Neuropsychological studies have provided evidence of disease-based cognitive loss in a substantial number of patients with MS, possibly as many as 50%. These cognitive deficits often go unnoticed by the physician, and may not be recognized even by the patients themselves. They can have an appreciable effect, however, on the lives of the patients and their family members. In addition to causing a significant amount of emotional distress, cognitive deficits are a primary cause of early departure from the workforce.

**COGNITIVE FUNCTION AFFECTED BY MS**

Though patients vary greatly, the following cognitive impairments have been most commonly reported:

- Slowed information processing
- Impaired attention and concentration, especially “alternating attention” (the need to shift attention back and forth between two stimuli) and “divided attention” (simultaneously attending to multiple stimuli)
- Impaired recent memory, especially “explicit memory” (explicitly instructed information meant for learning and remembering) and “episodic memory” (the memory of events and of information that is seen, read, or heard)
- Impaired executive functions, such as concept formation, reasoning, problem-solving, and planning and sequencing

Cognitive impairment is difficult to predict on the basis of clinical indicators. In general, relapse rates and changes in neurologic disability are poor predictors of the degree of cognitive dysfunction. Patients may be mildly affected physically but present with significant cognitive dysfunction.
Severely disabled persons, on the other hand, may experience no cognitive declines. As a group, secondary progressive patients are more likely to demonstrate cognitive symptoms.

Recent attention has been directed toward MRI predictors of cognitive impairment. Several indices of cerebral damage have been positively correlated with the severity of cognitive loss, including lesion volume scores, third ventricle size, corpus callosum size, and ventricular-brain ratios and overall cerebral atrophy. There is also a correlation between the degree of left frontal lobe plaque involvement and poor performance on tests of abstraction, memory, and word-finding.

**ASSESSMENT OF COGNITIVE IMPAIRMENT**

Unfortunately, there is no established method for quickly and accurately assessing cognitive loss in MS. The Mini-Mental Status Examination (MMSE) is not sensitive in this diagnosis, and a complete neuropsychological assessment is often unrealistic in the limited managed care setting. When cognitive loss is suspected, the clinician might begin the screening process by posing a series of ad hoc questions, such as whether the patient has noticed a problem with remembering appointments or conversations, understanding or remembering written material, or focusing attention on a task without becoming distracted. A patient who reports recent onset or a worsening of these types of problems should be referred for a brief neuropsychological screening battery to assess performance in the most common areas of deficit, and determine if further intervention is necessary. A screening battery takes approximately one to two hours. Recommended tests include:

<table>
<thead>
<tr>
<th>Cognitive Function</th>
<th>Instrument</th>
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<tr>
<td>Processing speed/working memory</td>
<td>Paced Auditory Serial Addition Test (PASAT); Symbol Digit Modalities Test (SDMT)</td>
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<tr>
<td>Learning/memory</td>
<td>California Verbal Learning Test—I (CVLT-I); Brief Visuospatial Memory Test—Rev. (BVRT-R)</td>
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<tr>
<td>Executive functions</td>
<td>California Card Sorting Test (CST)</td>
</tr>
<tr>
<td>Visual perception/spatial processing</td>
<td>Judgment of Line Orientation Test (JLO)</td>
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<tr>
<td>Language</td>
<td>Controlled Oral Word Association Test (COWAT)</td>
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**TREATMENT OF COGNITIVE LOSS**

Data are limited regarding the effects of immunomodulating agents on cognitive dysfunction. However, clinical trials have suggested that they may improve some aspects of performance. The possibility that they may reduce disease progression, and thereby slow cognitive decline, supports the move toward early treatment with these agents. Donepezil (Aricept®), a drug that
has been approved by the FDA for the treatment of memory disorders in Alzheimer’s disease, was found in a recent study of 69 MS patients with memory deficits to have modest benefits for verbal memory (the ability to remember a list of words). A forthcoming multi-center trial of Aricept® should provide more definitive evidence concerning the effectiveness of this drug for people with MS.

The best management approach at this point appears to be to recognize and diagnose cognitive loss early, and to provide appropriate social or vocational protection. This may include cognitive retraining, and an individualized plan for compensatory strategies utilizing intact functions and external aids such as “memory books.” The overall success of cognitive rehabilitation and other specific interventions in MS patients has not been thoroughly assessed, however.

The family plays an important role, both in diagnosis and management. The steady support of family members is key in assisting the patient’s process of acceptance and in facing any social or vocational role changes. Family members themselves must become personally involved if the cognitive loss necessitates adaptive changes in social and family roles.

Referral to neuropsychologists for more comprehensive assessment is recommended in many cases. Rehabilitation psychologists, occupational therapists, and speech/language pathologists may also be of great help in assisting the adaptive process.

**SOURCES**


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