Microbiota-Gut-Brain Axis Protocol‡

DEVELOPED IN COLLABORATION WITH OUR SCIENTIFIC AND MEDICAL ADVISORS

This protocol was designed with our clinician partners to help you deliver the most effective care and support for your patients. Included are recommendations to support foundational health and focused interventions to address common clinical objectives related to the microbiota-gut-brain axis.‡

FOUNDATIONAL SUPPORT

In addition to a healthy diet and lifestyle, consider the following foundational supplements to support overall health and well-being:‡

- PureGenomics® Multivitamin (PGM26)
- O.N.E.™ Omega (ONO6 / ONO3)
- ProbioMood (PBM6)
- Digestive Enzymes *Ultra* (DEU1 / DEU9) or Digestive Enzymes *Ultra* with Betaine HCl (DEUB1 / DEUB9)

  Some patients may benefit from the addition of Betaine HCl, however, HCl can irritate the gastric mucosa and may be contraindicated in patients with upper GI symptoms. Use of Betaine HCl is advised only in clinical evidence of inadequate HCl production.

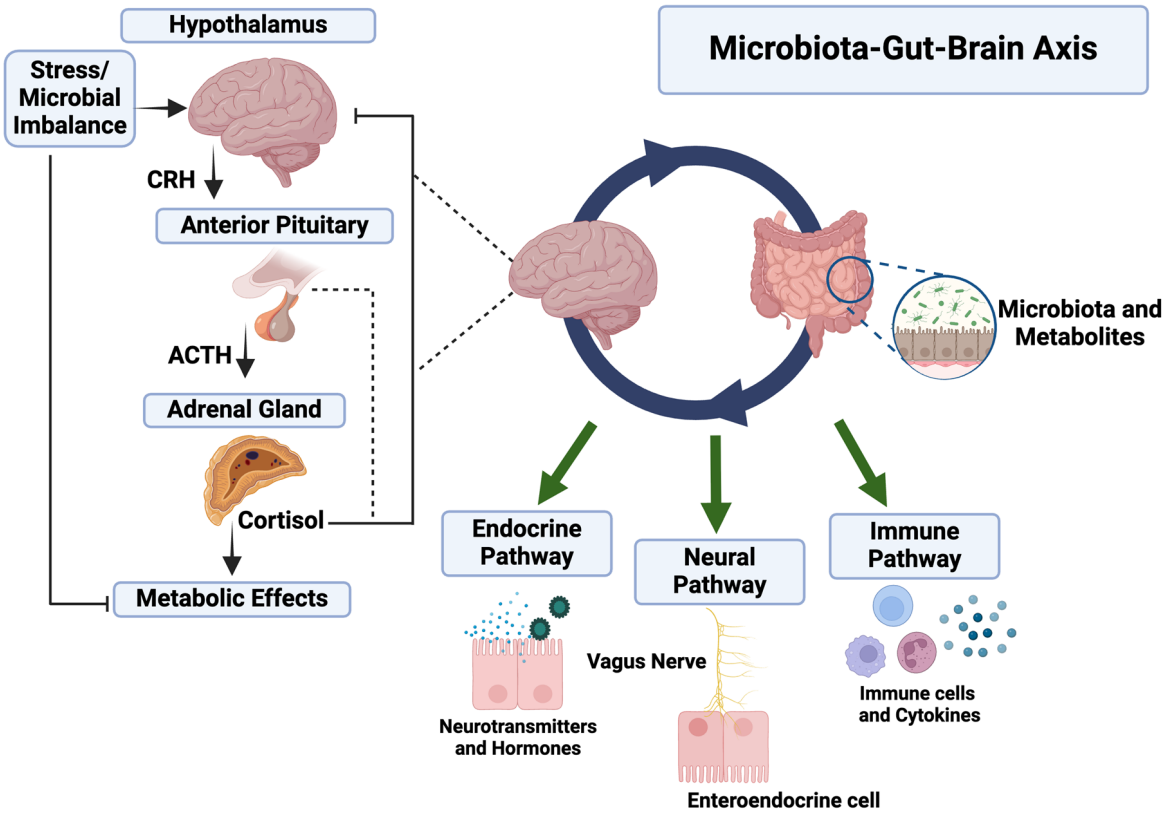
TARGETED NUTRIENTS

Stand-alone nutrients should be considered in addition to foundational support based upon lab results and/or symptoms. Retesting is recommended to determine the need for extended use.

- Vitamin D_3 25 mcg (1,000 IU) (VD11 / VD12 / VD16)
  Assessment: 25-hydroxyvitamin D
- PureGenomics® B-Complex (BGB1) or B-Complex Plus (BCP1 / BCP6)
  Assessment: MTHFR genotype, Serum or methylmalonic acid, Organic acids
- PureMelt B_{12} Folate (PMLB9)
  Assessments: Urinary Methylmalonic acid and Formiminoglutamic acid
- Zinc 30 (Z31 / Z36)
  Assessment: Zinc RBC, Copper/Zinc ratio

FOCUSED SUPPORT

The microbiota-gut-brain axis is a bidirectional communication system linking the central nervous system (CNS) with the enteric nervous system (ENS) via neural, endocrine, immune and metabolic pathways.[1] Microbes in the gut can synthesize or act upon various metabolites including hormones, vitamins and other bioactive compounds that influence numerous biological functions. Thus, the microbiota-gut-brain axis has a wide-reaching effects on human health, including the stress response, emotions and memory, in addition to its impacts on cognitive, neurological, gastrointestinal, immune, reproductive and metabolic health.



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Adapted from: Góralczyk-Bińkowska A et al. Int J Mol Sci. 2022;23(19):11245. doi:10.3390/ijms231911245

STRESS AND MOOD

Altered microbial balance and composition, along with increased intestinal permeability, have been observed in individuals with low mood.[2,3] Gut microbes can influence brain function through neurotransmitter production, immune modulation and neuroendocrine signaling.[4] The gut microbiota produce neurotransmitters like serotonin, dopamine and gammaminobutyric acid (GABA) that help regulate mood.

Crosstalk occurs between the hypothalamic-pituitary adrenal (HPA) axis and the microbiota-gut-brain axis.

The **gut microbiota** activate the HPA axis through numerous mediators and metabolites like cytokines, prostaglandins and SCFAs that cross the blood-brain barrier.[5] Conversely, persistent elevations of cortisol and its effect on the HPA axis can impact the intestinal barrier, alter gut microbiota composition and promote a decrease in beneficial species. This can lead to reduction in metabolites like SCFAs that support gut-brain communication, neurotransmitter activity, mood and behavior.[6]

FOCUSED SUPPORT FOR MOOD AND STRESS

Supporting GI motility, microbial balance, intestinal barrier integrity and overall digestive health can support emotional resilience under stress.[7]

Beneficial strains of bacteria from the *Lactobacillus* and *Bifidobacterium genera* have been shown to improve global mood and stress scores.[8] Non-digestible fibers found in prebiotics can also promote beneficial microbial growth and influence cortisol awakening response, potentially improving stress resilience and emotional health.[9]

For targeted approaches to mood and stress, refer to:

Positive Mood Protocol‡

Stress Management and Relaxation Protocol‡

COGNITIVE AND NEUROLOGICAL HEALTH

The microbiota-gut-brain axis plays a crucial role in cognitive health by modulating immune responses in the brain, neurotransmitter production and intestinal permeability.

Microbial imbalance is associated with increased intestinal permeability, allowing cytokines to enter circulation, affecting the integrity of the blood brain barrier and impacting cognition. SCFAs produced by gut bacteria communicate to the brain both systemically and through vagal pathways and have potential neuroprotective effects by promoting serotonin biosynthesis, modulating levels of neurotrophic factors, increasing neurogenesis and reducing neuroimmune response. The interaction of SCFAs and the microbiota-gut-brain axis can positively affect emotion and cognitive function.[10]

Patients experiencing age-related mild cognitive decline exhibit altered microbial balance along with increased immune activity in the gut, lower SCFA levels and higher circulating lipopolysaccharides (LPS), which can contribute to cognitive changes.[11,12]

FOCUSED SUPPORT FOR COGNITIVE AND NEUROLOGICAL HEALTH

Dietary changes like increased dietary fiber along with stress management and probiotic support can positively influence the microbiota-gut-brain axis and support cognitive function.[8,13,14‡]

For a targeted approach to neurological health and mild age-related cognitive decline, refer to:

Mild Age-Related Cognitive Decline Protocol‡

Mental Alertness and Concentration Support Protocol‡

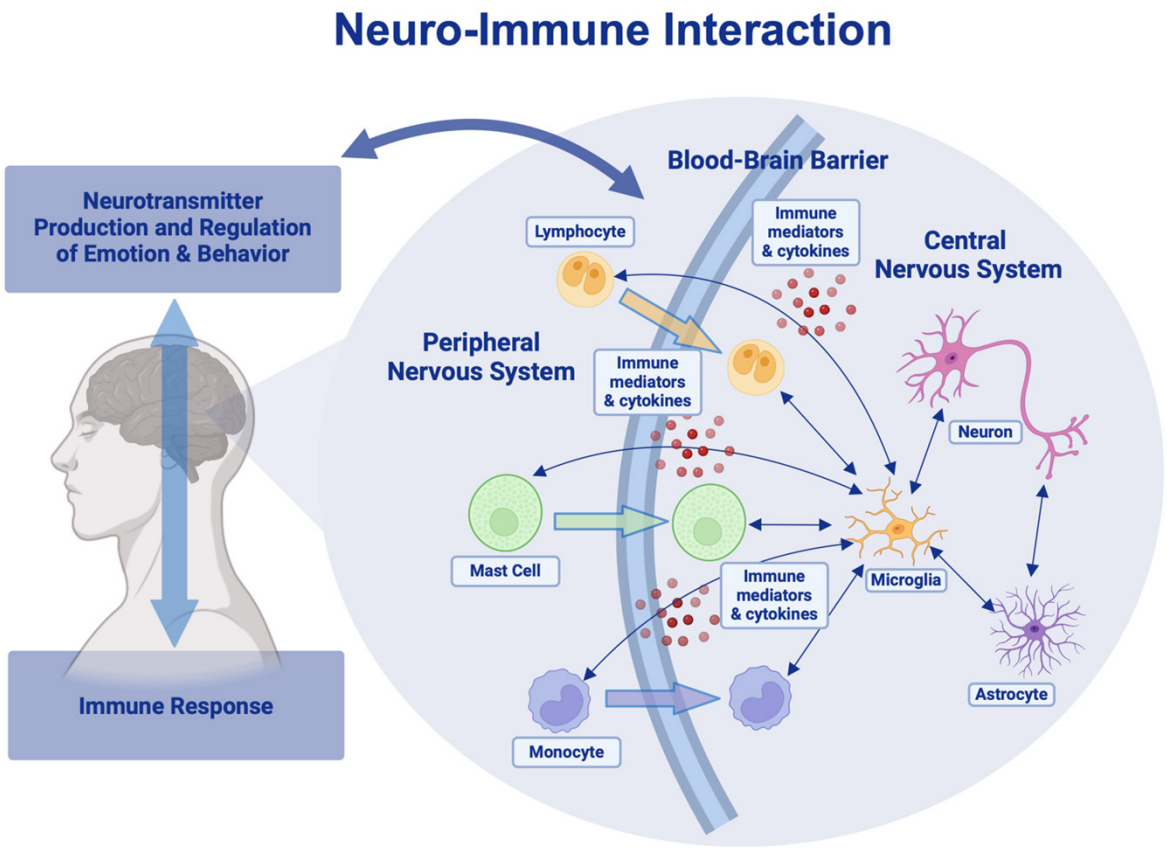
Memory Support Protocol‡

IMMUNE HEALTH

The microbiota-gut-brain axis plays a crucial role in immune system regulation, influencing cytokine production, immune cell function and the defense against non-beneficial microorganisms and self-tissue responses. The gut microbiota communicate with the immune system through metabolites, neurotransmitters and direct interaction with immune cells, affecting both local gut immunity and systemic immune responses.

In addition, the bidirectional connection and communication between the brain and immune system influences mood regulation.[15,16,17] Immune cells, including microglia, astrocytes and cytokines, interact directly with neurons, contributing to the modulation of mood and cognitive function.[18,19]

Studies suggest that systemic immune activation can affect the nervous system via production of cytokines, including interleukin-1 beta (IL-1b), interleukin-6 (IL-6), interleukin-8 (IL-8) and tumor necrosis factor-alpha (TNF-α), which can cross the blood-brain barrier.[20] Alteration of the immune/brain interaction can affect neurotransmitter balance, affecting the production of serotonin, GABA, dopamine and norepinephrine, which are critical for mood stabilization.[15]



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FOCUSED SUPPORT FOR IMMUNE HEALTH

Targeted strategies for supporting the microbiota-gut-brain axis and cytokine modulation can positively influence both immune response and mood.

For targeted support for mood and immune health, refer to:

Positive Mood Protocol‡

Immune Defense and Resilience Protocol‡

Self-Tissue Response Protocol‡

GASTROINTESTINAL HEALTH

The microbiota-gut-brain axis is involved in functional gastrointestinal disorders. Alterations in gut microbiota can alter gut motility, increase visceral sensitivity and activate immune responses in the GI tract, leading to gastrointestinal symptoms.[21] Disruptions in the gut microbial ecosystem can lead to increased bacterial growth and gastrointestinal symptoms.

Evidence also suggests that individuals with a self-tissue response in the intestines have a reduction of beneficial bacterial species in the gastrointestinal tract.[22]

FOCUSED SUPPORT FOR GASTROINTESTINAL HEALTH

Combining diet, lifestyle modifications and microbiome-targeted care can improve gastrointestinal health and patient outcomes.

For targeted support for gastrointestinal health, refer to:

Leaky Gut Protocol‡

Functional GI Health Protocol‡

METABOLIC HEALTH

The microbiota-gut-brain axis significantly impacts metabolic health by enabling a two-way communication between the gut bacteria and the brain, influencing factors like appetite, energy expenditure, and glucose regulation.[23] The microbiota have been recognized as key drivers in metabolic changes. Gut and metabolic changes occur through mechanisms like hormone signaling and immune system modulation. This can lead to changes in appetite regulation, excess adipose tissue, impaired glucose metabolism and immune response with fat accumulation in the liver.[24,25]

FOCUSED SUPPORT FOR METABOLIC HEALTH

A Mediterranean-type diet and personalized lifestyle interventions can support the gut microbiome and improve metabolic markers and overall health in patients.[26] Probiotic and prebiotic intervention studies have revealed a positive effect on immune response, glucose metabolism and other metabolic markers.[27,28,29]

FOCUSED SUPPORT FOR METABOLIC HEALTH *CONTINUED*

For targeted support related to metabolic health, refer to:

Cardiometabolic Health Protocol‡

Metabolic Liver Support Protocol‡

Healthy Weight† Management Protocol‡

HORMONE HEALTH

The microbiota-gut-brain axis plays a role in regulating hormone health through bidirectional communication between the gut microbiota, endocrine system and central nervous system. Gut microbes influence hormone production, metabolism and signaling through microbial metabolites, neurotransmitters and immune modulation.

REPRODUCTIVE HORMONES

Gut microbiota regulate the metabolism of the reproductive hormones estrogen, progesterone and testosterone. Beta-glucuronidase producing bacteria, including *Clostridium, Bacteroides, Bifidobacterium* and *Escherichia* make up the estrobolome, a collection of gut bacteria involved in estrogen metabolism and the regulation of estrogen reabsorption.[30] Increased *Bacteroidetes* and decreased *Firmicutes* in the gut can contribute to androgen excess and metabolic changes.[31]

Women with menstrual and metabolic irregularities have exhibited altered gut microbiota and cytokine activity.[32] Menopausal women have been shown to have reduced gut microbiota diversity, leading to lower estrogen levels and increased risk of bone loss, while probiotic interventions in menopausal women have improved estrogen metabolism and bone health.[33,34]

THYROID HORMONES

The microbiome affects thyroid health by its interaction with minerals in the gut. Microbiota influence iodine uptake, degradation and enterohepatic cycling. Microbiota also play a role in the uptake of minerals necessary for thyroid function and hormone synthesis, particularly selenium, iron, and zinc.[35] Altered microbial composition has been found in patients with suboptimal thyroid function.[36,37] Certain bacterial species, *Lactobacillus* and *Bifidobacterium* have been linked to improved thyroid function and reduced immune response in patients with suboptimal thyroid function.[37]

FOCUSED SUPPORT FOR HORMONE HEALTH

For targeted support related to hormone health, refer to:

Men's Health Protocol‡

PMS Protocol‡

Menopausal Comfort Protocol‡

Thyroid Support Protocol‡

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