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THE GUT–BRAIN–DIGITAL AXIS: INTEGRATING MICROBIOME SCIENCE WITH AI-DRIVEN MENTAL WELLNESS INTERVENTIONS

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ABSTRACT

This review introduces the gut–brain–digital axis as a unifying conceptual framework integrating microbiome science, artificial intelligence (AI), and digital health technologies to advance mental health care. Adopting a narrative and integrative approach, the review synthesises interdisciplinary evidence from microbiology, neuroscience, psychiatry, and digital health to examine biological mechanisms, analytical innovations, and their clinical translation. Growing evidence indicates that the gut microbiome exerts a profound influence on neurobiological function through interlocking neural, immune, and metabolic pathways, with compositional shifts linked to depression, anxiety, and neurodevelopmental conditions. AI has proven indispensable for navigating the high-dimensional, multimodal datasets that characterise this field, enabling predictive modelling, personalised diagnostics, and adaptive interventions. Digital phenotyping and real-time monitoring technologies capture continuous behavioural and physiological data that enrich biological profiles. A central contribution is the formal articulation of the gut–brain–digital axis as a systems-oriented model integrating biological signalling with computational intelligence. Clinical applications—from microbiome-informed therapies to AI-powered platforms—demonstrate promise for improving outcomes across diverse populations. Pressing challenges in data standardisation, ethical governance, privacy, and equitable access are also identified. Realising this paradigm's potential will require sustained interdisciplinary collaboration, robust ethical and regulatory frameworks, and deliberate investment in inclusive digital health systems.

Keywords: *Gut–brain axis; Artificial intelligence; Microbiome; Mental health; Digital health; Precision medicine*

1. INTRODUCTION

Research on the microbiota–gut–brain axis has fundamentally reshaped how we understand the interplay between physiological and psychological systems. For much of the twentieth century, the brain was treated as the unchallenged orchestrator of bodily functions, with peripheral biological influences attracting relatively little attention. That picture began to change as mounting evidence revealed the gut microbiota to be an active participant in a regulatory network extending to cognition, behaviour, and emotional regulation (Cryan & Dinan, 2012). This paradigm shift has repositioned the gut microbiome as a determinant of overall health and catalysed a more integrative orientation in biomedical research.

The microbiota–gut–brain axis is now understood as a complex, bidirectional communication system operating through neural, immune, endocrine, and metabolic pathways. The gut microbiota modulates brain function via vagal signalling, microbial metabolite production, and immune-mediated cascades (Mayer *et al*., 2015). Foster *et al*. (2017) demonstrate that these interactions are functionally significant, shaping emotional and cognitive processing. Preclinical studies using germ-free animal models show that the absence of a commensal microbiota leads to marked alterations in stress responsiveness and neurochemical profiles (Clarke *et al*., 2013), while microbiota transplantation can transfer behavioural phenotypes, establishing a causal link between microbial composition and brain function (Sharon *et al*., 2016).

Clinical research has translated these insights into human contexts. Dysbiosis has been implicated in depression, anxiety disorders, and autism spectrum disorders (Dinan & Cryan, 2017), fuelling interest in microbiome-targeted therapies. Probiotics, prebiotics, and dietary modifications may restore microbial equilibrium and influence well-being (Sherwin *et al*., 2018). Mechanistically, microbial metabolites such as short-chain fatty acids modulate immune responses, maintain intestinal barrier integrity, and regulate neurotransmitter systems including serotonin and gamma-aminobutyric acid (Fröhlich *et al*., 2016; Cryan *et al*., 2019). Early-life colonisation represents a critical window, with disruptions potentially leaving lasting imprints on brain development (Cryan *et al*., 2019).

Despite this progress, inter-individual variability in microbiome composition and methodological inconsistencies limit generalisability. This review provides a comprehensive synthesis of current knowledge on the microbiota–gut–brain axis, examining key biological pathways, evaluating empirical evidence, identifying knowledge gaps, and exploring translational implications for clinical practice and public health.

1.1 The Evolution of the Gut–Brain Axis Concept

The conceptualisation of the gut–brain axis has evolved from a narrow neurocentric model emphasising the autonomic nervous system and the vagus nerve (Mayer *et al*., 2015) into a multidimensional framework incorporating microbial, immunological, and metabolic influences. Cryan and Dinan (2012) laid the groundwork for recognising the gut microbiota as integral to this network, giving rise to the microbiota–gut–brain axis. Foster *et al*. (2017) demonstrated that microbial activity modulates stress responses and cognitive processes, while Clarke *et al*. (2013)

showed that germ-free conditions produce profound neurodevelopmental and behavioural alterations. Dinan and Cryan (2017) linked microbial dysbiosis to neuropsychiatric disorders, and Sherwin *et al*. (2018) highlighted the promise of microbiome-targeted interventions. These developments reflect a paradigm shift toward a systems-oriented understanding of the gut–brain axis.

1.2 Mental Health Burden and the Need for Integrative Models

Mental health disorders constitute a pressing global challenge, and their multifactorial nature demands integrative models beyond reductionist frameworks (Johnson & Steenbergen, 2020). Sarkar *et al*. (2016) and Kelly *et al*. (2016) link alterations in gut microbiota to depressive-like behaviours, while Sanders *et al*. (2019) highlight the therapeutic promise of microbiome-targeted interventions. Recent work by Verma, Inslicht and Bhargava (2024) and Liu *et al*. (2025) draws on advanced methods to further elucidate microbiota–mental health interactions. The burden is not uniformly distributed: Bosch *et al*. (2022) identify significant ethnic and contextual variations in depression, reinforcing the need for culturally sensitive models. Initiatives such as the saNeuroGut programme exemplify this approach in underrepresented populations (O'Hare *et al*., 2025; Kuponiyi & Akomolafe, 2025).

1.3 Rise of Digital Mental Health and Artificial Intelligence

Digital technologies have reshaped mental health care through AI, mobile health applications, and telehealth. Traditional systems are constrained by limited access and workforce shortages (Insel, 2017), and digital platforms have shown promise in expanding access and supporting self-management (Mohr *et al*., 2017). AI amplifies these capabilities through predictive analytics, pattern recognition, and adaptive interventions (Shatte *et al*., 2019; Topol, 2019), while digital phenotyping enables continuous monitoring through smartphones and wearable devices (Torous & Keshavan, 2020). AI-powered chatbots offer scalable mental health support in underserved regions (Frempong *et al*., 2020), and the expansion of telehealth has demonstrated the feasibility of remote delivery (Omotayo & Kuponiyi, 2020).

1.4 Toward the Gut–Brain–Digital Axis Framework

The convergence of microbiome science, neuroscience, and digital technology has produced a novel conceptual paradigm: the gut–brain–digital axis. This integrative framework extends the traditional microbiota–gut–brain axis by incorporating digital systems and AI as mediating components of health monitoring, analysis, and intervention (Johnson & Steenbergen, 2020). Wu *et al*. (2025) and Krynicka *et al*. (2025) argue that coupling digital tools with biological data enables more precise health profiling, while Bhuiyan *et al*. (2025) and Mosquera *et al*. (2024) demonstrate how AI-driven analytics synthesise large-scale, multimodal datasets aligned with computational psychiatry (Bzdok & Meyer-Lindenberg, 2018). Digital infrastructure enhances continuous monitoring (Allali *et al*., 2021) and clinical translation (Brewster *et al*., 2019), with digital twin technologies enabling simulation of individual health trajectories (Taiwo *et al*., 2022). Adeyemi-Benson (2025) contends that this framework represents a critical step toward holistic, systems-oriented healthcare.

2. BIOLOGICAL FOUNDATIONS OF THE GUT–BRAIN AXIS

The biological underpinnings of the gut–brain axis reside in intricate, dynamic interactions between the gut microbiota and host physiological systems, operating through neural, immune, endocrine, and metabolic pathways. At the centre of this network sits the gut microbiome—a diverse, highly adaptive community of microorganisms critical to host homeostasis and neurological function.

The Human Microbiome Project (2012) provided detailed characterisations of microbiome composition and function, revealing core functional capabilities for metabolic processes, immune modulation, and nutrient synthesis despite substantial inter-individual variation (Turnbaugh *et al*., 2007). Knight *et al*. (2018) further illuminate the ecological complexity of these communities. The Integrative Human Microbiome Project (2019) linked microbial dynamics to specific disease states, and Valles-Colomer *et al*. (2019) demonstrated associations between specific microbial taxa and measures of depression and quality of life.

At the mechanistic level, microbial metabolites serve as critical mediators: Strandwitz (2018) highlights the microbiota's role in producing neurotransmitters including GABA, while short-chain fatty acids contribute to immune modulation and intestinal barrier integrity. The immune system constitutes another critical interface, with dysregulation potentially leading to chronic inflammation and altered neural signalling (Allali *et al*., 2021).

Maghini *et al*. (2025), through an African microbiome atlas, demonstrate significant geographic and cultural variations in microbial composition, addressing longstanding gaps in a field dominated by Western populations. Multi-omics approaches combining genomic, transcriptomic, proteomic, and metabolomic data have advanced understanding of microbiome function (Knight *et al*., 2018), and the microbiome's responsiveness to dietary changes (Turnbaugh *et al*., 2007) underscores the potential for targeted interventions.

2.1 Microbiome Composition and Functional Dynamics

The Human Microbiome Project Consortium (2012) revealed that the gut harbours vast microbial diversity while maintaining core functional redundancy ensuring biological stability. Knight *et al*. (2018) describe the microbiome as an ecological network shaped by environmental, dietary, and genetic factors, with continuous fluctuations influencing metabolic and immunological functions. The Integrative Human Microbiome Project (2019) linked temporal changes in composition to disease states. Allali *et al*. (2021) emphasise that microbial functions—metabolite production and immune modulation—are central to understanding health outcomes, necessitating integrative models that capture both structure and function. Maghini *et al*. (2025) reveal geographic variations challenging the generalisability of existing models and highlighting the necessity of globally representative research.

2.2 Communication Pathways in the Gut–Brain Axis

Bidirectional gut–brain communication is sustained by interconnected neural, endocrine, immune, and metabolic pathways operating simultaneously (Mayer *et al*., 2015). The vagus nerve provides the most direct route, with microbial modulation of vagal signalling playing a critical role in stress responses and behavioural regulation (Cryan *et al*., 2019; Clarke *et al*., 2013). Microbial metabolites constitute a second channel: certain gut bacteria produce neurotransmitters such as GABA (Strandwitz, 2018), while short-chain fatty acids contribute to immune modulation and neurochemical regulation (Fröhlich *et al*., 2016). Immune signalling adds further complexity, with inflammatory responses affecting brain function (Cryan *et al*., 2019). Sharon *et al*. (2016) provide direct evidence of causality, demonstrating that microbiota transfer alters behavioural phenotypes.

2.3 Microbiome and Mental Health Disorders

The relationship between the gut microbiome and mental health disorders has emerged as a focal point in neurobiological research. Kelly *et al*. (2016) demonstrated that transplanting microbiota from individuals with depression into animal models induced depressive-like behaviours, suggesting a causal connection. Sarkar *et al*. (2016) showed that gut microbiota alterations are associated with stress-related behavioural changes, while Sharon *et al*. (2016) confirmed that microbiota transfer modifies behavioural phenotypes.

Dinan *et al*. (2015) link dysbiosis to depression and anxiety through immune activation, neurotransmitter modulation, and disrupted stress responses. Malan-Müller *et al*. (2018) and Hemmings *et al*. (2017) extend this work to trauma-related disorders in diverse population contexts such as South Africa. Emerging evidence implicates microbiome alterations in schizophrenia (Rust *et al*., 2025) and age-related cognitive decline. Verma, Inslicht and Bhargava (2024) highlight integrative analytical approaches, and Sanders *et al*. (2019) underscore the therapeutic potential of microbiome-targeted interventions across diverse clinical contexts.

3. ARTIFICIAL INTELLIGENCE IN MICROBIOME AND MENTAL HEALTH RESEARCH

The integration of AI into microbiome and mental health research represents one of the most significant methodological advances in recent biomedical science. As biological data grow in complexity and scale, AI has become indispensable for analysing multidimensional datasets, uncovering latent patterns, and advancing precision medicine (Topol, 2019). The microbiome operates as a highly complex ecological system requiring advanced computational techniques (Knight *et al*., 2018), and machine learning algorithms can synthesise multimodal data—microbiome profiles, behavioural indicators, and clinical variables—to generate predictive insights and personalised treatment strategies (Bhuiyan *et al*., 2025; Wu *et al*., 2025).

AI-driven models enhance understanding of individual variability in microbiome composition and its effects on mental health, supporting precision psychiatry. Integrative analytical frameworks bridge the gap between data generation and clinical practice (Allali *et al*., 2021). AI's capacity for longitudinal, real-time analysis allows identification of temporal patterns informing clinical decision-making (Bhuiyan *et al*., 2025), and by combining microbiome data with clinical records, lifestyle data, and environmental factors, AI models provide comprehensive representations of individual health profiles (Wu *et al*., 2025). Despite these advances, challenges of data quality, standardisation, model interpretability, and ethical concerns around privacy and consent remain significant (Knight *et al*., 2018; Johnson & Steenbergen, 2020).

3.1 AI-Driven Microbiome Analytics

AI-driven microbiome analytics addresses the high dimensionality and interconnectedness of microbiome data through computational methods capable of identifying meaningful patterns and predictive relationships (Knight *et al*., 2018). Machine learning models synthesise multimodal data to identify microbial biomarkers associated with mental health conditions (Bhuiyan *et al*., 2025) and model complex, non-linear relationships within microbiome data (Wu *et al*., 2025). Computational frameworks bridge large-scale data generation and actionable clinical insights, supporting personalised treatment strategies (Allali *et al*., 2021) and integrating diverse data sources for a holistic health perspective (Johnson & Steenbergen, 2025).

3.2 AI in Mental Health Diagnostics and Intervention

AI enables more accurate diagnosis, early detection, and personalised treatment in mental health. Digital tools extend traditional services through continuous monitoring (Mohr *et al*., 2017), and digital phenotyping captures behavioural patterns through smartphones and wearables (Torous & Keshavan, 2020). Machine learning identifies subtle patterns that conventional assessment may miss (Shatte *et al*., 2019), while computational psychiatry supports predictive tools for at-risk identification (Dwyer *et al*., 2018; Bzdok & Meyer-Lindenberg, 2018).

AI-driven decision support systems assist clinicians in evidence-based decision-making (Kuponiyi, Omotayo & Akomolafe, 2023), and predictive modelling enables anticipation of disease trajectories (Tafirenyika, 2023). AI-powered chatbots and digital health assistants offer scalable support for mental health needs (Ezeh *et al*., 2024), while emerging applications in neurodevelopmental modelling (Omolayo *et al*., 2024) and disease prediction (Sagay *et al*., 2024) are central to the future of precision psychiatry (Dwyer & Koutsouleris, 2022).

4. THE GUT–BRAIN–DIGITAL AXIS: CONCEPTUAL INTEGRATION

The conceptualisation of the gut–brain–digital axis represents a significant evolution in integrative health science, incorporating digital infrastructures and AI as essential enablers of data integration, real-time monitoring, and precision intervention. This framework responds to the recognition that mental health disorders are shaped by multifactorial interactions that reductionist paradigms cannot adequately capture (Johnson & Steenbergen, 2025).

At the heart of this framework lies the convergence of biological signalling systems with computational intelligence. Digital technologies enhance the capacity to capture and interpret gut–brain interactions at unprecedented scale and resolution. Wu *et al*. (2025) and Krynicka *et al*. (2025) note that digital platforms enable continuous collection of multimodal data—microbiome composition, physiological indicators, behavioural metrics, and environmental exposures—supporting personalised care strategies. AI-driven models identify non-linear relationships and latent patterns inaccessible through traditional statistics, generating predictive insights into disease onset, progression, and treatment response (Mosquera *et al*., 2024).

The biological foundation remains anchored in the microbiota–gut–brain axis. Sharon *et al*. (2016) provide compelling evidence that alterations in gut microbiota induce changes in behaviour and brain function. Digital systems amplify rather than replace the capacity to observe and modulate these interactions. Wearable devices and mobile health platforms enable ongoing physiological and behavioural data collection, supporting a shift from reactive treatment to preventive care.

Digital twin technologies exemplify this potential. As described by Taiwo *et al*. (2022), digital twins are virtual representations of biological systems enabling simulation of microbiome–brain–environment interactions, prediction of outcomes, and evaluation of interventions before clinical implementation. AI-driven neurodevelopmental modelling further broadens the scope, elucidating mechanisms underlying complex neurological conditions when integrated with microbiome data (Omolayo *et al*., 2024).

4.1 Framework for GBDA Interaction

The GBDA framework conceptualises health as an emergent property of interactions between gut microbiota, neural processes, and digitally mediated data systems (Johnson & Steenbergen, 2025). Biological signals from bidirectional gut–brain communication (Sharon *et al*., 2016) are continuously captured and contextualised through digital systems. AI serves as the central analytical engine, integrating multimodal datasets to support predictive modelling and personalised interventions (Mosquera *et al*., 2024). Digital twin systems expand operational scope through simulation and scenario testing (Taiwo *et al*., 2022), while AI-driven neurodevelopmental modelling enables deeper insights into brain–microbiome interactions (Omolayo *et al*., 2024). Together, these components establish the GBDA framework as a dynamic, data-driven model for integrative and personalised healthcare.

4.2 Digital Phenotyping and Microbiome Correlation

Digital phenotyping enables continuous, real-time collection of behavioural and physiological data through personal digital devices, providing a dynamic representation of mental health status (Torous & Keshavan, 2020; Onnela & Rauch, 2016). Insel (2018) highlights its potential for early detection and personalised intervention. Integrating this with microbiome research enables identification of complex interactions between lifestyle factors, microbial composition, and mental health outcomes (Bhuiyan *et al*., 2025).

Correlating digital phenotypes with microbiome data requires robust frameworks for high-dimensional, temporally variable datasets, with data reliability and validity being essential (Huckvale *et al*., 2019). Advanced computational models align longitudinal behavioural data with microbiome fluctuations, supporting identification of predictive markers and causal pathways. Adeyemi-Benson (2025) argues that this convergence provides a holistic view of individual health, enhancing early intervention and understanding of the interplay between behaviour, biology, and environment.

5. AI-DRIVEN INTERVENTIONS TARGETING THE GUT–BRAIN AXIS

AI-driven interventions offer novel strategies for modulating the microbiota and improving mental health outcomes by combining insights from microbiome science, digital health technologies, and computational analytics. Psychobiotics—probiotics and prebiotics conferring mental health benefits—can modulate neurotransmitter production, reduce inflammation, and influence stress pathways (Dinan *et al*., 2015; Sanders *et al*., 2019). However, their effectiveness is highly individualised, necessitating AI-driven personalisation.

Mosquera *et al*. (2024) demonstrate that AI models can integrate microbiome, behavioural, and clinical variables to identify optimal therapeutic approaches for individual patients, predicting how specific interventions will influence microbiome composition and downstream mental health outcomes. Rosas-Sánchez *et al*. (2025) further highlight AI's potential for optimising therapies through adaptive treatment planning.

Digital health platforms enhance delivery and scalability. AI-powered chatbots provide accessible, continuous support (Abd-alrazaq *et al*., 2019), and when combined with microbiome data, digital health assistants can guide targeted dietary and lifestyle modifications (Ezeh *et al*., 2024; Kuponiyi & Akomolafe, 2024). These interventions also address health disparities: O'Hare *et al*. (2025) stress culturally sensitive approaches for underrepresented regions, and AI technologies support scalable interventions accounting for local factors.

Unlike static treatment models, AI-driven systems adjust recommendations based on real-time data, responding to fluctuations in microbiome composition and behavioural patterns (Mosquera *et al*., 2024)—a significant advancement over approaches relying on periodic assessments and standardised protocols.

6. CLINICAL APPLICATIONS AND CASE STUDIES

The clinical application of the gut–brain–digital axis has gained increasing traction as microbiome science and AI converge to inform diagnostic and therapeutic strategies. Kelly *et al*. (2016) provide foundational evidence through transplantation studies linking gut microbiota from depressed individuals to depressive-like behaviours in recipients, informing clinical approaches targeting microbial composition through dietary interventions, probiotics, and personalised treatment plans.

Machine learning applications in psychiatric diagnostics improve classification and prediction of mental disorders (Dwyer *et al*., 2018; Bzdok & Meyer-Lindenberg, 2018), particularly when combined with microbiome data. Hemmings *et al*. (2017) and Malan-Müller *et al*. (2018) demonstrate associations between microbiome alterations and trauma-related disorders in South African populations, while Bosch *et al*. (2022) emphasise socio-cultural influences on mental health outcomes.

Emerging applications extend to neurodegenerative conditions: Lwere *et al*. (2025) provide evidence from Uganda on Alzheimer's disease, while AI-driven models enable early detection of age-related diseases (Sagay *et al*., 2024) and neurodevelopmental disorders (Omolayo *et al*., 2024). In resource-constrained environments, AI systems improve access to care despite limited infrastructure (Kuponiyi & Akomolafe, 2024). Maghini *et al*. (2025) highlight the importance of population diversity for designing effective interventions. AI-driven longitudinal analysis supports adaptive, personalised care models.

7. CHALLENGES, ETHICAL CONSIDERATIONS, AND FUTURE DIRECTIONS

The integration of AI, microbiome science, and digital health within the gut–brain–digital axis introduces methodological, ethical, and structural challenges alongside its opportunities. The heterogeneity of microbiome data complicates standardisation and limits cross-study comparability (Knight *et al*., 2018), while clinical translation requires analytical frameworks maintaining accuracy and reproducibility (Allali *et al*., 2021). Digital phenotyping raises concerns about data quality and validity (Huckvale *et al*., 2019; Onnela & Rauch, 2016), calling for rigorous validation protocols.

Ethical considerations are central. The use of sensitive personal data raises issues of privacy, consent, and data ownership (Essien *et al*., 2023). Federated learning approaches offer promising avenues for enhancing privacy through distributed analysis (Omolayo *et al*., 2024), though they introduce technical complexities. Equity and access remain critical: digital health systems may exacerbate inequalities where technology and infrastructure are limited (Ojeikere *et al*., 2024), and culturally sensitive approaches are essential (O'Hare *et al*., 2025). AI models trained on non-representative datasets risk biased outcomes (Brewster *et al*., 2019), and algorithmic opacity hinders clinical adoption and accountability (Allali *et al*., 2021).

Looking ahead, priorities include interdisciplinary collaboration spanning microbiology, neuroscience, data science, and ethics; global standards for data collection and reporting; investment in infrastructure and digital literacy for clinicians and patients; and robust ethical frameworks balancing innovation with accountability, equity, transparency, and patient autonomy.

8. CONCLUSION

This review has examined the evolving intersection of microbiome science, mental health, and digital innovation through the lens of the gut–brain–digital axis. The gut microbiome plays a central role in modulating neurological and psychological processes through neural, immune, and metabolic pathways, and AI significantly enhances the capacity to analyse complex, multimodal datasets for predictive modelling, personalised interventions, and improved diagnostic accuracy.

A central contribution is the formal articulation of the gut–brain–digital axis as an integrative framework bridging biological and technological domains. Digital phenotyping, AI-driven analytics, and computational models such as digital twins enable continuous monitoring and adaptive care, with clinical applications spanning mental health disorders, neurodevelopmental conditions, and age-related diseases across diverse populations.

Critical challenges persist in data standardisation, ethical governance, and equitable access. The integration of microbiome science and AI offers a transformative pathway for mental health research and practice, but realising this potential requires interdisciplinary collaboration, ethical and regulatory frameworks, and inclusive digital infrastructure to deliver equitable, effective, and sustainable benefits worldwide.

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