Factors influencing the microbiome and gut-brain axis

Dietary components

Dietary fibre

- There is now overwhelming evidence of the health benefits of dietary fibre consumption and its association with high concentrations of short-chain fatty acids (SCFAs) in the gut (1)
- The microbiome depends on dietary fibre to thrive and consumption of dietary fibre appears to be a critical determinant for gut bacterial ecology, diversity, and function (2). Consumption of dietary fibre has a direct effect on the microbiome composition (3)
- Bacterial fermentation of dietary fibre generates SCFAs such as butyrate, an essential metabolite for intestinal homeostasis (4). Butyrate is the preferred energy source for colonocytes, contributes to gut barrier integrity and suppresses gut inflammation. A diet lacking in fibre can lead to chronic GI inflammation and a compromised gut barrier (3)

Dietary protein

- Dietary protein serves as the major source of nitrogen for colonic microbial growth and is essential to the assimilation of carbohydrates and production of beneficial products such as SCFAs. Hence, a combination of protein and carbohydrates in the large bowel can contribute to bowel health (5)
- High-protein diets, however, increase detrimental metabolites in faeces and high intake of animal protein is associated with an increased risk of IBD (6)
- The gut microbiota is affected by excess protein fermentation in the colon. The effect of protein digestion is determined by the amount and source of protein. Dietary strategies with judicious selection of source and supplementation of dietary protein to benefit gut health are important (7)

Dietary fat

- Several *in vivo* studies have shown that a high-fat diet is associated with a decrease in butyrate-producing bacteria and increased GI inflammation. Dietary fats, particularly trans and saturated fats, also alter diurnal patterns of gut microbiota structure and function (3,8)
- Omega-3 polyunsaturated fatty acids (n-3-PUFAs), primarily eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), may improve or prevent some neurological and neuroimmune disorders (for example, depression and AD) (3)
- A randomized trial found that supplementation with n-3-PUFA induces a reversible increase in several SCFA-producing bacteria (9)
- These observations suggest that n-3-PUFA supplementation may represent an effective way to modify the production of SCFAs and in turn improve GI homeostasis (3)
- DHA and EPA are available commercially as purified supplements, however, they are present in high quantities in fish, especially cold-water fatty fish, such as salmon, mackerel, low-mercury tuna, herring and sardines

Dietary polyphenols

- A novel and relevant strategy in reducing neuroinflammation and oxidative stress, improving memory and cognitive function, as well as modulating the gut microbiota, making them promising nutraceuticals to combat neurological disorders (10)
- Abundant in fruits, vegetables, red wine, green and black tea (3)
- Citrus flavanones (e.g. hesperidin and naringin) are able to influence the microbiota composition and activity and exert beneficial effects on intestinal barrier function and gastrointestinal inflammation (11)
- While studies clearly underscore the potential benefits of polyphenols in modifying and modulating the gut microbiota, most of these studies have been carried out using experimental models. Therefore, more clinical trials are needed to fully appreciate their benefit (3)

Vitamins	**Vitamin A** • Plays an important role in neurological function as well as regulating the CNS development • Promotes intestinal immunity and maintains gut barrier integrity • Influences the microbiome profile, including in children with ASD (3,12,13) **Vitamin D** • Several neuroimmune and neuroinflammatory diseases which are associated with microbiome alterations such as MS, ASD and AD, have been associated with vitamin D deficiency (3) • Evidence for the efficacy of vitamin D in altering the microbiota in neuroimmune and neuroinflammatory diseases is limited and supported by indirect evidence, however, there is substantial evidence supporting its role in maintaining GI homeostasis by regulating mucosal inflammatory responses and maintaining intestinal barrier function (3) **B Vitamins** • B vitamins are acquired through diet or from the gut microbiota, and their deficiencies are often found in patients with intestinal malabsorption. B vitamin deficiencies lead to deleterious neurological effects including polyneuropathy, diabetic polyneuropathy, optic atrophy, myelopathy and cerebellar ataxia (3) • Vitamin B_{12} is made in significant quantities by commensal bacteria in the large intestine; however, the necessary transport receptors in humans are primarily in the small intestine, suggesting that the B_{12} produced by the microbiota is primarily consumed by the microbiota. Accordingly, B_{12} supplementation may represent an effective way to modulate the gut microbiota, particularly in the small intestine (14)
Probiotics	• Probiotics have recently attracted attention in the context of brain function and health because they serve to alter gut microflora toward a beneficial state, which could affect the gut-brain axis (15). Certain probiotics may positively impact the pathogenesis of neurological disorders, however, most of the studies are based on indirect evidence (3) • A recent meta-analysis concluded that probiotics may have a positive effect on psychological symptoms in healthy individuals, however, the effect may be significantly reduced in individuals suffering from existing chronic conditions, particularly those associated with dysbiosis, immune function changes and psychological comorbidities such as IBS and rheumatoid arthritis (16) • The term 'psychobiotics' is defined as any live organism that, when ingested in adequate amounts, produces a health benefit in patients suffering from psychiatric illness (17) • Psychobiotics are by definition a subgroup of probiotics with the added emphasis on mental illness. Most psychobiotics are capable of producing or promoting the endogenous synthesis of neurotransmitters which influence the gut-brain axis and mental health. Biogenic amines implicated in neuroimmune disease pathology, such as brain-derived neurotrophic factor (BDNF), dopamine, gamma-aminobutyric acid (GABA) and glutamate, are influenced by gut microbes (3) • Fermented foods may be a useful dietary strategy for mental and brain health (8) • Consuming probiotics from the *Bifidobacterium* and *Lactobacillus* genera reduces negative mood in healthy individuals (18)
Harmful dietary components	• It is important to consider the emerging evidence regarding the harmful impact of components of 'junk' and processed foods, including dietary emulsifiers, artificial sweeteners and high-fat, refined-sugar diets on gut and brain health (23) • Emulsifiers, compounds commonly used in a variety of foods, promote gut microbiota alteration and gut barrier dysfunction, leading to negative metabolic alterations resulting in weight gain low-grade inflammation and metabolic disorders (24) • Artificial sweetener consumption has been linked to gut dysbiosis and metabolic abnormalities (9,25)