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Definition and Characteristics of Multiple Sclerosis with Predominant Cognitive Presentation

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Commentary

We recently reported a longitudinal MRI and cognitive follow-up of a patient with multiple sclerosis with predominant cognitive presentation (MSCP), showing the evolution of the disease and the difficulty in its early diagnosis [1]. In this commentary, we will briefly overview the definition and clinical manifestations of MSCP.

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system, resulting in recurrent episodes of acute neurological dysfunction or progressive neurological decline [2], usually having physical deficits affecting motricity, sensitivity, balance, or vision. The occurrence of cognitive impairment (CI) associated with motor deficits is frequent, with a prevalence of approximately 65% [3]. Although CI is not a central symptom and is not part of the McDonald criteria for diagnosing the disease, it is possible for patients to present early CI [4], compromising the information processing speed (IPS), executive function, episodic memory, verbal fluency, and visuospatial skills [5]. Although frequent, CI is generally associated with the presence of marked motor deficits in the disease, being rare its manifestation as a predominant symptom without major physical impairment [5]. MSCP can also present with predominantly mood and psychiatric symptoms, such as anxiety, depression, and psychosis, and can occur in all clinical phenotypes of the disease [1,6,7]. Vieira et al. [1] recently described a patient with MSCP, primary progressive multiple sclerosis phenotype, whose condition began in childhood with depressive, behavioral symptoms and learning difficulties, progressing in adulthood with severe psychotic symptoms that were difficult to control.

Older studies define MSCP as an individual with impairment in multiple domains in executive function, memory and processing speed [8]. Posteriorly, Staff et al. [7] showed that two different clinical presentations could occur in this type of patient: (1) progressive onset and evolution of symptoms, (2) subacute and fulminant type related to the attack (isolated or with relapses). More recent studies, such as Zurawskia et al. [5], define MSCP based on the Expanded Disability Status Scale (EDSS), as the presence of Cerebral Functional System (FS) ≥ 3 and remaining EDSS FS subscores ≤ 2 (vision, brainstem, pyramidal, cerebellar, gait and sensory function). Another recent study evaluated 1,212 patients with MS, separating them into 5 cognitive phenotypes according to results in the Brief Repeatable Battery of Neuropsychological Tests (BRB-N) and Stroop Color and Word Test (SCWT): (1) preserved cognition (19.4%); (2) mild–verbal memory/semantic fluency commitment (29.9%), showed only mildly decreased performance in Selective Reminding Test (SRT) and Word List Generation (WLG); (3) mild-multidomain commitment (19.5%), who showed mildly decreased performance in SRT, Symbol Digit Modalities Test (SDMT), SCWT and Paced Auditory Serial Addition Task (PASAT) and, mildly decreased performance in SRT, SPART, SDMT and WLG; (4) severe–executive/attention commitment (13.8%), who showed severely decreased performance in SCWT and PASAT, and (5) severe–multidomain commitment (17.5%), who showed severely decreased performance in SRT, SDMT, SCWT, PASAT and WLG and mildly decreased performance in 10/36 Spatial Recall Test (SPART) [9].

As well as diagnosis, monitoring cognitive functions in these individuals is very important. An initial screening with annual follow-up is recommended, for this reason, the SDMT is a good test for this purpose [10]. The SDMT is a brief, reliable and sensitive test that is easy to apply and can be widely used to monitor the cognition of these individuals, particularly the IPS [3,11].

In relation to brain structural changes, an important predictor of CI in patients with MS is thalamus and hippocampal atrophy, which is associated with worse cognitive outcomes, mainly related to IPS, visual and verbal memory [9,12]. Another parameter related to cognitive decline is cerebellar atrophy, which is associated with verbal and non-verbal memory impairment, executive function, visuospatial processing, attention and IPS, in addition to cerebellar changes generally occurring concomitantly with changes in motor ability [13]. Damage to the white matter microstructure, gray matter lesions, cortical and deep gray matter atrophy are also related to CI in MS [3,14,15]. Studies on functional imaging also associate CI with changes in the frontal, occipital and temporal subregions, in addition to the hippocampus, parahippocampal gyrus and superior temporal cortex [12].

Some treatments have been studied to treat cognitive dysfunction in MS, including cognitive rehabilitation, exercise, and pharmacological management [16]. The development of appropriate treatment strategies that address cognitive decline in MS still needs development. Administering highly effective therapy early in the disease can help reduce cognitive decline in MS [17].

In conclusion, MSCP is a rare form, with few obvious motor symptoms, making it difficult to diagnose early. Therefore, the assessment of cognitive function is essential in patients with MS and can be carried out simply and quickly during follow-up of these patients, through easy-to-apply cognitive tests, such as SDMT, to assist in the diagnosis of CI, and even MSCP.

Conflict of Interest Statement

The authors declare no competing interests.

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