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Butyrate — The Gut-Brain Axis Connector That Influences Mood and Cognition

Analysis by Dr. Joseph Mercola | November 24, 2026

STORY AT-A-GLANCE

- Butyrate, produced by gut bacteria when they ferment dietary fiber, acts as a signaling molecule in the gut-brain axis — a communication network that may influence stress, pain sensitivity, immunity, and brain health
- Laboratory and animal research suggests that, through multiple mechanisms, including specific enzyme inhibition and NF-κB pathway regulation, butyrate may help calm neuroinflammation, which is a process implicated in neurodegenerative conditions like Alzheimer's and Parkinson's disease. However, protection against these diseases has not been shown in people
- Research, mostly in animals, suggests that butyrate and other gut-derived compounds may influence key neurotransmitters including GABA and dopamine, and that butyrate may increase brain-derived neurotrophic factor (BDNF), which supports neuronal growth and cognitive function
- The vagus nerve links the gut and the brain, carrying signals involved in mood, stress response, and immune function. Animal research suggests butyrate may trigger some of these signals
- Rebuilding gut health step by step — starting with easily digested carbs like white rice and ripe whole fruit, gradually adding fiber as your gut tolerates it, and eating homemade fermented foods — may help promote butyrate production and support a healthy gut-brain connection

Butyrate, a short-chain fatty acid (SCFA) produced in your colon through the bacterial fermentation of dietary fiber, is a metabolite byproduct that nourishes your colonocytes (i.e., the cells lining your colon). Interestingly, it's also an important signaling molecule within the complex communication network between your gut and your brain, known as the gut-brain axis.

As explained in a review published in Nutrients,[1] the gut-brain axis is a bidirectional communication system that involves a dynamic interplay of neural, hormonal, immune, and metabolic pathways, enabling constant information exchange between your gastrointestinal tract and your central nervous system.

The exchange of information between your gut and brain may influence a multitude of functions, from stress and pain sensitivity to immunity,[2] brain function, and even mood.

Butyrate's Potential Role in Neuroinflammation

When inflammation within the brain (neuroinflammation) becomes chronic, it can contribute to neuronal damage, synaptic dysfunction, and, ultimately, cognitive decline.

Neuroinflammation is widely recognized as a key factor in the development and progression of a wide range of neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and multiple sclerosis.

Within this context, researchers sought to understand whether and how butyrate, which originates from the gut, may support brain health.

- **Butyrate may support mitochondrial function in brain cells —** In a review published in Neuroscience Letters,[3] researchers hypothesized that butyrate may promote brain health because of its diverse modes of action that influence the gut-brain axis. Notably, they proposed that the butyrate produced through fermentation of dietary fiber could support the health of mitochondria located in the brain, while noting that no studies had yet examined this effect of gut-derived butyrate directly.

> *"While the metabolic events in the colon may appear disconnected from that of the brain, it's important to consider the immense energy demands of the brain and the energy dyshomeostasis that occurs in the brain in many neurological diseases. Perhaps the best cited example is the reduced glucose utilization in the Alzheimer's brain, which occurs at the earliest stages of the disease and well before memory loss …*
>
> *However, we hypothesize that if sufficient butyrate levels could be reached in the brain, butyrate could stand in as an energy substrate, as in the colon, and restore energy homeostasis," the researchers said.*[4]

- **The dangers of reduced glucose availability in the brain —** The study authors highlighted this problem, which "is believed to contribute to mitochondrial dysfunction in acute and chronic neurological diseases."[5] This observation is consistent with what I've written about before — **the health dangers of following a low-carb diet** — as your body, and especially your brain, relies on carbohydrates to function at an optimal state.

- **Butyrate and colon cells —** Based on the evidence reviewed by the researchers, butyrate activates GPR109a (a G protein-coupled receptor found on the surface of cells), which belongs to the larger family of G protein-coupled receptors (GPCRs).

  This receptor is present in colonocytes (cells lining the colon) and T cells (immune cells). The reviewers note that GPR109a expression is reduced in human colon cancer cells, and that forcing these cancer cells to express it in the laboratory induced programmed cell death (apoptosis) — a finding that has not been shown to lower colon cancer risk in people.

A Deeper Dive Into How Butyrate May Affect Neuroinflammation

Research suggests butyrate may also inhibit pro-inflammatory signaling pathways, such as the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway, a master regulator of inflammation. The featured Neuroscience Letters paper describes a

related finding for β-hydroxybutyrate, a compound with a similar name that acts on the same GPR109a receptor:[6]

> *"Treatment with β-hydroxybutyrate induced anti-inflammatory effects in both in vitro and in vivo models of Parkinson's disease through GPR109a activation and down regulating NF-κB activation. The neurons were also protected from LPS-induced [editor's note: endotoxin-induced] injury and improved behavioral outcomes in the animal models."*

Editor's Note: *β-hydroxybutyrate is a ketone body made mainly by the liver; it is not the gut-derived butyrate discussed in this article, so this finding does not directly test butyrate.*

In mouse research summarized in a 2023 review, butyrate reduced NF-κB activation and the production of inflammatory mediators like cytokines,[7] which, in an inflamed central nervous system, can promote synaptic dysfunction.[8]

- **Butyrate inhibits histone deacetylases (HDACs)**[9] **—** These enzymes modify histones, proteins around which DNA is wrapped, thereby influencing gene expression.

- **HDAC inhibition and brain inflammation —** By inhibiting HDACs, butyrate can induce epigenetic modifications that alter gene expression in brain cells. In a 2023 study in rats with brain hemorrhage, sodium butyrate given as an HDAC inhibitor increased histone acetylation in the motor cortex and was accompanied by improved motor function.[10]

  That featured study did not measure inflammation, but other research, described below, suggests these gene-expression changes may shift brain immune cells toward fewer pro-inflammatory and more anti-inflammatory molecules, which may help dampen the inflammatory response in the brain.

Going deeper, a 2024 systematic review and meta-analysis of animal studies, published in Frontiers in Neuroscience, provides a more nuanced look at how butyrate's HDAC-limiting activity may affect neuroinflammation associated with ischaemic stroke:[11]

> *"In addition to its role as an antitumor agent, butyrate partially achieves its anti-inflammatory effects by inhibiting HDAC.*
>
> *For example, butyrate reduced neuroinflammation caused by microglia in IS [ischaemic stroke] mice by inhibiting HDAC, thereby altering the gene initiation of histone-3-lysine 9-acetylation (H3K9ac) in microglia. In conclusion, butyrate modulates microglia in the brain to attenuate neuroinflammation in IS through multiple mechanisms."*

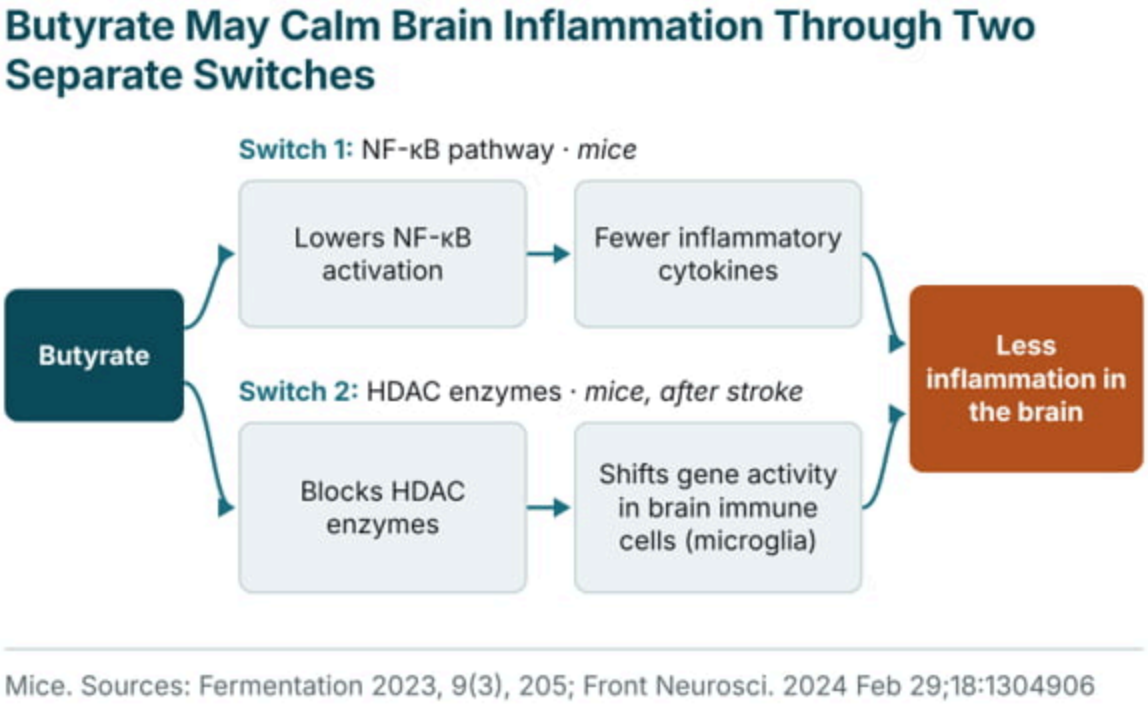

Figure 1. In mouse research, butyrate dampened brain inflammation along two paths: lowering NF-κB activation and blocking HDAC enzymes in brain immune cells (microglia).

- **Butyrate and Alzheimer's research in mice —** Another study, which used a mouse model of early-stage Alzheimer's disease, found that male mice fed a diet supplemented with sodium butyrate (5 or 15 mg/kg each day) for 12 weeks had about 40% lower brain amyloid-beta levels and showed a 25% stronger response on memory-related fear-conditioning tests than control mice.

  For context, amyloid-beta buildup is a pathological hallmark of the disease.[12] The authors concluded that sodium butyrate warrants further investigation — it has not been shown to lower the risk of Alzheimer's disease in people.

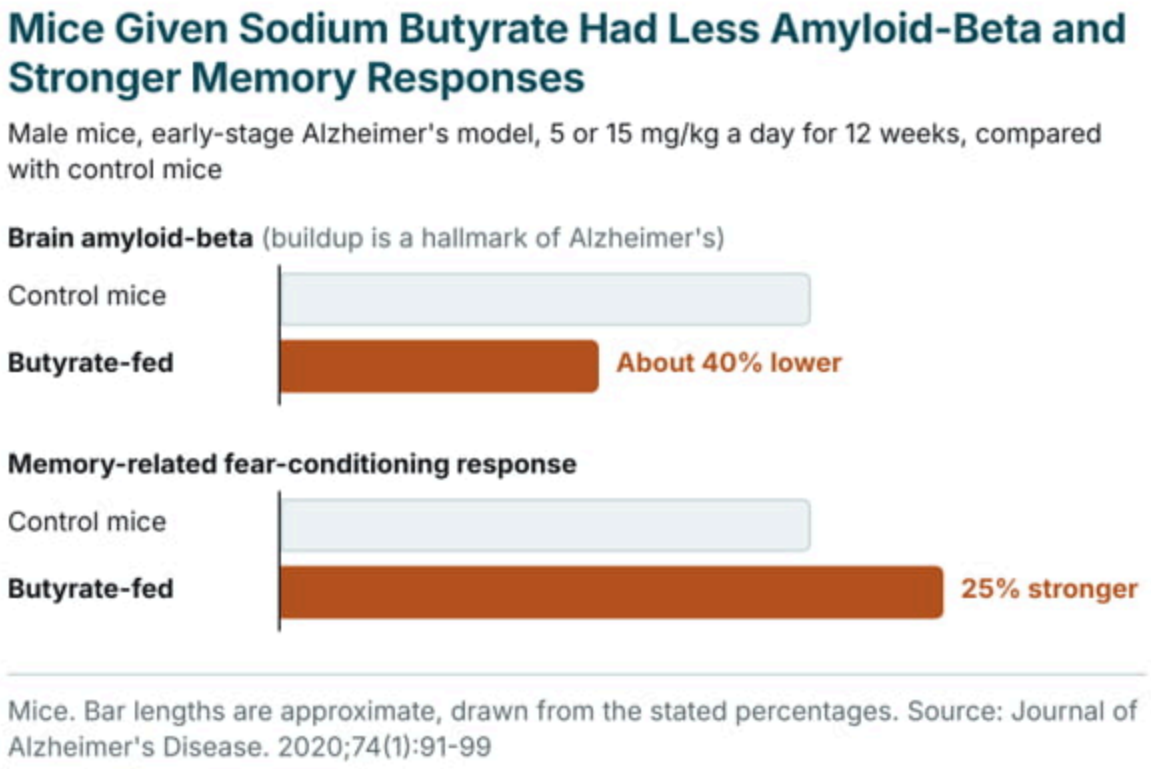

Figure 2. Male mice given sodium butyrate for 12 weeks had about 40% lower brain amyloid-beta and a 25% stronger memory-related response than control mice.

- **Butyrate, GLP-1, and Parkinson's disease research —** In mouse models of Parkinson's disease, butyrate has shown protective effects that appear to involve stimulation of glucagon-like peptide-1 (GLP-1) secretion in the colon.[13] GLP-1 and

GLP-1 receptor agonists (medications that mimic GLP-1) are being actively studied as potential treatments for Parkinson's disease because they appear to have neuroprotective effects.

In addition to possibly reducing brain inflammation, GLP-1 is being studied for its potential to protect dopamine-producing neurons, which are damaged in Parkinson's disease, possibly by reducing oxidative stress and supporting mitochondrial function. In other tissues, GLP-1 has also been shown to:

- **Enhance autophagy —** The cell's natural cleaning process that removes damaged proteins and cellular components. GLP-1-based approaches have been shown to boost autophagy in the fat tissue surrounding blood vessels and in kidney cells and diabetic rats.[14,15] Whether the same happens in the brain is still being studied, but it is of interest because Parkinson's disease involves the accumulation of misfolded proteins (especially alpha-synuclein).*

- **Influence metabolic function —** A 2015 review describes how GLP-1 acting in the brain helps regulate glucose metabolism, including insulin sensitivity.[16] Brain energy metabolism is often impaired in Parkinson's disease, and better energy metabolism may help neurons function more effectively and resist damage.*

**These findings are from laboratory or animal research and may not directly apply to human health.*

The Role of Butyrate in Neurotransmitter Function and Mood

Neurotransmitters are chemical messengers that transmit signals between nerve cells (neurons) in the brain, orchestrating a vast array of brain functions, including mood, behavior, cognition, sleep, and appetite. And based on published evidence, gut microbes and their metabolites, including SCFAs such as butyrate, appear to influence the production, release, and signaling of several key neurotransmitters, including GABA (gamma-aminobutyric acid) and dopamine.[17]

- **GABA is the primary inhibitory neurotransmitter in your brain —** It acts as a natural calming agent by reducing neuronal excitability and is thought to help relieve anxiety.[18]

  Interestingly, certain gut bacteria also produce GABA — a 2021 laboratory study found this among human intestinal Bacteroides strains.[19] Furthermore, GABA-producing bacteria are being explored as possible future therapies for recurrent abdominal pain and functional bowel disorders[20] — an example of the two-way relationship of the gut-brain axis.

- **Dopamine is central to your reward responses —** A neurotransmitter associated with motivation, movement, and pleasure, dopamine also appears to be influenced by SCFAs, which can affect the expression of tyrosine hydroxylase, which is an enzyme involved in making dopamine.[21]

  A 2022 review notes that butyrate can cross the blood-brain barrier and affect microglial function and development, and describes research in weaning piglets in which supplementation with the butyrate-producing bacterium Clostridium butyricum was associated with higher dopamine levels in the hypothalamus.[22]

Because these neurotransmitter systems are closely involved in mood, researchers are investigating whether butyrate plays a role in mood disorders such as anxiety and depression. Studies have reported associations between altered gut microbiota composition, reduced butyrate production, and these conditions,[23] although associations like these cannot show that one causes the other.

Butyrate and Brain-Derived Neurotrophic Factor

Brain-derived neurotrophic factor (BDNF) is a member of the neurotrophin family of growth factors, which are essential for the survival, growth, differentiation, and maintenance of neurons. BDNF plays a vital role in neuronal plasticity, the brain's ability to change and adapt its structure and function in response to external stimuli, which is fundamental for learning and memory formation.[24,25]

- **Butyrate may increase BDNF —** In animal studies, butyrate has been shown to increase BDNF expression in brain regions essential for learning and memory, such as the hippocampus, by inhibiting HDACs.[26] BDNF itself promotes neurogenesis (the birth of new neurons),[27] has been shown in cultured neurons to strengthen existing neuronal connections (synapses),[28] and has shown neuroprotective potential in preclinical research.[29]

- **Low BDNF and neurological conditions —** Reduced BDNF levels have been implicated in the pathophysiology of various neurological and psychiatric conditions, including depression[30] and Alzheimer's disease,[31] although the Alzheimer's review notes that some findings conflict. Whether raising butyrate production increases BDNF enough to protect against these conditions in people has not been tested, but the connection is an active area of research.

Butyrate's Role in Vagus Nerve Crosstalk

The vagus nerve, often referred to as the "wandering nerve" due to its extensive network throughout the body, is the longest cranial nerve and serves as a major communication highway between the gut and the brain.[32]

- **The vagus nerve allows your gut and brain to communicate —** Essentially, the vagus nerve functions as the information highway of the gut-brain axis, affecting a wide array of neural/digestive functions, including mood regulation, stress response, appetite control, and immune function.

- **Butyrate-related signals travel along the vagus nerve —** Sensory information arising from the gut, including signals related to the presence and concentration of butyrate, is thought to travel along the vagus nerve to reach various brain regions, influencing their activity and function.

- **Butyrate may directly stimulate nerve endings located in the gut lining —** Animal research cited in a 2016 review found that butyrate could directly stimulate afferent fibers of the vagus nerve, which carry electrical and chemical signals from the gut

to the brain.[33]

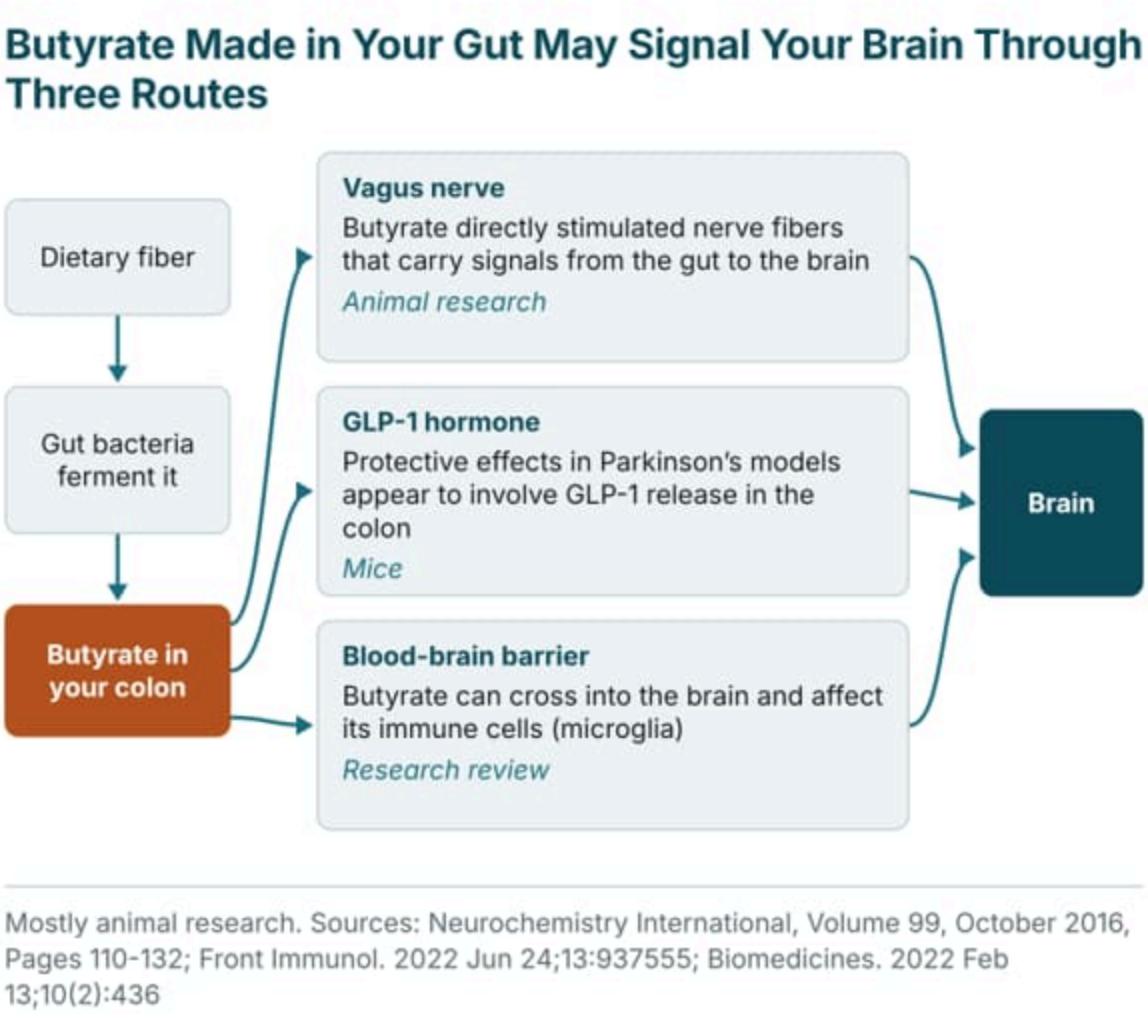

Figure 3. Research, mostly in animals, points to three routes from gut butyrate to the brain: the vagus nerve, GLP-1 release in the colon, and crossing the blood-brain barrier.

Integrating Gut Health and Brain Health

Dietary fiber is the main fuel your gut bacteria use to produce butyrate and other SCFAs. From there, butyrate works on the gut-brain axis in ways that may help support cognitive function. But how do you increase butyrate production safely? While the obvious answer seems to be increasing your fiber intake, there are important caveats. Most people have a damaged gut microbiome, and in that setting, a high-fiber diet can increase endotoxin production and do more harm than good.

- **Start with healthy carbs —** If you have only moderate gut issues, you'll be able to start with options like white rice and ripe, whole fruits right away.

- **Severe gut issues require a different approach —** If your gut health is severely compromised, it's important to build it from the ground up again.

  I recommend slowly sipping dextrose water throughout the day as a transitional solution, then gradually progressing to fruit juice with pulp, pulp-free juice (also sipped slowly), and whole fruit before moving on to complex carbs and starches like white rice. Unlike complex carbohydrates, dextrose is metabolized in the small intestine and doesn't feed the bad bacteria in your colon.

- **Add more dietary fiber in the long run —** As your gut begins to improve, you'll be able to gradually add more fiber-rich veggies and starches, increasing slowly as long as you're not experiencing digestive problems. But dietary fiber isn't the only aspect that's emphasized when optimizing overall gut health. It's also wise to add more fermented foods to your diet. This approach may help restore a balanced gut microbiome, meaning your good bacteria keep pathogenic bacteria in check.



Figure 4. Rebuilding your gut moves from dextrose water through juice, whole fruit, and white rice before more fiber is added; moderate gut issues can start at fruit and rice.

Here are additional recommendations that may help support your gut-brain connection further:

1. **Make your own fermented foods at home —** Creating fermented foods at home helps ensure you receive fresh, live probiotics. Homemade options like yogurt, kefir, and sauerkraut contain a diverse array of beneficial bacteria that support a healthy gut microbiome.

   Plus, making your own fermented foods is cost-effective and allows you to control the ingredients, avoiding unnecessary additives, genetically modified ingredients, and refined sugars found in mass-produced probiotic goods.

2. **Avoid pasteurized commercial fermented foods —** Commercially available fermented foods are often pasteurized to extend shelf life, which kills the live bacteria necessary for gut health. If you're unable to make fermented vegetables at home, opt for traditionally fermented, unpasteurized products sourced from reputable businesses. But again, a better solution is preparing them yourself to maximize the health benefits.

3. **Incorporate various fermented foods into your diet —** Diversity is key when it comes to fermented foods. Different types offer unique strains of probiotics that may work together to support your gut microbiome's resilience.

   Include a range of options such as kimchi, natto, homemade yogurt, and homemade fermented vegetables in your daily meals. Variety helps support a robust and balanced microbiome, which is important for healthy gut-brain communication.

4. **Maintain consistent consumption —** Regularly consuming fermented foods may help sustain a healthy gut microbiome over the long-term. That matters because the modern Western diet is filled with ingredients that can harm beneficial gut bacteria, so regularly reseeding your gut with probiotic foods is worthwhile.

Make it a habit to include fermented foods in your everyday diet, whether through meals or snacks. Consistency may help maintain gut microbiota diversity, which research has linked to lower inflammation, steadier neurotransmitter signaling, and better mood and cognitive function.

Frequently Asked Questions About Butyrate's Role in the Gut-Brain Axis

Q: What is butyrate and why is it important?

A: Butyrate is a short-chain fatty acid produced when beneficial bacteria in your colon ferment dietary fiber. Beyond nourishing cells in your colon, butyrate also serves as an important signaling molecule along the gut-brain axis that appears to help regulate inflammation, mood, and energy metabolism.

Q: How might butyrate affect neuroinflammation and brain health?

A: Laboratory and animal research suggests that butyrate may inhibit inflammatory pathways, particularly the NF-κB pathway, and may support mitochondrial function in brain cells. Because neuroinflammation is implicated in neurodegenerative diseases like Alzheimer's, Parkinson's, and multiple sclerosis, researchers are studying whether these effects could help protect neurons — but this has not been shown in people.

Q: How does butyrate influence mood and neurotransmitter function?

A: Research suggests butyrate and other gut-derived SCFAs may influence key neurotransmitters, including GABA and dopamine. These neurotransmitters play critical roles in mood, anxiety, and reward responses. Animal studies have reported

antidepressant-like effects, and lower levels of butyrate-producing bacteria have been observed in people with depression, but whether butyrate eases symptoms of anxiety or depression in people have not been established.

Q: What does research show about butyrate and colon cells?

A: Studies highlight that butyrate activates a receptor called GPR109a on colon cells (colonocytes) and certain immune cells. This receptor is reduced in human colon cancer cells, and in laboratory experiments, forcing these cells to express it triggered apoptosis (programmed cell death). These are laboratory findings; they do not show that butyrate prevents colon cancer in people.

Q: How can I increase my butyrate levels for gut-brain benefits?

A: Dietary fiber (especially from starches, fruits, and vegetables) is the main fuel for butyrate production, but it should be increased gradually as your gut tolerates it. For most people, the first step is easily digested carbs like white rice and ripe whole fruit.

Fermented foods like homemade yogurt, kefir, and sauerkraut may further support a healthy gut microbiome. If your gut is severely compromised, starting with dextrose water sipped slowly, then progressing gradually through fruit juice and whole fruit before adding more fiber, is a gentler way to rebuild your gut health over time.

This article is for informational purposes only and does not constitute medical advice. Consult a qualified health care provider before making changes to your health regimen.

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