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From Gut to Grey Matter: Exploring the Gut–Brain Axis in Older Adults – Implications for Mental Health in Primary Care

Dr Mohammad Mazharuddin[1*], Dr Ameen Shamsudeen[2]

[1]MD Physician, Dip.in Neurology (UCL), MRCPsych (U.K), Consultant Psychiatrist, Leabaib Health Centre, Primary Health Care Corporation (PHCC), Doha, Qatar
[2]MBBS, FRCPCH (U.K); Consultant Paediatrician, PHCC, Doha, Qatar; Dept – Paediatrics; Muaither Health Centre

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***Corresponding author:** Dr Mohammad Mazharuddin
MD Physician, Dip.in Neurology (UCL), MRCPsych (U.K), Consultant Psychiatrist, Leabaib Health Centre, Primary Health Care Corporation (PHCC), Doha, Qatar

Abstract **Review Article**

The gut–brain axis (GBA) is a two-way communication system between the gastrointestinal tract and the central nervous system. Dysbiosis (alterations in the composition of the gut microbiota) has been linked to mental health outcomes in older adults. Dysbiosis in older adults is linked with increased inflammation, neurotransmitter dysregulation, and reduced cognitive resilience. Common medications such as antibiotics, proton pump inhibitors, and psychotropics can exacerbate microbial imbalance. Emerging therapies like probiotics and Mediterranean-style diets show promise in improving mental health outcomes. The GBA offers a clinically relevant, modifiable target for improving mental well-being in older adults. GPs and psychiatrists are well placed to integrate gut health awareness into holistic mental health assessments and care plans. This narrative review explores how the gut microbiota changes with age and how these changes may be connected to mental health conditions such as depression, anxiety, and cognitive decline. The review also considers how commonly used medications can affect the gut microbiome. Finally, it examines potential interventions—including probiotics, dietary strategies, and faecal microbiota transplantation (FMT)—that may help support mental well-being in older adults.

Keywords: Gut-brain axis (GBA), Dysbiosis, Older adults, Mental health, Gut microbiota.

INTRODUCTION

The connection between the gut and the brain is no longer a fringe scientific idea-it is now a recognised clinical concept with real implications for practice. The gut–brain axis is a two-way communication system between the gut and the brain. It works through the vagus nerve, hormones, the immune system, and gut bacteria. These signals help link digestive and mental health (Appleton, 2018).

This interaction becomes particularly relevant in later life. Mental health issues such as depression, anxiety, and cognitive decline are increasingly prevalent with age, which consequently lead to complex relationship with the gut-brain axis (Lerner *et al*., 2017). At the same time physiological changes associated with aging can disrupt the balance of the gut microbiota, potentially exacerbating mental health challenges (Grenham *et al*., 2011).The other factors which affect GBA are the impact of medication, reduced microbial diversity and increased inflammation, all of which are common in older adults (Martin *et al*., 2018).

Recent research suggests that gut dysbiosis may contribute to late life depression and anxiety (Clapp *et al*., 2017). Cognitive decline, including dementia, has also been linked to alterations in the gut microbiome (Halverson & Alagiakrishnan, 2020).]. This emerging evidence urges a more integrated, systems-based approach to mental health—one that includes the gut as a key component of care. Primary care physicians are often the first point of contact for older adults experiencing mental health problems, an understanding of GBA becomes essential in delivering effective and integrated care.

This review examines the role of the ageing gut microbiome in mental health disorders, the impact of medications commonly prescribed to older adults, and emerging microbiome-targeted interventions. The main purpose of this review is to bring awareness among

clinicians about how gut health and aging interact to affect mental health in older adults.

Ageing and the Gut Microbiome

In healthy individuals the gut microbiome is diverse. It consists of various bacterial species that support important functional pathways such as carbohydrate and amino acid metabolism, oxidative phosphorylation and fermentation (Durack & Lynch, 2018).

The gut microbiota undergoes significant changes with age, influenced by a combination of physiological changes, diet, medication, and lifestyle factors (DeJong *et al*., 2020). After sixth decade of life, the gut microbial diversity decreases and there is an increase in pathogenic bacteria, resulting in dysbiosis, chronic inflammation, and reduced production of essential metabolites like short-chain fatty acids (Romo-Araiza & Ibarra, 2019).

There is a shift away from beneficial species such as faecal bacterium and bifidobacteria (Arboleya *et al*., 2016) and there is an increase in an opportunistic or inflammatory taxa such as Escherichia coli (Coman & Vodnar, 2020). This imbalance contributes to chronic low grade inflammation or inflammaging, which accelerates age related diseases and impairs cognitive function (Haran & McCormick, 2020).

Age-related changes in the gut include reduced intestinal barrier function, also known as "leaky gut," which allows the translocation of microbial products into the circulation and this further exacerbates systemic inflammation (Walrath *et al*., 2020). Dietary habits play a crucial role in shaping the gut microbiota in older adults (Guarino *et al*., 2013). A diet low in fibre and high in processed foods promotes the growth of detrimental bacteria. Factors such as reduced fibre intake, institutionalisation, dentition loss and decreased gastric acid production leads to gut dysbiosis in elderly people.

Gut Dysbiosis and Mental Health in Older Adults

Late life Depression and Anxiety:

The connection between gut dysbiosis and mental health disorders, particularly depression and anxiety, has received a lot of attention in geriatric research. Gut dysbiosis can lead to increased intestinal permeability and systemic inflammation, which can affect brain function and neurotransmitter production (Ragonnaud & Biragyn, 2021).Inflammation can disrupt the hypothalamic-pituitary-adrenal axis, which plays a role in stress response and mood regulation.

A cohort study emphasized that an imbalance in gut microbiota has been found in patients with mental disorders, including anxiety and depression (Delanote *et al*., 2024). Additionally, research indicates the gut microbiome is important for mediating both the efficacy and adverse effects of a variety of medications, including psychotropics (Bastiaanssen & Cryan, 2021).

When the gut microbiome becomes unbalanced, it can weaken the gut lining—sometimes referred to as a "leaky gut." This allows harmful bacterial substances, like lipopolysaccharides, to leak into the bloodstream, where they can spark inflammation throughout the body. These microbial products can trigger neuroinflammation, which damages neurons and impairs cognitive function (Zhong *et al*., 2021). At the same time, this imbalance can affect the gut's ability to support the production of key brain chemicals such as serotonin, dopamine, and GABA, all of which are essential for managing mood.

Cognitive Decline and Dementia:

Researchers are increasingly discovering that the gut microbiome may play a role in keeping the brain healthy. Imbalances in gut bacteria (gut dysbiosis) — have been linked to problems with memory and thinking and may even contribute to conditions like Alzheimer's disease (disease (Wu *et al*., 2021). Certain beneficial gut bacteria, particularly those that produce butyrate, play a key role in maintaining brain health. A reduction in these bacteria can compromise the integrity of the blood–brain barrier. This may increase the risk of neuroinflammation. In turn, it can contribute to cognitive impairments and exacerbate symptoms of depression.

Medication Effects on the Gut–Brain Axis

Older adults are often prescribed multiple medications which can significantly affect the gut microbiota and thereby the gut-brain axis (Rogers *et al*., 2016). Antibiotics, proton pump inhibitors, nonsteroidal anti-inflammatory drugs and even some psychiatric medications can disrupt the balance of the gut microbiota, leading to dysbiosis and increased intestinal permeability.

Antibiotics are crucial for treating bacterial infections. However, they can kill both harmful and helpful bacteria. This disrupts the natural balance of the gut microbiome. As a result, harmful bacteria like *Clostridium difficile* may grow and cause infection.

Proton pump inhibitors (PPIs), often used to reduce stomach acid, can unintentionally change the environment of the gut. They change the pH levels in the gut. This helps some bacteria grow while stopping others. Over time, this can upset the gut's natural balance.

Nonsteroidal anti-inflammatory drugs can cause intestinal inflammation and increase gut permeability. This disruption can exacerbate systemic inflammation and negatively impact mental health outcomes in older adults (Silva *et al*., 2020).

SSRI's and antipsychotics can disrupt gut microbiota balance, leading to gastrointestinal side effects and potentially affecting their efficacy through interactions with the gut-brain axis.

Metformin, a widely used treatment for type 2 diabetes, doesn't just help control blood sugar—it also affects the gut microbiome. Studies have shown that it can increase levels of helpful bacteria which supports a healthy gut lining and helps reduce inflammation (Rodriguez *et al*., 2018). These findings highlight the complex interplay between medications, the gut microbiota, and overall health in older adults.

Emerging Microbiome-Based Interventions

Supporting mental health in older adults may be possible by gently reshaping the gut microbiome. Approaches like probiotics, prebiotics, synbiotics, and dietary changes have shown encouraging results — both in early research and in clinical studies — offering new hope for improving emotional and cognitive well-being (Thangaleela *et al*.,).

Probiotics:

Giving live microbes, known as probiotics, can help balance gut bacteria. Studies show they may ease anxiety and depression. They might also boost thinking and memory. Probiotics support gut health in other ways too. They may increase mucus, protect gut lining, and reduce harmful substances like lipopolysaccharides (Cristofori *et al*., 2021).

A meta-analysis of randomized controlled trial showed that probiotic supplementation can positively influence brain function and emotional regulation even in healthy individuals (Rode *et al*., 2022).Several studies on MCI and Alzheimer's patients are found to significantly improve cognitive function by use of probiotics *(Cristofori et al*., 2021).

Prebiotics and Synbiotics:

Prebiotics like inulin and galacto-oligosaccharides stimulate the growth and activity of beneficial bacteria already present in the gut and have demonstrated efficacy in improving mood and reducing anxiety symptoms in certain populations. When used with probiotics, they may reduce stress, lower cortisol and improve emotional regulation (Selhub *et al.*, 2014).Dietary fibres from whole grains legumes, fruits, and vegetables serve as prebiotics, nourishing beneficial gut bacteria and promoting a diverse and balanced gut microbiota.

Mediterranean Diet:

A Mediterranean-style diet, rich in fruits, vegetables, whole grains, and healthy fats, has been associated with improved mental health in older adults. Evidence suggests it may reduce the risk of depression and slow cognitive decline (Zwilling *et al*., 2024). This diet gives the body nutrients and fibre that feed good gut bacteria. These, in turn, produce helpful compounds for brain health.

Faecal Microbiota Transplantation (FMT)

FMT is an emerging experimental intervention. Faecal microbiota transplant (FMT) involves transferring stool from a healthy donor to a recipient whose gut bacteria are out of balance. It's already shown strong results in treating repeated *Clostridium difficile* infections and is now being studied for its potential to improve brain and mental health by influencing the gut-brain connection.

FMT in patients with constipation and depression improved both GI and mood symptoms. A pilot RCT by Green *et al*., in patients with major depressive disorder showed that FMT resulted in a greater reduction in depression symptoms compared to placebo (Green *et al*., 2020)

However, FMT is an invasive procedure and comes with safety concerns, including the risk of transmitting infectious agents. Therefore, it must be conducted with caution and under strict medical supervision.

Research shows a clear link between gut bacteria and mood. Studies on prebiotics, probiotics, and antibiotics support this. These treatments may help reduce symptoms of anxiety and depression. They offer a possible new approach to managing mood disorders (Liu & Zhu, 2018).

Clinical Applications in Primary Care

Primary care physicians often serve as the first point of contact for older adults experiencing symptoms of depression, anxiety, or cognitive decline. They play a key role in spotting mental health issues early. This allows for a quick support and treatment.

Integrating gut-brain axis considerations into primary care practice requires a holistic approach that encompasses comprehensive assessment, personalized interventions, and interdisciplinary collaboration (Minuti *et al*., 2022)

Primary care is central to recognising and acting on GBA disturbances in older adults. Clinicians can:

Take A Gut Mind History: Enquire about diet, bowel habits, medication and their adherence, and previous use of antibiotics. Assess and stratify older people according to their risk factors.

Review Medications: deprescribing where possible of medications that can disrupt the gut microbiota or mental health.

Encourage a Comprehensive Approach to Wellness: Encourage habits that support a healthy and diverse gut.

Eat plenty of fibre, prebiotics, and probiotics. Stay active and manage stress regularly.

Recommend Evidence-Based Probiotics and Prebiotics: This can modify the gut microbiota composition to reduce the anxiety levels. A balanced gut microbiota can be restored by consuming ancestral microbiota, that are unaffected by modernisation and industrialisation (Kali, 2016).

Refer Collaboratively: In more complex cases, it can be helpful for primary care physicians to work closely with specialists like psychiatrists, psychologists, or gastroenterologists. This kind of team-based approach ensures that both the mental and physical health needs of older adults are fully addressed — especially when symptoms are severe or don't improve with initial treatment.

Challenges and Research Gaps: In recent years, there has been growing interest in nutritional approaches—particularly the use of probiotics and psychobiotics—as potential tools for managing depression and anxiety. While initial evidence is promising, further research is needed to better understand how these interventions work and to establish the most effective dosages within a nutritional framework. Despite the growing interest in the gut-brain axis, several challenges and research gaps remain that warrant further investigation.

Causality is Unclear: Although gut dysbiosis has been linked to neurodegenerative and psychiatric conditions, its exact role in causing these illnesses is not yet fully understood. Long-term studies are needed to clarify the timing of these changes and determine whether dysbiosis plays a direct causal role.

Variability: The human microbiome is highly individual. What's healthy for one person is not necessarily healthy for another. There are huge interpersonal differences in the gut microbial composition of the human population; this is driven by multiple factors, including genetics, age, diet, and medication.

Standardisation: Probiotic trials use different strains and doses. There is a lack of standardized protocols for assessing gut microbiota composition and function, making it difficult to compare results across studies.

Long Term Safety: The long-term effects of microbiome manipulation, especially in frail elders, remain unknown. Long-term studies are needed to assess the safety and effectiveness of gut-brain axis interventions over time. This is especially important for vulnerable groups, such as older adults with comorbidities.

Researchers are increasingly investigating how microbiome-based biomarkers might help identify those at higher risk of developing psychiatric conditions. There is also a growing focus on personalised psychobiotic treatments, designed to match an individual's specific gut microbiome makeup.

At the same time, large randomised controlled trials are examining whether faecal microbiota transplantation (FMT) can be effective in treating depression, anxiety, and neurodegenerative disorders. The use of faecal microbiota transplantation as a potential therapeutic intervention for modulating the gut-brain axis in neurological and psychiatric disorders (Forssten *et al*., 2022).

CONCLUSION

The gut–brain axis offers a new frontier for addressing mental health in older adults. Age-related changes in gut microbiota—exacerbated by diet, lifestyle, and medications—can contribute to depression, anxiety, and cognitive decline.

Encouragingly, the gut microbiome is a modifiable system. General practitioners and psychiatrists can play a key role in promoting healthy ageing by using simple, evidence-based strategies—such as offering dietary guidance, reviewing medications, and exploring on the use of probiotics—to support both mental and physical well-being.

Gaining a deeper understanding of how the gut and brain communicate—and what this means for mental health—offers valuable opportunities for primary care. Insights into the gut-brain axis could lead to new ways of diagnosing and treating mental health conditions, ultimately supporting healthy ageing and enhancing the overall well-being of older adults (Singh *et al*., 2022).

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