# Behavioral Neurology of Multiple Sclerosis and Autoimmune Encephalopathies

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### **KEYWORDS**

• Multiple sclerosis • Cognition • Behavioral change • Depression

### **KEY POINTS**

- Cognitive impairment may start at an early stage in multiple sclerosis (MS), and approximately 50% of the patients may face such difficulty.
- Different areas of cognitive domains are involved in MS patients, including memory, information-processing speed, attention, and executive function.
- Lability, irritability, inflexibility, aggression, impatience, and apathy are the most common behavioral symptoms among patients with MS.
- Management of cognitive and behavioral abnormalities in MS should include both pharmacologic and nonpharmacologic approaches to achieve the best results. Particular attention to diagnose and manage behavioral impairments should start immediately after diagnosis.
- Multicenter controlled studies aimed at treating cognitive and neurobehavioral problems in MS should be planned, and cognitive tests should be considered as an outcome measure in future disease-modifying trials.

#### INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune disorder that usually affects young adults. The disease frequently starts in a relapsing course with different signs and symptoms that may lead to a progressive phase in which the patients experience progression of disability with or without exacerbations. A diagnosis of MS often has

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The authors have no conflict of interest to disclose.

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profound social and psychological impacts on the patient's life not only for physical disabilities but also for its special features. MS starts at the most productive years of life, and unpredictability of the clinical course, the impact on education, employment, sexual and family functioning, friendships, and activities of daily living are some of the features making MS different from other neurologic diseases.<sup>2</sup>

Neuropsychiatric symptoms are well documented in MS and can be divided into cognitive and behavioral symptoms. Although changes in cognitive abilities in MS are not universal and uniform, some cases may experience changes in cognitive abilities from the beginning of the disease even at the stage of clinically isolated syndrome, and many patients face this problem with a progression of physical disabilities.<sup>3,4</sup> Actually, most of the mild to moderate cognitive and neurobehavioral changes may be ignored or may receive less attention by the clinicians because of their special focus on the physical aspects of the disease and the misconception of intellectual abilities being spared in MS. Even most of the pivotal trials on approved medications did not consider this point seriously, and the major outcome measures were annual relapse rate and level of disability. During the last 2 decades, thanks to the development of more sensitive neuropsychological tests, many studies have demonstrated the high prevalence of cognitive problems in MS and its special impact on quality of life regardless of physical disabilities. Cognitive impairment has been reported in 40% to 60% of patients based on the type of home-based or communitybased studies.4,5

Frank dementia is rare and may be seen in less than 10% of the patients. Several aspects of life, such as driving, employment, and social activities, have been demonstrated to be affected by changes in cognitive performance. 7,8

Different areas of cognitive domains are involved in MS patients, including memory, information processing, attention, and executive function. Any disorder in the above-mentioned areas can affect the person's behavioral trends. Actually, cognitive impairment and behavioral changes are closely related and both of them should be taken into account in the management of such patients.

In this review, first a summary of most important cognitive domains that are involved in MS is provided and then some important aspects of behavioral changes in clinical practice are described. Also a brief review on the management of cognitive declines and behavioral problems in MS is provided.

## COGNITIVE PROBLEMS Information Processing

The information-processing speed is affected more frequently and at an earlier stage than other cognitive domains in MS.<sup>10,11</sup> It has been proven that there is a direct relationship between the information-processing speed and T2 lesion volume and brain atrophy.<sup>12</sup> In addition, it has been demonstrated that the extent of corpus callosum atrophy is directly correlated with information-processing speed disorder.<sup>13</sup> Information-processing speed disorder may directly affect the patient's behavior. These patients may find it difficult to learn new information.<sup>14</sup> Moreover, information-processing speed disorder can decrease the speed of planning and problem-solving.<sup>15</sup> Furthermore, it has been reported that information-processing speed has a direct relationship to anxiety, depression, and apathy in MS.<sup>16–18</sup>

## Memory

Memory disorders, especially in long-term memory, have been reported in MS patients. Memory disorder is associated with reduced hippocampal activity and male

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