ECRONICON OPEN ACCESS

EC NEUROLOGY
Editorial

Cognitive Impairment as a Biomarker in Multiple Sclerosis

Grigorios Nasios[1]* and Lambros Messinis[2]

[1]*Department of Speech and Language Therapy, School of Health Sciences, University of Ioannina, Ioannina, Greece*
[2]*Neuropsychology Section, Departments of Neurology and Psychiatry, University of Patras Medical School, Patras, Greece*

***Corresponding Author**: Grigorios Nasios, Department of Speech and Language Therapy, School of Health Sciences, University of Ioannina, Ioannina, Greece.

Received: February 27, 2020; **Published:** March 09, 2020

Although Multiple Sclerosis (MS) is a single disease entity, no one person living with MS (pwMS) has the same clinical profile with another. The classical pathoanatomical study of Lucchinetti., *et al.* [1], classifies the disease into four subtypes based on material from biopsies and autopsies of patient's brains. Neuroimaging studies on the other hand have identified four different subtypes based on the relationship between brain lesions and atrophy [2].

On a clinical level the diversity of motor, sensory, cognitive and psychological symptoms and signs and the wide range of severity may lead to an accumulation of disabilities, which in general accumulate within the decades of the disease course, but some patients present these disabilities earlier in the course of the disease and with more severe disability and others much later on and with less severe disability. Some patients may even present with a largely debated condition known as "benign" MS. In this disease course patients experience little disease progression and minimal accumulation of disability decades after developing the disease.

Sayao., *et al.* [3] presented such a study with benign MS patients 20 years after disease diagnosis. In contrast to this much debated group other patients are characterized as having "malignant" or "aggressive" MS [4], less than 5 years after diagnosis.

According to a very recent study by Harel., *et al.* [5] who classified an MS Sample with disease duration of 20 years, based on physical and cognitive disability, reported that there are two sides of a coin; a "bright side" that represents 21.7% of the total and a "dark side" that represents 12% of the total. On the "bright side" 21,7% of these patients live with mild motor difficulties and normal cognitive functions, and on the "dark side"12% of pwMS presented with major motor disability with an Expanded Disability Status Scale (EDSS > 6), but also with severe cognitive impairment.

Findings such as the above require our urgent attention so as to develop valid methods of classifying pwMS adequately in order to offer them the most suitable type of treatment adjusted to their individual needs. The correct classification of pwMS according to their individual needs might not have been as important 20 years ago, when only interferon's-b, glatiramer acetate and a few other medications from the chemotherapy arena were available, but today 18 disease modifying drugs (DMDs) have been approved for use in pwMS. Chitnis and Prat [6] recently published an article on this issue, entitled "A roadmap to precision medicine for multiple sclerosis", which has provided excellent material for "thought and discussion".

Amongst other things, they discuss the urgent need to adopt different types of emerging biomarkers, which will enhance decision-making in MS management and more specifically, the ability to make earlier and more valid diagnoses, prognoses, predictions related to the outcome of specific treatments, monitoring the course of the disease, and possibly even preventing the disease in high risk populations. It is very important that Chitnis and Prat suggest on a clinical level that for every patient visual dysfunction, motor disability, bladder dysfunction, cognitive disability, fatigue and mood should be assessed.

These biomarkers may be clinical, neuroimaging, or biochemical. Technology will contribute to this on numerous levels (for e.g., the analysis of data from wearable biosensors). In our opinion, continuous assessment, timely detection and the monitoring of cognitive and mental functions, in conjunction with other symptoms and impairments may significantly contribute to clinical decision making (e.g., onset and type of treatment, or change to another DMD treatment.

Cognition is a complex process which allows a person to use and process information from the environment and through past experiences form behaviors and adaptive strategies. In this respect, a dysfunction of cognitive functions in MS may lead to profound functional limitations, affecting daily functional capacity, socialization, behavior and mood, and may lead to behavioral disturbances such as aggression or impulsivity and depression or apathy. On the other hand cognitive deficits may affect balance and mobility since impaired attention and distractibility force MS patients to actively think about their walking to reduce potential falls. MS patients with cognitive impairment may also limit their social interaction activities fearing apparent forgetfulness, slowness in thinking, or processing information and consequently develop depression. Furthermore, they may show decreased compliance with their medication regimen by forgetting to take it or by taking it in the wrong way [7].

Another important issue is that cognitive difficulties are not frequently reported by patients among the initial symptoms of MS although there is sufficient evidence that cognitive impairment is present from the early stage of the disease [8] or even before the time of diagnosis [9].

Moreover, cognitive impairment may be present in the early stages of the disease in patients with relatively low or mild physical disability (see for e.g. the studies by Ruggieri., *et al.* [10] and Messinis., *et al.* [11]), who found cognitive deficits in patients with an EDSS disability score of ≤ 3.5, that had not yet been influenced significantly in their daily functional abilities.

Unfortunately, neurologists are not able to detect CI by routine clinical evaluation, including the through the utilization of the well known and frequently used EDSS. Romero., *et al.* [12] found that "Neurologists' accuracy" to detect CI in pwMS "was not significantly different from chance". In this respect, these types of symptoms may escape the proper attention of patients, family, and unfortunately the treating clinicians, loosing valuable "time and brain". For this reason we recently proposed a practical algorithm for the timely detection and monitoring of cognitive impairment in pwMS [13].

One important reason that cognitive disorders or deficits remain "undetected" is the ability of the brain to reorganize itself via neuroplasticity mechanisms thereby "hiding" these cognitive weaknesses [14]. This "secretive" or "hidden" part of the iceberg significantly delays the initiation of any therapeutic scheme in this important (window) period with the available treatments. Especially in patients that present with cognitive impairment early on in the disease process, and specifically in patients with a "motor - cognitive split", with a clinical picture characterized by poor cognitive function with normal motor ability, i.e. low EDSS score; or when cognitive impairment develops during the course of the disease, this should be reason enough to start a more aggressive treatment scheme.

Therefore, this is the main reason that we suggest detection of cognitive impairment be utilized as a clinical biomarker via continuous and tactic standardized neuropsychological assessment, from the diagnosis and annually thereafter, or when we are suspicious of a cognitive relapse or due to progression of disability.

Bibliography

1. Lucchinetti C., *et al*. "Heterogeneity of multiple sclerosis lesions: Implications for the pathogenesis of demyelination". *Annals of Neurology* 47.6 (2000): 707-717.

2. Tauhid S., *et al*. "MRI phenotypes based on cerebral lesions and atrophy in patients with multiple sclerosis". *Journal of the Neurological Sciences* 346.1-2 (2014): 250-254.

3. Sayao AL., *et al*. "The psychosocial and cognitive impact of longstanding "benign" multiple sclerosis". *Multiple Sclerosis Journal* 17.11 (2011): 1375-1383.

4. Menon S., *et al*. "Characterising aggressive multiple sclerosis". *Journal of Neurology, Neurosurgery, and Psychiatry* 84.11 (2013): 1192-1198.

5. Harel Y., *et al*. "Cognitive function in multiple sclerosis: A long-term look on the bright side". *PLoS One* 14.8 (2019): e0221784.

6. Chitnis T and Prat A. "A roadmap to precision medicine for multiple sclerosis". *Multiple Sclerosis Journal* 22 (2020): 1352458519881558.

7. Messinis L., *et al*. "Neuropsychological Features of Multiple Sclerosis: Impact and Rehabilitation: Editorial". *Behavioural Neurology* (2018).

8. Messinis L., *et al*. "Neuropsychological Functions and Cognitive Neurorehabilitation in Multiple Sclerosis". *IntechOpen* (2019).

9. Cortese M., *et al*. "Preclinical disease activity in multiple sclerosis: A prospective study of cognitive performance prior to first symptom". *Annals of Neurology* 80.4 (2016): 616-624.

10. Ruggieri RM., *et al*. "Cognitive impairment in patients suffering from relapsing-remitting multiple sclerosis with EDSS ≤ 3.5". *Acta Neurologica Scandinavica* 108 (2003): 323-326.

11. Messinis L., *et al*. "Cognitive deficits in relapsing remitting multiple sclerosis patients with low disability status". In: Proceedings of the 7th International Congress on the Improvement of the Quality of life on Dementia, Parkinson's disease, Epilepsy, MS, Muscular Disorders and Neuroethics (2009): 31-35.

12. Romero K., *et al*. "Neurologists accuracy in predicting cognitive impairment in multiple sclerosis". *Multiple Sclerosis and Related Disorders* 4.4 (2015): 291-295.

13. Bakirtzis C., *et al*. "The Rationale for Monitoring Cognitive Function in Multiple Sclerosis: Practical Issues for Clinicians". *The Open Neurology Journal* 31.12 (2018): 31-40.

14. Nasios G., *et al*. "Cognitive impairment and brain reorganization in MS: underlying mechanisms and the role of neurorehabilitation". *Frontiers in Neurology* (2020).

Volume 12 Issue 4 April 2020