Brain-Gut-Microbiome Axis & Neuroinflammation

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Abstract

Recent studies highlight the microbiota-gut-brain axis as a central player in the development of neurological and psychiatric disorders. This analysis reviews five case-based studies encompassing Alzheimer's disease, major depressive disorder, neurosarcoidosis, pediatric acute neuropsychiatric syndrome with Crohn's disease, and anti-NMDAR autoimmune encephalitis across varied etiologies, common threads, altered gut microbiota, and inflammatory signaling. Select interventions targeting the immune or endocannabinoid systems yielded symptomatic improvements. These findings showcase the therapeutic potential of microbiome-based or immune-modulatory strategies.

Introduction

The gastrointestinal system, commonly known as the digestive system, refers to a group of organs responsible for numerous processes, including the breakdown of food, absorption of nutrients, and elimination of waste. Controlling among the most important functions, this system plays a key role in maintaining body homeostasis through its key elements: gastrointestinal flora, stomach acid, gut immunity; it is a complex environment of microorganisms. Whenever gut health is affected, gastrointestinal diseases tend to affect the digestive tract, often presenting common symptoms such as pain and bloating; however, recent studies have shown that gut microbiota changes affect brain functioning and impact psychological conditions.

The brain is an elaborate organ, the most complex one in our body. Controlling basic body activities to elaborate thinking and emotions, it is commonly addressed as the control center of the nervous system in vertebrates.

The enteric nervous system (one of the three divisions of the autonomic nervous system) controls the digestive system, connecting through the central nervous system and sympathetic nervous system. It is a network of neurons present in the walls of the gastrointestinal tract. Its neurons are arranged in thousands of ganglia which are sorted into Myenteric ganglia and Submucosal ganglia. Myenteric ganglia consist of groups of ganglia found within the myenteric plexus. This plexus represents a complex arrangement of nerve fibers and ganglia positioned between the inner circular and outer longitudinal layers of smooth muscle in the gastrointestinal system containing mainly motor neurons. The submucosal nodes, commonly referred to as Meissner's plexus, are networks of neurons and ganglia situated within the intestinal wall, extending from the esophagus to the rectum, most of the afferent sensory neurons.

Quoting from the book Neuroscience, 2nd edition: “An enormous number of neurons are specifically associated with the gastrointestinal tract to control its many functions; indeed, more neurons are said to reside in the human gut than in the entire spinal cord. As already noted, the activity of the gut is modulated by both the sympathetic and the parasympathetic divisions of the visceral motor system.” This perfectly summarizes the relationship between these two systems and how gut health affects the brain.

Objectives

- Review documented case studies and clinical reports linking gut dysbiosis with rare neurological diseases involving neuroinflammation.

- Identify patterns in microbiome composition and associated neurological outcomes.

Content

Neuroinflammation

According to an article published in PMC, neuroinflammation is defined as an inflammatory response directly related to the spinal cord and the brain. This condition might vary in intensity in response to the context: injury, infection, or stress; therefore it is crucial to identify the cause before prescribing treatment. Key aspects such as physiological, biochemical, and behavioral consequences influence the duration of these responses; however, it is viewed that in many cases, neuroinflammatory responses are not always inherently negative.

Neuroinflammation can be benign; it is an immunological response to injury and is capable of further recovery and healing. Among its positive aspects, it drives brain tissue repair and neuroprotection, enhancing plasticity. Microglia, known as innate immune cells of the central nervous system, mediate these responses. This last one produces cytokines (small proteins that act like signaling molecules) which contribute to the regulation of immune responses, commonly acting as communicators between these cells and other cells in the body. It is worth highlighting that microglias also produce chemokines (small proteins that attach blood cells to site inflammation or infection) and reactive oxygen species (highly reactive molecules containing oxygen that can act as signaling molecules), however, each of these cells has a positive and negative effect on the cells, which is a reason why a controlled parameter must be met.

Neuroinflammatory Markers

Cytokines: can be divided into two wide groups:

- Pro-inflammatory(triggers a heighten inflammation): TNF-α, IL-1β, IL-6, IFN-γ.

Tumor Necrosis Factor-alpha (TNF-α)
Source: Activated microglia, astrocytes, macrophages.
Functions:

- Promotes inflammation by activating NF-κB signaling.
- Increases BBB permeability, allowing immune cell infiltration.
- It can induce neuronal apoptosis (cell death) in excess.

Role in Disease(suppresses inflammation): Elevated in Alzheimer's, multiple sclerosis (MS), and depression.

Interleukin-1 Beta (IL-1β)
Source: Microglia, astrocytes.

Functions:

- Stimulates further cytokine release (e.g., IL-6, TNF-α).
- Enhances neurotoxicity by promoting excitotoxicity (via NMDA receptor overactivation).
- Linked to fever and sickness behavior.

Role in Disease: High levels of Parkinson's, traumatic brain injury (TBI), and major depressive disorder (MDD).

Interleukin-6 (IL-6)
Source: Microglia, astrocytes, endothelial cells.

Functions:

- Acute phase: Helps in tissue repair.
- Chronic elevation → neurodegeneration, synaptic dysfunction.
- Can signal via trans-signaling (soluble IL-6R) to exacerbate inflammation.

Role in Disease: Associated with cognitive decline, MS, and autism spectrum disorder (ASD).

Interferon-gamma (IFN-γ)
Source: T-cells, NK cells.

Functions:

- Activates microglia and macrophages.
- Increases MHC class II expression (enhances antigen presentation).
- Can be neuroprotective or damaging, depending on context.

Role in Disease: Key in multiple sclerosis (MS) and viral encephalitis.

- Anti-inflammatory: IL-10, TGF-β.

Interleukin-10 (IL-10)

Source: Regulatory T-cells (Tregs), microglia, astrocytes.

Functions:

- Suppresses TNF-α, IL-1β, IL-6.
- Promotes tissue repair and resolution of inflammation.
- Protects against excessive microglial activation.

Role in Disease: Low IL-10 linked to chronic neuroinflammation (e.g., Alzheimer's).

Transforming Growth Factor-beta (TGF-β)

Source: Microglia, astrocytes, Tregs.

Functions:

- Inhibits pro-inflammatory cytokine production.
- Promotes neuronal survival and synaptic plasticity.
- Helps maintain immune tolerance in the CNS.
- Role in Disease: Dysregulation seen in ALS and brain tumors.

Chemokines:

- CXCL8, CCL2 (MCP-1), CCL5 (RANTES).

CXCL8 (IL-8)

Source: Microglia, astrocytes, endothelial cells.

Functions:

- Recruits neutrophils to sites of inflammation.
- Enhances BBB breakdown.
- Role in Disease: Elevated in stroke and bacterial meningitis.

CCL2 (MCP-1 – Monocyte Chemoattractant Protein-1)

Source: Microglia, astrocytes, neurons.

Functions:

- Attracts monocytes/macrophages to the brain.
- Promotes neuroinflammation in chronic conditions.
- Role in Disease: High in HIV-associated dementia, and Alzheimer's.

CCL5 (RANTES – Regulated on Activation, Normal T-cell Expressed and Secreted)
Source: Microglia, T-cells.

Functions:
- Recruits T-cells, eosinophils, and monocytes.
- Linked to viral infections (e.g., HIV, Zika).

Role in Disease: Implicated in neuropathic pain and MS.

Reactive Oxygen Species (ROS) & Nitric Oxide (NO):
- Contribute to oxidative stress.
  Low levels (eNOS/nNOS): Neuroprotective (vasodilation, synaptic plasticity).

  High levels (iNOS): Forms peroxynitrite ($ONOO^-$) → damages neurons.

Gut health relation

The gut and the brain communicate bidirectionally, referring to a two-way influence between these two parts of the body. The communication is done through the brain-gut axis, a complex network involving the enteric nervous system. It can be said that the gut regulates the immune system, and any imbalance may lead to systemic inflammation; this dysbiosis leads to neuroinflammation frequently triggered by endotoxins.

When talking of the gut-brain axis, one must not leave aside the vagus nerve. This last one is a neural pathway connecting the gut and the brain directly. Vagus nerve damage can lead to gastroparesis, food not moving into your intestines.

Another significant factor that fixes into this division is "leaky gut" and bacteria translocation. Whenever the tight junctions between gut epithelial cells weaken (caused by factors such as chronic stress, poor diet, and infections) endotoxins (such as lipopolysaccharide also known as LPS), bacterial fragments, and undigested proteins enter the bloodstream which trigger the peripheral immune cells releasing inflammatory cytokines and chronic microglial activation

leads to neurodegeneration and mood disorders. In other words, it raises the chances of Alzheimer's, Parkinson's, depression, and anxiety.

Bacterias found in the gut induce the production or modulation of neurotransmitters that influence brain function. Taking as an example the serotonin, about 90% is made in the gut, this one regulates mood and sleep patterns. When Dysbiosis disrupts these pathways, contributing to depression, ADHD, and Parkinson's disease.

Common gut-influenced conditions

The gut microbiome plays a key role in numerous disorders, sorted into four major groups we highlight:

Neurodegenerative

- Alzheimer's Disease (AD)
  Featured by high levels of LPS which reduces neuroprotection. AD patients have altered gut microbiota.

- Parkinson's Disease (PD)
  The α-synuclein (a protein that regulates neurotransmitter release and synaptic vesicle trafficking) starts misfolding, beginning in the gut, this change spreads to the brain, and this constipation often precedes motor symptoms over years. PD patients have higher pro-inflammatory and fewer SCFA producers.

- Amyotrophic Lateral Sclerosis (ALS)
  A leaky gut influences systemic inflammation resulting in motor neuron damage. ALS patients often have gut dysbiosis.

Autoimmune & Neuroinflammatory Disorders

- Multiple Sclerosis (MS)
  Characterized by elevated levels of Akkermansia muciniphila, a mucus-degrading bacterium. Short-chain fatty acids (SCFAs), particularly butyrate, regulate T-regulatory cells (Tregs), which suppress autoimmunity. MS patients have altered gut microbiota and those on high-fiber diets experience fewer relapses.

- Autism Spectrum Disorder (ASD)
  Linked to increased intestinal permeability ("leaky gut"), allowing neurotoxic metabolites like propionic acid to reach the brain. Overgrowth of Clostridia bacteria contributes to

harmful compounds that affect behavior. Children with ASD often experience gastrointestinal symptoms, and probiotic treatments (e.g., L. reuteri) have been shown to improve social behavior in animal models.

Psychiatric & Mood Disorders

- Depression & Anxiety
  Associated with reduced gut microbial diversity, leading to lower serotonin production (90% of serotonin is synthesized in the gut). Inflammatory molecules like LPS and cytokines disrupt the GABA/glutamate balance. Depressed individuals often show increased Bacteroides and decreased Faecalibacterium (an anti-inflammatory genus). Probiotic interventions, termed "psychobiotics," have been shown to reduce anxiety symptoms.

- Schizophrenia
  Characterized by increased gut permeability and immune activation, contributing to glutamate/NMDA receptor dysfunction. Patients frequently exhibit microbial imbalances, including reduced Lactobacillus and elevated Candida species.

Metabolic & Immune Disorders

- Obesity & Type 2 Diabetes
  Defined by an altered Firmicutes/Bacteroidetes ratio that enhances calorie absorption. Lipopolysaccharides (LPS) from gram-negative bacteria contribute to systemic inflammation and insulin resistance.

- Irritable Bowel Syndrome (IBS)
  Mediated by mast cell activation leading to visceral hypersensitivity and pain amplification in the brain. Low-FODMAP diets alleviate symptoms by reducing fermentable substrates for gut bacteria.

- Rheumatoid Arthritis (RA)
  Linked to an overgrowth of Prevotella copri, which promotes autoimmunity. Increased gut permeability permits microbial fragments to enter circulation and trigger joint inflammation.

Sometimes, diseases cannot be classified into a specific group due to the multiple overlapping of their complexity.

Examples of this are:

- Crohn's Disease
  A type of inflammatory bowel disease causing chronic inflammation in the digestive tract often accompanied by diarrhea, abdominal pain, fatigue, and malnutrition. The immune system attacks the gut, leading to ulcers and strictures. Consequences of this occurrence include reduced microbial diversity and an overgrowth of pro-inflammatory bacteria. This way, it promotes leaky gut, cytokine release, and vagus nerve dysfunction.

- Pediatric Acute-onset Neuropsychiatric Syndrome (PANS)
  PANS refers to a sudden onset of OCD, tics, anxiety, aggression, and cognitive decline in children often triggered by infection or immune activation. There is no exact cause, however, it is highly related to infections, metabolic disturbances, or other inflammatory reactions. This one triggers infections which leads to autoantibodies production to attack neurons.

Data Collection

1. Cannabinoid extract in microdoses ameliorates mnemonic and nonmnemonic Alzheimer's disease symptoms: a case report

Data	**Description**
Case No.	1
Disease	Alzheimer's Disease (AD)
Patient Info	- 75-year-old white male - autonomous farmer - no major comorbidities - ex-smoker
Neuro Symptoms	- Memory loss - spatial/temporal disorientation - repetitive storytelling - Executive dysfunction - mood issues - sleep disturbance
Gut Symptoms/ Microbiome Data	No Gastrointestinal symptoms were reported; a gut-brain connection was hypothesized via the endocannabinoid system.
Inflammatory Markers	Not directly assessed; anti-inflammatory effect hypothesized via cannabinoid action
Microbiome-Related interventions (if applicable)	Cannabinoid microdosing (oral, THC: CBD 8:1) targeting the endocannabinoid system.
Outcome/notes	Long-term cognitive and mood improvement, improved MMSE and ADAS-Cog scores, no side effects.
Extra (?)	Suggests microdose cannabinoids may restore endocannabinoid/gut-brain balance in AD.

2. Neuroinflammation, Microbiota-Gut-Brain Axis, and Depression: The Vicious Circle

Data	**Description**

Case No.	2
Disease	Major depressive disorder (MDD)
Patient Info	- Various studies involving both humans and mice, including specifically Chinese and American patients and Polish women
Neuro Symptoms	- MDD, which includes: - anxiety - lower cognition - delayed thinking - irritability - feelings of worthlessness and guilt - low energy - insomnia - suicidal thoughts
Gut Symptoms/ Microbiome Data	- increased levels of isovaleric acid in stool - lack of equilibrium of short-chain fatty acid levels in stool (significantly lower or higher levels than average) - alterations in bile acid
Inflammatory Markers	- increased IL-6, IL-12, IL-1 β and TNF
Microbiome-Related interventions (if applicable)	None
Outcome/notes	Gut dysbiosis -> cytokines traveling through bloodstream to CNS
Extra (?)	None

3. Corticosteroid treatment for acute hydrocephalus in neurosarcoidosis: a case report

Data	**Description**
Case No.	3
Disease	Neurosarcoidosis with acute hydrocephalus and seizures
Patient Info	- 29-year-old Caucasian male

	- history of Mediterranean anemia
Neuro Symptoms	- Vertigo - ataxia - bilateral papillary edema - epileptic seizure - headache - visual field changes
Gut Symptoms/ Microbiome Data	No gastrointestinal or microbiome data was reported.
Inflammatory Markers	- Elevated CSF proteins - lymphocytic pleocytosis - oligoclonal bands - ↑CD4/CD8 ratio - granulomas
Microbiome-Related interventions (if applicable)	None
Outcome/notes	Complete recovery with high-dose corticosteroids; stable MRI and EEG findings.
Extra (?)	Non-surgical management of hydrocephalus was successful; a rare case of medical-only resolution.

4. Whole-exome sequencing in a subject with fluctuating neuropsychiatric symptoms, immunoglobulin G1 deficiency, and subsequent development of Crohn's disease: a case report

Data	**Description**
Case No.	4
Disease	- Pediatric acute/onset neuropsychiatric syndrome (PANS) - Crohn's disease
Patient Info	- Non-Hispanic Caucasian female - Initial symptoms at age 9 - Diagnosed with Crohn's at 15

Neuro Symptoms	- Severe anxiety - school phobia - persistent headache - fatigue - sleep disturbance - symptoms resembling POTS
Gut Symptoms/ Microbiome Data	- Chronic abdominal pain - diagnosis of Crohn's disease with lesions in the terminal ileum - Infected with Yersinia enterocolitis
Inflammatory Markers	- Elevated IL-1β, TNF-α, and IL-6 levels linked to NLRP12 mutation - reduced cytokines after anakinra treatment
Microbiome-Related interventions (if applicable)	Not direct, but NLRP12 mutation affects gut microbiome tolerance and diversity; anakinra (IL-1β blocker) improved symptoms.
Outcome/notes	Anakinra markedly improved symptoms; ustekinumab was later used successfully for Crohn's flare-up; highlighting gene-environment-immune interactions.
Extra (?)	Whole-exome sequencing revealed NLRP12 (loss-of-function) and IRF2BP2 (gain-of-function) mutations; paternal inheritance; TNF blockers were ineffective.

5. Gut dysbiosis correlates with the symptom severity of anti-NMDA receptor autoimmune encephalitis: a multi-patient study

Data	**Description**
Case No.	5
Disease	Anti-NMDA receptor autoimmune encephalitis
Patient Info	-21 individuals: mostly young adults and some adolescents -Diagnosed clinically with anti-NMDAR encephalitis, some had prior infections or gut-symptoms
Neuro Symptoms	-Seizures -Memory loss and loss of consciousness

	-Confusion -Psychosis -Abnormalities in behavior and movements -Cognitive decline -Speech disorder
Gut Symptoms/ Microbiome Data	-No gastrointestinal symptoms -Elevated gut permeability/"leaky gut" markers -Altered microbiota -Increased levels of pro-inflammatory bacteria (e.g: enterobacteriaceae) -Decreased levels of beneficial bacteria (e.g: faecalibacterium)
Inflammatory Markers	-Elevated LPS (marker of bacterial toxins) -Elevated D-lactate (a marker of microbial metabolite) -Elevated DAO (an enzyme that reveals gut permeability) -Cytokine imbalance (e.g: elevation of IL-6, TNF-α, IFN-γ indicating inflammation)
Microbiome-Related interventions (if applicable)	-No gut treatments -Anticipated future applications of probiotics
Outcome/notes	Most patients showed neurological improvement with immunotherapy, but their microbiota remained altered for some time. Elevated gut permeability and inflammation markers correlate with more severe symptoms, indicating the vital role of gut health in disease progression.
Extra (?)	Higher LPS, D-lactate, and DAO were statistically correlated with high MRS levels, meaning worse short-term outcomes.

Analysis

Neurodegenerative Disorders

Alzheimer's Disease (AD)

- Involves endocannabinoid system (ECS) dysregulation, contributing to neuroinflammation. No reported GI symptoms or microbiome tests, but ECS is closely linked to gut-brain signaling.

- Suggested mechanism: ECS imbalance affects cognitive decline via neuroimmune pathways.

- Intervention: Oral cannabinoid microdosing (THC: CBD 8:1) for 22 months.

- Outcome: Improvement in memory, mood, and cognitive tests (MMSE, ADAS-Cog).

- Insight: Implies gut-brain-immune interaction through ECS, even in absence of GI symptoms.

Psychiatric & Mood Disorders

Major Depressive Disorder (MDD)

- Marked by increased pro-inflammatory cytokines and microbiota imbalance.

- Microbiome findings: Elevated Bacteroides, decreased butyrate-producing bacteria (e.g., Faecalibacterium).

- Immune profile: High IL-6, IL-12, IL-1β, and TNF-α.

- Metabolic profile: Abnormal SCFAs, bile acids, and isovaleric acid levels

- Outcome: No interventions were applied; however, inflammation and dysbiosis were correlated with symptom severity.

- Insight: Supports the gut-immune-brain model of depression pathogenesis.

Autoimmune & Inflammatory CNS Disorders

Neurosarcoidosis with Acute Hydrocephalus

- Sarcoid granulomas infiltrating CNS pathways. No microbiome data was reported.

- CSF findings: High protein, low glucose, elevated ACE, lymphocytic pleocytosis, high CD4/CD8 ratio.

- Intervention: High-dose corticosteroids (methylprednisolone + oral prednisone).

- Outcome: Full neurological recovery without the need for neurosurgical intervention.

- Insight: Purely immune-driven; demonstrates CNS inflammation responding to systemic immunosuppression.

Overlap Disorders (Neuroimmune + GI)

Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) + Crohn’s Disease

- Genetic mutation (NLRP12) is linked to abnormal inflammasome regulation and microbiota intolerance.

- Trigger: Yersinia enterocolitica infection.
- Immune profile: Elevated IL-1β, TNF-α, IL-6.
- GI symptoms: Chronic diarrhea, intestinal ulcers, anemia.
- Neuropsychiatric symptoms: Tics, aggression, insomnia, OCD.
- Intervention: Anakinra (IL-1β antagonist) and later ustekinumab (IL-12/23 blocker).
- Outcome: Reduction in both psychiatric and gastrointestinal symptoms.
- Insight: Demonstrates direct gut-brain-immune axis disruption via genetics, infection, and inflammation.

Anti-NMDAR Autoimmune Encephalitis

- Autoantibodies target NMDA receptors in the brain, accompanied by concurrent alterations in the gut microbiome.
- Microbiome: Decreased butyrate-producers; increased LPS-producing bacteria and gut permeability.
- Immune profile: High IL-6, TNF-α, IFN-γ, LPS, D-lactate, DAO.
- Intervention: Standard immunotherapy, no microbiota-specific treatment.
- Outcome: Clinical symptom relief, but persistent microbiome dysbiosis and systemic inflammation.

Discussion

How do alterations in the gut microbiome correlate with neuroinflammatory symptoms in patients with rare neurological disorders?

Research shows that an unhealthy gut microbiome (called dysbiosis) may play a major role in brain inflammation. This is because gut bacteria influence how the immune system functions, how the body processes certain chemicals, and how effectively the barrier between the gut and brain maintains its integrity.

Gut Bacteria and Immune System Overactivation

In anti-NMDAR encephalitis, there were more harmful bacteria that produced toxins (like LPS) and fewer helpful ones like Faecalibacterium. These changes were linked to higher levels of inflammatory chemicals in the blood, which may affect the brain. This kind of immune overreaction can make brain symptoms worse.

In PANS (linked to Crohn's disease), genetic mutations cause the immune system to overreact to gut bacteria. This led to inflammation in both the gut and the brain. Treatments that reduced immune activity helped improve the patient's brain symptoms, showing how closely the gut and brain are connected.

Gut Chemicals and Brain Health

Several of these disorders showed low levels of butyrate, a chemical made by good bacteria. Butyrate helps protect the brain and gut barriers. When it's absent, harmful molecules may pass through and cause inflammation in the brain.

Patterns Across Conditions

Even when gut data wasn't available—like in neurosarcoidosis—the immune response looked similar. This suggests that the same types of inflammation might be happening in different diseases, even if the gut isn't clearly involved.

Conclusion

Alterations in the gut microbiome correlate strongly with neuroinflammatory symptoms in rare neurological disorders through mechanisms involving systemic cytokine elevation, loss of beneficial metabolites, and increased gut permeability. While these findings remain correlative in most cases, therapeutic responses to microbiome- or cytokine-targeted interventions (e.g., anakinra, dietary modification, cannabinoids) support a causal role. Future research should prioritize longitudinal, multi-omic studies to define microbiota-based biomarkers and interventions for neuroimmune diseases.

References

Brain Anatomy and How the Brain Works. (n.d.). Johns Hopkins Medicine. Retrieved May 24, 2025, from https://www.hopkinsmedicine.org/health/conditions-and-diseases/anatomy-of-the-brain

Definition of gastrointestinal system - NCI Dictionary of Cancer Terms - NCI. (n.d.). National Cancer Institute. Retrieved May 24, 2025, from https://www.cancer.gov/publications/dictionaries/cancer-terms/def/gastrointestinal-system

Donato, A. (n.d.). *Enteric nervous system - Queensland Brain Institute - University of Queensland*. Queensland Brain Institute. Retrieved May 24, 2025, from https://qbi.uq.edu.au/brain/brain-anatomy/peripheral-nervous-system/enteric-nervous-system

The Enteric Nervous System - Neuroscience. (n.d.). NCBI. Retrieved May 24, 2025, from https://www.ncbi.nlm.nih.gov/books/NBK11097/

Godbout, J. (n.d.). *Neuroinflammation: The Devil is in the Details*. PubMed Central. Retrieved May 30, 2025, from https://pmc.ncbi.nlm.nih.gov/articles/PMC5025335/

The gut-brain connection. (2023, July 18). Harvard Health. Retrieved May 24, 2025, from https://www.health.harvard.edu/diseases-and-conditions/the-gut-brain-connection

Jyonochouchi, H., & Geng, L. (2022, May 11). *Whole-exome sequencing in a subject with fluctuating neuropsychiatric symptoms, immunoglobulin G1 deficiency, and subsequent development of Crohn's disease: a case report.* Journal of Medical Case Reports. https://doi.org/10.1186/s13256-022-03404-9

PANDAS and PANS (for Parents) | Nemours KidsHealth. (n.d.). Kids Health. Retrieved May 31, 2025, from https://kidshealth.org/en/parents/pandas.html

PANS | PANS: Pediatric Acute-onset Neuropsychiatric Syndrome | Stanford Medicine. (n.d.). Stanford Medicine. Retrieved May 31, 2025, from https://med.stanford.edu/pans

Purves, D. (Ed.). (2001). *Neuroscience*. Oxford University Press, Incorporated.

P Zheng, B Zheng, C Zhou, M Liu, Z Fang, X Xu, L Zeng, J Chen, S Fan, X Du, X Zhang, D Yang, Y Yang, H Meng, W Li, Melgiri, N. D., Licinio, J., H Wei, & P Xie. (2016, June). *Gut microbiome remodeling induces depressive-like behaviors through a pathway mediated by the host's metabolism*. Molecular Psychiatry. https://doi.org/10.1038/mp.2016.44

Ruver-Martins, A. C., Assunção Bicca, M., Soares de Araujo, F., de Noronha Sales Maia, B. H. L., Pamplona, F. A., Gomes da Silva, E., & Pinto Nascimento, F. (2022, July 12). *Cannabinoid extract in microdoses ameliorates mnemonic and nonmnemonic Alzheimer's disease symptoms: a case report*. Journal of Medical Case Reports. https://doi.org/10.1186/s13256-022-03457-w

Sandy Reyes-Martínez, Lorena Segura-Real, Ana Pamela Gómez-García, Emiliano Tesoro-Cruz, Luis A. Constantino-Jonapa, Amedeo Amedei, María M. Aguirre-García. Neuroinflammation, Microbiota-Gut-Brain Axis, and Depression: The Vicious Circle. *J. Integr. Neurosci.* **2023**, 22(3), 65. https://doi.org/10.31083/j.jin2203065

Stefanis, L. (n.d.). *α-Synuclein in Parkinson's Disease - PMC*. PubMed Central. Retrieved May 30, 2025, from https://pmc.ncbi.nlm.nih.gov/articles/PMC3281589/

Vagus Nerve: What It Is, Function, Location & Conditions. (n.d.). Cleveland Clinic. Retrieved May 30, 2025, from https://my.clevelandclinic.org/health/body/22279-vagus-nerve

What are Cytokines? Types & Function. (n.d.). Cleveland Clinic. Retrieved May 30, 2025, from https://my.clevelandclinic.org/health/body/24585-cytokines