REVIEW ARTICLE

Fatigue Associated With Stroke and Other Neurologic Conditions: Implications for Stroke Rehabilitation

Marleen H. de Groot, MSc, Stephen J. Phillips, MB, Gail A. Eskes, PhD

ABSTRACT. de Groot MH, Phillips SJ, Eskes GA. Fatigue associated with stroke and neurologic conditions: implications for stroke rehabilitation. Arch Phys Med Rehabil 2003;84: 1714-20.

Objectives: To examine the general phenomenon of fatigue in stroke and other neurologic disorders and to review what is currently known about its occurrence, including its frequency, duration, severity, and associated factors, to develop a strategy for treatment.

Data Sources: Computerized databases (eg, PubMed, PsycInfo, Science Citation Index, Ovid EMBASE, Ovid MEDLINE) searched from inception to May 2002. Additional references were identified from bibliographies of pertinent articles and books.

Study Selection: Over 1000 articles were identified as relevant to fatigue experienced by patients with neurologic or nonneurologic disorders. Articles on fatigue in stroke and neurologic disorders, mechanisms, and/or treatment were selected for inclusion.

Data Extraction: Authors reviewed the articles and assessed the purpose, study design, and conclusions for validity and relevance to the topic of fatigue in stroke.

Data Synthesis: Fatigue is a common complaint among patients with neurologic disorders including stroke. Few studies have documented the high frequency of fatigue in poststroke patients and its negative impact on daily functioning and quality of life. Little is known about associated factors or about therapeutic strategies that may be used to alleviate it. Examination of fatigue in other neurologic populations suggests common characteristics and associated factors that may be useful in the development of potential therapeutic strategies. Pharmacologic and nonpharmacologic therapeutic interventions, such as stimulants, amantadine, or sleep and stress-management education, have been used with some success in neurologic and other patient populations (eg, multiple sclerosis, human immunodeficiency virus, acquired immune deficiency syndrome, cancer), but evidence of effectiveness based on randomized clinical trials is rare.

Conclusions: Poststroke fatigue is common. Therapeutic strategies have been used to treat fatigue in other patient populations, but it is unclear whether these will be beneficial to poststroke patients. Frequency, severity, duration, impact, predisposing factors, and causes of poststroke fatigue, as well as the development of effective treatment, require further research. Criteria for assessment of fatigue and potential therapeutic interventions are outlined as a first step for stimulating further research.

Key Words: Cerebrovascular disorders; Fatigue; Neurologic disorders; Quality of life; Recovery of function; Rehabilitation; Review [publication type].

FOR COUNTLESS PEOPLE suffering from diverse neurologic disorders, fatigue plays an overwhelming role.[1] Often accepted and endured as part of the disease process, fatigue appears to be a ubiquitous symptom and a common complaint among patients with chronic neurologic problems. It may well be because of its universal occurrence, vague or subjective definition, and largely undetermined cause that fatigue remains an underdiagnosed and undertreated symptom.

Research has focused on fatigue as it occurs in such varied neurologic disorders as multiple sclerosis[2-8] (MS); head or brain injury,[9-15] Parkinson's disease,[4,16-20] and postpolio syndrome.[4,21-23] More recently, a few studies have examined fatigue after stroke[24-29] (for reviews, see Staub and Bogousslavsky[30,31] and Michael[32]). The studies in stroke have revealed that fatigue is a prevalent symptom that can occur independently of poststroke depression and can persist for long periods of time after the stroke has occurred.

The relevance of fatigue to poststroke rehabilitation and recovery of function has not yet been examined. Discussion of this issue is important, because fatigue is potentially detrimental to physical and psychologic recovery after stroke. Fatigue poses one of the greatest barriers to rehabilitation and has negative impact on quality of life[32] (QOL). For these reasons, a review of what is currently known about the phenomenon of fatigue after stroke, in addition to other neurologic disorders, appears warranted to begin to identify possible causes, associated factors, methods of assessment, and potential interventions.

METHODS

Data Sources

Computerized databases including PubMed, PsycInfo, Science Citation Index, Ovid EMBASE, and Ovid MEDLINE were searched from inception to May 2002 for articles on fatigue in patients with neurologic disorders by using key words such as *fatigue*, *stroke*, *MS*, *brain injury*, or *fatigue* and *treatment*. References were also identified from bibliographies of pertinent articles and books. More than 1000 articles were initially identified as relevant.

Study Selection

Articles specific to fatigue in neurologic disorders, its mechanisms, and its treatment were selected for detailed review.

From the Departments of Psychology (de Groot, Eskes), Medicine (Neurology) (Phillips, Eskes), and Psychiatry (Eskes), Dalhousie University, Halifax, NS, Canada.

Supported by the Canadian Institutes of Health Research and Natural Sciences and Engineering Research Council of Canada (grant no. A0305) and by the Nova Scotia Health Research Foundation (infrastructure grant).

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the author(s) or upon any organization with which the author(s) is/are associated.

Reprint requests to Gail Eskes, PhD, Dept of Psychiatry, Dalhousie University, Rm 9216 AJLB, 5909 Veterans Memorial Ln, Halifax, NS B3H 2E2, Canada, e-mail: *gail.eskes@dal.ca.*

0003-9993/03/8411-7215$30.00/0
doi:10.1053/S0003-9993(03)00346-0

Data Extraction and Synthesis

We reviewed the articles and assessed the purpose, study design, and conclusions for validity and relevance to the topic of fatigue in stroke and other neurologic disorders. All articles on fatigue in stroke patients were included in this review. Relevant articles on frequency of fatigue, its characteristics, correlated factors, and treatment in other neurologic disorders (MS, brain injury, Parkinson's disease, postpolio syndrome) were also examined. Most of the information on fatigue mechanisms and treatment stems from work on patients with cancer or human immunodeficiency virus or acquired immune deficiency syndrome (AIDS); therefore, information from these domains was included when relevant to stroke.

Defining Fatigue

It is generally accepted that "normal" fatigue is a state of general tiredness that is the result of overexertion and can be ameliorated by rest. In contrast, "pathologic" fatigue is a state characterized by weariness unrelated to previous exertion levels and is usually not ameliorated by rest.[33] These 2 types of fatigue can be further distinguished by their onset and time course.[33,34] Normal fatigue is more acute, with a rapid onset and shorter duration. It is thought of as protective, restorative, and likely because of a single, readily identifiable cause. Pathologic fatigue is chronic in nature, likely has multiple or unknown causes, and is perceived to be abnormal or excessive. For the purposes of this review, fatigue was defined as a feeling of physical tiredness and lack of energy that was described as pathologic, abnormal, excessive, chronic, persistent, or problematic.

Poststroke Fatigue

Frequency and duration. Fatigue is a common complaint after stroke.[30-32] Using interviews or mailed questionnaires, 4 recent studies[24-26,28] examined fatigue as an independent phenomenon and found that the frequency of occurrence can range from 30% to 68% of stroke survivors. In the first systematic study of poststroke fatigue, Ingles et al[24] found that 68% of 88 respondents at 3 to 13 months poststroke reported fatigue problems, as measured by the Fatigue Impact Scale (FIS), compared with only 36% of 56 elderly control subjects ($P<.001$). In addition, when asked if they felt full of energy on a depression rating scale, 78% of the stroke group answered no, compared with 51% of control subjects ($P<.001$). In a second study, van der Werf et al[25] mailed questionnaires to persons at a median time of 2 years after stroke. Van der Werf reported that 50% (45/90) of stroke respondents answered yes when they were asked if fatigue was their main complaint, but only 16% (8/50) of control subjects answered yes ($P<.01$). Fifty-one percent of the stroke group also had elevated scores on the Checklist Individual Strength (CIS) fatigue subscale, whereas the scores of only 12% of the control subjects were elevated ($P<.01$). A larger study[28] assessed the prevalence of fatigue independent of depression approximately 30 months poststroke by a mail-out questionnaire. Of the 3667 patients who returned the questionnaire and did not report chronic depression, 39.2% reported moderate to severe fatigue in answer to the question, "Do you feel tired?" Another study[26] of fatigue after stroke published in abstract form reported that 30% of 43 poststroke patients reported problems with "early exhaustion after physical or mental activity, weariness and aversion to effort."

Other studies have reported fatigue within the context of a poststroke syndrome,[35-37] as a symptom of poststroke depression,[38-40] or in relation to cognitive impairments.[41] One study,[36] of psychosocial functioning of 50 individuals poststroke, reported general tiredness in a large number of respondents at 3 months (54%), 1 year (44%), 2 years (42%), and 3 years (44%) poststroke, compared with 38% with general tiredness prestroke. Fatigue was also frequently endorsed as one of several diffuse symptoms at 6 to 26 months after cerebral (75%, n=44) and myocardial (70%, n=40) infarction.[35] In an investigation of cognitive functioning 6 to 45 months after a single supratentorial lacunar infarct, 38% of 16 patients reported changes in fatigue levels after the infarct, compared with 12% (2/16) of matched healthy controls.[41] In addition, the frequency of possible, definite, or marked fatigue associated with depression was 67% among 97 individuals who were 7 years poststroke.[40] Complaints of fatigue also were reported in studies of subarachnoid hemorrhage[29] (SAH) and can continue up to 4 to 7 years after insult.[27]

Severity and functional implications. Little is known about fatigue severity and the overall impact that it has on poststroke recovery and return to activities of daily living (ADLs). Ingles[24] reported that 40% of stroke patients rated it as either their worst symptom or among their worst symptoms. Overall, when fatigue was present (ie, in 60/88 stroke patients, in 20/56 control subjects), it was experienced more frequently in the poststroke group than in the control group ($P<.05$), and 27% of stroke respondents experienced fatigue every day. Furthermore, stroke survivors who reported fatigue attributed more functional limitations to it in both physical and psychosocial (but not cognitive) domains than did control subjects with fatigue.

In the long-term follow-up population study by Glader et al,[28] fatigue independently predicted decreased functional independence, institutionalization, and mortality, even after adjusting for age. Glader, suggested, however, that the relationship between fatigue and these outcome measures is likely not unidirectional—that is, impairments after stroke likely contribute to fatigue, which, in turn, contributes to impairment. Similarly, fatigue was found to correlate significantly with measures of functional disability and neuropsychologic problems in a study by van der Werf.[25]

Interestingly, stroke survivors with less severe physical or cognitive disability after stroke tend to rate fatigue as a more severe symptom.[24,31,41] There is also anecdotal evidence to suggest that fatigue is more prevalent in younger than in older poststroke patients (but see Glader[28]). There may be several reasons for this. First, it may be that the relative lack of other sequelae makes fatigue a more salient poststroke symptom. Second, it may be that the expectation for things to return to normal is greater for patients with more subtle poststroke disabilities. It may also be the case that, for younger poststroke patients, the demands of daily life are qualitatively different from those for older poststroke patients, making fatigue more of an obstacle to accomplishing the tasks required of them.

Factors associated with poststroke fatigue. There are few identified predictors of poststroke fatigue, although the available evidence is currently limited. Glader[28] found that older women were most likely to report fatigue, but other studies[24,25] have found no association between fatigue and demographic variables. Other factors present before stroke that were associated with poststroke fatigue included living alone or in an institution, impairment in ADLs and previous stroke.[28] Self-reported fatigue 2 years poststroke was associated with poor general health, anxiety, pain, and depression.[25,28] In some studies,[24,26,31] however, fatigue was independent of depression. For example, Ingles[24] found that, although the frequency of depression (defined as a score of ≥ 11 on the Geriatric Depression Scale) was higher in poststroke patients than in controls, it occurred independently of fatigue in 39% of 88 subjects. Ad-

ditionally, only 4 of 123 patients with SAH reported new-onset clinical depression, which indicates that depression in these patients was an unlikely explanation for the presence of elevated fatigue.[27]

The occurrence of fatigue or increased fatigue severity, duration, and frequency in poststroke patients was not associated with several stroke-related variables, including time since the stroke occurred[24-26,31] or type or severity of stroke.[24,28] Although side of lesion (right hemisphere, left hemisphere) did not seem to be related to reports of fatigue,[24,26,31] a small group study[26] published in abstract form reported that it was found mainly in patients with brainstem infarct (6/11), less often in patients with subcortical infarct (6/16), and rarely in patients with cortical infarct (1/16). Given the limited sample size, however, further study is needed to replicate these findings.

Fatigue in Patients With Other Neurologic Disorders

Patients with neurologic disorders other than stroke also complain of problems with acute and/or chronic fatigue, and comparisons between these groups and stroke suggest some potential common features that deserve investigation.[4,42] Groups included in this review are patients with MS, brain injury, Parkinson's disease, and postpolio syndrome.

Multiple sclerosis. Fatigue is reported by a large number of patients with MS (≈70%), and for approximately one third of patients (33%–40%) fatigue is described as problematic or severe.[2,4-6,8] It is often associated with, or precedes, other symptoms.[8] It is frequently present even at rest and is usually not ameliorated by rest.[8] Fatigue has both physical and cognitive impact, because patients often report that the effort required to perform both mental and physical tasks is disproportionately high.[4,7] Despite the large amount of descriptive information gathered to date on patients with MS, the associated factors and/or underlying mechanisms of fatigue in this patient population appear elusive. Fatigue in patients with MS can be worsened by stress and by increases in temperature,[8] but it does not appear to correlate with age, neurologic impairment, or sleep disturbances.[4,8]

Brain injury. Studies looking at outcomes after traumatic brain injury have found that significant numbers of patients experience fatigue after their injury and that it is not necessarily related to severity of injury.[10] In 1 study,[15] 70% of patients (449/639) with minor head injury endorsed it as a symptom on assessment at 2 weeks postinjury. A subset of patients with more severe symptoms was asked to return at 6 weeks postinjury for follow-up, and 84% (151/179) who returned reported it at this time as well. One study[14] compared a heterogeneous group of 30 patients with brain injury (due to both traumatic and neurologic insult), an average of 44.3 months postinjury, to an age and sex-matched healthy control group on 3 separate fatigue scales (visual analog scale for fatigue, Fatigue Severity Scale [FSS], FIS), as well as an objective measure (thumb pressing). Results of all measures supported the hypothesis that patients with brain injury experience significantly more fatigue than healthy control subjects. Fifty percent of patients in this study also rated fatigue as their worst symptom or among their worst symptoms,[14] similar to ratings obtained in stroke by Ingles et al.[24]

As with stroke patients, fatigue appears to remain an issue for long periods of time postinjury in the brain injury population. It was among the top 6 complaints endorsed on a checklist by 67 patients at 1 month (57% reported fatigue), at 3 months (61%), and at 6 and 12 months (45%) postinjury.[10] A chronic presentation was also supported by another study showing that fatigue remained a problem for approximately 70% of patients 2 to 5 years postinjury,[11] even with mild, moderate, or severe head injury, as determined by Glasgow Coma Scale scores.[9,12]

It has been suggested that fatigue in patients with brain injury results from common difficulties initiating or maintaining sleep.[13] One study[13] looking at sleep disturbance 1 year after injury in 86 patients reported that, overall, 63% had significant problems with fatigue. Half also reported some type of problem with sleep, which was associated with significant fatigue during the day in a majority (80%) of subjects. Objective laboratory investigations of sleep complaints after brain injury are needed to support these observations.

Parkinson's disease. About 40% of patients with Parkinson's disease report fatigue among their main symptoms.[4] Schenkman et al[17] reported that 44% of 70 patients reported it when surveyed about their symptoms, although the term was not defined explicitly. In a study designed to investigate its relationship with other symptoms, 44% (103/233) of patients, compared with 18% (18/100) of healthy elderly controls, were found to be fatigued on the Nottingham Health Profile.[16] When patients with depression, dementia, or sleep disturbances were excluded, fatigue reports were still significantly higher in the patient group (43.5% or 20/46) than in the control group (4.5% or 3/66), which indicates that, although depression and cognitive impairment co-occurred with fatigue in some patients, these factors did not account for all fatigue experienced.[16] A similar percentage of patients with Parkinson's without dementia, who scored 25 or more on the Folstein Mini-Mental State Examination, were found to have elevated scores on the FSS (40% or 40/99) when assessed for the presence of nonmotor symptoms of Parkinson's.[18] As with stroke and MS, fatigue may be manifested in both mental and physical domains in Parkinson's disease.[19] Lou et al[19] found that patients with Parkinson's disease (n=39) scored significantly higher on the Multidimensional Fatigue Inventory, and on each of its 5 subscales, than the age-matched normal control group (n=32). In addition, although patients showed elevated levels of both mental and physical fatigue, these 2 types of fatigue appeared to be independent phenomena.[19]

Not surprisingly, fatigue tends to be chronic in Parkinson's disease. One longitudinal study[20] showed the persistence of fatigue for more than 9 years on the Fatigue Assessment Instrument. Collectively, the findings of studies on fatigue in Parkinson's disease point to its pervasive and persistent nature in this patient population.

Postpolio syndrome. Approximately 25% to 40% of survivors of polio develop postpolio syndrome,[4] which comprises several musculoskeletal complaints, with fatigue being the most commonly reported symptom.[4,21,22] Although abnormalities in the peripheral nervous system (at the neuromuscular junction or within the muscle fibers themselves) have been implicated in the generation of the neuromuscular fatigue exhibited by these patients,[23] central neurologic abnormalities caused by polioencephalitic damage are thought to be responsible for the generalized fatigue these patients report.[4,21,22]

Summary of Fatigue in Stroke and Neurologic Disorders

Fatigue among patients with neurologic disorders such as MS, brain injury, Parkinson's disease, postpolio syndrome, and stroke shares a number of characteristics.[24-26] It can exist independently of depression—although it also can accompany depression and may be exacerbated by it—and is typically chronic and pervasive. When present, fatigue is often described as among the worst symptoms of the disorder or injury. The severity of fatigue is not necessarily related to age, gender, severity of brain injury, or to the amount of disability. It seems reasonable, therefore, that at least some of the underlying

Table 1: Factors Contributing to Poststroke Fatigue

Physiologic factors
Altered nutritional status
Malnutrition
Hypovolemia/dehydration
Biochemical abnormalities
Electrolyte imbalance
Hypoglycemia
Systemic states or disorders
Hypothyroidism
Infection/fever
Anemia
Renal failure
Diabetes
Chronic pain
Congestive heart failure
Inflammatory disorders
Medication side effects
Hypnotics/tranquilizers
Anticonvulsants
Corticosteroids
Antihypertensives
Antihistamines
Opiates
β-blockers
Sleep disorders
Chronic sleep disturbance because of
Hospitalization
Pain/discomfort
Illness-related stress
Sleep apnea or other sleep-disordered breathing
Hypersomnia/insomnia
Immobility/inactivity
Disuse
Physical deconditioning
Excessive rest
Physical impairment
Psychologic factors
Levels of perceived effort
Perceived increase in:
Mental effort or strain
Physical effort or strain
Illness-related stress
Stressors:
Neurologic, physical, and/or cognitive impairment
Stroke as a chronic disease
Life-altering effects of stroke
Comorbid mood disorders
Anxiety disorder
Depression or other mood disorder
Stress-related disorder

mechanism(s) of fatigue may be similar in these neurologic disorders. It also seems reasonable to expect that the fatigue associated with these disorders may respond to similar treatments.

Assessment and Treatment of Poststroke Fatigue

A myriad of factors may predispose to fatigue (table 1), and, consequently, assessment and treatment is challenging. Given the paucity of our knowledge of the mechanisms of fatigue, aiming treatment toward predisposing factors is likely to be of most benefit. A multidisciplinary approach toward the assessment and treatment of these factors in the rehabilitation setting is presented below and summarized in table 2 and figure 1.

Assessment. The first step in treatment of fatigue should consist of a physical examination with a thorough evaluation of its history and characteristics. This evaluation would have 2 goals: (1) to ascertain whether the fatigue is normal or pathologic and (2) to identify possible predisposing factors. Although there is no accepted definition of abnormal fatigue in stroke, we suggest a set of criteria (table 2) that is modified from those determined for cancer-related fatigue[43,44] and that includes items from previous definitions and descriptions used for stroke-related fatigue.[24,31] For the purposes of assessment, characteristics to be noted should include onset, duration, severity, daily pattern, any factors that increase or decrease fatigue, and associated impact on daily living. Objective assessment tools used to investigate fatigue in stroke have included the FIS[24] and the CIS.[25] These scales could be used to quantify fatigue characteristics for initial diagnosis and to monitor the outcome of treatment. Scales or measures used in the study of fatigue in other patient populations may also prove useful for application to poststroke fatigue, although these have not yet been used in poststroke patients specifically.[32,34]

Medical and pharmacologic treatment. Many physiologic or biochemical parameters, when disrupted, can result in fatigue—for example, malnutrition, hypovolemia and dehydration, hypoglycemia, hypomagnesemia, hypophosphatemia, hypocalcemia, or hypokalemia (see table 1).[43-47] Common endocrine disturbances (eg, hypothyroidism, diabetes), as well as comorbid medical conditions (eg, renal failure, congestive heart failure, anemia, infections, chronic inflammatory disorders) have all been associated with it.[1,45,47,48] Fatigue has also been attributed to chronic pain.[43,44] A number of medications used in the stroke population, including hypnotics, anticonvulsants, corticosteroids, antihypertensives, antihistamines, opiates, and β-blockers, can also lead to fatigue (as reviewed in Swain[1] and Soucy[49]). Initial treatment should, therefore, focus on identification and optimum management of these potential factors associated with fatigue, which are common in the aging stroke population. Consultation with a clinical dietitian can provide nutritional assessment and interventions that may allow patients to maintain energy levels and alleviate feelings of fatigue because of inadequate dietary intake.[50] Chronic pain or discomfort, both of which can contribute to, or exacerbate, fatigue, can be treated with analgesics.[1] Additionally, an evaluation of current medications is warranted, and those medications that have fatigue as a side effect should be reduced or eliminated if possible.[44]

Patients should be screened for depression, because antidepressants such as fluoxetine and other selective serotonin reuptake inhibitors can sometimes reduce fatigue levels.[1,8,44,51] Antidepressants with stimulatory properties, such as bupropion, may be more successful in treating fatigue directly.[51,52] These medications should be used with caution, however, and only in appropriately diagnosed patients, because the effects of antidepressants on poststroke fatigue in patients without poststroke depression have yet to be determined.

Although the number of randomized control studies is few, various other pharmacologic interventions, including stimulants and amantadine, have been used with some success to treat fatigue in other patient populations (eg, postpolio syndrome, MS).[3,4,8,44] Recently, modafinil (Provigil), a wakefulness-promoting psychostimulant used in the treatment of narcolepsy, has been used with some success to alleviate fatigue in MS patients[53] and patients with other neurologic disorders including stroke.[42] A detailed review of this literature is beyond the scope of this article, but a list of these drugs is presented in

Table 2: Proposed Criteria for Poststroke Fatigue

The following symptoms should be present every day or nearly every day during a 2-week period in the past month:
Significant fatigue (defined as overwhelming feelings of exhaustion or tiredness), diminished energy or increased need to rest, disproportionate to any recent exertion levels, plus any 3 of the following:
Experience of sleep or rest as unrefreshing or nonrestorative
Disrupted balance between motivation (preserved) and effectiveness (decreased)
Perceived need to struggle to overcome inactivity
Difficulty completing or sustaining daily tasks attributed to feeling fatigued
Postexertional malaise lasting several hours
Marked concern about feeling fatigued

NOTE. Modified from Cella et al[43] and Portenoy and Itri.[44]

figure 1. Controlled trials need to be performed to determine whether these agents benefit patients with poststroke fatigue.

There are several lines of evidence that suggest sleep can be fundamentally disrupted in stroke patients.[31,54,55] These disruptions can take the form of hypersomnia, insomnia, or sleep-disordered breathing. Patterns, quantity, and quality of sleep should be investigated in cases in which a patient presents with fatigue. Polysomnographic assessment and treatment of existing sleep disorders, such as sleep apnea or other forms of sleep-disordered breathing, may be beneficial, particularly given the reported common association between sleep apnea and stroke.[8,43,44,54-56] In other cases, use of nocturnal hypnotic treatments could be advised.[1]

Nonpharmacologic treatment. Work on improving sleep-hygiene parameters and minimizing sleep disturbances could prove beneficial in alleviating fatigue. Some patients have found that the scheduling of regular naps or rest periods can be of help.[43,46] For some people, napping is a concept associated with negative images of aging, weakness, and illness. Changing these conceptualizations and replacing them with images of rejuvenation and refueling may convince even the most skeptical patients to use napping as a fatigue management strategy. Patients should be cautioned, however, regarding the potential deleterious effects of excessive rest and inactivity.

Decreased mobility or inactivity is often a part of the response to the global illness or stroke-induced sensorimotor

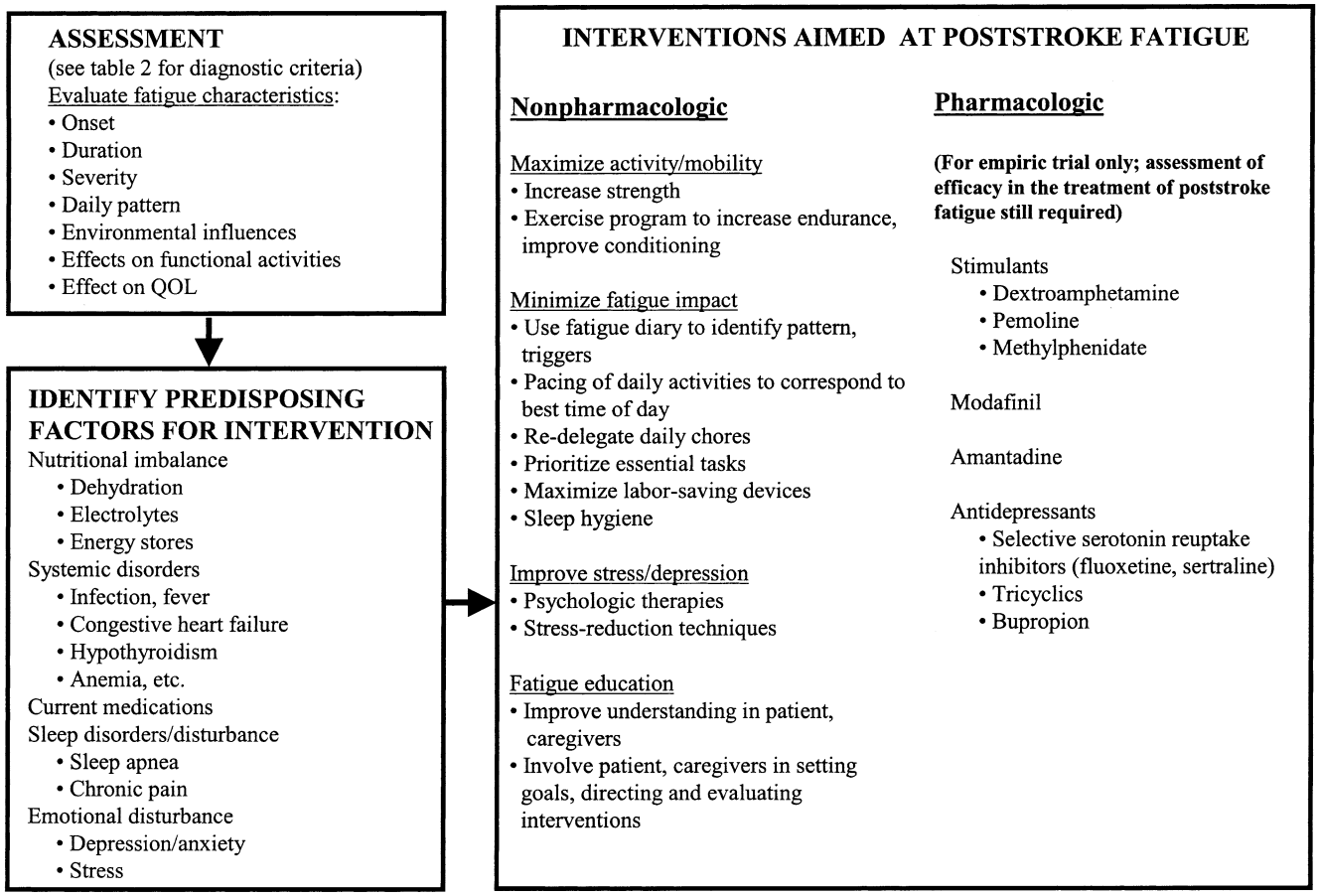

Fig 1. Assessment and intervention for poststroke fatigue.

impairment and imbalance. This inactivity can then lead to increased fatigability and further physical deconditioning.[57,58] Additionally, patients presenting with fatigue are often told to take it easy and to rest by family and caregivers.[58] To reduce fatigue, patients themselves will often avoid fatiguing activities.[47,59] Thus, the appropriate balance between rest and activity is not achieved. Although it may at first seem counterintuitive to patients, exercise has been shown to be an important treatment for fatigue in MS and could be applied to stroke.[8,60] Assessment of physical abilities and development of an exercise program with physiotherapists to ensure maximal benefit with minimal deleterious effects of overexertion can be tailored to each patient. Increased physical activity, no matter how slight, can prove beneficial in combating the self-perpetuating cycle of inactivity, deconditioning, and fatigue.[8,23,44,46]

Several strategies can be adopted by occupational therapists to minimize the impact of fatigue on QOL parameters and tasks of daily living.[1,43-45,61] It may be beneficial for both the patient and the caregiver(s) to keep a diary detailing the experience of fatigue and its characteristics. This information could then be used to identify triggers and patterns of occurrence. Patients experiencing problems with fatigue should be encouraged to restructure the timing of daily activities so to minimize its deleterious effects.[32] Depending on the daily patterns of fatigue, activities requiring the most effort should be scheduled at a time when it is at its lowest, and rest should be scheduled at those times when the likelihood of fatigue is high. Delegating daily chores or other required tasks to other family members or caregivers so that less of a burden falls on the patient may be a necessary step in circumventing the negative effects of fatigue. The use of labor-saving devices can also be helpful, as can the postponing of nonessential tasks.

The stress related to the life-altering effects and/or chronic disability of a stroke may well be overwhelming and could easily be considered a significant contributing factor.[1,31] Psychologic interventions by mental health professionals, such as cognitive behavior therapy, group therapy, or stress management techniques, have been used to treat fatigue in several patient populations.[46,62] In addition to this, patients can be taught stress reduction or relaxation techniques.[44] Other techniques, such as hypnosis, guided imagery, or distraction, may also prove beneficial in reducing fatigue by reducing stress.[44]

Patient education regarding fatigue after stroke should be made available for patients, caregivers, and family.[32] This information could include how to recognize abnormal fatigue and possible reasons for experiencing it, the likelihood of a problem, its potential impact on daily living, and suggestions regarding different fatigue management strategies that may prove beneficial. Education about fatigue has been tried with, and continues to be recommended for, patients exhibiting cancer- and AIDS-related fatigue,[23,43-45,61] however, educational efforts should be tailored to the stroke patient population. It is important that the patient is made aware that it is a real and not imagined symptom. Recognition by the patient, caregivers, and family members that it is a genuine symptom of disease can be crucial to the psychologic well-being of the patient.[4,8] It also ensures that the patient does not feel as if fatigue is simply to be endured, but that strategies may, in fact, reduce or alleviate it.[45]

CONCLUSIONS

Poststroke fatigue is a real and complex phenomenon. Although a great number of factors contributing to fatigue have been identified, its underlying causes remain elusive. Additional research on poststroke fatigue is required in areas such as diagnosis, prevalence, severity, duration, and associated factors to better understand causal mechanisms and predisposing factors. The identification of effective therapeutic strategies for poststroke fatigue is also critical to optimize recovery and rehabilitation. The recognition of fatigue as a genuine poststroke disorder requiring assessment and treatment is the first step toward the development of a comprehensive therapeutic program to address the problem.

Acknowledgments: We thank Dr. G. Gubitz and the anonymous reviewers for their helpful feedback and suggestions on an earlier draft of the manuscript.

References

1. Swain MG. Fatigue in chronic disease. Clin Sci 2000;99:1-8.
2. Fisk JD, Pontefract A, Ritvo PG, Archibald CJ, Murray TJ. The impact of fatigue on patients with multiple sclerosis. Can J Neurol Sci 1994;21:9-14.
3. Krupp LB, Coyle PK, Doscher C, et al. Fatigue therapy in multiple sclerosis: results of a double-blind, randomized, parallel trial of amantadine, pemoline, and placebo. Neurology 1995;45:1956-61.
4. Krupp LB, Pollina DA. Mechanisms and management of fatigue in progressive neurological disorders. Curr Opin Neurol 1996;9: 456-60.
5. Vercoulen JH, Hommes OR, Swanink CM, 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;53:642-9.
6. van der Werf SP, Jongen PJ, Lycklama á Nijeholt GJ, Barkhof F, Hommes OR, Bleijenberg G. Fatigue in multiple sclerosis: interrelations between fatigue complaints, cerebral MRI abnormalities and neurological disability. J Neurol Sci 1998;160:164-70.
7. Krupp LB, Elkins LE. Fatigue and declines in cognitive functioning in multiple sclerosis. Neurology 2000;55:934-9.
8. Comi G, Leocani L, Rossi P, Colombo B. Physiopathology and treatment of fatigue in multiple sclerosis. J Neurol 2001;248: 174-9.
9. Masson F, Maurette P, Salmi LR, et al. Prevalence of impairments 5 years after a head injury, and their relationship with disabilities and outcome. Brain Inj 1996;10:487-97.
10. van der Naalt J, van Zomeren AH, Sluiter WJ, Minderhoud JM. One year outcome in mild to moderate head injury: the predictive value of acute injury characteristics related to complaints and return to work. J Neurol Neurosurg Psychiatry 1999;66:207-13.
11. Olver JH, Ponsford JL, Curran CA. Outcome following traumatic brain injury: a comparison between 2 and 5 years after injury. Brain Inj 1996;10:841-8.
12. Hillier SL, Sharpe MH, Metzer J. Outcomes 5 years post-traumatic brain injury (with further reference to neurophysical impairment and disability). Brain Inj 1997;11:661-75.
13. Clinchot DM, Bogner J, Mysiw WJ, Fugate L, Corrigan J. Defining sleep disturbance after brain injury. Am J Phys Med Rehabil 1998;77:291-5.
14. LaChapelle DL, Finlayson MA. An evaluation of subjective and objective measures of fatigue in patients with brain injury and healthy controls. Brain Inj 1998;12:649-59.
15. Haboubi NH, Long J, Koshy M, Ward AB. Short-term sequelae of minor head injury (6 years experience of minor head injury clinic). Disabil Rehabil 2001;23:635-8.
16. Karlsen K, Larsen JP, Tandberg E, Jorgensen K. Fatigue in patients with Parkinson's disease. Mov Disord 1999;14:237-41.
17. Schenkman M, Wei Zhu C, Cutson TM, Whetten-Goldstein K. Longitudinal evaluation of economic and physical impact of Parkinson's disease. Parkinsonism Relat Disord 2001;8:41-50.
18. Shulman LM, Taback RL, Bean J, Weiner WJ. Comorbidity of the nonmotor symptoms of Parkinson's disease. Mov Disord 2001; 16:507-10.
19. Lou JS, Kearns G, Oken B, Sexton G, Nutt J. Exacerbated physical fatigue and mental fatigue in Parkinson's disease. Mov Disord 2001;16:190-6.
20. Friedman JH, Friedman H. Fatigue in Parkinson's disease: a nine-year follow-up. Mov Disord 2001;16:1120-2.
21. Bruno RL, Cohen JM, Galski T, Frick NM. The neuroanatomy of post-polio fatigue. Arch Phys Med Rehabil 1994;75:498-504.

22. Bruno RL, Creange SJ, Frick NM. Parallels between post-polio fatigue and chronic fatigue syndrome: a common pathophysiology? Am J Med 1998;105:66S-73S.
23. Dalakas MC, Mock V, Hawkins MJ. Fatigue: definitions, mechanisms, and paradigms for study. Semin Oncol 1998;25(Suppl): 48-53.
24. Ingles JL, Eskes GA, Phillips SJ. Fatigue after stroke. Arch Phys Med Rehabil 1999;80:173-8.
25. van der Werf SP, van der Broek HL, Anten HW, Bleijenberg G. Experience of severe fatigue long after stroke and its relation to depressive symptoms and disease characteristics. Eur Neurol 2001;45:28-33.
26. Staub F, Annoni JM, Bogousslavsky J. Fatigue after stroke: a pilot study [abstract]. Cerebrovasc Dis 2000;10:62.
27. Ogden JA, Utley T, Mee EW. Neurological and psychosocial outcome 4 to 7 years after subarachnoid hemorrhage. Neurosurgery 1997;41:25-34.
28. Glader EL, Stegmayr B, Asplund K. Poststroke fatigue: a 2-year follow-up study of stroke patients in Sweden. Stroke 2002;33: 1327-33.
29. Eskesen V, Sorensen EB, Rosenorn J, Schmidt K. The prognosis in subarachnoid hemorrhage of unknown etiology. J Neurosurg 1984;61:1029-31.
30. Staub F, Bogousslavsky J. Post-stroke depression or fatigue? Eur Neurol 2001;45:3-5.
31. Staub F, Bogousslavsky J. Fatigue after stroke: a major but neglected issue. Cerebrovasc Dis 2001;12:75-81.
32. Michael K. Fatigue and stroke. Rehabil Nurs 2002;27:89-94, 103.
33. Piper BF. Fatigue: current bases for practice. In: Funk SG, Tornquist EM, Champagne MT, Archer Copp L, Weise RA, editors. Key aspects of comfort: management of pain, fatigue, nausea. New York: Springer; 1989. p 187-98.
34. Aaronson LS, Teel CS, Cassmeyer V, et al. Defining and measuring fatigue. Image J Nurs Scholarship 1999;31:45-50.
35. Leegaard OF. Diffuse cerebral symptoms in convalescents from cerebral infarction and myocardial infarction. Acta Neurol Scand 1983;67:348-55.
36. Åström M, Asplund K, Åström T. Psychosocial function and life satisfaction after stroke. Stroke 1992;23:527-31.
37. Kihara M, Nishikawa S, Nakasaka Y, Tanaka H, Takahashi M. Autonomic consequences of brainstem infarction. Auton Neurosci 2001;86:202-7.
38. Schubert DS, Taylor C, Lee S, Mentari A, Tamaklo W. Physical consequences of depression in the stroke patient. Gen Hosp Psychiatry 1992;14:69-76.
39. Ramasubbu R, Robinson RG, Flint AJ, Kosier T, Price TR. Functional impairment associated with acute poststroke depression: the Stroke Data Bank Study. J Neuropsychiatry Clin Neurosci 1998;10:26-33.
40. Dam H. Depression in stroke patients 7 years following stroke. Acta Psychiatr Scand 2001;103:287-93.
41. Van Zandvoort MJ, Kappelle LJ, Algra A, De Haan EH. Decreased capacity for mental effort after single supratentorial lacunar infarct may affect performance in everyday life. J Neurol Neurosurg Psychiatry 1998;65:697-702.
42. Cochran JW. Effect of modafinil on fatigue associated with neurological illnesses. J Chronic Fatigue Syndrome 2001;8:65-70.
43. Cella D, Peterman A, Passik S, Jacobsen P, Breitbart W. Progress toward guidelines for the management of fatigue. Oncology (Huntington) 1998;12:369-77.
44. Portenoy RK, Itri LM. Cancer-related fatigue: guidelines for evaluation and management. Oncologist 1999;4:1-10.
45. Groopman JE. Fatigue in cancer and HIV/AIDS. Oncology (Huntington) 1998;12:335-44.
46. Stone P, Richards M, Hardy J. Fatigue in patients with cancer. Eur J Cancer 1998;34:1670-6.
47. Barroso J. A review of fatigue in people with HIV infection. J Assoc Nurses AIDS Care 1999;10:42-9.
48. Murtagh JE. Making fatigue less tiresome. Med J Aust 1996;164: 580-1.
49. Soucy MD. Fatigue and depression: assessment in human immunodeficiency virus disease. Nurse Pract Forum 1997;8:121-5.
50. Kalman D, Villani LJ. Nutritional aspects of cancer-related fatigue. J Am Diet Assoc 1997;97:650-4.
51. Burks TF. New agents for the treatment of cancer-related fatigue. Cancer 2001;92:1714-8.
52. Valentine AD, Meyers CA. Cognitive and mood disturbance as causes and symptoms of fatigue in cancer patients. Cancer 2001; 92:1694-8.
53. Rammohan KW, Rosenberg JH, Lynn DJ, Blumenfeld AM, Pollak CP, Nagaraja HN. Efficacy and safety of modafinil (Provigil) for the treatment of fatigue in multiple sclerosis: a two centre phase 2 study. J Neurol Neurosurg Psychiatry 2002;72:179-83.
54. Parra O, Arboix A, Bechich S, et al. Time course of sleep-related breathing disorders in first-ever stroke or transient ischemic attack. Am J Respir Crit Care Med 2000;161:375-80.
55. Mohsenin V. Sleep-related breathing disorders and risk of stroke. Stroke 2001;32:1271-6.
56. Culebras A. Balancing sleep and breathing [comment]. Stroke 2001;32:1277-8.
57. McComas AJ, Miller RG, Gandevia SC. Fatigue brought on by malfunction of the central and peripheral nervous systems, In: Gandevia SC, Enoka RM, McComas AJ, Stuart DG, Thomas CK, editors. Fatigue: neural and muscular mechanisms. New York: Plenum Pr; 1995. p 495-512.
58. Winningham ML. Strategies for managing cancer-related fatigue syndrome: a rehabilitation approach. Cancer 2001;92:988-97.
59. Dimeo FC, Stieglitz RD, Novelli-Fischer U, Fetscher S, Keul J. Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. Cancer 1999;85:2273-7.
60. Di Fabio RP, Soderberg J, Choi T, Hansen CR, Schapiro RT. Extended outpatient rehabilitation: its influence on symptom frequency, fatigue, and functional status for persons with progressive multiple sclerosis. Arch Phys Med Rehabil 1998;79:141-6.
61. Mock V. Fatigue management: evidence and guidelines for practice. Cancer 2001;92:1699-707.
62. Deale A, Chalder T, Marks I, Wessely S. Cognitive behavior therapy for chronic fatigue syndrome: a randomized controlled trial. Am J Psychiatry 1997;154:408-14.