Brain Atrophy and Disability in Multiple Sclerosis

A Roundtable Discussion
Counseling Points™
Brain Atrophy and Disability in Multiple Sclerosis

Continuing Education Information

Target Audience
This educational activity is designed to meet the needs of nurses who treat patients with multiple sclerosis.

Purpose
To meet MS nurses’ educational needs on current topics in multiple sclerosis, acknowledging the nurse’s role in patient counseling.

Learning Objectives
Upon completion of this educational activity, the participant should be able to:

• Identify forms of atrophy associated with disability in multiple sclerosis (MS)
• Describe the evaluation and management of disability in patients with MS
• Discuss patient education on disability in MS
• Review current data on the prevention of brain atrophy in MS

Continuing Education Credit
This continuing nursing education activity was approved by the Wisconsin Nurses Association Continuing Education Approval Program Committee, an accredited approver by the American Nurses Credentialing Center’s Commission on Accreditation.

This activity has been approved for 1.0 contact hours.
Approximate time to complete this activity is 1 hour.
This program expires June 30, 2011.

Disclaimer
Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any medications, diagnostic procedures, or treatments discussed in this publication should not be used by clinicians or other health care professionals without first evaluating their patients’ conditions, considering possible contraindications or risks, reviewing any applicable manufacturer’s product information, and comparing any therapeutic approach with the recommendations of other authorities.
Dear Colleague,

The concept of brain atrophy gets to the heart of what disability in multiple sclerosis (MS) is all about—the tissues of the brain are literally shrinking due to the damaging effects of this disease. New research has shown that the effects of MS on gray matter, white matter, and other structures of the brain and spinal cord occur much earlier in the disease course than we had previously believed. We have also seen that decreases in brain volume can be measured over fairly short time intervals. But even with sophisticated research techniques, brain atrophy can be difficult to pin down: We know that it correlates strongly with disability in MS, but the degree of correlation and the types of disability vary among individual patients and according to study design.

While research on whether disease-modifying treatments specifically prevent brain atrophy is still inconclusive, it stands to reason that reducing the number of lesions on magnetic resonance imaging (MRI) would stave off damage down the road, further highlighting the importance of getting our patients on treatment early.

Brain atrophy represents permanent change, and once the damage has occurred the patient with MS will have permanent deficits in many areas. These deficits need to be evaluated and managed. A number of assessment tools are available for measuring disability. An MS-specific physical therapy evaluation is also recommended to evaluate status and find solutions before patients become disabled.

Many of our patients want to know whether they qualify for disability benefits if their ability to work has become impaired, and some may need guidance while going through this process. The panel for this edition of MS Counseling Points™ discusses these issues from the specific point of view of a nurse treating MS patients.

Beginning this year, MS Counseling Points™ is offering nurses continuing education (CE) credit. We hope that you find it a valuable learning experience, and we encourage you to complete the evaluation form and posttest to receive your credit.

We would like to thank Teva Neuroscience for providing an educational grant for this program.

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It doesn’t take a skilled radiologist to distinguish between a magnetic resonance imaging (MRI) scan of a healthy young individual and a scan from a person with long-standing multiple sclerosis (MS) (Figure 1). Pronounced tissue loss, or atrophy, can be observed in many areas of the brain. In the past, the number of active lesions seen on MRI was believed to be the major predictor of disability in MS, but increasing numbers of studies have shown that brain atrophy may be a stronger and more consistent indicator of disability.1-4

Several long-held beliefs about atrophy in MS are being challenged with newer research. The traditional view is that inflammation occurs first, triggering demyelination, with axonal loss and tissue atrophy occurring much later in the course of disease. In contrast, some researchers have proposed an “inside-out model” of MS—a sort of “chicken or egg” theory—whereby the axon is injured by an infection or toxin, triggering a vicious cycle of inflammation and tissue damage.5

Current research also shows that brain atrophy begins earlier in the course of MS than previously believed and that atrophy can progress over fairly short periods of time.6 Harde meier and colleagues compared results from 3 MRI scans taken over a 3-month period (mean 76±20 days) in untreated patients with early MS awaiting enrollment in a treatment trial.7 Brain volume reductions were observed between scan 1 and scan 3. If atrophy were to continue in a linear manner at that pace (not necessarily the case), the investigators estimated an annualized atrophy rate of about –1.06%.

In addition, there is now substantial evidence showing that atrophy occurs in white matter, gray matter, and spinal cord tissue; MS is no longer considered a disease of primarily white matter.1,8 The mechanisms causing tissue atrophy in MS are complex, and different mechanisms may be involved in gray matter atrophy versus atrophy in the white matter or spinal cord.9 Spinal cord atrophy in particular has been associated with progressive forms of MS.10

The study of atrophy in MS is hampered by several challenges associated with measuring brain volume. Imaging technology is still evolving. Brain sizes vary among individuals, and few MS patients have had a baseline MRI prior to symptom onset. Many factors can contribute to brain atrophy, including normal aging, concomitant disease, and alco-

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**Figure 1**

Non-contrast T1-weighted magnetic resonance imaging (MRI) shows brain volume in normal controls in the fifth decade (A and B) compared with age-matched patients with multiple sclerosis (C and D) showing prominent atrophy.

holism. Even temporary changes such as hydration status can affect how brain volume appears on MRI. Some have proposed that treating MS with disease-modifying therapies (DMTs) reduces inflammation, which may create an appearance of reduced brain volume, or pseudoatrophy. One approach introduced to quantify brain atrophy is measuring brain parenchymal fraction (BPF), which is the ratio of brain parenchymal volume to total intracranial volume.

How Brain Atrophy Correlates With Disability in MS

The Expanded Disability Status Scale (EDSS) and the MS Functional Composite (MSFC) are standardized measures of disability in MS often used in clinical trials. Many studies of brain atrophy and disability have been conducted to determine how degree of atrophy (or rate of change in brain volume) correlates to these scales (Tables 1 and 2).

An early study of brain atrophy by Fisher and colleagues involving 160 MS patients showed that brain atrophy (via BPF) correlated with both EDSS and MSFC scores at each follow-up point during an 8-year study (baseline, 1, 2, and 8 years). The changes in BPF over that time period also correlated with changes in disability among these patients.

A recent study from The Netherlands showed that atrophy is measurable in the earliest stages of MS. Jasperse et al measured brain volume and other MRI parameters in 89 treatment-naïve MS patients at the time of diagno-

Table 1. Kurtzke Expanded Disability Status Scale (EDSS)

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>Normal neurological examination</td>
</tr>
<tr>
<td>1.0</td>
<td>No disability, minimal signs in one functional system (FS)</td>
</tr>
<tr>
<td>1.5</td>
<td>No disability, minimal signs in more than one FS</td>
</tr>
<tr>
<td>2.0</td>
<td>Minimal disability in one FS</td>
</tr>
<tr>
<td>2.5</td>
<td>Mild disability in one FS or minimal disability in two FS</td>
</tr>
<tr>
<td>3.0</td>
<td>Moderate disability in one FS, or mild disability in three or four FS. Fully ambulatory</td>
</tr>
<tr>
<td>3.5</td>
<td>Fully ambulatory but with moderate disability in one FS and more than minimal disability in several others</td>
</tr>
<tr>
<td>4.0</td>
<td>Fully ambulatory without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability; able to walk without aid or rest some 500 meters</td>
</tr>
<tr>
<td>4.5</td>
<td>Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability; able to walk without aid or rest some 300 meters.</td>
</tr>
<tr>
<td>5.0</td>
<td>Ambulatory without aid or rest for about 200 meters; disability severe enough to impair full daily activities (work a full day without special provisions)</td>
</tr>
<tr>
<td>5.5</td>
<td>Ambulatory without aid or rest for about 100 meters; disability severe enough to preclude full daily activities</td>
</tr>
<tr>
<td>6.0</td>
<td>Intermittent or unilateral constant assistance (cane, crutch, brace) required to walk about 100 meters with or without resting</td>
</tr>
<tr>
<td>6.5</td>
<td>Constant bilateral assistance (canes, crutches, braces) required to walk about 20 meters without resting</td>
</tr>
<tr>
<td>7.0</td>
<td>Unable to walk beyond approximately 5 meters even with aid, essentially restricted to wheelchair; wheels self in standard wheelchair and transfers alone; up and about in wheelchair some 12 hours a day</td>
</tr>
<tr>
<td>7.5</td>
<td>Unable to take more than a few steps; restricted to wheelchair; may need aid in transfer; wheels self but cannot carry on in standard wheelchair a full day; may require motorized wheelchair</td>
</tr>
<tr>
<td>8.0</td>
<td>Essentially restricted to bed or chair or perambulated in wheelchair, but may be out of bed itself much of the day; retains many self-care functions; generally has effective use of arms</td>
</tr>
<tr>
<td>8.5</td>
<td>Essentially restricted to bed much of day; has some effective use of arms; retains some self-care functions</td>
</tr>
<tr>
<td>9.0</td>
<td>Confined to bed; can still communicate and eat.</td>
</tr>
<tr>
<td>9.5</td>
<td>Totally helpless bed patient; unable to communicate effectively or eat/swallow</td>
</tr>
<tr>
<td>10.0</td>
<td>Death due to MS</td>
</tr>
</tbody>
</table>

Table 2. Multiple Sclerosis Functional Composite (MSFC)

- 25-foot walk (2 trials)
- 9-hole peg test (2 trials each hand)
- Paced auditory serial addition test (PASAT-3 version)

Note: A training videotape and administration and scoring manual are available from the National Multiple Sclerosis Society (www.nmss.org).
sis and again 2 years later. Disability was assessed based on the EDSS score. The percent of volume change during the 2 years correlated significantly with the EDSS score, with a higher rate of change associated with an increase in clinical disability. This study also showed that patients with contrast-enhancing lesions at baseline had a faster rate of atrophy, suggesting that such methods may be helpful in predicting the rate of progression in MS.

A recent study by Rudick and colleagues looked at whole brain, gray matter, and white matter atrophy in a group of patients with MS or a clinically isolated syndrome (CIS) and normal controls over a 6.6-year period. In this study, gray matter atrophy was strongly predictive of disability on the MSFC, but not on the EDSS.

Evaluating Disability in MS

It may not be surprising that research shows better correlation of brain atrophy with a broader scale such as the MSFC. The EDSS gives an incomplete picture of the patient’s condition because this scale is heavily weighted toward gait and mobility issues and does not consider other functional problems, particularly cognition. Cognitive disturbances may start early in MS and are among the many pervasive and disabling “invisible” symptoms of MS (Table 3).

Cognitive problems and other invisible symptoms—such as fatigue, pain, and visual impairment—can create significant disability in the patient with MS, sometimes well before motor dysfunction becomes evident. This is why an early comprehensive evaluation is recommended for patients.

Table 3. Visible and Invisible Symptoms of MS

<table>
<thead>
<tr>
<th>Visible Symptoms</th>
<th>Invisible Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired gait</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Significant weakness (paresis/paralysis)</td>
<td>Cognitive impairment</td>
</tr>
<tr>
<td>Balance or coordination problems</td>
<td>Abnormal sensation</td>
</tr>
<tr>
<td>Spasticity</td>
<td>Impaired vision</td>
</tr>
<tr>
<td>Contractures</td>
<td>Heat sensitivity</td>
</tr>
<tr>
<td>Tremor</td>
<td>Depression</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>Pain</td>
</tr>
<tr>
<td></td>
<td>Dysphagia</td>
</tr>
<tr>
<td></td>
<td>Bowel/bladder problems</td>
</tr>
<tr>
<td></td>
<td>Sexual problems</td>
</tr>
</tbody>
</table>

Although many patients are not evaluated by a physical therapy (PT) specialist until their deficits interfere with functioning, experts in this area strongly advocate an early baseline PT evaluation for all patients. The goals for this assessment in MS are outlined in Table 4. Ideally, an evaluation should be scheduled soon after diagnosis, if the patient is ready to accept it. While rehabilitation cannot directly affect disease progression, it can help patients manage some of the effects of the disease as they occur. Even subtle changes that may go unnoticed by the patient can lead to deconditioning and adaptive techniques that result in “bad habits” relating to gait, energy management, or daily functioning. It is best not to wait until the patient is challenged and frustrated by fatigue, difficulty walking, or other functional limitations before initiating a rehabilitation program. Some of the tests that may be used in this evaluation are summarized in Table 5.

World Health Organization International Classification of Functioning (ICF)

The ICF is a classification system developed by the World Health Organization (WHO) to provide standard, univer-
Sally accepted language to describe health status in various forms of disability.20 The ICF views disability based on the patient’s ability to participate in life activities and also takes the person’s environment into consideration. Components of the ICF are categorized as:

- **Impairments**: problems in body function or structure (significant deviation or loss);
- **Activity limitations**: difficulties performing in a uniform environment;
- **Participation restrictions**: problems in executing a task or involvement in life in the patient’s current environment.20

Specific examples of how MS symptoms can be classified according to ICF categories are listed in Table 6. A number of MS-specific standardized tests are available for evaluating the MS patient according to these criteria (Table 7).

### Disability Benefits for MS Patients

Eventually, many patients with MS will apply for and receive Social Security Disability Insurance (SSDI) benefits. Some patients try to apply for benefits immediately after receiving a diagnosis, while others delay the process. There is a threshold of real disability that must be demonstrated (and appropriately documented) before benefits will be granted.

SSDI criteria for determining a person to be disabled, sometimes called “the Listings” are readily available online.21 MS-specific criteria are outlined in Table 8. Although initial acceptance rates seem to be improving, nearly two-thirds of persons applying for disability benefits are still turned down on their first application, based on national data.22 According to MS disability expert Tom Stewart, initial success rates are somewhat higher for patients with neurologic disorders and in some geographic areas.22

Stewart points out that this almost-inevitable rejection of the first application creates an interesting financial dilemma for MS patients.22 In order to apply for benefits, a person’s income must not exceed a certain threshold. For 2009, the maximum yearly income is $14,160.21 For every $2 the person earns over that limit, $1 is withheld from benefits. So a person earning $40,000 would have approximately $13,000 withheld from benefits. For many people, this entails quitting one’s job to qualify. But if the person then fails to receive SSDI benefits, what is

### Table 6. ICF Components: Clinical Examples in MS20

<table>
<thead>
<tr>
<th>Body Structure and Function</th>
<th>Activities and Participation</th>
<th>Environmental Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Increased tone</td>
<td>• Bed mobility</td>
<td>• Work and leisure</td>
</tr>
<tr>
<td>• Decreased range of movement</td>
<td>• Transfers</td>
<td>• Accessibility of buildings, sidewalks</td>
</tr>
<tr>
<td>• Decreased functional strength</td>
<td>• Activities of daily living (ADLs)</td>
<td>• Transportation</td>
</tr>
<tr>
<td>• Abnormal sensation</td>
<td>• Dynamic standing for hygiene/ADLs</td>
<td>• Return to life roles</td>
</tr>
<tr>
<td>• Pain</td>
<td>• Mobility/gait in home/community</td>
<td>• Attitudes of community</td>
</tr>
<tr>
<td>• Sexual dysfunction</td>
<td>• Social participation</td>
<td>• Community interaction</td>
</tr>
<tr>
<td>• Balance disorders (vestibular)</td>
<td>• Work</td>
<td></td>
</tr>
<tr>
<td>• Speech and swallowing disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Cognition impairments</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Bladder/bowel problems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Impaired vision</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ICF = International Classification of Functioning.

### Table 7. Standardized Measures in MS Focusing on ICF Components

<table>
<thead>
<tr>
<th>Body Structure and Function</th>
<th>Activities and Participation</th>
<th>Environmental Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• MS Functional Composite (MSFC)</td>
<td>• Expanded Disability Status Scale (EDSS)</td>
<td>• Work and leisure</td>
</tr>
<tr>
<td>• Expanded Disability Status Scale (EDSS)</td>
<td>• MS Fatigue Impact Scale (MSFIS)</td>
<td>• Accessibility of buildings, sidewalks</td>
</tr>
<tr>
<td>• MS Fatigue Impact Scale (MSFIS)</td>
<td>• MS Functional Composite (MSFC)</td>
<td>• Transportation</td>
</tr>
<tr>
<td>• MS Functional Composite (MSFC)</td>
<td>• Expanded Disability Status Scale (EDSS)</td>
<td>• Return to life roles</td>
</tr>
<tr>
<td>• Expanded Disability Status Scale (EDSS)</td>
<td>• Disease Steps (DS)</td>
<td>• Attitudes of community</td>
</tr>
<tr>
<td>• Disease Steps (DS)</td>
<td>• MS Walking Scale–12 (MSWS–12)</td>
<td>• Community interaction</td>
</tr>
</tbody>
</table>

ICF = International Classification of Functioning.
Proper Documentation Is Key

This type of dilemma underscores the importance of advocating for patients, which means proper documentation by the health care team. People who find the application process straightforward are often those with good access to medical care and well-documented impairments—especially mobility impairments. Unfortunately this is not always a “slam dunk” case with cognitive impairment. According to Stewart, “many MS patients who are unable to work because of cognitive difficulties and fatigue may have a normal or near-normal neurological examination reflected in their medical records.”

Furthermore, patients with cognitive impairment and/or fatigue are particularly likely to be overwhelmed by the red tape involved in applying for disability benefits.

The MS nurse can be a valuable advocate to guide patients through this process. The entire health care team must recognize that the way in which impairments are documented in the medical record can impact a disability claim. Stating in the medical record that the “patient is doing well” or the “patient is clinically stable” will not help the patient’s case. The person may be doing well relative to his or her last visit (or relative to those with severe MS), but a caveat should be added that ongoing deficits (e.g., with cognition, pain, fatigue, or psychological distress) continue to create certain problems at home or at work.

Patients who do not strictly meet the SSDI Listings may still qualify for benefits based on a Residual Functional Capacity exam (also called a functional capacity evaluation or FCE). This exam is performed by an occupational therapist (OT) with special training. If a PT or OT’s opinion is included in the application, there should also be a statement by the neurologist concurring with the results. For patients for whom cognitive impairment is the primary disability, a comprehensive evaluation by a neuropsychiatrist and/or speech therapist may be the key to documenting disability.

Adapting the Work Environment

Advocating for the patient may also mean encouraging the patient or employer to explore workplace adaptation
as an alternative to receiving disability insurance. Adapting a job to meet the needs of a person with disabilities is obviously preferable to having the person quit working altogether, and is mandated by the Americans With Disabilities Act (ADA). The ADA requires all US employers with 15 or more employees to provide reasonable accommodation for individuals with disabilities, unless it would cause undue hardship. A reasonable accommodation is any change in the work environment or in the way a job is performed that enables a person with a disability to enjoy equal employment opportunities. For example, if the person’s job requires a lot of standing or walking, reassignment to a desk-based job would comprise a reasonable accommodation. Computer software could be incorporated to increase type size on job-specific programs or databases used by the employee. More frequent breaks could be incorporated into the workday. More information about the ADA can be found at www.ADA.gov.

Does the Patient Need a Disability Attorney?

A routine web search on disability benefits will spring a lot of lawyers’ names from the woodwork. Many ads claim that hiring an attorney is the only way to ensure success, but this is not necessarily the case. Hiring an attorney may be warranted if the patient is turned down when he or she is clearly disabled, or if the patient has tried and failed to get benefits on a few separate attempts.

The National Multiple Sclerosis Society (NMSS) is a good resource for both patients and health professionals on this subject. The website contains informational articles, templates for health care providers, and other resources.

Can Disability From Brain Atrophy be Prevented?

Research has shown promising evidence for remyelination of nerves in MS, but atrophy appears to represent irreversible tissue loss. Thus, it is a key target for prevention. DMTs for MS—which include the β-interferons and glatiramer acetate—have been clearly shown to prevent exacerbations of the disease, reduce progression of disability, and reduce the number of gadolinium-enhancing (Gd+) lesions seen on MRI. Does this also mean that they prevent brain tissue or spinal tissue atrophy? According to Rudick, “because [DMTs] are effec-

tive in reducing measures of disease related to brain inflammation (e.g., relapses, Gd+ lesions) and because brain inflammation has been linked to irreversible brain tissue injury, [these drugs] should be effective in reducing the rate of brain atrophy progression.”

Thus far, data specifically demonstrating prevention of atrophy have been mixed, as described in a review by Rudick. Studies of each of the first-line DMTs (interferon β-1a subcutaneous or intramuscular; interferon β-1b, and glatiramer acetate) looking at brain volume changes have shown no significant treatment effect in some trials, and promising reductions in brain atrophy progression in others (Table 9). Other therapies shown to have a significant effect on brain volume in relapsing-remitting MS include intravenous (IV) methylprednisolone, natalizumab, and IV immunoglobulin. Studies in progressive forms of MS have so far not shown a significant effect of disease modification on brain atrophy measures.

Discussion Disease Modification with the Patient

Patients with early MS can have near-normal functioning for many years while insidious neuronal damage and tissue atrophy continue. Patients need to understand that this activity is ongoing even when they feel “just fine,” in the absence of exacerbations. In discussing DMTs with patients, particularly those newly diagnosed, it’s helpful to think in terms of preventing tissue loss. It cannot be overstated: Delaying or slowing disability is much easier than trying to reverse it. Anything that can be done to help maintain or improve the patient’s current level of functioning and protect his or her brain tissue should be done, as this strategy represents the best opportunity for preventing disability down the line.

In counseling patients, you might try this analogy to hypertension: If you found out you had high blood pressure, you would likely take medication immediately to control it, not wait until you had a heart attack or stroke before starting treatment.

Anything that can be done to help maintain or improve the patient’s current level of functioning and protect his or her brain tissue should be done, as this strategy represents the best opportunity for preventing disability down the line.
pressure, would you wait until you had a heart attack to treat it? Visual aids showing that treatment can delay the progression to later stages of disability can be helpful in convincing patients that staying on their therapy offers them the best chance of delaying their disability significantly compared with the natural history of this disease (Figure 2).  

Adherence and Financial Considerations

DMTs cannot prevent neurologic damage and disability if they are not used consistently and correctly. If a patient’s condition progresses more rapidly than expected, a change in therapy may be warranted.  

Before this decision is made, however, the nurse may want to explore whether the patient could be cutting corners on the therapy. For instance, during the current recession, clinicians are finding that some patients are trying to “stretch” the medication by diluting it or using it less frequently in an attempt to save money. This is probably more of a financial problem than an adherence problem, per se. Most patients will not volunteer this information during a routine follow-up visit, but some probing on the nurse’s part (“How many doses have you missed?” “Are you having trouble affording your medications?”) may give the patient “permission” to answer honestly. Patients who are experiencing difficulty paying for their medication should be directed to financial assistance programs, such as those offered by the pharmaceutical industry, as well as other drug-coverage programs.

For people who are stretching their budget in many areas, cutting back on their medication may seem like a satisfactory short-term solution. The patient may think, “I’ve skipped several doses in the last three months and nothing has happened—I’m fine.” It is critical to counsel

Table 9. Studies of Disease-Modifying Therapies on Brain Atrophy in MS

<table>
<thead>
<tr>
<th>Treatment (Dosage)</th>
<th>Duration in Months (No. of Patients)</th>
<th>Effect of Treatment on Brain Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trials in Relapsing-Remitting MS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IFNβ-1a IM (Avonex®) (30 µg weekly)</td>
<td>24 (140)</td>
<td>S (12–24 months)</td>
</tr>
<tr>
<td>IFNβ-1a IM (Avonex®) (30 µg/wk &amp; 60 µg/wk)</td>
<td>36 (386)</td>
<td>S (12-24 mo): lower dose</td>
</tr>
<tr>
<td>IFNβ-1a IM (Avonex®) (30 µg/wk vs no treatment)</td>
<td>36 (54)</td>
<td>S (24-36 mo): higher dose</td>
</tr>
<tr>
<td>IFNβ-1a SC (Rebif®) (66 µg/wk or 132 µg/wk)</td>
<td>24 (519)</td>
<td>NS</td>
</tr>
<tr>
<td>IFNβ-1a SC (Rebif®) (66 µg/wk or 132 µg/wk)</td>
<td>84 – 96 (382)</td>
<td>NS</td>
</tr>
<tr>
<td>Glatiramer acetate (Copaxone®) (20 mg/day)</td>
<td>18 (239)</td>
<td>NS</td>
</tr>
<tr>
<td>Glatiramer acetate (Copaxone®) (20 mg/day)</td>
<td>18 (194)</td>
<td>S in placebo-controlled and open-label phases</td>
</tr>
<tr>
<td>Glatiramer acetate (Copaxone®) (20 mg/day)</td>
<td>24 (27)</td>
<td>S (0-24 mo)</td>
</tr>
<tr>
<td>Glatiramer acetate (Copaxone®) (20 mg/day)</td>
<td>80.4 (135)</td>
<td>S (0-80.4 mo)</td>
</tr>
<tr>
<td>IV methylprednisolone (1 g/day for 5 days)</td>
<td>60 (81)</td>
<td>S (0-60 mo)</td>
</tr>
<tr>
<td>Natalizumab (Tysabri®)</td>
<td>24 (942)</td>
<td>S (12-24 mo)</td>
</tr>
<tr>
<td><strong>Trials in Clinically Isolated Syndrome</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IFNβ-1a SC (Rebif®) (22 µg/wk)</td>
<td>24 (163)</td>
<td>S (0-24)</td>
</tr>
</tbody>
</table>

IM=intramuscular; IV=intravenous; NS=nonsignificant; S=significant; SC=subcutaneous.
patients that MS progression is often not clinically evident, and that this type of cutting corners is likely to be very costly in the long run.

**Conclusion**

Researchers appear to be on the brink of many discoveries that will advance the study of brain atrophy in MS. Sophisticated methods of imaging and calculating changes in the brain may soon provide more information about which MS patients are susceptible to disease progression, the mechanisms causing neurologic damage, and the effects of specific treatments.32,33 The nurse continues to serve a key function in advocacy, education, evaluation, and caregiving for MS patients.

**References**

Brain atrophy correlates with disability in multiple sclerosis (MS) and may be a stronger predictor of disability status than measures of inflammation or lesion load.

Brain atrophy occurs much earlier in the course of MS and progresses more rapidly than was previously believed. Deterioration occurs in all forms of tissue; gray matter atrophy has been recognized as an important factor in the pathogenesis of MS.

The mechanisms of atrophy are complex. Some investigators believe that atrophy may actually precede inflammation in MS, rather than the reverse. However, atrophy or tissue loss is regarded to be permanent.

Standard measures of disability in MS include the Expanded Disability Status Scale (EDSS) and the MS Functional Composite (MSFC), as well as the World Health Organization (WHO) International Classification of Functioning.

An early physical therapy evaluation can be valuable for all MS patients, to help establish a baseline and help patients adapt appropriately to subtle deficits.

The US Social Security Administration has issued a set of disability measures (“the Listings”) that must be demonstrated for a US citizen to receive disability insurance.

The nurse can serve as an important advocate for patients applying to receiving disability insurance. Appropriate documentation of deficits, especially in cognitive areas, can help patients receive the benefits to which they are entitled.

Patients who are able to continue working should explore modifications to the workplace required by the Americans With Disabilities Act.

In treating MS, it is essential to try to prevent atrophy, since lost brain tissue is not regenerated.

Many disease-modifying therapies (DMTs), including some β-interferon formulations, glatiramer acetate, and intravenous methylprednisolone, have been shown to prevent reductions in brain volume in various clinical studies.

Results of many clinical trials have been mixed or inconclusive in regard to brain atrophy. More research and better ways of characterizing atrophy are needed to establish how and to what degree the available treatments prevent brain tissue loss in patients with MS.
1. Which of the following statements has been proven FALSE?
   A. Brain atrophy is a strong predictor of disability in multiple sclerosis (MS)
   B. Brain atrophy and inflammation may be part of a “vicious cycle” of disease in MS
   C. Brain atrophy does not occur until late in the disease course of MS
   D. Atrophy can affect gray matter, white matter, and spinal cord tissue

2. Challenges in studying and measuring brain volume in MS include all of the following EXCEPT that:
   A. brain tissue volume varies among individuals
   B. brain volume cannot be measured via MRI
   C. normal changes in brain volume occur with aging
   D. alcohol use, hydration, and other factors may temporarily affect brain volume

3. The appearance of reduced brain volume resulting from anti-inflammatory treatment of MS is called:
   A. anti-inflammatory volume reduction
   B. brain parenchymal fraction
   C. normal-appearing white matter
   D. pseudoatrophy

4. A disadvantage of the Expanded Disability Status Scale (EDSS) in characterizing disability in MS is that:
   A. it emphasizes cognitive deficits over mobility factors
   B. it emphasizes deficits in mobility over cognitive deficits or fatigue
   C. EDSS scores do not correlate with disability in clinical trials of MS
   D. none of the above

5. “Invisible” symptoms of MS include all of the following EXCEPT:
   A. depression
   B. fatigue
   C. heat sensitivity
   D. spasticity

6. Bed mobility, activities of daily living (ADL), and social participation are components in which category of the World Health Organization (WHO) Classification of Functioning?
   A. Activities and Participation
   B. Body Structure and Function
   C. Environmental Factors
   D. None of the above

7. Current national data show that approximately ____ of all patients applying for Social Security Disability Insurance (SSDI) are turned down on their first application:
   A. one-tenth
   B. one-quarter
   C. half
   D. two-thirds

8. Steps made by the health care team that could be DETRIMENTAL to a patient applying for disability insurance include:
   A. proper documentation of impairments in medical records
   B. referral to the National Multiple Sclerosis Society for resources
   C. stating in the chart that the patient is clinically stable
   D. referring for a Residual Functional Capacity Exam

9. “Reasonable accommodations” in the work environment for a person with a disability are required by the Americans With Disabilities Act for:
   A. companies with 15 or more employees
   B. companies with 50 or more employees
   C. federal and state employees only
   D. companies receiving federal or state funding

10. The potential to slow the deterioration of brain volume in MS has been demonstrated in clinical trials involving which of the following therapies?
    A. Glatiramer acetate but not interferon β-1a
    B. Interferon β-1a but not glatiramer acetate
    C. Interferon β-1a but not natalizumab
    D. Glatiramer acetate, interferon β-1a, and natalizumab
Counseling Points™: Program Evaluation Form
Brain Atrophy and Disability in Multiple Sclerosis

Using the scale provided, Excellent = 5 and Poor = 1, please complete the program evaluation so that we may continue to provide you with high quality educational programming. Please fax this form to (201) 612-8282.

5 = Excellent  4 = Good  3 = Satisfactory  2 = Fair  1 = Poor

To what extent did the program enable you to achieve the following objectives? (Please circle the appropriate number on the scale.)

1. Identify forms of atrophy associated with disability in multiple sclerosis (MS) ................................................................. 5 4 3 2 1
2. Describe the evaluation and management of disability in patients with MS ................................................................. 5 4 3 2 1
3. Discuss patient education on disability in MS .......................................................................................................................... 5 4 3 2 1
4. Review current data on the prevention of brain atrophy in MS .................................................................................. 5 4 3 2 1

To what extent was the content...

5. Well-organized and clearly presented ............................................................................................................................................ 5 4 3 2 1
6. Current and relevant to your area of professional interest .............................................................................................................. 5 4 3 2 1
7. Free of commercial bias ................................................................................................................................................................5 4 3 2 1

General Comments

8. As a result of this continuing education activity (check only one):
   ☐ I will modify my practice. (If you checked this box, how do you plan to modify your practice?)

   ☐ I will wait for more information before modifying my practice.
   ☐ The program reinforces my current practice.

Suggestions for future topics/additional comments:

Follow-up

As part of our continuous quality improvement effort, we conduct post-activity follow-up surveys to assess the impact of our educational interventions on professional practice. Please check one:

☐ Yes, I would be interested in participating in a follow-up survey.
☐ No, I would not be interested in participating in a follow-up survey.

There is no fee for this educational activity.

Posttest Answer Key

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Via the Web: Applicants can access this program at the International Organization of MS Nurses website, www.IOMSN.org. Click on Counseling Points and follow the instructions to complete the online posttest and application forms.