



# What is neuroinflammation?

Inflammation is an essential biological process triggered by injury, infection, and trauma suffered by cells or tissues. A successful inflammatory response eliminates invading pathogens and initiates wound healing and angiogenesis. However, unresolved inflammation can adversely affect recovery and lead to tissue degeneration.<sup>1</sup>

**Neuroinflammation** is a defence mechanism associated with the response of all brain cells, including neurons, macroglia, and microglia. <sup>1-3</sup> Neuroinflammation is an important feature of many neurodegenerative diseases such as multiple sclerosis, Alzheimer's disease, amyotrophic lateral sclerosis, and Parkinson's disease. <sup>1,4</sup> Neuroinflammation is involved in migraine headaches, cerebrovascular diseases, neurological conditions such as epilepsy, and psychiatric disorders such as depression, bipolar disorder and schizophrenia. <sup>5-7</sup>

## Neuroinflammation and the blood brain barrier'

In the past, it was believed that due to the blood-brain barrier (BBB), the central nervous system (CNS) was immunoprivileged; however, increasing evidence has disputed this belief. CNS cells seem to be reactive to peripheral inflammatory factors, and peripheral immune cells can infiltrate the brain. A Neuroinflammatory diseases cause an impairment of the BBB. The BBB integrity can be impacted by traumatic brain injury, stroke, and even environmental toxins such as aluminium and mercury.



# **KEY HIGHLIGHTS:**

- Neuroinflammation is crucial in neurodegenerative diseases affecting the brain's response to injury and infection.
- O Genetic predisposition, ageing, traumatic brain injury, chronic stress, environmental toxins, and gut inflammation can influence neuroinflammation.
- Neuroinflammation can be assessed through neuroimaging, electroencephalography, blood markers of inflammation, and stool testing.
- Symptoms of neuroinflammation include brain fog, low mood, poor memory, concentration issues, fatigue, headaches, digestive disturbances, and increased pain sensitivity.
- Early intervention is key. Treatment includes stress management, dietary changes, physical activity, sleep improvement, and supplementation with anti-inflammatory nutrients like zinc, magnesium, vitamin C, vitamin D, and omega-3 fatty acids.

Information about neuroinflammation can generally be obtained by conducting a thorough clinical assessment including a history of past and current stressors, traumatic brain injuries, dietary intake, sleep quality, viral infections, and physical activity.



# What triggers neuroinflammation?

There are several environmental and genetic factors that can trigger, exacerbate, and prolong neuroinflammation. These include:

- Certain genetic predispositions, ageing, traumatic brain injury, chronic physical and psychological stress, exposure to environmental toxins, viral infections, autoimmune disease, obesity, and metabolic conditions such as metabolic syndrome and diabetes.1,4
- Gut inflammation is also associated with neuroinflammation. Lipopolysaccharides (LPS), a major component of the outer membrane of Gram-negative bacteria, instigate systemic inflammatory responses, ultimately triggering an inflammatory response in the CNS.10
- Foods, sleep patterns, and physical activity also play a role in neuroinflammation.11-13
- Prenatal stress and childhood trauma also affect the activity of microglia, the resident immune cells of the brain. 14-16

### How to test for neuroinflammation?

Identifying what is happening in the brain can be difficult. Neuroimaging and electroencephalography can provide some insights into neuroinflammation, however specialist referral is required. Assessing for inflammatory biomarkers in the cerebrospinal fluid can be undertaken in exceptional circumstances.<sup>17</sup> Blood markers of inflammation, such as C-reactive protein and cytokine panels, and concentrations of blood markers of autoimmunity can suggest neuroinflammation.<sup>17,18</sup> Blood concentrations of these markers, however, may not translate into reliable measures of the processes occurring in the brain.

Gut health can be assessed with stool testing. Microbial testing can provide some insights into general gut function and inflammation.<sup>19</sup>

Reported symptoms of brain fog, low mood, poor memory and concentration, fatigue, headaches, migraines, digestive disturbances, and increased pain sensitivity can indicate potential neuroinflammation. This information can be obtained from a clinical interview and validated self-report questionnaires and symptom diaries.

Early intervention provides the best treatment outcomes, as prolonged neuroinflammation can lead to irreversible neurological damage.

The brain is incredibly resilient and neuroplasticity can occur despite long-standing neuroinflammation.<sup>20</sup>

As with any condition, the key is identifying potential causes or contributors to a person's neuroinflammation and applying appropriate treatment strategies. These can include teaching stress management, implementing dietary changes, recommending moderate physical activity, incorporating sleeprelated changes and education about lifestyle or environmental changes to minimise exposure to environmental pollutants.

**Supplementation** with certain macro- and micronutrients and herbal or plant-based compounds may also be helpful.

## Anti-inflammatory nutrients include:

- magnesium
- vitamin D
- omega-3 fatty acids
- zinc<sup>21,22</sup>
- vitamin C

Anti-inflammatory compounds found in plants, fruits and vegetables, may provide neuroprotective benefits and lower neuroinflammation, include:

- berberine
- quercetin
- curcumin
- resveratrol<sup>2,23</sup>
- epigallocatechin gallate

Specialised pro-resolving mediators (SPMs) are another potential option to reduce neuroinflammation. SPMs are cell-signalling molecules formed in cells by the metabolism of polyunsaturated fatty acids. SPM supplementation may help support the resolution of neuroinflammation.24

Preliminary research presents **probiotics** as another treatment option. Evidence in animal trials indicates that probiotics can reduce LPS-induced neuroinflammation.<sup>25,26</sup>

# **SUMMARY**

Neuroinflammation is a condition that is associated with an extensive array of conditions and symptomatic profiles.

Understanding the potential role of neuroinflammation in our clients and implementing strategies to reduce neuroinflammation is important for all health practitioners; not only those practitioners who treat 'brain-related conditions'.

- Shabab, T., et al., Neuroinflammation pathways: a general review. Int. J. Neurosci, 2017. 127(7): p. 624-633.

  Kaur, N., et al., Neuroinflammation Mechanisms and Phytotherapeutic Intervention: A SystWematic Review. ACS Chem Neurosci, 2020. 11(22): p. 3707-3731.

  Gilhus, N.E. and G. Deuschi, Neuroinflammation a common thread in neurological disorders. Nat Rev Neurol, 2019. 15(8): p. 429-430.
- Kolliker-Fres R, et al., Neuroinflammation: An Integrating Overview of Reactive-Neuroimmune Cell Interactions in Health and Disease. Mediators Inflamm, 2021; 2021; p. 9999146.

  Dunn, G.A., J.M. Loftis, and E.L. Sullivan, Neuroinflammation in psychiatric disorders: An introductory primer. Pharmacol Biochem

- Dunn, CA-, J.M. Lottis, and E.L. Sullivan, Neuronniammation in psycriauric usorues and introduced y parties in additionable behavious parties of the property of the property
- in Brain Microvascular Endothelial Cells for Prevention and Treatment of BBB Dysfunction, Front Cell Neurosci, 2021, 15: p. 661838.
- Batista, C.R.A., et al., Lipopolysaccharide-Induced Neuroinflammation as a Bridge to Understand Neurodegeneration. Int J Mol Sci, and the Company of the C
- Batista, C.H.A., et al., Lipopolysacchande-induced Neurontiammation as a bringge to Understand Neurodegeneration. Inf J Mol Sci. 2019;20(9).
  Wang, M., et al., Exercise suppresses neuroinflammation for alleviating Alzheimer's disease. J Neuroinflammation, 2023;20(1):p. 76.
  Zielinski, M.R. and A.J. Gibbons, Neuroinflammation, Siega, and Circadian Phythms. Front Cell Infect Microbiol, 2022;12:p. 853096.
  Bok. E., et al., Dietary Restriction and Neuroinflammation: A Potential Mechanistic Link. Int. J Mol Sci., 2019;20(3).
  Luris DJ. An Integrative Approach to Neuroinflammation in Psychiatric disorders and Neuropathic Pain. J Exp Neurosci, 2018;12:p.

- 1179069518793639. Poletti, S., et al., Long-term effect of childhood trauma: Role of inflammation and white matter in mood disorders. Brain Behav Immun
- Foletti, S., et al., Long-term effect of childhood trauma: Hole of inflammation and white matter in mood disorders. Brain Behavimmu, Health, 2022. 26, p. 1005.29.

  Diz-Chaves, Y., et al., Prenatal stress causes alterations in the morphology of microglia and the inflammatory response of the hippocampus of adult female mics. J Neuroinflammation, 2012. 9, p. 71.

  Bechter, K., The Challenge of Assessing Mild Neuroinflammation in Severe Mental Disorders. Front Psychiatry, 2020. 11, p. 773.

  Ransohoff, R.M., et al., Neuroinflammation. Ways in Which the Immune System Affects the Brain. Neurotherapeutics, 2015. 12(4): p. 2020. 2020.

- Dumitrescu, L., et al., Serum and Fecal Markers of Intestinal Inflammation and Intestinal Barrier Permeability Are Elevated in
- Dumitrescu, L., et al., Serum and Fecal Markers of Intestinal Inflammation and Intestinal Barrier Fermeability Are Elevated in Parkinson's Diseases. Front Neurosci, 2021; 15, p. 689723.

  Voss, P., et al., Dynamic Brains and the Changing Rules of Neuroplasticity: Implications for Learning and Recovery, Front Psycho 2017; 8, p. 1657.

  Holton, K.F., Micronutrients May Be a Unique Weapon Against the Neurotoxic Triad of Excitotoxicity, Oxidative Stress and Neuroinflammation: A Perspective, Front Neurosci, 2021; 15; p. 726457.

  Devassy, J.G., et al., Omega-3 Polyursaturated Fatty Acids and Oxylipins in Neuroinflammation and Management of Alzheimer
- Disease, Adv Nutr. 2016, 7(5): p. 905-16.
- Disease. An Avail, 2010. 10(1): 200-201. W.W.X., Y.Yan, and Q. Zhang, Neuroinflammation and Modulation Role of Natural Products After Spinal Cord Injury. J Inflamm Res, 2021.14; p.5713-5737.

  Valente, M. et al., Specialized Pro-Resolving Mediators in Neuroinflammation: Overview of Studies and Perspectives of Clinical Applications. Molecules, 2022.27(15).
- Applications in Notice in the Secretary of the Conference of the C
  - Anderson, R.C., Can probiotics mitigate age-related neuroinflammation leading to improved cognitive outcomes? Front Nutr, 2022 9: p. 1012076



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