activity due to an imbalance in the availability, utilization, and/or restoration of resources needed to perform activity" (p. 46). This definition has more clarity than other definitions of fatigue because it avoids words such as *exhaustion* and *tiredness* that are open to misinterpretation. Furthermore, this definition includes a cause of fatigue, an imbalance in needed resources, and a way of looking at a treatment for fatigue—the restoration of needed resources.

When discussing fatigue that is specific to MS, researchers have distinguished two types of fatigue: primary and secondary (Bakshi, 2003; Kos, Kerckhofs, Nagels, D'hooghe, & Ilsbroukx, 2007). Primary fatigue is thought to be caused by factors related to the disease process, whereas secondary fatigue is caused by some of the pathological consequences of the disease (Bakshi; Kos et al., 2007). Clinically, primary fatigue and secondary fatigue may be difficult to differentiate, as the manifestations are similar; however, secondary fatigue can be ruled out if none of the causes of this type of fatigue, such as insomnia or depression, are present (Bakshi; Crayton, Heyman, & Rossman, 2004).

Others discuss MS fatigue similarly but use different terms. Iriarte, Subira, and Castro (2000) named three types of fatigue in MS: (a) asthenia, (b) fatigability, and (c) worsening of other symptoms. *Asthenia* is defined as fatigue at rest and is believed to be associated with immunoactivation (Iriarte et al.). *Fatigability* is defined as fatigue during or after

Questions or comments about this article may be directed to Susan L. Johnson, BSN RN, at slj6@u.washington.edu. She is a staff nurse at Tacoma General Hospital and a master of nursing student at the University of Washington–Tacoma.

exercise and seems to be associated with pyramidal-tract involvement (Iriarte et al.). In addition, fatigue in the patient with MS can be cognitive (Bakshi, 2003; Barak & Achiron, 2006; Bryant, Chiaravalloti, & DeLuca, 2004; Olsson, Lexell, & Soderberg, 2005). Cognitive fatigue occurs in the absence of related dementia and manifests when sustained cognitive attention is required. It includes decreased ability to concentrate and complete a task, decreased visual and verbal memory, and decreased ability to problem solve (Barak & Achiron; Krupp & Elkins, 2000).

Prevalence of Fatigue in People with MS

Fatigue is reported to be the most common and persistent symptom of people with MS and is often the symptom with the greatest impact on patients' health-related quality of life (Egner et al., 2003; Flesner & Lindencrona, 2002; Mathiowetz, 2003). It can be the first symptom that a patient complains of, manifesting even before a diagnosis of MS is made (Iriarte et al., 2000). Patients in all stages of MS, from mild to severe, can exhibit significant fatigue (Bakshi, 2003).

In one study, which looked at people with advanced MS over the course of a 2-year period, 80% of the sample consistently reported experiencing severe fatigue, whereas 100% of the sample reported symptoms of fatigue at some point after diagnosis (Egner et al., 2003). In other studies of patients with MS, 50%–93% of participants reported that they experienced fatigue (Barak & Achiron, 2006; Forbes et al., 2006; Iriarte et al., 2000; Lerdal, Celius, & Moum, 2003). Fatigue in the population with MS tends to be persistent; some patients report fatigue symptoms that last for more than 1 year (Barak & Achiron; Egner et al.).

Contributing Factors

Environmental factors such as heat can increase the likelihood that an individual will manifest a symptom such as fatigue. Personal factors such as age, socioeconomic status, race, and gender also can contribute to the likelihood that symptoms of fatigue will occur (Carrieri-Kohlman, Lindsey, & West, 2003). In this section, factors that place individuals with MS at a greater risk for experiencing fatigue are examined.

Environmental Risk Factors

Hot, humid weather is an environmental factor that places patients with MS at risk of experiencing fatigue (Bakshi, 2003; Crayton et al., 2004). Some people with MS have reported that ingesting hot drinks and food exacerbates their fatigue (Flesner & Lindencrona, 2002). Several studies have shown that reducing core body temperature in patients with MS helped alleviate their fatigue (Flesner & Lindencrona; NASA/MS Cooling Study Group, 2003). Neural conductivity is decreased in demyelinated nerves that are exposed to high temperatures and increased when these nerves are cooled; it is hypothesized that this increased conductivity reduces fatigue (Bakshi; NASA/MS Cooling Study Group).

Personal and Developmental Risk Factors

Gender and race have not been found to be associated with MS-related fatigue (Barak & Achiron, 2006; Egner et al., 2003; Iriarte et al., 2000; Lerdal et al., 2003). One study found a possible positive association between fatigue and age (Lerdal et al.), while others found that no such association exists (Barak & Achiron; Iriarte et al.; Kroencke, Lynch, & Denney, 2000). In one study, education level was found to be negatively correlated with fatigue (Lerdal et al.). Two studies (Iriarte et al.; Kroencke et al.) found that duration of illness was not associated with the likelihood of experiencing fatigue, while a third study found a possible correlation between duration of illness and fatigue (Lerdal et al.).

Disease subtype has not been associated with fatigue. Patients with primary-progressive MS are just as likely to experience fatigue as those with the relapsing-remitting form (Forbes et al., 2006; Kroencke et al., 2000). Disability, on the other hand, may be a factor in predicting fatigue, although the results of studies on this factor are mixed. Forbes and colleagues reported that patients in each of the diagnosis subcategories who had more severe disease and disability scored higher on the fatigue scale. Likewise, Kroencke and associates found that disability was a significant predictor of fatigue. However, two other studies found no correlation between severity of disability and fatigue experience (Barak & Achiron, 2006; Egner et al., 2003).

Likewise, studies that examined how fatigue correlates with sleep in the population with MS yielded mixed results. Iriarte and colleagues (2000) found no difference in fatigue levels in patients with MS who sleep well and those who do not. Others reported that sleep disturbance does contribute to fatigue in this population (Bakshi, 2003; Kos et al., 2007; Stanton, Barnes, & Silber, 2006). Medications (Bakshi; Oken et al., 2006) and infections (Bakshi) also increase the risk of fatigue in people with MS.

Pathological Processes and Consequences

Although the causes of fatigue in patients with MS are unknown, there is some indication that primary fatigue results from physical changes caused by MS, such as demyelinization, inflammation, and axonal loss in the central nervous system (Bakshi, 2003; Kos et al., 2007). Immune factors have been associated with primary fatigue (Bakshi; Kos et

al., 2007) and asthenia (Iriarte et al., 2000), while fatigability has been associated with pyramidal-tract involvement (Iriarte et al.). Secondary fatigue in MS arises from disturbed sleep, deconditioning, depression, and other psychological factors, such as feelings of hopelessness and reduced feelings of self-efficacy (Kos et al., 2007).

Fatigue can lead to declines in overall health in the person with multiple sclerosis.

Fatigue has several pathological consequences for the person with MS. Fatigue in this population limits social activities and the ability to hold down a job (Forbes et al., 2006; Iriarte et al., 2000). The U.S. Social Security Administration lists fatigue as a leading cause of disability in persons with MS (Bakshi, 2003). Independent of MS disability scores (i.e., the Expanded Disability Status Scale [EDSS]), fatigue reduces health-related quality of life in persons with MS (Forbes et al.; Merkelbach, Sittinger, & Koenig, 2002). Furthermore, people with MS who experience fatigue say there is "no fun in life" (Olsson et al., 2005). Fatigue also can lead to deconditioning and exercise intolerance in people with MS, as patients are likely to curtail their physical activity to try to minimize fatigue (Bakshi; Crayton et al., 2004; Rampell et al., 2007). Decreased exercise can create other problems, such as increased spasticity and constipation (Crayton et al.).

Fatigue can also affect cognitive function. It has been shown to cause impairment on cognitive tests in MS patients who are not otherwise cognitively impaired (Bryant et al., 2004). In addition, fatigue can lead to declines in overall health in the person with MS, inasmuch as it has been identified as a barrier to health-promoting behaviors and activities in this population (Becker & Stuifbergen, 2004).

Depression: A Related Pathophysiological Concept

Depression is a pathophysiological concept that is related to, but distinct from, fatigue. Fatigue lies in Ferrell and colleagues' (1996) physical well-being domain, while depression lies in the psychological well-being domain. It is often hard to distinguish between fatigue and depression because fatigue can be a symptom of depression and depression can be a consequence of fatigue (Aaronson et al., 1999; Kos et al., 2007). The relationship is further confounded because instruments that measure depression generally include questions about fatigue (Aaronson et al.).

Depression is a common comorbidity of MS (Egner et al., 2003). In one study of people with MS, 75% of the participants complained of symptoms of depression, making it the second most common complaint after fatigue (Forbes et al., 2006). The study found that depression and fatigue in the population with MS were interactive, but that one did not cause the other (Forbes et al.). Kroencke and colleagues (2000) found that the mean rates of depression in their patients with MS were higher than the mean for healthy people. This finding held up even when items that measured fatigue were removed from the scale used for measuring depression (Kroencke et al.).

Anxiety and depression have been found to be predictive of chronic fatigue in long-term survivors of testicular cancer (Fossa, Dahl, & Loge, 2003), and the same has been found to be true in the population with MS (Iriarte et al., 2000; Kroencke et al., 2000). Depression has been cited as a factor that causes secondary fatigue in people with MS (Kos et al., 2007). However, some researchers argue that depression does not cause fatigue in patients with MS (Egner et al., 2003; Forbes et al., 2006; Iriarte et al.). Egner and colleagues found that depression often subsided with treatment and that it had no impact on fatigue levels. Nevertheless, it is important to treat depression in patients with MS because reducing depression can lead to increased physical activity and overall improvements in health-related quality of life (Bakshi, 2003; Crayton et al., 2004).

Manifestations and Surveillance

Fatigue in people with MS has many different manifestations that are unique to each person (Bakshi, 2003). Therefore, when measuring fatigue in the clinical setting, subjective assessments, rather than objective measures, should be used (Bakshi; Ream & Richardson, 1996). It is important to assess the presence of fatigue and to document both its severity and its impact on the patient's life (Bakshi; Mathiowetz, 2003). Fatigue should be measured separately from level of disability because it can lead to limitations in activities in patients who are not otherwise physically disabled (Egner et al., 2003; Merkelbach et al., 2002). People with MS who have fatigue may not report their fatigue if they regard it as an inevitable consequence of MS, so it is important for clinicians to ask specific questions that can identify its presence (Bakshi).

Presenting symptoms of fatigue include lack of energy (Kos et al., 2007), inability to sustain performance of a task or to tolerate physical activity (Bakshi, 2003; Iriarte et al., 2000; Kos et al., 2007), and feelings of malaise (Bakshi; Olsson et al., 2005). Patients also may complain of difficulty concentrating or completing a mental task (Bakshi; Barak & Achiron, 2006; Kos et al., 2007). People with MS

describe the fatigue as relentless and omnipresent (Barak & Achiron; Iriarte et al.; Olsson et al.), leading to sleepiness (Kos et al., 2007) and an intense need to rest (Olsson et al.). Other descriptions that people with MS use to characterize their fatigue include "heavy body" and "a feeling of not being connected to the world" (Olsson et al.).

Measuring Fatigue

Fatigue has proven to be a difficult concept to define and measure clinically (Dittner, Wessely, & Brown, 2004; Schwid, Covington, Segal, & Goodman, 2002). Upwards of 30 different instruments have been developed to measure fatigue, but none has emerged as the definitive measure (Dittner et al.; Kos, Nagels, D'Hooghe, Duportail, & Kerckhofs, 2006; Schwid et al.). Two instruments often used in research and clinical settings to measure fatigue in the population with MS are the Fatigue Severity Scale (FSS) and the Fatigue Impact Scale (FIS; Kos et al., 2006; Schwid et al.).

Fatigue Impact Scale

The FIS assesses the effect of fatigue on activities of daily living (Dittner et al., 2004). It has been used with stroke patients (Ingles, Eskes, & Phillips, 1999), postpolio patients (Yagiz, Oncu, Atamaz, & Durmaz, 2006), and people with MS (Dittner et al.; Mathiowetz, 2003; Vanage, Gilbertson, & Mathiowetz, 2003; Wingerchuk et al., 2005). It has been identified by the Multiple Sclerosis Council for Clinical Practice Guidelines "as the most appropriate for assessing the impact of MS-related fatigue on quality of life" (Mathiowetz, 2003, p. 389).

The scale measures physical, cognitive, and social fatigue for a total fatigue score, as well as subscores for each area (Mathiowetz, 2003; Schwid et al., 2002). The scale consists of 40 statements that respondents rate on a Likert scale of 0 (*no problem*) to 4 (*extreme problem*). Higher scores indicate that fatigue is negatively affecting the respondent's life (Mathiowetz). The FIS is a retrospective tool; it measures the impact of fatigue over the past month (Fisk & Doble, 2002).

A drawback of the FIS is that it takes 10–20 minutes to administer and 5 minutes to score (Kos et al., 2006; Mathiowetz, 2003). However, two versions of this scale, the Modified Fatigue Impact Scale (M-FIS) and the Daily Fatigue Impact Scale (D-FIS), are quicker to administer and possess levels of reliability and validity similar to the FIS (Benito-Leon et al., 2007; Dittner et al., 2004; Kos et al., 2006; Mathiowetz). The M-FIS contains 21 questions that cover physical, cognitive, and psychosocial status; a general fatigue score is obtained by totaling these items (Kos et al., 2006; Tellez et al., 2005). A score of 38 or more is indicative of fatigue (Tellez et al.) The D-FIS consists of 8 questions (Fisk & Doble, 2002). It was developed for use in studying flulike illnesses (Fisk & Doble) but has been assessed for use with MS patients (Benito-Leon et al.). It could prove to be a useful tool for assessing fatigue in the clinical setting because it is short and easy to use and captures current fatigue levels. Patients could be asked to use it to keep a fatigue diary that clinicians could review at clinic visits (Benito-Leon et al.).

Fatigue Severity Scale

The FSS is another instrument commonly used in the population with MS (Dittner et al., 2004; Kos et al., 2006). Contrary to what the name implies, this scale measures the impact of fatigue on the respondent's daily life, rather than its overall severity (Dittner et al.; Schwid et al., 2002). The scale consists of 9 statements, to which patients are asked to respond using a 7-point Likert scale (Mathiowetz, 2003; Schwid et al., 2002). Responses are added together and averaged to determine the overall score. Scores greater than 4 are considered to be indicative of significant fatigue (Egner et al., 2003).

Clinical Management Strategies

The first step in treating MS-related fatigue is to identify and treat secondary factors, such as insomnia, depression, infection, hypothyroidism, and pain, that might be exacerbating the fatigue (Bakshi, 2003; Crayton et al., 2004; Kos et al., 2007; Schwid et al., 2002). Some nonpharmacologic strategies for managing and reducing fatigue in people with MS are exercise training, energy conservation, and cooling therapy (Bakshi; Crayton et al.; Kos et al., 2007; Schwid et al.). Medications that have been used to treat MS-related fatigue include amantadine, pemoline, modafinil, and aspirin (Bakshi; Kos et al., 2007; Schwid et al.; Wingerchuk et al., 2005).

Exercise has been recommended cautiously for people with MS due to the fact that an increase in body temperature can exacerbate symptoms (Bakshi, 2003). However, several studies have shown that participation in an exercise program such as yoga or using a stationary bicycle can reduce fatigue symptoms in people with MS (Mostert & Kesselring, 2002; Oken et al., 2004). Furthermore, contrary to common belief, the exercise programs of yoga and stationary bicycling were not found to worsen participants' MS (Oken et al., 2004).

Another method of mitigating fatigue in patients with MS is energy conservation. Energy-conservation strategies include adjusting daily routines so that more strenuous activities occur early in the day and allowing time for rest or naps between

strenuous activities (Bakshi, 2003). Several studies have empirically examined whether energy conservation is effective in reducing fatigue by including participants in a course wherein they are taught energy-conservation techniques, and afterward measuring their fatigue levels (Mathiowetz, Finlayson, Matuska, Chen, & Luo, 2005; Matuska, Mathiowetz, & Finlayson, 2007; Vanage et al., 2003). A significant mitigation of fatigue was found in those patients who attended the classes and continued to use energy-conservation strategies (Mathiowetz et al.; Matuska et al.; Vanage et al.).

Several studies have shown that MS fatigue can be reduced through the use of special cooling suits (Flesner & Lindencrona, 2002; NASA/MS Cooling Study Group, 2003). However, unless these suits become easy to obtain, cooling therapy will not be a practical option for most people with MS. Drinking cool beverages might also help reduce fatigue (Crayton et al., 2004).

A Conceptual Model: The Symptom Management Model

The Symptom Management Model is a useful tool that clinicians and researchers can use (a) to help them understand the symptom experience, (b) to evaluate symptom-management strategies, and (c) to evaluate the outcomes of these management strategies (Dodd et al., 2001). By taking these three aspects into consideration, symptoms can be effectively managed to prevent or delay further negative outcomes. The model also can be used to examine symptoms, such as fatigue and depression, that often occur in a cluster and can be generalized for use in all diseases (Dodd et al.).

The model is placed in the context of the nursing domains of person, environment, and health and illness. The person domain includes demographic, psychological, sociological, and physiological variables that can influence how an individual reacts to and manages his or her symptoms. The health and illness domain takes into account health history, disabilities, risk factors, and injuries. The environment domain examines the physical, social, and cultural variables that might impact the symptom experience (Dodd et al., 2001).

The three elements of the Symptom Management Model are (a) symptom experience, (b) components of symptom-management strategies, and (c) outcomes. In the realm of symptom experience, the clinician or researcher examines, from the perspective of the patient and his or her support system, how the symptom is perceived, how life-threatening or limiting the symptom is viewed to be, and how the patient and his or her support system respond to the symptom. The component of symptom management includes the person who manages the symptom, how and where the symptom is managed, and the recipient of the intervention. When examining the outcomes of symptom management, one determines costs that may be incurred as well as the effect of management strategies on functional status, emotional status, mortality, morbidity, quality of life, and ability for self-care. Outcomes lead back to the symptom experience as management strategies are revised as needed. The model also takes into account the fact that symptom-management strategies fail when it is difficult for the individual to adhere to them (Dodd et al., 2001).

This model can provide a useful framework for examining how fatigue in the population or the individual with MS is experienced and managed. For example, a nurse caring for a patient experiencing fatigue would first examine the impact of the fatigue on the patient and his or her support network. The nurse, with the help of the patient and his or her support system, would then develop specific strategies for ameliorating the fatigue. Finally, the nurse would evaluate whether the strategies were effective and modify them as needed. The Symptom Management Model can be used to examine a constellation of related symptoms simultaneously (Dodd et al., 2001). This is particularly useful for MS because fatigue is often interrelated with other MS symptoms, such as depression, exercise intolerance, and cognitive difficulties (Crayton et al., 2004).

Summary

Fatigue is a common symptom for people with MS. It can severely impact their health-related quality of life, including their ability to work. It is important that healthcare practitioners be proactive in treating this symptom, as it can lead to the worsening of other MS symptoms. Nurses can play an important part on the treatment team by taking the time to assess patients' fatigue and related symptoms, developing treatment strategies with the patient and his or her support system, and assessing and modifying these strategies as needed. Although a variety of treatment options are available for MS-related fatigue, no single option has emerged as the best. Therefore, further research on the treatment and management of this symptom in the MS population is needed.

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