

Studies on Gut Microbiome and Neurological and Neuropsychiatric Disorders

STUDIES

A Gut-Derived Metabolite Alters Brain Activity And Anxiety Behaviour In Mice

Integration of sensory and molecular inputs from the environment shapes animal behaviour. A major site of exposure to environmental molecules is the gastrointestinal tract, in which dietary components are chemically transformed by the microbiota and gut-derived metabolites are disseminated to all organs, including the brain. In mice, the gut microbiota impacts behaviour, modulates neurotransmitter production in the gut and brain and influences brain development and myelination patterns.

In this study researchers identified biosynthetic genes from the gut microbiome that mediate the conversion of dietary tyrosine to 4-ethylphenol (4EP), and bioengineered gut bacteria to selectively produce 4EPS in mice. 4EPS entered the brain and was associated with changes in region-specific activity and functional connectivity. Gene expression signatures revealed altered oligodendrocyte function in the brain, and 4EPS impaired oligodendrocyte maturation in mice and decreased oligodendrocyte–neuron interactions in ex vivo brain cultures. Mice colonized with 4EP-producing bacteria exhibited reduced myelination of neuronal axons. Altered myelination dynamics in the brain have been associated with behavioural outcomes. Moreover, mice exposed to 4EPS displayed anxiety-like behaviours, and pharmacological treatments that promote oligodendrocyte differentiation prevented the behavioural effects of 4EPS.

The findings of the study reveal that a gut-derived molecule influences complex behaviours in mice through effects on oligodendrocyte function and myelin patterning in the brain.

Source: Brittany D. Needham, Division Of Biology And Biological Engineering, California Institute Of Technology, Pasadena, CA, USA. A Gut-Derived Metabolite Alters Brain Activity And Anxiety Behaviour In Mice. *Nature* 602, 647–653 (2022). <https://doi.org/10.1038/s41586-022-04396-8>

The Role Of Microbiome In Brain Development And Neurodegenerative Diseases

This review article explains that the makeup of the microbiome is impacted by a variety of factors, such as genetics, health status, method of delivery, environment, nutrition, and exercise, and improves the present understanding of the role of gut microbiota and its metabolites in the preservation of brain functioning and the development of the aforementioned neurological illnesses.

Scientists have discussed current breakthroughs in the use of probiotics, prebiotics, and synbiotics to address neurological illnesses. Further, they have also discussed the role of **boron-based diet in memory**, boron and microbiome relation, boron as anti-inflammatory agents, and boron in neurodegenerative diseases.

Source: Narayan S. Hosmane, Department Of Chemistry And Biochemistry, Northern Illinois University, DeKalb, USA. The Role Of Microbiome In Brain Development And Neurodegenerative Diseases. *Molecules*. (2022); 27(11):3402. <https://doi.org/10.3390/molecules27113402>

Isoorientin Affects Markers Of Alzheimer's Disease (AD) Via Effects On The Oral And Gut Microbiota In APP/PS1 Mice

This study examines the effects of oral administration of ISO (Isoorientin is anti-inflammatory and alleviates markers of AD) on AD-related markers and the oral and gut microbiota in mice.

Study result shows that the high-dose ISO treatment significantly decreased amyloid beta 42-positive deposition by 38.1% and 45.2% in the cortex and hippocampus, respectively, of AP mice. Compared with the AP group, both ISO treatments reduced brain phospho-Tau, phospho-p65, phospho-inhibitor of NF- κ B, and brain and serum LPS and TNF- α by 17.9%-72.5% and increased brain and serum IL-4 and IL-10 by 130%-210% in the AP + ISO-L and AP + ISO-H groups.

Abundances of 26, 25, and 23 microbial taxa in oral, fecal and cecal samples, respectively, were increased in both the AP + ISO-L and AP + ISO-H groups relative to the AP group [linear discriminant analysis (LDA) >3.0 ; $P < 0.05$]. **Gram-negative bacteria, Alteromonas, Campylobacteriales**, and uncultured **Bacteroidales bacterium** were positively correlated ($\rho = 0.28-0.59$; $P < 0.05$) with the LPS levels and responses of inflammatory cytokines.

This study concluded that the microbiota-gut-brain axis is a potential mechanism by which ISO reduces Alzheimer's disease (AD) related markers in AP mice.

Source: Zhongyi Wu, Beijing Agro-Biotechnology Research Center, Beijing Academy Of Agriculture And Forestry Sciences, Beijing, China. Isoorientin Affects Markers Of Alzheimer's Disease (AD) Via Effects On The Oral And Gut Microbiota In APP/PS1 Mice. *The Journal of Nutrition*, Volume 152, Issue 1, January (2022), Pages 140–152, <https://doi.org/10.1093/jn/nxab328>

Changes To Gut Amino Acid Transporters And Microbiome Associated With Increased E/I Ratio In Chd8+/- Mouse Model Of ASD-Like Behavior

Autism spectrum disorder (ASD), a group of neurodevelopmental disorders characterized by social communication deficits and stereotyped behaviors, may be associated with changes to the gut microbiota. In this study researchers used chromodomain helicase DNA-binding protein 8 (CHD8) haploinsufficient mice as a model of ASD to elucidate the pathways through which the host and gut microbiota interact with each other.

Scientists found that increased levels of amino acid transporters in the intestines of the mouse model of ASD contribute to the high level of serum glutamine and the increased excitation/inhibition (E/I) ratio in the brain. In addition, elevated α -defensin levels in the haploinsufficient mice resulted in dysregulation of the gut microbiota characterized by a reduced abundance of *Bacteroides*. Furthermore, supplementation with *Bacteroides uniformis* improved the ASD-like behaviors and restored the E/I ratio in the brain by decreasing intestinal amino acid transport and the serum glutamine levels.

This study demonstrates associations between changes in the gut microbiota and amino acid transporters, and ASD-like behavioral and electrophysiology phenotypes, in a mouse model.

Source: Fangqing Zhao, Beijing Institutes Of Life Science, Chinese Academy Of Sciences; University Of Chinese Academy Of Sciences, Beijing. Changes To Gut Amino Acid Transporters And Microbiome Associated With Increased E/I Ratio In Chd8+/- Mouse Model Of ASD-Like Behavior. Nat Commun 13, 1151 (2022). <https://doi.org/10.1038/s41467-022-28746-2>

Caudovirales Bacteriophages Are Associated With Improved Executive Function And Memory In Flies, Mice, And Humans

This study shows that subjects with increased *Caudovirales* and *Siphoviridae* levels in the gut microbiome had better performance in executive processes and verbal memory.

Conversely, increased *Microviridae* levels were linked to a greater impairment in executive abilities. Microbiota transplantation from human donors with increased specific *Caudovirales* (>90% from the *Siphoviridae* family) levels led to increased scores in the novel object recognition test in mice and up-regulated memory-promoting immediate early genes in the prefrontal cortex. Further, supplementation of the *Drosophila* diet with the 936 group of *lactococcal Siphoviridae* bacteriophages resulted in increased memory scores and upregulation of memory-involved brain genes. Thus, bacteriophages warrant consideration as novel actors in the microbiome-brain axis.

Source: José-Manuel Fernández, Department Of Diabetes, Endocrinology, And Nutrition, Dr. Josep Trueta University Hospital; Nutrition, Eumetabolism, And Health Group, Girona Biomedical Research Institute (Idibgi), Girona, Spain; Centro De Investigación Biomédica En Red Fisiopatología De La Obesidad Y Nutrición (CIBEROBN), Madrid, Spain And Department Of Medical Sciences, School Of Medicine, University Of Girona, Girona, Spain. Caudovirales Bacteriophages Are Associated With Improved Executive Function And Memory In Flies, Mice, And Humans. Cell Host & Microbe, Volume 30, Issue 3 (2022), Pages 340-356.e8, ISSN 1931-3128. <https://doi.org/10.1016/j.chom.2022.01.013>

The Role Of Gut Microbiota—Gut—Brain Axis In Perioperative Neurocognitive Dysfunction

This article reviews the mechanism of the role of gut microbiota-gut-brain axis in Perioperative Neurocognitive Dysfunction (PND) which helps to explore reasonable early treatment strategies.

Source: Youming Zong, Department Of Anesthesiology, The Second Hospital Of Jiaxing, The Second Affiliated Hospital Of Jiaxing University, Jiaxing And Department Of Anesthesiology, Bengbu Medical College, Bengbu, China. Front. Pharmacol. 13:879745, 14 June, (2022). doi: 10.3389/fphar.2022.879745.

The Gut Microbiota Of Environmentally Enriched Mice Regulates Visual Cortical Plasticity

Exposing animals to an enriched environment (EE) has dramatic effects on brain structure, function, and plasticity. The poorly known “EE-derived signals” mediating the EE effects are thought to be generated within the central nervous system. This study shows that gut microbiota signals are crucial for EE-driven plasticity.

Developmental analysis reveals striking differences in intestinal bacteria composition between EE and standard rearing (ST) mice, as well as enhanced levels of short-chain fatty acids (SCFA) in EE mice. Depleting the microbiota of EE mice with antibiotics strongly decreases short chain fatty acids (SCFA) and prevents activation of adult ocular dominance plasticity, spine dynamics, and microglia rearrangement. SCFA treatment in ST mice mimics EE induction of ocular dominance plasticity and microglial remodeling. Remarkably, transferring the microbiota of EE mice to ST recipients activates adult ocular dominance plasticity. Thus, experience-dependent changes in gut microbiota regulate brain plasticity.

Source: Paola Tognini, BIO@SNS Lab, Scuola Normale Superior And Department Of Translational Research And New Technologies In Medicine And Surgery, University Of Pisa, Pisa, Italy. The Gut Microbiota Of Environmentally Enriched Mice Regulates Visual Cortical Plasticity. Cell Reports, Volume 38, Issue 2, 110212, January 11 (2022). <https://doi.org/10.1016/j.celrep.2021.110212>

Combination Of Gut Microbiota And Plasma Amyloid-B As A Potential Index For Identifying Preclinical Alzheimer's Disease: A Cross-Sectional Analysis From The SILCODE Study

Plasma amyloid- β ($A\beta$) may facilitate identification of individuals with brain amyloidosis. Gut microbial dysbiosis in Alzheimer's disease (AD) is increasingly being recognized.

Study result shows that on comparing with the CN- group ($A\beta$ -negative cognitively normal [CN-]), the CN+ group ($A\beta$ -positive cognitively normal [CN+]) shows significantly reduced plasma $A\beta_{42}$ and $A\beta_{42}/A\beta_{40}$. The relative abundance of phylum *Bacteroidetes* was significantly enriched, whereas phylum *Firmicutes* and class *Deltaproteobacteria* were significantly decreased in CN+ individuals in comparison with that in CN- individuals. Particularly, the relative abundance of phylum *Firmicutes* and its corresponding *short chain fatty acids* (SCFA)-producing bacteria exhibited a progressive decline tendency from CN- to CN+ and CI (cognitive impairment). Besides, the global brain $A\beta$ burden was negatively associated with the plasma $A\beta_{42}/A\beta_{40}$, family *Desulfovibrionaceae*, genus *Bilophila* and genus *Faecalibacterium* for all CN participants. Finally, the combination of plasma $A\beta$ markers, altered gut microbiota, and cognitive performance reached a relatively good discriminative power in identifying individuals with CN+ from CN-.

This study provided the evidence that the gut microbial composition was altered in preclinical Alzheimer's disease (AD). The combination of plasma $A\beta$ and gut microbiota may serve as a non-invasive, cost-effective diagnostic tool for early AD screening. Further, targeting the gut microbiota may be a novel therapeutic strategy for AD.

Source: Ying Han, Department Of Neurology, Xuanwu Hospital Of Capital Medical University, Beijing; Key Laboratory Of Biomedical Engineering Of Hainan Province, School Of Biomedical Engineering, Hainan University, Haikou; Center Of Alzheimer's Disease, Beijing Institute For Brain Disorders, Beijing And National Clinical Research Center For Geriatric Diseases, Beijing, China. Combination Of Gut Microbiota And Plasma Amyloid-B As A Potential Index For Identifying Preclinical Alzheimer's Disease: A Cross-Sectional Analysis From The SILCODE Study. *Alz Res Therapy* 14, 35 (2022). <https://doi.org/10.1186/s13195-022-00977-x>

Implications Of Gut Microbiota In Neurodegenerative Diseases

The morbidity associated with neurodegenerative diseases (NDs) is increasing, posing a threat to the mental and physical quality of life of humans. The crucial effect of microbiota on brain physiological processes is mediated through a bidirectional interaction, termed as the gut-brain axis (GBA), which is being investigated in studies. Many clinical and laboratory trials have indicated the importance of microbiota in the development of NDs via various microbial molecules that transmit from the gut to the brain across the GBA or nervous system.

This review summarizes that the implications of gut microbiota in ND, which will be beneficial for understanding the etiology and progression of NDs that may in turn help in developing ND interventions and clinical treatments for these diseases.

Source: Wei Wang, Innovative Institute Of Animal Healthy Breeding, College Of Animal Sciences And Technology, Zhongkai University Of Agriculture And Engineering, Guangzhou And Key Laboratory Of Zoonosis Research, Ministry Of Education, Jilin University, Changchun, China. Implications Of Gut Microbiota In Neurodegenerative Diseases. *Front. Immunol.* 13:785644, 14 February (2022), doi: 10.3389/fimmu.2022.785644.

Clinical, Gut Microbial And Neural Effects Of A Probiotic Add-On Therapy In Depressed Patients: A Randomized Controlled Trial

A promising new treatment approach for major depressive disorder (MDD) targets the microbiota-gut-brain (MGB) axis, which is linked to physiological and behavioral functions affected in MDD. This randomized controlled trial determines whether short-term, high-dose probiotic supplementation reduces depressive symptoms along with gut microbial and neural changes in depressed patients.

Researchers have found that *Hamilton Depression Rating Scale HAM-D scores* were decreased over time and interactions between time and group indicated a stronger decrease in the probiotics relative to the placebo group. Probiotics maintained microbial diversity and increased the abundance of the genus *Lactobacillus*, indicating the effectivity of the probiotics to increase specific taxa. The increase of the *Lactobacillus* was associated with decreased depressive symptoms in the probiotics group. Finally, putamen activation in response to neutral faces was significantly decreased after the probiotic intervention.

Further, an add-on probiotic treatment ameliorates depressive symptoms (HAM-D) along with changes in the gut microbiota and brain, which highlights the role of the MGB axis in MDD and emphasizes the potential of microbiota-related treatment approaches as accessible, pragmatic, and non-stigmatizing therapies in MDD.

Source: André Schmidt, University Of Basel, Department Of Psychiatry (UPK), Basel, Switzerland. Clinical, Gut Microbial And Neural Effects Of A Probiotic Add-On Therapy In Depressed Patients: A Randomized Controlled Trial. *Transl Psychiatry* 12, 227 (2022). <https://doi.org/10.1038/s41398-022-01977-z>

The Alleviation Of Gut Microbiota-Induced Depression And Colitis In Mice By Anti-Inflammatory Probiotics NK151, NK173, And NK175

In this study researchers examined whether the fecal microbiota of *Inflammatory bowel disease (IBD) patients with depression (IBDD)* and their *gut microbiota culture (iGm)* could cause depression and colitis in mice and anti-inflammatory probiotics could mitigate depression in iGm-transplanted or immobilization stress (IS)-exposed mice.

Scientists found that *fecal microbiota transplantation (FMT)* from IBDD patients exhibited *Enterobacteriaceae*-rich gut microbiota, and its gut microbiota culture (iGm) increased depression-like behaviors in mice. Their treatments heightened the blood *lipopolysaccharide (LPS)* level and colonic IL-1 β and IL-6 expression. However, FMT from healthy volunteers or sulfasalazine treatment alleviated cGm-induced depressive-like behaviors and hippocampal and colonic inflammation in mice.

Further, oral administration of *Lactobacillus plantarum* NK151, *Bifidobacterium longum* NK173, and *Bifidobacterium bifidum* NK175, which inhibited LPS-induced IL-6 expression in macrophages, alleviated cGm-induced depression-like behaviors, hippocampal NF- κ B+Iba1+ cell numbers and IL-1 β and IL-6 expression, blood LPS, IL-6, and creatinine levels, and colonic NF- κ B+CD11c+ number and IL-1 β and IL-6 expression in mice.

Treatment with NK151, NK173, or NK175 mitigated immobilization stress (IS)-induced depressive-like behaviors, neuroinflammation, and gut inflammation in mice. NK151, NK173, or NK175 also decreased IS-induced blood LPS, IL-6, and creatinine levels. The transplantation of *Enterobacteriaceae*-rich gut microbiota can cause depression and colitis, as IS exposure, and anti-inflammatory NK151, NK173, and NK175, may alleviate stress-induced fatigue, depression, and colitis by regulating the expression of proinflammatory and anti-inflammatory cytokines through the suppression of gut bacterial LPS.

Source: Dong-Hyun Kim, Neurobiota Research Center, College Of Pharmacy, Kyung Hee University, 26, Kyunghedae-Ro, Dongdaemun-Gu, Korea. *The Alleviation Of Gut Microbiota-Induced Depression And Colitis In Mice By Anti-Inflammatory Probiotics NK151, NK173, And NK175*. *Nutrients*. (2022); 14(10):2080. <https://doi.org/10.3390/nu14102080>

Mechanistic Insights Into Gut Microbiome Dysbiosis-Mediated Neuroimmune Dysregulation And Protein Misfolding And Clearance In The Pathogenesis Of Chronic Neurodegenerative Disorders

This review highlights the functional pathways and mechanisms, particularly gut microbe-induced chronic inflammation, protein misfolding, propagation of disease-specific pathology, defective protein clearance, and autoimmune dysregulation, linking gut microbial dysbiosis and neurodegenerations.

In addition, researchers have also discussed how pathogenic transformation of microbial composition leads to increased endotoxin production and fewer beneficial metabolites, both of which could trigger immune cell activation and enteric neuronal dysfunction. These can further disrupt intestinal barrier permeability, aggravate the systemic pro-inflammatory state, impair blood-brain barrier permeability and recruit immune mediators leading to neuroinflammation and neurodegenerations.

Further, continued biomedical advances in understanding the microbiota-gut-brain axis will extend the frontier of neurodegenerative disorders and enable the utilization of novel diagnostic and therapeutic strategies to mitigate the pathological burden of these diseases.

Source: Anumantha G. Kanthasamy, Parkinson's Disorder Research Laboratory, Department Of Biomedical Sciences, Iowa State University, Ames, IA And Department Of Physiology And Pharmacology, Center For Brain Sciences And Neurodegenerative Diseases, University Of Georgia, Athens, GA, United States. *Mechanistic Insights Into Gut Microbiome Dysbiosis-Mediated Neuroimmune Dysregulation And Protein Misfolding And Clearance In The Pathogenesis Of Chronic Neurodegenerative Disorders*. *Front. Neurosci.* 16:836605, 25 February (2022). doi: 10.3389/fnins.2022.836605.

Convergent Pathways Of The Gut Microbiota–Brain Axis And Neurodegenerative Disorders

In this review researchers have provided an overview of the gut microbiota axis pathways to lay the groundwork for upcoming sessions on the links between the gut microbiota and neurodegenerative disorders. They have also discussed how the gut microbiota may act as an intermediate factor between the host and the environment to mediate disease onset and neuropathology.

Source: Livia H. Morais, Division Of Biology & Biological Engineering, California Institute Of Technology, Pasadena, CA, USA. *Convergent Pathways Of The Gut Microbiota–Brain Axis And Neurodegenerative Disorders*. *Gastroenterology Report*, Volume 10 (2022), goac017. <https://doi.org/10.1093/gastro/goac017>

New Hope For Parkinson's Disease Treatment: Targeting Gut Microbiota

This review focused on the current understanding of the connection between Parkinson's disease and gut microbiota, to provide potential therapeutic targets for Parkinson's Disease (PD).

Source: Feng Zhang, Laboratory Animal Center And Key Laboratory Of Basic Pharmacology Of Ministry Of Education And Joint International Research Laboratory Of Ethnomedicine Of Ministry Of Education And Key Laboratory Of Basic Pharmacology Of Guizhou Province, Zunyi Medical University, Zunyi, Guizhou, China. New Hope For Parkinson's Disease Treatment: Targeting Gut Microbiota. CNS Neuroscience And Therapeutics, 13 July (2022). <https://doi.org/10.1111/cns.13916>

The Microbiota–Gut–Brain Axis in Depression: The Potential Pathophysiological Mechanisms and Microbiota Combined Antidepressant Effect

Many studies have demonstrated that the disorder of the intestinal microbial system structure plays a crucial role in depression. The gut–brain axis manifests a potential linkage between the digestion system and the central nervous system (CNS) This article reviewed the mechanism of bidirectional interaction in the gut–brain axis and existing symptom-relieving measures and antidepressant treatments related to the gut microbiome is reviewed in this article.

Source: Tingtao Chen, Departments Of Geriatrics, The Second Affiliated Hospital Of Nanchang University And National Engineering Research Center For Bioengineering Drugs And Technologies, Institute Of Translational Medicine, Nanchang University, China. The Microbiota–Gut–Brain Axis in Depression: The Potential Pathophysiological Mechanisms and Microbiota Combined Antidepressant Effect. Nutrients (2022), 14(10), 2081. <https://doi.org/10.3390/nu14102081>

Gut Microbiota In Monozygotic Twins Discordant For Parkinson's Disease

Differences in gut microbiota between Parkinson's disease (PD) patients and controls seem to depend on multiple – frequently unmeasured – confounders. Monozygotic twins offer a unique model for controlling several factors responsible for interpersonal variation in gut microbiota. Fecal samples from 20 monozygotic twin pairs (N=40) discordant for PD were studied (metagenomic shotgun analysis).

Researchers have found that paired-data analysis detected minimal differences in bacterial taxa abundance at species level (*Bacteroides pectinophilus* [P=0.037], *Bifidobacterium pseudocatenulatum* [P=0.050] and *Bifidobacterium catenulatum* [P=0.025]) and in predicted metabolic pathways (primary bile acid biosynthesis [P=0.037]). Further, additional studies are required to understand the role of gut microbiota in the pathogenesis of PD.

Source: Emanuele Cereda MD, PhD; Clinical Nutrition and Dietetics Unit, Fondazione IRCCS Policlinico San Matteo, Viale Golgi, Italy. Gut Microbiota In Monozygotic Twins Discordant For Parkinson's Disease. Annals Of Neurology, 19 July (2022). <https://doi.org/10.1002/ana.26454>

Pre- And Probiotics In The Management Of Children With Autism And Gut Issues: A Review Of The Current Evidence

Manipulation of the gut microbiome offers a promising treatment option for children with autism spectrum disorder (ASD) for whom functional gastrointestinal disorders (FGIDs) are a common comorbidity. Both ASD and FGIDs have been linked to dysfunction of the microbiome-gut-brain (MGB) axis. The aim of this review is to investigate the gut microbiome as a therapeutic target for children with ASD.

Findings of the study suggest that there is limited, but preliminary evidence of efficacy in relieving GI distress, improving ASD-associated behaviours, altering microbiota composition, and reducing inflammatory potential.

Source: Leanne K. Mitchell, Child Health Research Centre, Faculty of Medicine, The University of Queensland, South Brisbane, QLD, Australia. Pre- And Probiotics In The Management Of Children With Autism And Gut Issues: A Review Of The Current Evidence. Eur J Clin Nutr 76, 913–921 (2022). <https://doi.org/10.1038/s41430-021-01027-9>

Longitudinal Study Of Stool-Associated Microbial Taxa In Sibling Pairs With And Without Autism Spectrum Disorder

The study result shows that overall microbiome composition (beta-diversity) is associated with specific Autism Spectrum Disorder (ASD)-related behavioral characteristics.

Source: Christine Tatarue, Department Of Microbiology, Oregon State University, Corvallis, OR, USA. Longitudinal Study Of Stool-Associated Microbial Taxa In Sibling Pairs With And Without Autism Spectrum Disorder. ISME COMMUN. 1, 80 (2021). <https://doi.org/10.1038/s43705-021-00080-6>

Autism-Related Dietary Preferences Mediate Autism-Gut Microbiome Associations

Researchers have found that negligible direct association between Autism Spectrum Disorder (ASD) diagnosis and the gut microbiome.

Study data support a model whereby ASD-related restricted interests are associated with less-diverse diet, and in turn reduced microbial taxonomic diversity and looser stool consistency. In contrast to ASD diagnosis, study dataset was well powered to detect microbiome associations with traits such as age, dietary intake, and stool consistency.

Overall, microbiome differences in ASD may reflect dietary preferences that relate to diagnostic features, and researchers caution against claims that the microbiome has a driving role in ASD.

Source: Jacob Gratten, Mater Research Institute, The University Of Queensland, Woolloongabba; Institute For Molecular Bioscience, The University Of Queensland, St Lucia And Cooperative Research Centre For Living With Autism (Autism CRC), Long Pocket, Queensland, Australia. Autism-Related Dietary Preferences Mediate Autism-Gut Microbiome Associations. *Journal Cell*, Volume 184, Issue 24, P5916-5931.E17, November 24, (2021), DOI: <https://doi.org/10.1016/j.cell.2021.10.015>

Regulation Of Neurotransmitters By The Gut Microbiota And Effects On Cognition In Neurological Disorders

In this study researchers have summarized the mechanisms whereby the gut microbiota regulate the production, transportation, and functioning of neurotransmitters. They have also discussed how microbiome dysbiosis affects cognitive function, especially in neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease.

Source: Yu Chen, Chinese Academy Of Sciences Key Laboratory Of Brain Connectome And Manipulation, Shenzhen Key Laboratory Of Translational Research For Brain Diseases, The Brain Cognition And Brain Disease Institute, Shenzhen Institute Of Advanced Technology, Chinese Academy Of Sciences, Shenzhen-Hong Kong Institute Of Brain Science-Shenzhen Fundamental Research Institutions; Shenzhen College Of Advanced Technology, University Of Chinese Academy Of Sciences And Guangdong Provincial Key Laboratory Of Brain Science, Disease And Drug Development, HKUST Shenzhen Research Institute, Shenzhen-Hong Kong Institute Of Brain Science, Shenzhen Fundamental Research Institutions, China. Regulation of Neurotransmitters by the Gut Microbiota and Effects on Cognition in Neurological Disorders. *Nutrients*. (2021); 13(6):2099. <https://doi.org/10.3390/nu13062099>

Gut Microbiota Regulation And Their Implication In The Development Of Neurodegenerative Disease

This review highlights the relationship between gut microbiota and neurodegenerative diseases, and to contribute to the understanding of the function of gut microbiota in neurodegeneration, as well as their relevant mechanism. Further, it also discusses the current application and future prospects of microbiota-associated therapy, including probiotics and fecal microbiota transplantation (FMT), potentially shedding new light on the research of neurodegeneration.

Source: Chuan Qin, NHC Key Laboratory Of Human Disease Comparative Medicine, Institute Of Laboratory Animal Sciences And Beijing Engineering Research Center For Experimental Animal Models Of Human Critical Diseases, Chinese Academy Of Medical Sciences (CAMS), China. Gut Microbiota Regulation And Their Implication In The Development Of Neurodegenerative Disease. *Microorganisms* 9, (2021), no. 11: 2281. <https://doi.org/10.3390/microorganisms9112281>

Healthy Gut, Healthy Brain: The Gut Microbiome In Neurodegenerative Disorders

The **central nervous system (CNS)** known to regulate the physiological conditions of human body, also itself gets dynamically regulated by both the physiological as well as pathological conditions of the body. These conditions get changed quite often, and often involve changes introduced into the gut microbiota which, as studies are revealing, directly modulate the CNS via a crosstalk. This cross-talk between the gut microbiota and CNS, i.e., the **gut-brain axis (GBA)**, plays a major role in the pathogenesis of many neurodegenerative disorders such as **Parkinson's disease (PD)**, **Alzheimer's disease (AD)**, **amyotrophic lateral sclerosis (ALS)**, **multiple sclerosis (MS)** and **Huntington's disease (HD)**. The aim of the study is to discuss how gut microbiota, through GBA, regulate neurodegenerative disorders such as PD, AD, ALS, MS and HD.

Researchers have concluded that alterations in the intestinal microbiota modulate various activities that could potentially lead to CNS disorders through interactions via the GBA.

Source: Prem P. Tripathi, CSIR- Indian Institute Of Chemical Biology (CSIR-IICB), Kolkata, India. Healthy Gut, Healthy Brain: The Gut Microbiome In Neurodegenerative Disorders. *Curr Top Med Chem.*, Volume 20, Issue 13, (2020); 20(13):1142-1153. DOI: 10.2174/1568026620666200413091101.

Gut Microbial Molecules In Behavioural And Neurodegenerative Conditions

In this study researchers have described bacterial metabolites with known or suspected neuromodulatory activity, define mechanisms of signalling pathways from the gut microbiota to the brain and discussed direct effects that gut bacterial molecules are likely to exert on specific brain cells.

Source: Sarkis K. Mazmanian, Division Of Biology & Biological Engineering, California Institute Of Technology, Pasadena, CA, USA. Gut Microbial Molecules In Behavioural And Neurodegenerative Conditions. *Nat Rev Neurosci* 21, 717-731 (2020). <https://doi.org/10.1038/s41583-020-00381-0>

The Progress Of Gut Microbiome Research Related To Brain Disorders

In this review, scientists have provided an overview of technical approaches used in gut microbiome studies; microbiota and immunity; gut microbiota and metabolites; microbiota-induced blood-brain barrier dysfunction; neuropsychiatric diseases; neurodegenerative diseases; and cerebrovascular disease.

Source: Xingdong Chen, State Key Laboratory of Genetic Engineering and Collaborative Innovation Center for Genetics and Development, School of Life Sciences, Fudan University; Fudan University Taizhou Institute of Health Sciences and Human Phenome Institute, Fudan University, China. *The Progress Of Gut Microbiome Research Related To Brain Disorders*. *J Neuroinflammation* 17, 25 (2020). <https://doi.org/10.1186/s12974-020-1705-z>

Microbiota Composition And Metabolism Are Associated With Gut Function In Parkinson's Disease

The objectives of the current study were to assess associations between microbiota composition, stool consistency, constipation, and systemic microbial metabolites in Parkinson's disease to better understand how intestinal microbes contribute to gastrointestinal disturbances commonly observed in patients.

This study concluded that compositional and metabolic alterations in the Parkinson's microbiota are highly associated with gut function, suggesting plausible mechanistic links between altered bacterial metabolism and reduced gut health in this disease. The systematic detection of elevated deleterious proteolytic microbial metabolites in Parkinson's serum suggests a mechanism whereby microbiota dysbiosis contributes to disease etiology and pathophysiology.

Source: Dr. Silke Appel-Cresswell, Pacific Parkinson's Research Centre, University Of British Columbia, Canada. *Microbiota Composition And Metabolism Are Associated With Gut Function In Parkinson's Disease*. *Movement Disorders*, 01 May (2020). <https://doi.org/10.1002/mds.28052>

Frailty, Cognitive Decline, Neurodegenerative Diseases and Nutrition Interventions

This review aims to describe the nutritional factors that have been researched so far which may lead to the development of frailty, and especially cognitive decline.

Source: Sara C. Zapico, International Forensic Research Institute And Chemistry Department, Florida International University And Anthropology Department, Smithsonian Institution, NMNH, MRC 112, 10th And Constitution Ave, NW, Washington, DC, USA. *Frailty, Cognitive Decline, Neurodegenerative Diseases and Nutrition Interventions*. *International Journal of Molecular Sciences*. (2019); 20(11):2842. <https://doi.org/10.3390/ijms20112842>

Unhealthy Gut, Unhealthy Brain: The Role Of The Intestinal Microbiota In Neurodegenerative Diseases

In this review scientists have illustrated two pathways implicated in the crosstalk between gut microbiota and CNS involving 1) the vagus nerve and 2) transmission of signaling molecules through the circulatory system and across the blood-brain barrier (BBB). This review summarizes the available evidence of the specific changes in the intestinal microbiota, as well as microorganism-induced modifications to intestinal and BBB permeability, which have been linked to several neurodegenerative disorders including ALS, AD, and PD. Even though each of these diseases arise from unique pathogenetic mechanisms, all are characterized, at least in part, by chronic neuroinflammation. It also provides an interpretation for the substantial evidence that healthy intestinal microbiota have the ability to positively regulate the neuroimmune responses in the CNS.

Source: Lindsay Joy Spielman, Department of Biology, Alexander College, Burnaby, BC, Canada. *Unhealthy Gut, Unhealthy Brain: The Role Of The Intestinal Microbiota In Neurodegenerative Diseases*. *Neurochemistry International*, Volume 120, November (2018), Pages 149-163. <https://doi.org/10.1016/j.neuint.2018.08.005>

The Gut-Brain Axis: Influence Of Microbiota On Mood And Mental Health

The gut-brain axis is a bidirectional communication network that links the enteric and central nervous systems. This network is not only anatomical, but it extends to include endocrine, humoral, metabolic, and immune routes of communication as well. The autonomic nervous system, hypothalamic-pituitary-adrenal (HPA) axis, and nerves within the gastrointestinal tract, all link the gut and the brain, allowing the brain to influence intestinal activities, including activity of functional immune effector cells; and the gut to influence mood, cognition, and mental health.

Source: Appleton J, former Faculty Member of the National University of Naturopathic Medicine, Portland, Oregon. *The Gut-Brain Axis: Influence of Microbiota on Mood and Mental Health*. *Integr Med (Encinitas)*. (2018) Aug;17(4):28-32. PMID: 31043907; PMCID: PMC6469458.

Fermented Milk Containing *Lactobacillus Casei* Strain *Shirota* Preserves the Diversity of the Gut Microbiota and Relieves Abdominal Dysfunction in Healthy Medical Students Exposed to Academic Stress

This study investigated the effects of the probiotic *Lactobacillus casei* strain *Shirota* on abdominal dysfunction, a double-blind, placebo-controlled trial was conducted with healthy medical students undertaking an authorized nationwide examination for academic advancement.

Researchers found that stress-induced increases in a visual analog scale measuring feelings of stress, the total score of abdominal dysfunction, and the number of genes with changes in expression of more than 2-fold in leukocytes were significantly suppressed in the *L. casei* strain *Shirota* group compared with those in the placebo group. Further, there was a significant increase in salivary cortisol levels before the examination in the placebo group. The administration of *L. casei strain Shirota*, but not placebo, significantly reduced gastrointestinal symptoms.

Further, 16S rRNA gene amplicon sequencing demonstrated that the *L. casei strain Shirota* group had significantly higher numbers of species, a marker of the alpha-diversity index, in their gut microbiota and a significantly lower percentage of *Bacteroidaceae* than the placebo group.

The findings of the study indicates that the daily consumption of probiotics, such as *L. casei strain Shirota*, preserves the diversity of the gut microbiota and may relieve stress-associated responses of abdominal dysfunction in healthy subjects exposed to stressful situations.

Source: Kouji Miyazaki, Yakult Central Institute, Izumi, Kunitachi, Tokyo, Japan. **Fermented Milk Containing *Lactobacillus casei* Strain *Shirota* Preserves the Diversity of the Gut Microbiota and Relieves Abdominal Dysfunction in Healthy Medical Students Exposed to Academic Stress.** *Appl Environ Microbiol.*, (2016) May 31;82(12):3649-58. DOI: <https://doi.org/10.1128/AEM.04134-15>

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