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# Neurofilament light chain – a marker of neuronal injury

FROM THE SPECIALTIES

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## Neurofilament light chain is released following neuronal injury and has been referred to as 'the neurologist's troponin'.

Measuring neurofilament light chain in cerebrospinal fluid has long been possible. With single molecule array (Simoa), neurofilament light chain can now also be measured in blood (1), and Akershus University Hospital offers analyses of both cerebrospinal fluid and serum.

## Diagnosis and prognosis

The highest levels of neurofilament light chain are seen in diseases with extensive axonal damage, such as frontotemporal dementia, Creutzfeldt-Jakob disease and amyotrophic lateral sclerosis, while mildly elevated or normal values can be observed in more slowly progressing conditions, such as Alzheimer's disease and Parkinson's disease (1). In neurodegenerative diseases, high levels generally indicate a poor prognosis (1).

## Amyotrophic lateral sclerosis

Neurofilament light chain has been particularly studied in multiple sclerosis and amyotrophic lateral sclerosis. The analysis can distinguish amyotrophic lateral sclerosis from relevant differential diagnoses with a sensitivity and specificity of over 80 % (1), and blood concentrations can rise several years before clinical symptoms are apparent (2). Specific treatments have been developed for certain hereditary forms of amyotrophic lateral sclerosis, and neurofilament light chain is recognised as a marker of treatment response (3).

## Multiple sclerosis

In multiple sclerosis, longitudinal measurements of neurofilament light chain in the blood can provide information about treatment response and prognosis (4). The most effective disease-modifying therapies reduce the concentration to normal levels. Blood concentrations rise during relapses and can remain elevated for several months (1). However, neurofilament light chain is not a replacement for MRI in assessing an active relapse, as the increase may not occur until several weeks later (5).

There are no official guidelines for measuring neurofilament light chain in multiple sclerosis. However, international experts recommend measuring it at the start of treatment and after 3–6 months, and escalating treatment in patients with persistently high levels (4). In Norway, most patients with relapsing multiple sclerosis are treated with rituximab. Persistently elevated neurofilament light chain should raise suspicion of treatment failure due to neutralising antibodies or other causes.

## Use and interpretation

All doctors can order an analysis of neurofilament light chain in blood, but the test's sensitivity and specificity are too low for it to be used as a screening tool. The analysis complements clinical assessment and other diagnostic methods but is not a replacement for these. We only recommend measuring neurofilament light chain for diagnosis and follow-up of patients with neurological diseases in specialist health care. The test can be especially useful when there is suspicion of diseases involving significant neuronal damage, such as amyotrophic lateral sclerosis, frontotemporal dementia, multiple system atrophy and progressive supranuclear palsy. The Norwegian Laboratory Code Registry's fee for neurofilament light chain analysis in blood is NOK 1274 as of April 2025.

It is known that levels of neurofilament light chain in cerebrospinal fluid and blood increase with age and are influenced by body mass index and comorbidities (1). Results therefore need to be interpreted by a specialist.

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