Microbiota (mi·cro·bi·o·ta) the microscopic organisms of a particular environment

Microbiome (mi·cro·bi·ome) a community of microorganisms

Prebiotics (pre·bi·ot·ic) a substance and especially a carbohydrate (such as inulin) that is nearly or wholly indigestible and that when consumed (as in food) promotes the growth of beneficial bacteria in the digestive tract

Probiotics (pro·bi·ot·ic) a microorganism (such as lactobacillus) that when consumed (as in a food or a dietary supplement) maintains or restores beneficial bacteria to the digestive tract

Dysbiosis (dĭs″bī-ō′sĭs) The condition that results when the natural flora of the gut are thrown out of balance, such as when antibiotics are taken.

Oral Health(Periodontal disease) and Alzheimers

https://pubmed.ncbi.nlm.nih.gov/26063967/ Porphyromonas gingivalis Periodontal Infection and Its Putative Links with Alzheimer's Disease 2015
Periodontal disease (PD) and Alzheimer's disease (AD) are inflammatory conditions affecting the global adult population. In the pathogenesis of PD, subgingival complex bacterial biofilm induces inflammation that leads to connective tissue degradation and alveolar bone resorption around the teeth. In health, junctional epithelium seals the gingiva to the tooth enamel, thus preventing bacteria from entering the gingivae. Chronic PD involves major pathogens (Porphyromonas gingivalis, Treponema denticola, and Tannerella forsythia) which have an immune armoury that can circumvent host's immune surveillance to create and maintain an inflammatory mediator rich and toxic environment to grow and survive. The neurodegenerative condition, AD, is characterised by poor memory and specific hallmark proteins; periodontal pathogens are increasingly being linked with this dementing condition. It is therefore becoming important to understand associations of periodontitis with relevance to late-onset AD. The aim of this review is to discuss the relevance of finding the **keystone periodontal pathogen P. gingivalis in AD brains** and its plausible contribution to the aetiological hypothesis of this dementing condition.
https://pubmed.ncbi.nlm.nih.gov/25522313/ Serum IgG antibody levels to periodontal microbiota are associated with incident Alzheimer disease 2014
Periodontitis and Alzheimer disease (AD) are associated with systemic inflammation. This research studied serum IgG to periodontal microbiota as possible predictors of incident AD.
Using a case-cohort study design, 219 subjects (110 incident AD cases and 109 controls without incident cognitive impairment at last follow-up), matched on race-ethnicity, were drawn from the Washington Heights-Inwood Columbia Aging Project (WHICAP), a cohort of longitudinally followed northern Manhattan residents aged >65 years. Mean follow-up was five years (SD 2.6). In baseline sera, serum IgG levels were determined for bacteria known to be positively or negatively associated with periodontitis (Porphyromonas gingivalis, Tannerella forsythia, Actinobacillus actinomycetemcomitans Y4, Treponema denticola, Campylobacter rectus, Eubacterium nodatum, and Actinomyces naeslundii genospecies-2). In all analyses, we used antibody threshold levels shown to correlate with presence of moderate-severe periodontitis. **Conclusions: Serum IgG levels to common periodontal microbiota are associated with risk for developing incident AD.**
https://pubmed.ncbi.nlm.nih.gov/36299333/ Association of periodontitis and oral microbiomes with Alzheimer's disease: A narrative systematic review 2022
Periodontitis is an infectious and inflammatory disease which mainly causes alveolar bone destruction and tooth loss. **Results:** This review included 26 articles based on the eligibility criteria. Epidemiologic researches and post-mortem **studies showed that the presence of periodontitis is associated with cognitive decline**, suggesting a possible role of periodontal pathogens in the pathogenesis of AD. The reported microbiome was inconsistent with those in gene sequencing studies. Nevertheless, **Gram-negative species may be possible candidates**.
https://pubmed.ncbi.nlm.nih.gov/36009350/ Oral Microbiota, Its Equilibrium and Implications in the Pathophysiology of Human Diseases: A Systematic Review 2022
Dysbiosis of the oral microbiota is implicated in the apparition and progression of cardiovascular, neurodegenerative and other major human diseases. The **reviewed scientific literature provides plausible vias of implication of dysbiotic oral microbiota in systemic human diseases,** and encourages further research to continue elucidating the highly relevant and still poorly understood implications of this niche microbiota in systemic health. P

Gut microbiome and Alzheimers (note best with selenium)

https://pubmed.ncbi.nlm.nih.gov/29051531/ Gut microbiome alterations in Alzheimer's disease 2017
Our analyses revealed that the **gut microbiome of AD participants has decreased microbial diversity** and is compositionally distinct from control age- and sex-matched individuals. We identified phylum- through genus-wide differences in bacterial abundance including **decreased Firmicutes, increased Bacteroidetes, and decreased Bifidobacterium in the microbiome of AD participants**.
https://pubmed.ncbi.nlm.nih.gov/31434623/ Mild cognitive impairment has similar alterations as Alzheimer's disease in gut microbiota 2019
Linkage to other major theories: **Escherichia was observed increased at genus level in both fecal and blood samples from AD and MCI**. For AD biomarker, postmortem brain tissue from patients with AD showed **lipopolysaccharides and gram-negative Escherichia coli fragments colocalize with amyloid plaque**. In this way, the amyloid pathogenesis for AD would be triggered during MCI by gut microbiota shifting. Besides, **systemic inflammatory reactions caused by compounds secreted by bacteria may impair the blood-brain barrier and promote neuroinflammation and/or neurodegeneration**. Furthermore, abnormal metabolites caused by microbial gene functions have an impact on neurodegeneration.
https://pubmed.ncbi.nlm.nih.gov/33523001/ Gut Microbiome Features of Chinese Patients Newly Diagnosed with Alzheimer's Disease or Mild Cognitive Impairment 2021
Conclusion: Patients newly diagnosed with AD or MCI have gut dysbiosis that includes the decrease of potentially protective microbiome, such as Bacteroides, and the increase of microbiome that can promote inflammation, such as Prevotella. Our results support a novel idea that the degree of gut dysbiosis is worsened with the disease stage from MCI to AD.
https://pubmed.ncbi.nlm.nih.gov/31628992/ Exercise, diet and stress as modulators of gut microbiota: Implications for neurodegenerative diseases 2020
. In fact, **gut dysbiosis (microbiota dysregulation) has been associated with a range of neurodegenerative diseases, including Alzheimer's**, Parkinson's, Huntington's and motor neuron disease, as well as multiple sclerosis. The gut microbiota constitutes a dynamic microbial system constantly challenged by many biological variables, including environmental factors. Since the gut microbiota constitute a changeable and experience-dependent ecosystem, they provide potential therapeutic targets that can be modulated as new interventions for dysbiosis-related disorders, including neurodegenerative diseases. This article reviews the evidence for environmental modulation of gut microbiota and its relevance to brain disorders, exploring in particular the implications for neurodegenerative diseases.
https://pubmed.ncbi.nlm.nih.gov/31476155/ "Muscle-Gut-Brain Axis": Can Physical Activity Help Patients with Alzheimer's Disease Due to Microbiome Modulation? 2019
Research shows that the treatment of intestinal dysbiosis with probiotics/synbiotics/eubiotics can prevent or alleviate the symptoms of these chronic neurological diseases. Studies also point to the positive effects of movement on the health of seniors. A positive correlation can be found between cognitive functions and physical stress, both in the elderly and in AD patients. Even short-term interventions with a relatively low frequency seem to produce positive results, while physical activities can be performed by using relatively simple and cost-effective means. In addition, **physical activity can significantly modulate gut microbiome**. Thus, it can be concluded that physical activity in humans seems to correlate with gut microbiome, which can prevent the incidence and development of AD.
https://pubmed.ncbi.nlm.nih.gov/36235612/ Altered Gut Microbiota and Its Clinical Relevance in Mild Cognitive Impairment and Alzheimer's Disease: Shanghai Aging Study and Shanghai Memory Study 2022
Erysipelatoclostridiaceae, Erysipelotrichales, Patescibacteria, Saccharimonadales, and Saccharimonadia, compared with NC group (p < 0.05), which were positively correlated with APOE 4 carrier status and Clinical Dementia Rating (correlation coefficient: 0.11~0.31, p < 0.05), and negatively associated with memory (correlation coefficient: -0.19~-0.16, p < 0.01). Our results supported the hypothesis that **intestinal microorganisms change in MCI and AD**.
https://pubmed.ncbi.nlm.nih.gov/34024839/ Altered Gut Microbiota in Adults with Subjective Cognitive Decline: The SILCODE Study 2021
Results: The **abundance of phylum Firmicutes, class Clostridia, order Clostridiales, family Ruminococcaceae, and genus Faecalibacterium showed a trend toward a progressive decline** from NC to SCD and CI. Specifically, the **abundance of the anti-inflammatory genus Faecalibacterium was significantly decreased in SCD** compared with NC.
https://pubmed.ncbi.nlm.nih.gov/36093178/ A comparison of the composition and functions of the oral and gut microbiotas in Alzheimer's patients 2022
Objective: **Alterations in the oral or gut microbiotas have been reported in patients with subjective and mild cognitive impairment or AD dementia.** However, whether these microbiotas change with the severity of the AD spectrum (mild, moderate, and severe AD) remains unknown. Thus, we compared alterations in the composition and gene functions of the oral and gut microbiota between different phases of AD.
Results: **In order of the severity of cognition impairment (from normal to mild and to moderate AD), the oral abundances of the phyla Firmicutes and Fusobacteria showed a gradual upwards trend,** while the **abundance of the Proteobacteria phylum gradually decreased. In contrast, the abundance of the Firmicutes and Bacteroidetes phyla in the gut decreased progressively, while that of the Proteobacteria, Verrucomicrobia and Actinobacteria phyla increased gradually.** Key differences were identified in the microbiomes when compared between the mild AD and moderate AD groups when applying the linear discriminant analysis effect size (LEfSe) algorithm. LEfSe analysis revealed alterations that were similar to those described above; furthermore, different

bacterial taxa were associated with MMSE scores and age. KEGG analysis showed that the functional pathways associated with the oral microbiota were mainly involved in membrane transport and carbohydrate metabolism, while the gene functions of the fecal microbiota related to metabolism of amino acids, energy, cofactors and vitamins; identified significant differences among the three groups. Venn diagram analysis revealed that the number of genera that were present in **both the oral and gut microbiota increased progressively from NC to mild AD and then to moderate AD.** Conclusions: This study is the first to report a comparative analysis of the oral and fecal microbiota of patients with mild and moderate AD. The **compositions and functions of the oral and gut microbiotas differed when compared between different stages of AD.**

https://pubmed.ncbi.nlm.nih.gov/35202456/ The Microbiota-Gut-Brain Axis in Alzheimer's Disease: A Review of Taxonomic Alterations and Potential Avenues for Intervention 2022

Results: Alpha diversity is reduced in patients with ad. Within Firmicutes, taxa that produce **beneficial metabolites are reduced in ad, including Clostridiaceae, Lachnospiraceae, Ruminococcus, and Eubacterium**. Within Bacteroidetes, findings were mixed, with studies showing either reduced or increased abundance of Bacteroides in mild cognitive impairment or ad patients. Proteobacteria that produce toxins tend to be increased in ad patients, including Escherichia/Shigella. A **Mediterranean-ketogenic dietary intervention significantly increased beneficial short-chain fatty acids and taxa that were inversely correlated with changes in ad pathological markers**. **Probiotic supplementation with Lactobacillus spp. and Bifidobacterium spp. improved cognitive function and reduced inflammatory and metabolic markers in patients with ad.**

https://pubmed.ncbi.nlm.nih.gov/35431236/ Cognitive Function Associated with Gut Microbial Abundance in Sucrose and S-Adenosyl-L-Methionine (SAMe) Metabolic Pathways 2022

Results: We found **significantly increased abundance of Firmicutes but decreased abundance of Bacteroidetes at phylum level in AD compared to NC**.

https://pubmed.ncbi.nlm.nih.gov/31477562/ Modified Mediterranean-ketogenic diet modulates gut microbiome and short-chain fatty acids in association with Alzheimer's disease markers in subjects with mild cognitive impairment 2019

Herein, we examine how the gut microbiome differs in older adults with mild cognitive impairment compared to cognitively normal counterparts, and whether and how a modified **Mediterranean-ketogenic diet (MMKD) alters the gut microbiome signature in association with cerebrospinal fluid (CSF) AD biomarkers**.

Interpretation: The data suggest that specific **gut microbial signatures may depict the mild cognitive impairment** and that the **MMKD can modulate the gut microbiome and metabolites in association with improved AD biomarkers** in CSF.

https://www.mdpi.com/2072-6643/14/1/20/htm . Probiotics for Alzheimer's Disease: A Systematic Review 2022

However, there is growing evidence that revealed the involvement of **gut microbiota in the neuropathology of AD**. Gut microbiota interact with the pathogenesis of AD via several pathways: neuroinflammation, Aβ abnormality, tau phosphorylation, neurotransmitter dysregulation, and oxidative stress. These pathways are dysregulated following a derangement in the microbiota composition and associated with the increase in BBB permeability that promotes neuroinflammation, neuronal cell loss, and ultimately AD [23].

Sun and co-workers (2020) inject the gastric wall of mice with Aβ1-42 oligomers and observe that the amyloid contributes in causing neuroinflammation and AD [25]. This inflammatory environment can potentiate neuroinflammation and brain dysfunction via systemic inflammation-derived proinflammatory cytokines.

Aβ aggregation in the brain remains the most important pathogenic process of AD. Studies have reported that **several bacteria populating in the gut microbiota are able to produce a significant amount of monomeric soluble LPS and Aβ**, which might play in the modulation of signalling pathway that will affect the host immune and nervous system [26]. Any breakdown in intestinal barrier function will lead to the activation of immune cells by the interaction between gut bacteria-derived LPS and toll-like receptor 4 (TLR4) signalling pathway [27]. The soluble form of Aβ might polymerize over time producing insoluble fibrous protein aggregates that might be responsible in the pathogenetic process of AD. S**everal studies also report the correlation changes between gut microbiota composition with Aβ deposition in the brain.** Li and co-workers (2020) report changes in gut microbiota of APPSWE mice are correlated with increase expression on amyloid precursor protein and amyloid deposition by stimulating the MAPK signalling pathway [28]. MAPK pathways mediate Aβ induced astrocyte activation, which is the crucial hallmark in the pathogenetic process of AD [29].

Microglia, which is the main myeloid cell in the brain, is maintained by host microbiota under steady state conditions to prepare for the innate immune response in the CNS. Erny and co-workers (2015) observe defects in microglia properties of a germ-free mouse as a result of loss of a complex host microbiota [24]. Evidence suggests that reactive microglia provide a protective barrier around amyloid deposits, preventing the accumulation of new Aβ onto existing plaques [30]. However, some of the microglial activities become static in chronic inflammation and disrupt its ability to clear off the amyloid deposition. Minter and co-workers (2016), show that antibiotic treatment in APPSWE mice alters the composition of gastrointestinal microbiome and correlates with the reduction in the Aβ deposition [31]. Additionally, Aβ secreted by the pathogens induces the release of pro-inflammatory cytokines such as interleukin IL-17A and IL-22, and these cytokines can cross the blood brain barrier (BBB), trigger immune activity, and participate in chronic neurodegenerative disease such as AD [32].

Several studies evaluate the **gut microbiota perturbation on tau protein phosphorylation in the pathoetiology of AD.** Tau is a microtubule-associated protein that is abnormally phosphorylated to make up the paired helical filaments of neurofibrillary tangles in AD. Vogt and co-workers (2018) report that the gut microbiota-derived metabolite, **Trimethylamine N-oxide (TMNO), is higher in the cerebrospinal fluid (CSF) of individuals with mild cognitive impairment and AD [33]**. The CSF TMNO can promote and enhance the assembly of hyperphosphorylated tau protein, which is potential contributor in the characteristic of AD pathology [34]. Wang and co-workers (2015) explore possible correlation between Helicobacter pylori and Alzheimer-like tau hyperphosphorylation [35]. The study finds that the H. pylori increases the tau hyperphosphorylation which is attenuated by the synthase kinase-3β (GSK-3β). The GSK-3β signalling pathway has been recently implicated in the outer membrane vesicle-induced tau hyperphosphorylation, leading to cognitive impairment [36]. The study by Kim and co-workers (2020) finds that **frequent transfer and transplantation of fecal microbiota from WT mice into AD-like pathology with amyloid and neurofibrillary tangles (ADLPAPT) transgenic mouse model ameliorates tau pathology and memory impairment** [37].

Neurotransmitters including Acetylcholine (Ach), GABA, dopamine, histamine, noradrenaline, and serotonin (5-HT) can modulate immune system pathways that influence behaviour, memory, and learning in neurodegenerative disorders. In fact, gut bacteria have been found to have the capability to produce neurotransmitters and play an important role in modulating the gut-brain axis. **Recent post-mortem brain of AD patients concluded that GABA and glutamate neurotransmitters level are considerably reduced,** indicating deficient synaptic function and neuronal transmission in AD [38]. Another study reports the causal effect of elevated GABA, which is a downstream product of Blautia- dependent arginine metabolism with a lower risk of AD [39]. GABA, the major CNS inhibitory neurotransmitter is also produced by the families Bifidobacterium, Lactobacillus, and Streptococcus [40]. 5-HT is a neurotransmitter synthesized from the degradation of amino acid, tryptophan, and plays a key role in regulating appetite, mood, sleep, and sexual function. A recent study provides evidence that **high dietary fibre intake upregulates the expression of 5-HT and inhibits neuroinflammation** [41]. In the gut, 5-HT is produced by E.coli, Streptococcus sp., and Lactobacillus sp. [40]. Catecholamines, such as noradrenaline and its precursor, are produced by pathogenic Escherichia coli, Proteus vulgaris, Serratia marcescens, and Bacillus species [40]. Dopamine can be produced by Staphylococcus in the human intestine by converting the precursor L-3,4,-dihydroxy-phenylalanine (L-DOPA) [42]. Alteration of the norepinephrine and dopamine have been reported in AD patients, whereby both catecholamines concentration are decreased [43].

The **brain of AD patients demonstrates an increase in oxidation during the course of the disease**. Gut microbiota may influence the level of oxidative state in AD, either by interfering with the level of reactive oxygen species (ROS) or antioxidant system. Gut **Lactobacilli and Bifidobacteria can convert nitrate and nitrite into nitric oxide (NO),** which becomes noxious under conditions of oxidative stress. The oxidative reductive reaction of NO will form toxic compounds known as ROS, which are associated with mitochondrial dysfunction and neuronal apoptosis [44]. Oxidative stress can accelerate Aβ deposition and trigger oxidative reaction [45]. In the study by Kanamaru and co-workers (2015), they report the enhancement of oxidative stress and Aβ deposition in double transgenic mouse model of AD [46]. This oxidation is suggested to be the pathological marker in the disease's progression of AD patients by increasing Aβ, tau hyperphosphorylation, and neuronal death [47].

Although the comprehensive etiopathogenesis of AD remains unclear, understanding the roles and mechanisms of **gut microbiota in the AD pathogenesis can help develop promising strategies in the AD treatments.**

4.2. Deficient of Probiotics in Alzheimer's Disease

Probiotics alterations greatly influence the progression of AD. In this case, it is proven that in AD there is a drastic **reduction in bacteria belonging to the genera Verrucomicrobia, Actinobacteria, Firmicutes, and Proteobacteria. At the same moment, it is common to notice a rise in genera Tenericutes and Bacteroidetes [48].** This distinct microbial constitution enhances the deposition of Aβ in cerebral [49]. Similarly, a clinical study reveals that composition of AD subjects' gut microbiota shows reduced microbial diversity and changes in bacterial abundance including decreased levels of Firmicutes and Bifidobacterium, and increased levels of Bacteroidetes [48]. However, the exact mechanism on the influence of probiotics in AD still remains elusive. Researchers have speculated this might be due to the brain-gut-microbiota axis mechanisms [49].

Alteration in gut microbiota may result in the colonisation of intrinsic pathogens. As a consequence, the permeability of the gut will increase, which might disrupt the gut-brain axis mechanism. In regards to this statement, the presence of enterobacteria further modulates the progression of AD by enhancing immune hemocyte recruitment to the brain. This triggers neurodegeneration mediated by TNF-JNK in AD [50]. In fact, certain intestinal opportunistic bacteria, namely, Escherichia coli, Mycobacterim spp., Salmonella spp., Staphylococcus aureus, Klebsiella pneumonia, and Streptococcus spp. have the ability to eliminate microbial exudates and LPS, which are also known as immunogenic components of amyloids [51].

LPS is found within Aβ in the amyloid plaque, suggesting that bacterial constituents can migrate from gut to brain through systemic circulation, thereby further exacerbate Aβ deposition in AD. This triggers a sequence of downstream conditions that led to hindered phagocytosis, causing a rise in the aggregation of Aβ42 [19,22]. Subsequently, certain brain regions such as the cerebellum and the hippocampus will become dysfunctional [52]. Nevertheless, it has been theorised that in AD patients with cognitive disability and brain amyloidosis, an increase of pro-inflammatory gut microbiota such as Escherichia spp. or Shigella spp. and a decrease of anti-inflammatory taxon like Enterococcus rectale have been observed [53]. This highly correlates with the neuroinflammation in peripheral in AD subjects. **This clearly indicates that alteration of certain bacterial strain plays a significant effect in the pathogenesis of cognitive deficits and progression of AD severity [54].**

This result contradicts with both Akbari and co-workers (2016) [110] and Agahi and co-workers (2018) [111], who state that no effect is **observed on antioxidant capacity** in the experimental group although they used the same bacterial species for the study. **The difference of outcome can be mainly due to the integration of selenium in probiotic supplements.** A test done by Ejtahed and co-workers (2012) shows that Lactobacillus acidophilus La5 and Bifidobacterium lactis Bb12 increase SOD, GPx and total antioxidant in RBC [119]. In regards to these strains, Tamtaji and co-workers (2018) [113] combine selenium in their clinical investigation. **The combination of this successfully eliminated radicals such as H2O2, hydroxyl radicals, and peroxynitrite via cooperation with selenium-dependent GPx [120]. The outcome, witnessed through clinical trials, further confirms the positive effect of probiotic supplements on slowing down AD progression.**

Covid and Gut microbiota

https://pubmed.ncbi.nlm.nih.gov/35978881/ Altered gut microbiota patterns in COVID-19: Markers for inflammation and disease severity 2022

Augmented inflammation is one of the major driving forces for COVID-19 symptoms and **gut microbiome disruption and is associated with disease severity**.

https://www.healthline.com/health-news/long-covid-linked-to-unbalanced-gut-microbiome-what-to-know-now#Balanced-gut-microbiome-was-beneficial Long COVID Linked to Unbalanced Gut Microbiome

Long-COVID patients had a less diverse gut microbiome than non-COVID patients. At 6 months, **people with long COVID also had fewer "friendly" bacteria and a greater abundance of "unfriendly" bacteria** than people who hadn't had COVID-19.

What this research shows, said Ghannoum, is that "if you have a microbiome that is not balanced — what we call **dysbiosis** — the likelihood of having these symptoms will be much higher."

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7818076/ COVID-19 and Gut Microbiota: A Potential Connection 2021

Human gastrointestinal (GI) tract is home to intricate community of commensal bacteria called as gut microbiota. The number of microorganisms found in GI tract has been predicted to exceed 10^{14}, which consists of 100 times the amount of genomic content (microbiome) as the human genome [1]. Gut microbiome contains **1000–1500 species of bacteria with an individual containing approximately 160 species depending upon the environmental and genetic factors**. Dysbiosis defined as changes in gut microbiota leading to microbial imbalance has not only been closely linked with the pathogenesis of many inflammatory diseases but plays a critical role in diverse infections as well. The gut microbiota has been shown to affect the lung health via interactions between the lungs and the gut through a phenomenon called 'gut lung axis'. [6] Gut lung axis is a bidirectional tool i.e., the gut microbial metabolites, endotoxins can affect the lungs and vice-versa. [7] The fact that time of eating was related to the presence of several bacteria was reported by Kaczmarek et al. [53]. Similarly, Thaiss et al. in mice models showed that **rhythmic food intake not only increases microbial abundance** but also leads to 15% fluctuations in commensal bacteria in the day. [54] Impact of meal timing in humans on gut microbiota was reported by Collado et al. in 2018 randomised crossover study. [55] **Probiotics are the non-pathogenic live organisms mainly found in the gastrointestinal tract**. They are safe and can also be provided as food or dietary supplements. The major genera of probiotics in the gut are ***Bifidobacterium, Lactobacillus* and *Saccharomyces* like *B. breve, B. longum*, *B. bifidum*, *L. reuteri, L. fermentum L. paracasei, L. rhamnosus.*** Probiotics usually interact with various immune cells. Other functions include **maintaining the pH of the intestine** and lowering the invasion and colonization by the pathogens. Studies have also reported that probiotic strains like ***BifidobacteriumLactis, Bifidobacterium breve* and *Lactobacillus rhamnosus* show a good result in maintaining the innate immune system and the inflammatory response** as seen in a mice-based study. Use of prebiotics can also be considered as **prebiotics** like **maize fibre, inulin, polydextrose** are known to improve the gut diversity, digestion and immunity especially in elderly individuals. Prebiotics have also shown to r**egulate various pro and anti- inflammatory cytokines** [7] like carbohydrates present in whole grain are known to reduce the levels of IL-6 (pro-inflammatory cytokines) [54] and **butylated high amylose maize starch is shown to increase the levels of IL-10 (anti-inflammatory cytokine)**.

Gut microbiota and inflammation

https://pubmed.ncbi.nlm.nih.gov/33086688/ The Gut Microbiota and Inflammation: An Overview

The **gut microbiota encompasses a diverse community of bacteria** that carry out various functions influencing the overall health of the host. These comprise nutrient metabolism, immune system regulation and natural defence against infection. The presence of **certain bacteria is associated with inflammatory molecules that may bring about inflammation** in various body tissues. Inflammation underlies many chronic multisystem conditions including obesity, atherosclerosis, type 2 diabetes mellitus and inflammatory bowel disease. Inflammation may be triggered by structural components of the bacteria which can result in a cascade of inflammatory pathways involving interleukins and other cytokines. **Similarly, by-products of metabolic processes in bacteria, including some short-chain fatty acids, can play a role in inhibiting inflammatory processes**. In this review, we aimed to provide an overview of the **relationship between the gut microbiota and inflammatory** molecules and to highlight relevant knowledge gaps in this field. Based on the current literature, it appears that as the **gut microbiota composition differs between individuals** and is contingent on a variety of factors like diet and genetics, s**ome individuals may possess bacteria associated with pro-inflammatory effects whilst others may harbour those with anti-inflammatory effects.**

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3257638/ Gut Microbiota and Inflammation

Systemic and local inflammation in relation to the resident microbiota of the human gastro-intestinal (GI) tract and administration of probiotics are the main themes of the present review. The dominating taxa of the human GI tract and their potential for aggravating or suppressing inflammation are described. The human GI microbiota starts already in the **mouth, which harbours a viable count of 10^8–10^{10}** colony forming units (CFU) of bacteria per g saliva. These bacteria are constantly fed to the GI channel by the swallowing reflex. The numbers are reduced in the stomach (around 10^3 CFU/g gastric juice), duodenum and jejunum (10^2–10^4 CFU/g content), and then increase again in **ileum and colon (around 10^{10} CFU/g content and 10^{10}–10^{12} CFU/g** content, respectively). On the other hand, most of the OTUs belonged to the phyla ***Firmicutes* (about 80%)**, ***Bacteroidetes* (about 20%)**, ***Actinobacteria* (about 3%)**, ***Proteobacteria* (1%) and *Verrumicrobia* (0.1%)**.

Table 1. Taxa dominating the bacterial microbiota of the GI-tract [(1)].

Phyla/Division	Class	Family	Genus	Gram [(2)]
Actinobacteria	*Actinobacteria*	*Micrococcaceae*	*Rothia* *	+
Firmicutes	*Clostridia*	*Clostridiaceae*	*Clostridium*	+
Firmicutes	*Clostridia*	*Clostridiaceae*	*Blautia*	+
Firmicutes	*Clostridia*	*Eubacteriaceae*	*Eubacterium*	+
Firmicutes	*Clostridia*	unclassified	*Collinsella*	+
Firmicutes	*Erysipelotrichia*	*Erysipelotrichaceae*	*Holdemania*	+
Proteobacteria	*Betaproteobacteria*	*Alcaligenaceae*	*Sutterella*	-
Proteobacteria	*Betaproteobacteria*	*Neisseriaceae*	*Neisseria*	-
Proteobacteria	*Deltaproteobacteria*	*Desulfovibrionaceae*	*Bilophila*	-
Proteobacteria	*Gammaproteobacteria*	*Pasteurellaceae*	*Haemophilus* *	-
Proteobacteria	*Gammaproteobacteria*	*Enterobacteriaceae*	*Enterobacter* *	-
Proteobacteria	*Gammaproteobacteria*	*Enterobacteriaceae*	*Serratia* *	-
Proteobacteria	*Gammaproteobacteria*	*Enterobacteriaceae*	*Escherichia*	-
Proteobacteria	*Gammaproteobacteria*	*Enterobacteriaceae*	*Klebsiella*	-
Proteobacteria	*Gammaproteobacteria*	*Moraxellaceae*	*Acinetobacter*	-
Proteobacteria	*Gammaproteobacteria*	*Pseudomonadaseae*	*Pseudomonas* *	-
Proteobacteria	*Gammaproteobacteria*	*Cardiobacteriaceae*	*Cardiobacterium*	-
Bacteroidetes	*Bacteroidia*	*Prevotellaceae*	*Prevotella* *	-
Bacteroidetes	*Bacteroidia*	*Porphyromonadaceae*	*Porphyromonas* *	-
Bacteroidetes	*Bacteroidia*	*Porphyromonadaceae*	*Parabacteroides*	-
Bacteroidetes	*Bacteroidia*	*Bacteroidaceae*	*Bacteroides*	-
Bacteroidetes	*Bacteroidia*	*Rikenellaceae*	*Alistipes*	
Fusobacteria	*Fusobacteria*	*Fusobacteriaceae*	*Fusobacterium*	-
Spirochaetae	*Spirochaetes*	*Brachyspiraceae*	*Brachyspira*	-
Verrucomicrobia	*Verrucomicrobiae*	*Verrucomicrobiaceae*	*Akkermansia*	-

For some chronic diseases, it has been suggested that the pathologic agent might be the disturbed microbiota rather than a single organism [57], and this presumably means a decreased bacterial diversity and/or different degrees of overgrowth by more aggressive fractions of residential bacteria, i.e., bacteria inducing inflammatory responses by the immune system. A key question is then which bacteria are the most forceful ones in causing inflammation? **Gram-negative bacteria contain lipopolysaccharide (LPS)** as the major constituent in the outer leaflet of the outer cell membrane. **LPS contains large regions of variable polysaccharide** and oligosaccharide regions and a relatively conserved lipid region (lipid A), which is the endotoxic and biologically active moiety responsible for septic shock. The interaction of **LPS with macrophages results in the release of pro-inflammatory cytokines** such as TNF-alpha, IL-6, and IL-1, Gram-negatives that typically contaminate foods, and so are ingested on a more or less regular basis, sometimes in high quantities, are mostly **Gammaproteobacteria, e.g., Enterobacteriaceaea and Pseudomonadaceae**. However, different diet components can also affect the gut microbiota, e.g., a **high-fat diet seems to increase the proportion of Gram-negatives in the gut but also increase the leakage of LPS through the intestinal barrier** [66] It should be stressed that it is **not only gram-negatives and LPS that can induce inflammation**; other cell components and metabolites can be involved, and there are also several gram-positive pathogenic and opportunistic pathogenic bacteria that can induce inflammation [68]. One example of the latter is **Enterococcus, which is frequently found as a contaminant in foods**. An attempt to look for correlation between systemic inflammation and faecal microbiota showed that about 9% of the total variability of the microbiota was related to the pro-inflammatory cytokines IL-6 and IL-8 [69]. All taxa that showed a slightly positive correlation with either IL-6 or IL-8 belonged to the phylum Proteobacteria [69].
Bacterial Neutralisation of Inflammation
There are fractions of the **resident GI microbiota that are less prone to inducing inflammation**, and there may even be certain taxa with the **ability to counteract inflammation**. This seemingly inflammation-suppressing effect can be a result of different actions. The inflammation-suppressing fractions of the microbiota may: (i) **counteract some of the inflammation-aggravating bacteria**, which will decrease the inflammatory tone of the system; (ii) **improve the barrier effect of the GI mucosa, which allows less inflammation-inducing components in the lumen** to translocate out into the body; (iii) more directly interact with inflammation-driving components of the immune system. All three actions may be at work simultaneously. When the systemic inflammatory tone measured as IL-6 and IL-8 was compared, some **members of the Clostridium cluster XIVa (**as defined by Collins et al. [54]) were inversely correlated with systemic inflammation [69]. The currently most studied inflammation-suppressing taxa of the GI microbiota are certain species/strains of **Lactobacillus and Bifidobacterium,** and those are also the fractions that are supported by administering probiotics (living microorganisms that upon ingestion exert health-beneficial effects), or certain **dietary fibres** that selectively stimulate resident Lactobacillus and Bifidobacterium (prebiotics).
In particular, **lactic acid fermented foods such as yoghurt, cheese, sauerkraut, salted gherkins, olives and capers can contain high amounts of live bacteria and often bacteria of the same Lactobacillus species that are now used for probiotics.** Yoghurt was launched in Paris 1906 with reference to the theories of Metchnikoff [80]. In search of strains with better resistance to the low pH of the stomach and the digestive juices of duodenum, Lactobacillus acidophilus was launched in USA in the 1930s, and in Japan during the same period, Lactobacillus casei (should probably be L. paracasei) started to be used as probiotics. Popular probiotic species used commercially include **L. paracasei, L. rhamnosus, L. Acidophilus, L. johnsonii, L. fermentum, L. reuteri, L. plantarum, Bifidobacterium longum and Bifidobacterium animalis.** However, the **phylogenetic differences are extremely wide between Lactobacillus and Bifidobacterium** as they belong to different phyla, but there are also great differences between **Lactobacillus species such as L. acidophilus, L. fermentum, L. reuteri and L. plantarum.** Even within different strains of the same species, the genomic differences can be considerable, which has been clearly demonstrated for L. paracasei [81]. Consequently, with major genetic **differences between different probiotics it is also to be expected that the human body will respond differently to different probiotics.**

Gut microbiome and psoriasis

https://www.medicalnewstoday.com/articles/323271 Can probiotics help with psoriasis?
Probiotics help to maintain a good balance of healthful gut bacteria. Researchers believe that probiotics can have a positive impact on controlling, and even preventing, chronic inflammation caused by psoriasis. A growing body of evidence suggests that an imbalance of bacteria in the gut, or gastrointestinal dysbiosis, can cause psoriasis and other inflammatory diseases.
A 2015 studyTrusted Source showed that people with psoriasis have less diversity in the gut microbiota than healthy individuals. A 2018 studyTrusted Source found increased diversity, but reduced stability of the skin's microbiome in people with psoriasis
https://www.medicalnewstoday.com/articles/323271 Can probiotics help with psoriasis?
Probiotics help to maintain a good balance of healthful gut bacteria. Researchers **believe that probiotics can have a positive impact on controlling, and even preventing, chronic inflammation caused by psoriasis**. A growing body of evidence suggests that an **imbalance of bacteria in the gut, or gastrointestinal dysbiosis, can cause psoriasis and other inflammatory diseases**. A 2015 studyTrusted Source showed that **people with psoriasis have less diversity in the gut microbiota** than healthy individuals. A 2018 studyTrusted Source found increased diversity, but reduced stability of the skin's microbiome in people with psoriasis. Probiotics are living microorganisms that can occur in certain foods. **Consuming these organisms increases the diversity of bacteria in the gut. This may help the body to control inflammation**. Probiotics can influence the immune system's inflammatory response by stimulating the cells that regulate inflammation. A 2018 study looked at the effects of probiotics on skin conditions such as eczema in mice. The researchers found that **certain probiotics reduced and may even prevent chronic skin inflammation**, including: **Lactobacillus salivarius LA307, Lactobacillus rhamnosus LA305**
Another study in mice considered the effects of **Lactobacillus pentosus GMNL-77 on psoriasis**. The authors found that this strain **prevented skin inflammation and reduced biomarkers of inflammation**.
How to add probiotics to the diet. A person can add helpful bacteria to their diet by consuming probiotic-rich foods, such as:
yogurt, kefir, which is a fermented, probiotic dairy drink, kombucha, a fermented tea made with bacteria and yeast, fermented cheeses, pickles, miso, a Japanese seasoning paste made with fermented soybeans, fermented vegetables, such as kimchi and sauerkraut
Probiotic supplements are another good option. Several varieties are available in supermarkets, health stores, and online. Always consult a healthcare provider before taking any supplement.
https://pubmed.ncbi.nlm.nih.gov/32545459/ Gut Microbiome in Psoriasis: An Updated Review 2020
Background: A growing body of evidence highlights that **intestinal dysbiosis is associated with the development of psoriasis**. The gut-skin axis is the novel concept of the interaction between skin diseases and microbiome through inflammatory mediators, metabolites and the intestinal barrier. The objective of this study was to synthesize current data on the gut microbial composition in psoriasis. Results: **All of the 10 retrieved studies reported alterations in the gut microbiome in patients with psoriasis**. Eight studies assessed **alpha- and beta-diversity**. Four of them reported a lack of change in alpha-diversity, but **all confirmed significant changes in beta-diversity**. At the phylum-level, at least two or more studies reported a **lower relative abundance of Bacteroidetes, and higher Firmicutes in psoriasis patients** versus healthy controls.
https://pubmed.ncbi.nlm.nih.gov/33117362/ Psoriasis Is Associated With Elevated Gut IL-1α and Intestinal Microbiome Alterations 2020
C**hanges in gut immunology and microbiota are important drivers of proinflammatory disorders** and could play a role in the pathogenesis of psoriasis. Psoriasis was associated with **alterations in gut Firmicutes, including elevated Faecalibacterium and decreased Oscillibacter and Roseburia abundance**, but no association was observed between gut microbial diversity or Firmicutes/Bacteroidetes ratios and disease status.
Conclusions: **Psoriasis may be associated with gut inflammation and dysbiosis.**
https://pubmed.ncbi.nlm.nih.gov/30920647/ Gut microbiota dysbiosis in a cohort of patients with psoriasis 2019
Results: Gut microbiota composition of **patients with psoriasis displayed a lower diversity and different relative abundance of certain bacterial taxa** compared with healthy individuals.
Conclusions: The g**ut microbiota profile of patients with psoriasis displayed a clear dysbiosis that can be targeted for microbiome-based therapeutic approaches**
https://pubmed.ncbi.nlm.nih.gov/33685393/ Dysbiosis of gut microbiota and its correlation with dysregulation of cytokines in psoriasis patients 2021
The **gut microbiome has become a hot topic in psoriasis** as it has been shown to affect both allergy and autoimmunity diseases in recent studies. Our objective was to identify differences in the fecal microbial composition of patients with psoriasis compared with healthy individuals to unravel the microbiota profiling in this autoimmune disease. Our results showed that different **relative abundance of certain bacterial taxa between psoriasis patients and healthy individuals, including Faecalibacterium and Megamonas, were increased** in patients with psoriasis. It's also implicated that **many cytokines act as main effect molecules in the pathology of psoriasis**. We selected the inflammation-related indicators that were abnormal in psoriasis patients and found the microbiome variations were associated with the level of them, especially interleukin-2 receptor showed a positive relationship with Phascolarctobacterium and a negative relationship with the Dialister. The **relative abundance of Phascolarctobacterium and Dialister can be regard as predictors of psoriasis activity**. The correlation analysis based on microbiota and Inflammation-related indicators showed that microbiota dysbiosis might induce an abnormal immune response in psoriasis. Conclusions: We concluded that the gut microbiome composition in psoriasis patients has been altered markedly and provides evidence to understand the relationship between gut microbiota and psoriasis.
https://pubmed.ncbi.nlm.nih.gov/36159864/ Association of the characteristics of the blood metabolome and gut microbiome with the outcome of methotrexate therapy in psoriasis 2022
metagenomic features at baseline; for example, patients who had high levels of serum nutrient molecular and more enriched gut microbiota had a poor response. **After 16 weeks of MTX, we observed a reduction in microbial activity pathways, and patients with a good response showed more microbial activity and less biosynthesis of serum fatty acid.** We also found an association between the serum metabolome and the gut microbiome before intervention with mtx. These findings suggest that the metabolic status of the blood and the **gut microbiome is involved in the effectiveness of MTX in psoriasis**, and that **inhibition of symbiotic intestinal microbiota may be one of the mechanisms of action of MTX**.
https://pubmed.ncbi.nlm.nih.gov/35382440/ The Role of the Gut Microbiome in Psoriasis: From Pathogens to Pathology 2022
Randomized, controlled trials have revealed that **gut microbial imbalances contribute to inflammatory cytokines as well as to the progression and development of psoriasis**. Perhaps more importantly, perturbations in the gut microbiome have been correlated to elevated plasma levels of claudin-3, zonulin, and intestinal fatty acid-binding protein, contributing to intestinal barrier dysfunction and permeability. This translocation results in systemic immune activation leading to phenotypic expression of psoriasis in genetically susceptible individuals. Conclusion: **A healthy diet positively impacts the gut microbiome, which can dampen inflammatory cytokines and lessen the severity of psoriasis. The use of probiotics can also influence this dynamic**.
https://pubmed.ncbi.nlm.nih.gov/33869074/ Deciphering Gut Microbiota Dysbiosis and Corresponding Genetic and Metabolic Dysregulation in Psoriasis Patients Using Metagenomics Sequencing 2021

. A **distinct gut microbial composition in patients with psoriasis was observed, with an increased abundance of the phyla Firmicutes, Actinobacteria and Verrucomicrobia and genera Faecalibacterium, Bacteroides, Bifidobacterium, Megamonas and Roseburia and a decreased abundance of the phyla Bacteroidetes, Euryarchaeota and Proteobacteria and genera Prevotella, Alistipes, and Eubacterium.**
https://pubmed.ncbi.nlm.nih.gov/25319745/ Decreased bacterial diversity characterizes the altered gut microbiota in patients with psoriatic arthritis, resembling dysbiosis in inflammatory bowel disease 2015
Results: **The gut microbiota observed in patients with PsA and patients with skin psoriasis was less diverse when compared to that in healthy controls.** This could be attributed to the reduced presence of several taxa. Samples from both patient groups showed a relative **decrease in abundance of Coprococcus species, while samples from PsA patients were also characterized by a significant reduction in Akkermansia, Ruminococcus, and Pseudobutyrivibrio. Supernatants of fecal samples from PsA patients revealed an increase in sIgA levels and decrease in RANKL levels**. Analysis of fatty acids revealed **low fecal quantities of hexanoate and heptanoate in both patients with PsA and patients with psoriasis**.
https://pubmed.ncbi.nlm.nih.gov/33924414/ Alterations of the Skin and Gut Microbiome in Psoriasis and Psoriatic Arthritis 2021
. It has been proven that the representation of **Cutibacterium, Burkholderia spp., and Lactobacilli is decreased and Corynebacterium kroppenstedii, Corynebacterium simulans, Neisseria spp., and Finegoldia spp. increased in the psoriasis skin** in comparison to healthy skin. **Alterations in the gut microbiome in psoriasis are similar to those observed in patients with inflammatory bowel disease**. In those two diseases, the F. p**rausnitzii, Bifidobacterium spp., Lactobacillus spp., Parabacteroides and Coprobacillus were underrepresented, while the abundance of Salmonella sp., Campylobacter sp., Helicobacter sp., Escherichia coli, Alcaligenes sp., and Mycobacterium sp. was increased.** Several research studies provided evidence for the significant influence of psoriasis treatments on the skin and gut microbiome and a positive influence of orally administered probiotics on the course of this dermatosis.
https://www.eatthis.com/major-effect-vitamin-c-has-on-your-gut/ One Major Effect Vitamin C Has On Your Gut, Says Science
One of the major effects vitamin C has on your gut is **helping to maintain a balance between good and bad bacteria in your gut microbiome.**

Probiotics and Alzheimers

https://pubmed.ncbi.nlm.nih.gov/35010895/ Probiotics for Alzheimer's Disease: A Systematic Review 2021
Alzheimer's disease (AD) is the most common form of neurodegenerative disorders affecting mostly the elderly. It is characterized by the presence of Aβ and neurofibrillary tangles (NFT), resulting in cognitive and memory impairment. **Research shows that alteration in gut microbial diversity and defects in gut brain axis are linked to AD**. **Probiotics are known to be one of the best preventative measures against cognitive decline in AD**. Numerous in vivo trials and recent clinical trials have proven the effectiveness of selected bacterial strains in slowing down the progression of AD. It is proven that **probiotics modulate the inflammatory process, counteract with oxidative stress, and modify gut microbiota**. Thus, this review summarizes the current evidence, diversity of bacterial strains, defects of gut brain axis in AD, harmful bacterial for AD, and the mechanism of action of probiotics in preventing AD. A literature search on selected databases such as PubMed, Semantic Scholar, Nature, and Springer link have identified potentially relevant articles to this topic. However, upon consideration of inclusion criteria and the limitation of publication year, only 22 articles have been selected to be further reviewed. The search query includes few sets of keywords as follows. (1) Probiotics OR gut microbiome OR microbes AND (2) Alzheimer OR cognitive OR aging OR dementia AND (3) clinical trial OR in vivo OR animal study. The results evidenced in this study help to clearly illustrate the relationship between probiotic supplementation and AD. Thus, this systematic review will help identify novel therapeutic strategies in the future as probiotics are free from triggering any adverse effects in human body
https://pubmed.ncbi.nlm.nih.gov/33169684/ Role of gut-brain axis, gut microbial composition, and probiotic intervention in Alzheimer's disease. 2020
Gut microbiota represents a diverse and dynamic population of microorganisms harboring the gastrointestinal tract, which influences the host health and disease. Gut microbiota communicates with the brain and vice versa through complex bidirectional communication systems - the gut-brain axis, which integrates the peripheral intestinal function with emotional and cognitive brain centers via neuro-immuno-endocrine mediators. Aging alters the gut microbial population, which not only leads to gastrointestinal disturbances but also causes central nervous system (CNS) disorders such as dementia. Alzheimer's disease (AD) is the most common form of dementia affecting the older person, characterized by beta-amyloid (Aβ) plaques and neurofibrillary tangles leading to the cognitive deficit and memory impairment. Multiple experimental and clinical studies revealed the role of gut microbiota in host cognition, and its dysbiosis associated with aging leads to neurodegeneration. Gut microbial dysbiosis leads to the secretion of amyloid and lipopolysaccharides (LPS), which disturbs the gastrointestinal permeability and blood-brain barrier. Thereby modulates the inflammatory signaling pathway promoting neuroinflammation, neuronal injury, and ultimately leading to neuronal death in AD. A recent study revealed the antimicrobial property of Aβ peptide as an innate immune response against pathogenic microbes. Another study showed that bacterial amyloid shares molecular mimicry with Aβ peptide, which elicits misfolding and aggregation of Aβ peptide, it's seeding, and propagation through the gut-brain axis followed by microglial cell activation. As aging together with poor diet and gut-derived inflammatory response due to dysbiosis contributes to the pathogenesis of AD, **modification of gut microbial composition by uptake of probiotic-rich food can act as a preventive/therapeutic option for AD**. The objective of the present review is to summarize the recent findings on the role of gut microbiota in the development of AD. Understanding the relationship between gut microbiota and CNS will help identify novel therapeutic strategies, especially probiotic-based supplementation, for the treatment of AD.
https://pubmed.ncbi.nlm.nih.gov/34596721/ Probiotics as potential therapeutic options for Alzheimer's disease 2021
In view of **the close relationships between gut microbiota and AD, probiotics have been suggested as potential therapeutic options for AD** in recent years. As for probiotics, a total of 13 studies employed single-strain probiotic, and the rest studies used multi-strain probiotics (ranged from 2 to 9 probiotic strains), 4 used probiotic-fermented milk or probiotic-fermented soybean, 2 studies used engineered probiotic strain, and 4 studies focused on the combined effect of probiotics with AD drug memantine, selenium, or exercise. **Bifidobacterium and Lactobacillus** species were the most frequently used probiotics in the included studies. Overall, currently available studies showed that probiotic administration conferred neuroprotective benefits and could attenuate cognitive deficits and modulate gut microbiota dysbiosis, which may be related to oxidative and inflammatory pathways. Several perspectives on future studies on this topic are proposed. Thus, **probiotics seem to be an attractive approach to combat AD**, which deserves to be further studied by well-designed large-scale clinical studies. KEY POINTS: •We discussed the recent progresses concerning the effects of probiotics administration to combat AD. •**A total of 35 associated studies consisted of 26 animal model studies and 9 human studies were included. •Most studies found that probiotic administration conferred neuroprotective benefits and could attenuate cognitive deficits.**
https://pubmed.ncbi.nlm.nih.gov/32066253/ *Lactobacillus* probiotics improved the gut microbiota profile of a *Drosophila melanogaster* Alzheimer's disease model and alleviated neurodegeneration in the eye 2020
Here, we showed the **potential AD-reversal effects of *Lactobacillus* probiotics** through feeding to our *Drosophila melanogaster* AD model. The administration of *Lactobacillus* strains was able to rescue the rough eye phenotype (REP) seen in AD-induced *Drosophila*, with a more prominent effect observed upon the administration of ***Lactobacillus plantarum* DR7 (DR7)**. Furthermore, we analysed the gut microbiota of the AD-induced *Drosophila* and found **elevated levels of *Wolbachia***. The administration of DR7 restored the gut microbiota diversity of AD-induced *Drosophila* with a **significant reduction in *Wolbachia*'s** relative abundance, accompanied by an increase of *Stenotrophomonas* and *Acetobacter*. Through functional predictive analyses, ***Wolbachia* was predicted to be positively correlated with neurodegenerative disorders, such as Parkinson's, Huntington's and Alzheimer's diseases**, while ***Stenotrophomonas* was negatively correlated with these neurodegenerative disorders**. Altogether, our data exhibited DR7's ability to ameliorate the AD effects in our AD-induced *Drosophila*. Thus, we propose that *Wolbachia* be used as a potential biomarker for AD.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8303183/ Probiotics for Mild Cognitive Impairment and Alzheimer's Disease: A Systematic Review and Meta-Analysis 2021
Accumulating evidence from animal studies supports the potential role of probiotics and prebiotics in alleviating neurodegenerative diseases. However, **whether dietary supplementation with probiotics improves cognitive function in patients with Alzheimer's disease (AD) or mild cognitive impairment (MCI) is unclea**r. Among the 294 articles identified, eight articles involving 174 patients with AD and 446 with MCI were included in the qualitative synthesis and seven studies were meta-analyzed. Our analysis detected high between-group heterogeneity (SMD = 0.43, 95% CI −0.02–0.88, $p < 0.0001$, $I^2 = 86.4\%$) in cognitive function across the included studies. Subgroup analyses identified a **significant effect of probiotics on cognitive function only in the studies involving people with MCI** ($I^2 = 44\%$, $p = 0.15$ for heterogeneity, $p = 0.0002$ for overall effect). Our findings suggest that dietary supplementation with probiotics improves cognitive function, especially in people with MCI. In this meta-analysis, we include the most recent RCTs of probiotic and prebiotic supplementation for MCI and AD. Compared with placebo or control interventions, **probiotic supplementation considerably improved cognitive function in the participants with MCI, but it only caused a modest cognitive improvement in those with AD.** Another study in physically healthy subjects also found that the consumption of a probiotic-containing yogurt for 3 weeks substantially improved mood [32]. Collectively, the results of this meta-analysis indicate that **probiotics, when supplemented at adequate amounts for 12 weeks or longer, may improve cognitive function in MCI or AD individuals**.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6340155/ Probiotic Supplementation in Patients with Alzheimer's Dementia - An Explorative Intervention Study 2018
Dysbiosis of intestinal microbiota in the elderly **can cause a leaky gut, which may result in silent systemic inflammation and promote neuroinflammation** - a relevant pathomechanism in the early course of Alzheimer's disease. In this study, routine laboratory tests in twenty outpatients (9 females, 11 males, aged 76.7 ± 9.6 years) with Alzheimer's disease were investigated. After treatment a decline of fecal zonulin concentrations and an increase in Faecalibacterium prausnitzii compared to baseline were observed. At the same time, serum kynurenine concentrations in-creased ($p < 0.05$). Delta values (before - after) of neopterin and the kynurenine to tryptophan ratios (Kyn/Trp) correlated significantly ($p < 0.05$). Results show that the **supplementation of Alzheimer's disease patients with a multispecies probiotic influences gut bacteria composition as well as tryptophan metabolism in serum.** The correlation between Kyn/Trp and neopterin concentrations points to the activation of macrophages and/or dendritic cells. Further studies are warranted to dissect the potential consequences of Probiotic supplementation in the course of Alzheimer's disease.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7138569/ Gut microbiota and pro/prebiotics in Alzheimer's disease 2020
Recently, in addition to the strongly developing ischemic etiology of Alzheimer's disease, it is suggested that the **gut microbiota may also participate in the development of this disease**. The brain and gut are thought to form a network called the "gut-brain-microbiota axis", and it is strongly supported idea that the intestinal microflora can be involved in Alzheimer's disease. **Lately, many new studies have been conducted that draw attention to the relationship between Alzheimer's disease and gut microbiota.** This review presents a possible relationship between Alzheimer's disease and a microbiome. It is a promising idea for prevention or therapeutic intervention. Modulation of the gut microbiota through a personalized diet or beneficial microflora intervention like pro/prebiotics, changing microbiological partners and their products, including amyloid protein, can become a new treatment for Alzheimer's disease. **In addition, Ozawa et al., [4] observed over 1,000 patients with Alzheimer's disease for 17 years, and found that the incidence of Alzheimer's disease decreased significantly with the increase in the consumption of milk and dairy products.**
https://pubmed.ncbi.nlm.nih.gov/24916840/ Milk and dairy consumption and risk of dementia in an elderly Japanese population: the Hisayama Study 2014

Individuals aged 60 and older without dementia (N = 1,081). Over 17 years of follow-up, 303 subjects developed all-cause dementia; 166 had AD, and 98 had VaD. The age- and sex-adjusted incidence of all-cause dementia, AD, and VaD significantly decreased as milk and dairy intake level increased (P for trend = .03 for all-cause dementia, .04 for AD, .01 for VaD). After adjusting for potential confounders, the linear relationship between milk and dairy intake and development of AD remained significant (P for trend = .03), whereas the relationships with all-cause dementia and VaD were not significant. The risk of AD was significantly lower in the second, third, and fourth quartiles of milk and dairy intake than in the first quartile.
Conclusion: Greater milk and dairy intake reduced the risk of dementia, especially AD, in the general Japanese population.

Antibiotics and Alzheimers

https://pubmed.ncbi.nlm.nih.gov/31118068/ Antibiotics, gut microbiota, and Alzheimer's disease 2019
Recently, it has been **hypothesized that AD may be associated with a dysbiosis of microbes in the intestine**. In fact, the intestinal flora is able to influence the activity of the brain and cause its dysfunctions.Given the growing interest in this topic, the purpose of this review is to analyze the **role of antibiotics in relation to the gut microbiota and AD**. Antibiotics are normally used to remove or prevent bacterial colonization in the human body, without targeting specific types of bacteria. As a result, broad-spectrum antibiotics can greatly affect the composition of the gut microbiota, reduce its biodiversity, and delay colonization for a long period after administration. Thus, the action of antibiotics in AD could be wide and even opposite, depending on the type of antibiotic and on the specific role of the microbiome in AD pathogenesis.**Alteration of the gut microbiota can induce changes in brain activity,** which raise the possibility of therapeutic manipulation of the microbiome in AD and other neurological disorders. This field of research is currently undergoing great development, but therapeutic applications are still far away. Whether a therapeutic **manipulation of gut microbiota in AD could be achieved using antibiotics is still not known**. The future of antibiotics in AD depends on the research progresses in the role of gut bacteria. We must first understand how and when gut bacteria act to promote AD. Once the role of gut microbiota in AD is well established, one can think to induce modifications of the gut microbiota with the use of pre-, pro-, or antibiotics to produce therapeutic effects.
https://www.alzinfo.org/articles/drugs-and-treatment-26/ Antibiotics, Alzheimer's and End-of-Life Care 2008
The study, published in the *Archives of Internal Medicine*, looked at 214 nursing-home residents with advanced dementia living in the Boston area. The researchers, from Beth Israel Deaconess Medical Center, found that antibiotic use increased the frailer and **further advanced the dementia**

https://pubmed.ncbi.nlm.nih.gov/36217542/ Safety and efficacy of probiotic supplementation in 8 types of inflammatory arthritis: A systematic review and meta-analysis of 34 randomized controlled trials
Results: A total of 37 records were finally included, involving 34 RCTs and 8 types of autoimmune disease (Hyperuricemia and gout, Inflammatory bowel disease arthritis, juvenile idiopathic arthritis [JIA], Osteoarthritis [OA], Osteoporosis and Osteopenia, Psoriasis, rheumatoid arthritis (RA), Spondyloarthritis). RA involved 10 RCTs (632 participants) whose results showed that probiotic intervention reduced CRP. Psoriasis involved 4 RCTs (214 participants) whose results showed that probiotic intervention could reduce PASI scores. Spondyloarthritis involved 2 RCTs (197 participants) whose results showed that probiotic intervention improved symptoms in patients. Osteoporosis and Ostepenia involving 10 RCTs (1156 participants) showed that probiotic intervention improved bone mineral density in patients. Hyperuricemia and gout involving 4 RCTs (294 participants) showed that probiotic intervention improved serum uric acid in patients. OA involving 1 RCTs (433 participants) showed that probiotic intervention improved symptoms in patients. JIA involving 2 RCTs (72 participants) showed that probiotic intervention improved symptoms in patients. Inflammatory bowel disease arthritis involving 1 RCTs (120 participants) showed that probiotic intervention improved symptoms in patients. **All of the above RCTs showed that probiotics did not increase the incidence of adverse events.**