EVALUATING NEUROPHYSIOLOGICAL MARKERS OF THE MICROBIOTA–GUT–BRAIN AXIS: IMPACT ON PSYCHOLOGICAL AND METABOLIC HEALTH

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Abstract: *By 2026, the microbiota–gut–brain axis (MGBA) is recognized as a fundamental regulator of systemic physiology, moving from purely associative rodent studies to a mechanistic understanding in human clinical populations. This review evaluates key neurophysiological markers used to understand how gut-derived signals influence the brain. We analyze anatomical highways like the vagus nerve, molecular signals such as short-chain fatty acids (SCFAs), and emerging neuroimaging markers like the DTI-ALPS index for glymphatic clearance. The synthesis of these markers reveals how dysbiosis drives psychological conditions—including anxiety and depression—and metabolic disorders such as obesity and Type 2 Diabetes.*

Keywords- *Microbiota–gut–brain axis, Vagus nerve, Short-chain fatty acids, DTI-ALPS index , Metabolic disorders ,Type 2 Diabetes.*

1. Introduction

In 2026, the concept of the "second brain" has evolved into a precision diagnostic framework. The gut microbiome, containing trillions of microorganisms, is a major source of bioactive signaling molecules that communicate with the central nervous system (CNS) through neural, endocrine, and immune pathways. Identifying consistent neurophysiological markers is critical for diagnosing and treating the growing global burden of psychiatric and metabolic illnesses.

2. Anatomical and Neural Markers: The Vagus Nerve

The vagus nerve is the primary anatomical link in the MGBA, functioning as a bidirectional sensor for microbial activity.

Vagal Tone as a Health Indicator: Clinical measurement of vagal tone, often derived from heart rate variability (HRV), is now a validated marker for psychological resilience. In 2026, low vagal tone is consistently linked to anxiety and depression symptoms.

Direct Causal Evidence: Recent 2025 studies provided direct evidence that gut bacteria are required for normal vagal nerve activity; germ-free mice exhibit significantly lower vagal firing, which can be restored upon introduction of a normal gut microbiome.

Vagus Integrity and Plasticity: Research confirms that the vagus nerve is required to relay the effects of stress-induced gut changes to the brain, specifically affecting hippocampal neurogenesis and depressive-like behaviors.

3. Biochemical and Metabolic Markers

Gut-derived metabolites serve as systemic messengers that orchestrate metabolic health and neuroinflammation.

Short-Chain Fatty Acids (SCFAs): By 2026, SCFAs (butyrate, acetate, propionate) are established markers for gut barrier integrity and mucosal health. Lower SCFA levels are associated with increased anxiety and impaired insulin signaling.

Bile Acids and BCAAs: Branched-chain amino acids (BCAAs) and bile acids are critical biomarkers for early diagnosis of metabolic disorders. High levels of BCAAs, often produced by dysbiotic bacteria like *Prevotella copri*, increase the risk of gestational diabetes and impair glucose responsiveness.

Neuroactive Neurotransmitters: Gut microbes modulate neurochemical pathways involving serotonin, dopamine, and GABA. Changes in these neuroactive metabolites are now directly linked to alterations in blood–brain barrier permeability and subsequent neurological malfunctions.

4. Emerging Neuroimaging Markers: The DTI-ALPS Index

A significant breakthrough in 2025–2026 is the use of the DTI-ALPS (Diffusion Tensor Imaging along the Perivascular Space) index as a non-invasive marker for glymphatic function and its correlation with gut health.

Glymphatic-Gut Connection: Recent 2025 studies on ulcerative colitis demonstrate that gut-driven inflammation correlates with brain glymphatic dysfunction, as measured by a reduced ALPS index.

Metabolic and Cognitive Correlation: In 2026, the DTI-ALPS index is utilized to assess cognitive impairment in Type 2 Diabetes patients, where a lower index correlates with higher glycated hemoglobin levels and reduced vitamin D.

Obesity Marker: Research confirms that participants with obesity have significantly lower DTI-ALPS index values, suggesting that chronic metabolic stress impairs the brain's waste clearance system.

5. Results

Synthesis of data from 2024–2026 studies reveals the following:

Psychological Health: Dysbiosis, specifically a reduction in SCFA-producing bacteria and a lower vagal tone, is a reliable predictor of anxiety and depression.

Metabolic Health: A reduced DTI-ALPS index and high BCAA/LPS levels are hallmark markers of insulin resistance and impaired metabolic homeostasis.

Integrative Outcomes: Therapeutic interventions such as psychobiotics and vagus nerve stimulation (VNS) have shown clinical promise in restoring these neurophysiological markers to normal levels, thereby improving both mood and metabolic function.

6. Discussion and Future Directions

While markers like the DTI-ALPS index and SCFAs offer high diagnostic value, limitations remain in 2026. Individual variability in microbiome composition necessitates personalized "precision microbiome" approaches. Future research is shifting toward "Digital Twins" of the gut-brain axis to simulate patient-specific responses to fecal microbiota transplantation (FMT) and precision dietary modulation.

7. Conclusion

In 2026, the evaluation of neurophysiological markers—vagal tone, SCFA levels, and glymphatic clearance—confirms the gut microbiota as a central modulator of human health. These markers provide a non-invasive "window" into the brain's health, allowing for early detection of both psychological and metabolic decline. Integrating these assessments into clinical practice marks a paradigm shift toward holistic, multidisciplinary care for chronic neuro-metabolic conditions.

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