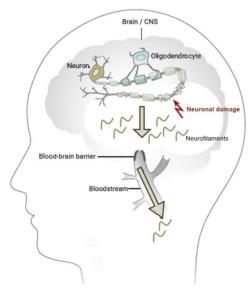
About neurofilaments

Neurofilaments are essential components of neurons and are involved in preserving the shape of nerve cells.¹ However, their role is not only structural but also functional as neurofilaments are crucial for signal transmission along the nerve cells.¹ Neurofilaments (Nf) consist of four subunits: Nf-light (NfL), Nf-medium (NfM), Nf-heavy (NfH) and α -internexin in the central nervous system (CNS), or peripherin in the peripheral nervous system.¹

Could neurofilaments be a potential biomarker in multiple sclerosis?

Neurofilaments as biomarkers of neurologic disorders



When axons from the CNS are damaged because of a trauma or a disease—their components, including neurofilaments, are released into the cerebrospinal fluid (CSF).²

Neurofilaments are also able to cross the blood–brain barrier and reach the bloodstream. Testing the neurofilament concentration in CSF or blood can therefore provide insights into the degree of neuronal damage.^{3,4}

As they are exclusively and abundantly expressed in neurons, neurofilaments (particularly NfL) have been identified as promising biomarkers of neuronal cell damage in some neurological disorders—such as multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS) and Parkinson's disease.⁵

A promising tool for MS clinical practice

MS is a chronic disease affecting the CNS, characterized by inflammatory and neurodegenerative processes resulting in lesions in both the white and grey matter. These lesions ultimately lead to physical and cognitive impairment.⁶

Currently, clinical investigation of CNS lesions in patients relies on magnetic resonance imaging (MRI). While white matter lesions can be visualized using different MRI protocols, grey matter lesions or diffuse microlesions are hardly visible.^{7–9}

An additional monitoring tool would therefore be very beneficial, especially if it could easily assess the disease course and treatment efficacy, as this has the potential to support optimization of the therapeutic strategy.¹⁰

In this context, neurofilament as a potential biomarker in MS is gaining increased interest and recent studies focusing specifically on NfL are promising. With improving techniques enabling the detection of low NfL concentrations, researchers are now focusing on serum NfL levels (sNfL). These can be measured through a simple blood test, representing a less invasive procedure for patients.^{3,10}

Why are sNfL a promising biomarker for MS?

- sNfL levels mirror the appearance of new CNS lesions.^{4,5}
- Recent studies showed that sNfL levels could also be used to help assess the course of MS (e.g. future relapse risk, disability worsening and treatment response).^{3–5,11}
- Collecting sNfL through blood sampling is simple, easily repeatable and less invasive for patients.

Reimagining care for people living with MS

Finding good biomarkers is challenging, as they should ideally reflect disease stage, prognosis and treatment efficacy. Responding to these criteria, NfL appear as promising biomarkers in MS. If implemented from the early stage of the disease, NfL could complement the clinical tools available to help physicians in their practice.^{7,8}

- MRI: visualization of the CNS lesions
- Expanded Disability Status Scale (EDSS): assessment of disability
- Relapse following: monitoring of the disease evolution
- NfL: evaluation and prognosis of the disease course as well as treatment efficacy

Therefore, NfL could potentially become a powerful decision-making tool for physicians, which is also cost effective and minimally invasive for patients. As a result, NfL could significantly improve MS patients' outcomes.

Novartis is committed to providing MS patients with the best therapeutic solutions. Reimagining care in MS for Novartis also means being at the forefront of NfL research to improve the assessment of disease activity in MS patients.

References

- 1. Yuan A, Rao MV, Nixon V, Nixon RA. Neurofilaments at a glance. J Cell Sci. 2012;125(Pt 14):3257–3263.
- 2. Deisenhammer F, Zetterberg H, Fitzner B, et al. The Cerebrospinal Fluid in Multiple Sclerosis. *Front Immunol.* 2019;10:726.
- 3. Disanto G, Barro C, Benkert P, et al. Serum Neurofilament light: A biomarker of neuronal damage in multiple sclerosis. *Ann Neurol.* 2017;81(6):857–870.
- Novakova L, Zetterberg H, Sundström P, et al. Monitoring disease activity in multiple sclerosis using serum neurofilament light protein. *Neurology*. 2017;89(22):2230–2237.
- 5. Khalil M, Teunissen CE, Otto M, et al. Neurofilaments as biomarkers in neurological disorders. *Nat Rev Neurol.* 2018;14(10):577–589.
- 6. Reich DS, Lucchinetti CF, Calabresi P. Multiple Sclerosis. N Engl J Med. 2018;378(2):169–180.
- Uitdehaag BMJ. Clinical outcome measures in multiple sclerosis. *Handb Clin Neurol*. 2014;122(3):393–404.
 Daumer M, Neuhaus A, Herbert J, Ebers G. Prognosis of the individual course of disease: the elements of time,
- heterogeneity and precision. *J Neurol Sci.* 2009;287(S1):50–55.
 Inglese M, Oesingmann N, Casaccia P, Fleysher L. Progressive Multiple Sclerosis And Gray Matter Pathology:
- An MRI Perspective. *Mt Sinai J Med.* 2011; 78(2): 258–267.
 Bhan A, Jacobsen C, Myhr KM, et al. Neurofilaments and 10-year follow-up in multiple sclerosis. *Mult Scler.* 2018;24(10):1301–1307.
- Varhaug KN, Torkildsen Ø, Myhr KM, Vedeler CA. Neurofilament Light Chain as a Biomarker in Multiple Sclerosis. Front Neurol. 2019;10:338.