

## Cognitive dysfunction in multiple sclerosis: Usually forgotten in the clinical assessment of MS patients

Sir,

In multiple sclerosis (MS) a lot of researches, indicate that 45-60% of patients are cognitively impaired.<sup>[1]</sup> It is seen in the subclinical radiologically isolated syndrome, clinically isolated syndrome, and all phases of clinical MS. In pediatric-onset MS, cognition is frequently impaired and worsens relatively rapidly cognitive impairment often affects personal life and vocational status.<sup>[2]</sup> Depression, anxiety and fatigue aggravate symptoms, whereas cognitive reserve partially protects it.<sup>[1]</sup> Although there are no predictors of which patients will suffer MS-related cognitive deficits. Disease duration and subtype, race, sex, and cognitive reserve may all play a role. Patients with progressive subtypes of MS are more likely to experience cognitive impairment, in general.<sup>[2]</sup> Adult African-American patients with MS develop cognitive deficits earlier in the disease course compared with adult Caucasian patients. The incidence and severity of cognitive deficits are higher in men. As with Alzheimer disease, MS patients with high levels of cognitive reserve are less likely to experience cognitive impairment.<sup>[2]</sup>

According to the recent studies both gray and white-matter lesions, which are frequently seen in the disease contribute to mental dysfunction in MS.<sup>[3,4]</sup> The correlation between multifocal white-matter and gray-matter lesions in cognitive dysfunction pathology has geared the disconnection theory. This model is based in the predilective topology of MS-associated lesions, predominantly involving subcortical periventricular fiber systems, which hinders distal flow of cortical cholinergic pathways. Disconnection occurs between cortical and subcortical regions interactions.<sup>[4,5]</sup>

There is a specific pattern of MS-related cognitive dysfunctions: The cognitive domains most commonly impaired in MS are including: Memory, attention, executive functions, speed of information processing, and visual-spatial abilities.<sup>[6]</sup>

Cognitive dysfunction could appear in the earliest stages of the disease as the first symptoms of MS.<sup>[7]</sup>

The cognitive domains impaired in MS seem to have an inter-patient variability, but a characteristic pattern may be defined: Memory, information processing efficiency, executive functioning, attention, processing speed, are the most commonly compromised functions.<sup>[8]</sup> Recent research shows that MS patients have difficulty with acquisition of new knowledge as opposed to retrieval from long-term storage.<sup>[9]</sup> Initially, based on the work of Rao *et al.* it was thought that memory difficulty was due to impaired retrieval, but more recent explanations are based in inadequate acquisition secondary to information processing insufficiency.<sup>[10]</sup>

Impaired speed of information processing has been identified as a key deficit in MS and is seen in 20-30% of patients.<sup>[11]</sup>

Information processing efficiency refers to the ability to maintain and manipulate information in the brain for short period and to the speed with which one can process that information. Processing speed deficits are observed on even the most basic tasks in MS patients and are related to decreased neuronal conduction speed secondary to demyelination. This slowed information processing may impact an individual's ability to complete tasks and to cope in demanding work.<sup>[12]</sup>

Executive functions concern to the cognitive abilities necessary to behavior directed to objectives and to the adaptation to environment demands and changes; examples are planning, organization, reasoning, and abstract conceptualization.

Up to 25% of MS patients had deficits in attention, especially in complex functions like selective and divided attention.<sup>[13]</sup>

The assessment of cognitive functions is undoubtedly important in MS patients. However, it is not wise to rely on the routine neurological consultation. Cognitive symptoms are usually hidden by more visible deficits (e.g., motor, sensory, cerebellar), may be masqueraded by emotional complains, as depression, by fatigue or pain and most times are not thoroughly recognized by the patients.

There is no evidence-based symptomatic drug treatment, nor are there optimal nonpharmacological approaches. Leisure activities enhance cognitive reserve. Cognitive rehabilitation in MS patients is still in its infancy. However, the importance of cognitive rehabilitation must be stressed.

Cognitive behavioral therapy, exercise, and education programs are promising psychosocial interventions to improve coping and lessen cognitive symptoms.

Multiple sclerosis neurologists should be aware of the importance of this usually forgotten subject. They should include cognitive evaluation of MS patients in clinical routine, since the presence of cognitive deficit may change their decisions in to the more appropriate therapy for better management and enhance the quality of life of the patients.

**Seyed Massood Nabavi, Bahram Sangelaji<sup>1</sup>**

Neurophysiology Clinic, Mostafa Center, Shahed University of Tehran, Tehran, Iran, <sup>1</sup>School of Physiotherapy, University of Otago, Dunedin, New Zealand

**Address for correspondence:** Dr. Seyed Massood Nabavi, University Clinic, Mostafa Center, Italia St., Tehran, Iran.  
E-mail: Massoodnabavi@yahoo.com

## REFERENCES

1. Jongen PJ, Ter Horst AT, Brands AM. Cognitive impairment in multiple sclerosis. *Minerva Med* 2012;103:73-96.
2. Rahn K, Slusher B, Kaplin A. Cognitive impairment in multiple sclerosis: A forgotten disability remembered. *Cerebrum* 2012;2012:14.
3. Dineen RA, Vilisaar J, Hlinka J, Bradshaw CM, Morgan PS, Constantinescu CS, *et al.* Disconnection as a mechanism for cognitive dysfunction in multiple sclerosis. *Brain* 2009;132:239-49.
4. Morgen K, Sammer G, Courtney SM, Wolters T, Melchior H, Blecker CR, *et al.* Evidence for a direct association between cortical atrophy and cognitive impairment in relapsing-remitting MS. *Neuroimage* 2006;30:891-8.
5. Amato MP, Bartolozzi ML, Zipoli V, Portaccio E, Mortilla M, Guidi L, *et al.* Neocortical volume decrease in relapsing-remitting MS patients with mild cognitive impairment. *Neurology* 2004;63:89-93.
6. Rao SM. Cognitive Function Study Group of the National Multiple Sclerosis Society. *A Manual for the Brief Repeatable Battery of Neuropsychological Tests in Multiple Sclerosis*. Milwaukee: Medical College of Wisconsin; 1990.
7. Schulz D, Kopp B, Kunkel A, Faiss JH. Cognition in the early stage of multiple sclerosis. *J Neurol* 2006;253:1002-10.
8. Rao SM, Leo GJ, Bernardin L, Unverzagt F. Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns, and prediction. *Neurology* 1991;41:685-91.
9. Chiaravalloti ND, DeLuca J. Cognitive impairment in multiple sclerosis. *Lancet Neurol* 2008;7:1139-51.
10. Rao SM, Grafman J, DiGuilio D, Mittenberg W, Bernardin L, Leo GJ, *et al.* Memory dysfunction in multiple sclerosis: Its relation to working memory, semantic encoding and implicit learning. *Neuropsychology* 1993;7:364-74.
11. Bergendal G, Fredrikson S, Almkvist O. Selective decline in information processing in subgroups of multiple sclerosis: An 8-year longitudinal study. *Eur Neurol* 2007;57:193-202.
12. Archibald CJ, Fisk JD. Information processing efficiency in patients with multiple sclerosis. *J Clin Exp Neuropsychol* 2000;22:686-701.
13. Nebel K, Wiese H, Seyfarth J, Gizewski ER, Stude P, Diener HC, *et al.* Activity of attention related structures in multiple sclerosis patients. *Brain Res* 2007;1151:150-60.