

# Relationship of Fatigue to Heat Sensitivity in Patients With Multiple Sclerosis: A Review for Management

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## ABSTRACT

Multiple sclerosis (MS) is a disabling progressive neurologic disorder in which fatigue is recognized as a significant symptom. However, an often self-reported complaint of patients with MS is heat sensitivity. A literature search was conducted to determine if there was a relationship between these 2 symptoms in patients with MS. The search yielded 10 studies published since 2006, all indicating a positive relationship between fatigue and heat sensitivity. Because fatigue and heat sensitivity are not routinely grouped together, the information in this article will provide recent evidence for nurse practitioners in the management of both fatigue and heat sensitivity in patients with MS.

**Keywords:** fatigue, heat sensitivity, management, multiple sclerosis, Uhthoff's phenomenon

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Multiple sclerosis (MS) is a significant health problem in the United States, affecting 2.1 million people worldwide.<sup>1</sup> As health care providers with advanced knowledge in disease pathology, diagnosis, and management, nurse practitioners (NPs) may be involved in the care of patients with MS. The pathophysiology of MS results in a disruption or loss of axonal myelin in the central nervous system, leading to the formation of scar tissue (sclerosis). Common clinical features of MS include fatigue; motor, sensory, cognitive, mood, and vision impairment; and sphincter dysfunction.<sup>2,3</sup> In caring for patients with MS, NPs are cognizant of these common features but may not be aware that many patients with MS often experience another challenging symptom known as heat sensitivity. In addition, NPs may not know that there is often an association between the common symptom of fatigue and heat sensitivity.<sup>4</sup> In particular, several complex environmental factors can be involved with worsening MS, including overheating caused by outdoor temperatures or overexertion.<sup>5</sup> Recent evidence

shows that patients with MS cannot regulate their body temperature, and even the slightest rise in temperature can cause a relapse in symptoms.<sup>6,7</sup>

Fatigue, defined by the Consortium of Multiple Sclerosis Centers guidelines as “a subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual and desired activities,”<sup>8(p2)</sup> can be a complex symptom. It is important for NPs to recognize that patients with MS are vulnerable to experiencing fatigue-related heat sensitivity even before heat or temperature elevations occur. There is evidence to suggest that even temperature elevations that are relatively small (0.5°C) have been recognized as a trigger of MS-related fatigue (ie, Uhthoff's phenomenon). Despite evidence of the problems patients with MS experience with thermoregulation, the management of heat sensitivity in patients with MS remains difficult because of the varied clinical signs and symptoms that occur over the illness trajectory.<sup>5,9</sup> The Consortium of Multiple Sclerosis Centers guidelines<sup>8</sup> recommend strategies to manage fatigue, including the avoidance

of overheating. The purpose of this article is to discuss the recent evidence of the relationship of both fatigue and heat sensitivity, which can impact the care of patients with MS in the primary care setting.

## BACKGROUND AND SIGNIFICANCE

The simplest possible model for MS posits that the only defect present is the loss of myelin. Demyelination is associated with corresponding changes in axonal physiology, including a loss of effective management of temperature. Immune responses in patients with MS are skewed toward a pro-inflammatory state, resulting in inflammation, demyelination, and, ultimately, loss of axons and disorganization within the central nervous system. The injury to neurons leaves patients vulnerable to heat sensitivity, defined as Uhthoff's phenomenon.

Uhthoff's phenomenon, which consists of visual disturbances during or after the elevation of body temperature, is a reflection of impaired myelin that functions inadequately regarding the transmission of electrical impulses.<sup>10</sup> Typically, the phenomenon is seen only in MS or other demyelinating disorders that mimic MS (demyelinating optic neuritis and vision loss in sarcoidosis).<sup>9,11,12</sup> Similarly, injury to the myelin sheath leading to Uhthoff's phenomenon also causes another MS symptom—fatigue.

Fatigue, which is a common symptom seen in the majority of patients with MS,<sup>2,13,14</sup> is exacerbated with increases in temperature. The pathological mechanism for this intensified fatigue is poorly understood but likely results from axonal damage through demyelination of nerve fibers with subsequent impulse conduction blockage.<sup>5,9</sup> Slight temperature increases may block action potentials in demyelinated nerves<sup>9</sup> and lead to relapse-type presentation. The exacerbation of fatigue and heat may precipitate other symptoms, such as numbness and cognitive deficits. Likewise, vision impairment, such as optic neuritis, may be experienced by the patient with MS. Bowel and bladder problems, which include both diarrhea and constipation, can be heightened.

Because fatigue is a primary symptom of MS, this article supports the need to discuss fatigue's relationship to heat sensitivity in patients with MS. Both fatigue and heat sensitivity are multifactorial in that they may be caused by the pathology of MS (eg, demyelination), the

exposure to heat, and unknown cell-mediated and/or immune factors. These studies highlight the significance of reviewing current evidence on both fatigue and heat sensitivity, which is expected to guide practice for NPs caring for patients with MS.

## METHODS

The literature from 2006 to 2017 was searched using the following keywords: *multiple sclerosis, body temperature regulation, cooling, thermoregulation, fatigue, and heat*. The databases searched included CINAHL, PubMed, PsycINFO, and the Cochrane Library. Our method was guided by Cooper et al's integrative review,<sup>15</sup> with stages of defining the purpose, problem, and question to be disclosed in the review. Review articles primarily discussed heat and the pathophysiology of MS and, thus, were excluded. An ancestry review from the references of other articles was also conducted. Quality studies with higher levels of evidence, including randomized controlled trials, cohort studies, and case-control articles, that discussed both fatigue and heat sensitivity were sought. Review articles were excluded. No systematic reviews and meta-analyses were found that discussed both fatigue and heat sensitivity. Results were limited to English and human studies, which included those with both fatigue and heat sensitivity. A total of 10 articles that were relevant and of sufficient quality were used for discussion once saturation was obtained<sup>15</sup> (Table, available online at <http://www.npjjournal.org/>).

## RESULTS

### Characteristics of the Studies

The 10 studies included in this review are summarized in the Table. Six of the 10 studies used both patient self-report of fatigue (the Fatigue Severity Scale and the Modified Fatigue Inventory Scale) and objective measures of heat sensitivity. All 10 studies concluded that fatigue was significantly influenced by heat in patients with MS compared with healthy controls.

### Findings

**Studies Using Self-report Measures of Fatigue and Heat Sensitivity.** Two Swedish descriptive cross-sectional studies explored whether fatigue and

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