Chapter 7

Probiotics, Prebiotics, and Psychobiotics – Therapeutic Modulation of the Gut-Brain Axis

The therapeutic modulation of the gut microbiota using probiotics, prebiotics, and psychobiotics has emerged as a promising strategy in the treatment of mental and neurological disorders. These interventions aim to restore microbial balance, enhance gut barrier integrity, and influence neurochemical and immune pathways involved in brain function. By targeting the microbiota–gut–brain axis, they may help regulate mood, stress responses, and cognitive processes. This chapter examines the mechanisms by which these agents exert their effects, reviews current preclinical and clinical evidence, and explores their potential clinical applications, positioning microbiota-targeted therapies as a novel frontier in neuropsychiatric and neurological care.

7.1 Definitions

- **Probiotics:** Live microorganisms that, when administered in adequate amounts, confer a health benefit to the host[1].
- **Prebiotics:** Substrates selectively utilized by host microorganisms that confer a health benefit[2].
- **Psychobiotics:** A class of probiotics or prebiotics that exert mental health benefits through the modulation of the microbiota–gut–brain axis[3].

7.2 Mechanisms of Action

Psychobiotics and other microbiota-modifying agents influence brain function through several mechanisms:

- **Production of neurotransmitters** such as GABA, serotonin, and dopamine
- **Regulation of HPA axis activity**, thus reducing stress-induced cortisol elevation
- **Immune modulation** via suppression of pro-inflammatory cytokines (e.g., IL-6, TNF-α)

• **Reinforcement of intestinal barrier integrity**, preventing LPS-induced systemic inflammation

• **Influencing vagus nerve activity**, which transmits gut-derived signals to the brain[4]

7.3 Clinical Evidence: Probiotics

Several clinical trials have evaluated the efficacy of probiotics in improving symptoms of depression, anxiety, and stress:

• **Meta-analyses** show that probiotics significantly reduce depressive symptoms compared to placebo[5].

• *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175 have been shown to reduce cortisol and psychological distress in both humans and rodents[6].

• In patients with **irritable bowel syndrome (IBS)**, which is highly comorbid with anxiety and depression, probiotics improved both GI and psychological symptoms[7].

7.4 Clinical Evidence: Prebiotics

Prebiotics, such as **fruc too ligosaccharides (FOS)** and **galac too ligosaccharides (GOS)**, nourish beneficial bacteria and impact emotional regulation:

•Supplementing with **galacto-oligosaccharides (GOS)**, a prebiotic fiber, has been shown to positively impact stress and emotional processing. One key finding is a **reduction in the cortisol awakening response (CAR)**—a biological marker of stress that reflects how sharply cortisol levels rise shortly after waking.A lower CAR suggests **reduced physiological stress levels**. Additionally, individuals receiving GOS showed **less attentional bias toward negative emotional stimuli**, meaning they were less likely to focus on or be influenced by negative facial expressions or emotionally charged images.[8].

• A lower cortisol awakening response (CAR) indicates **reduced physiological stress**, reflecting a calmer stress response system. Additionally, individuals who received GOS were **less focused on negative emotional cues**, such as angry or sad faces, suggesting a **more positive or balanced emotional outlook**. This points to GOS's potential role in supporting mental well-being by reducing stress and negative emotional reactivity.[9].

7.5 Synbiotics and Postbiotics

• **Synbiotics** (combinations of probiotics and prebiotics) offer synergistic benefits in modulating mood and stress levels[10].

• **Postbiotics**, the non-viable bacterial products or metabolites (e.g., SCFAs), also demonstrate neuroactive effects, especially in animal studies, and are increasingly explored as therapeutic agents[11]

7.6 Safety and Limitations

• Probiotics are generally considered safe for healthy individuals. However, **immunocompromised patients** may be at risk of bacteremia or fungemia.

• Current limitations include:

• **Variability in probiotic strains** and dosage across studies

• **Short-term trials** with small sample sizes

• **Lack of standardized psychobiotic guidelines**

Future research should focus on strain-specific effects, long-term safety, and personalized psychobiotic regimens.

7.7 Future Directions

Certainly! Here's a slightly expanded version with more explanation for each point:

• **Customized Probiotics**: These are probiotics specifically formulated based on an individual's unique **gut microbiome composition** and **genetic profile**. The goal is to create more effective, personalized treatments that address specific microbial imbalances and optimize gut-brain communication.

• **Microbiota-Targeted Nutrition**: These are specially engineered or selected **foods designed to nourish and support specific beneficial microbial populations** in the gut. By encouraging the growth of targeted bacteria, these foods can help modulate immune function, metabolism, and even mood.

• **FMT and Live Biotherapeutics**: **Fecal microbiota transplantation (FMT)** and **live biotherapeutic products** (e.g., FDA-approved microbial therapies) are emerging treatments aimed at restoring a healthy microbiome. They are especially promising for **psychiatric and neurodegenerative conditions**

that are resistant to conventional therapies, offering a more direct and targeted approach to correcting dysbiosis.

• **Modulating Microbial Metabolites**: This approach focuses on developing **drugs or supplements that mimic or influence neuroactive compounds** produced by gut microbes, such as **short-chain fatty acids (SCFAs)**, **tryptophan metabolites**, and **bile acids**. These compounds have a profound effect on brain function, inflammation, and neurotransmitter regulation, and may offer new therapeutic strategies for mental and neurological health.

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