Title: Cognition in Multiple Sclerosis: Bridging Neurology and Psychiatry

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Introduction:

Multiple sclerosis (MS) is increasingly recognized as a disorder extending beyond conventional neurological disability. Cognitive and neuropsychiatric symptoms are common, clinically meaningful, and frequently under-recognized, yet their complex interplay challenges the traditional distinction between neurological and psychiatric manifestations. Cognitive dysfunction may emerge early in the disease course and progress independently of clinical relapses, suggesting that it may provide a sensitive marker of otherwise clinically silent disease activity.

Objectives:

To review the current evidence on cognitive dysfunction in MS, focusing on its clinical relevance, biological substrates, relationship with neuropsychiatric symptoms, and implications for the interface between Neurology and Psychiatry.

Methods:

A semi-structured literature search was conducted in PubMed and other major scientific databases, focusing on recent systematic reviews, meta-analyses, longitudinal studies, and emerging evidence on cognitive progression in MS

Results:

Cognitive impairment affects approximately one-third of patients with relapsing-remitting MS. Processing speed, attention, learning and memory and executive functions are among the most consistently affected domains. Importantly, cognitive dysfunction is not adequately captured by conventional measures of neurological disability and may occur in the absence of clinical relapses.

Recent longitudinal evidence has established the concept of cognitive progression independent of relapse activity (cognitive PIRA), demonstrating that cognitive decline may represent an

independent dimension of MS progression. Emerging neuroimaging data further implicate cortical and deep grey-matter pathology, brain atrophy, network disconnection, and chronic "smouldering" inflammation in cognitive deterioration.

The interface with Psychiatry is particularly relevant. Depression, anxiety, and fatigue frequently coexist with cognitive dysfunction and may influence both subjective cognitive complaints and objective performance. Depressive symptoms have been associated with deficits across several cognitive domains, whereas apathy appears particularly related to executive dysfunction. Conversely, cognitive impairment may contribute to reduced autonomy, occupational dysfunction, social withdrawal, and psychological distress, suggesting a bidirectional relationship between cognition and neuropsychiatric symptoms.

Conclusion:

Cognitive dysfunction should be regarded as a core manifestation of MS, rather than a secondary consequence of physical disability or psychiatric comorbidity. Its occurrence independently of relapses, together with its association with neuropsychiatric symptoms, places cognition at the intersection of Neurology and Psychiatry. Integrating cognitive and psychiatric assessment into routine MS care may improve the detection of clinically silent progression and enable more comprehensive, individualized treatment strategies.