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Neuroimaging Review

Mood, Food, and the Microbiome

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The Signs of Depression: Current Treatment and Limitations

Major depressive disorder (MDD) is a prevalent and debilitating condition that affects both men and women. The prevalence of depressive symptoms is much higher and has increased significantly in women over the last decade (Figure 1). Although the exact cause of major depressive disorder is unknown, research points to a series of interactions between the brain, the endocrine, and the immune systems, including the gut microbiome. Although the current treatments for depression are effective for many individuals, several shortcomings in current treatments are evident. Accordingly, in the World Health Organization (WHO), annual 100-500 billion dollar loss in productivity, the need for more effective treatments for depression is apparent. Moreover, a significant percentage of individuals with depression do not seek treatment because of the stigma associated with mental illness. This review will discuss the current treatments for depression, their limitations, and the emerging research on the gut microbiome as a novel therapeutic target.

Figure 1. Gender differences in prevalence of major depressive disorder.

We know that antidepressants targeting monoamine neurotransmitters like serotonin and noradrenaline are not universally effective (e.g., Trivedi, Kansagara and Sanderson-Cimino, 2025). Moreover, the most recently approved drug, esketamine, and the mainstay of treatment for depression, Ketamine, this is more effective than placebo, but only for a subset of individuals (Wilkinson et al., 2018). Moreover, the mechanisms underlying the antidepressant effects of ketamine are not well understood, which contributes towards rational dosing.

Psychotherapy is a non-invasive treatment option and of the above therapies. Firstly, psychological therapies are not universally effective, and secondly, they are time-consuming and expensive. Cognitive behavioral therapy (CBT) is the most studied psychotherapy for treatment-resistant depression (TRD). Secondly, meditations seem to be more effective in severe disorders and when combined with other treatments (Kuyken et al., 2016). Finally, Electroconvulsive therapy (ECT) is a highly effective treatment for severe depression, but it is invasive and has significant side effects, including memory loss. The prevalence of such side effects, the reluctance of patients to undergo ECT, and the stigma associated with it, limit its clinical utility. The latter, for example, includes Antepartum depression, which affects approximately 10% of pregnant women and is associated with adverse outcomes for the mother and the child. However, the current treatment options are limited because of the concerns about the safety of the developing fetus. Moreover, the current treatment options are limited because of the concerns about the safety of the developing fetus. Moreover, research that relays about antepartum depression and its treatment options, including psychotherapy, pharmacotherapy, and neuromodulation, is sparse. Moreover, research that relays about antepartum depression and its treatment options, including psychotherapy, pharmacotherapy, and neuromodulation, is sparse. In conclusion, the current treatments for depression are not universally effective, and there is a need for more research into the development of novel treatments and a better understanding of the mechanisms underlying treatment-resistant depression, including the role of the gut microbiome in both depression and disease.

Fecal Microbiota Transplantation: Current Research and Clinical Applications

Fecal microbiota transplantation (FMT) is a medical procedure that involves transferring stool from a healthy donor into the gastrointestinal tract of a recipient to restore a balanced gut microbiome. This procedure has gained significant attention in recent years for its potential to treat various gastrointestinal and neurological disorders, including recurrent Clostridium difficile infection, inflammatory bowel disease, and even some neurological conditions like depression and anxiety. The rationale behind FMT is rooted in the concept that restoring a healthy gut microbiome can alleviate dysbiosis, reduce inflammation, and potentially influence brain function through the gut-brain axis. While the procedure has shown promising results in clinical trials, its long-term safety, efficacy, and mechanisms of action are still being investigated. As research continues, FMT may emerge as a novel therapeutic approach for various conditions, but its widespread adoption will depend on further scientific evidence and regulatory approvals.

Food, Mood and the Gut Microbiome: Current Knowledge

The proposed mechanisms of action for psychobiotics are diverse and interdependent, with evidence suggesting interactions between the immune system, the vagus nerve, and various neurotransmitter systems. The anti-inflammatory properties of certain psychobiotics may indirectly influence mood by reducing systemic inflammation, which has been linked to depressive symptoms. The vagus nerve, which connects the gut to the brain, is a key pathway through which gut microbes can potentially influence mood and behavior. Some psychobiotics have also demonstrated the ability to modulate the production of neurotransmitters like serotonin, dopamine, and GABA, which are crucial for mood regulation. However, the specific strains and dosages required to exert these effects may vary depending on individual factors and the specific mental health condition being addressed. While the potential of psychobiotics to influence mood through the gut-brain axis is an exciting area of research, more clinical trials are needed to fully understand their efficacy, optimal dosages, and long-term effects on mental health. As the field progresses, it may lead to the development of personalized psychobiotic interventions tailored to individual gut microbiome profiles and specific mental health challenges.

Why Nutrition Matters: Nutritional Psychiatry and Psychobiotics

Nutritional Psychiatry is a relatively new field that explores the impact of diet and nutrition on mental health. There is increasing evidence that the gut microbiome plays a significant role in this relationship, with the concept of the gut-brain axis being central to understanding this connection. Psychobiotics, a term which refers to beneficial bacteria such as probiotics that can positively influence mental health through their interaction with the gut microbiome, are a key area of research in this field.

A modified Mediterranean-style diet was shown to facilitate remission in populations suffering from moderate to severe depression. The study demonstrated that participants who followed a modified Mediterranean-style diet were more likely to experience significant improvements in their depressive symptoms. In comparison to supportive therapy such as befriending, dietary interventions showed a higher probability of achieving remission from depression. The study suggests that adherence to a nutritious, Mediterranean-style diet may be a viable and effective approach for improving mental health in individuals with depression, potentially offering a complementary or alternative treatment option to conventional therapies. However, more research is needed to confirm these findings and to understand the mechanisms by which dietary changes can influence mental health outcomes in individuals with depression.

Research investigating the neurological benefits of ketogenic diets, such as those conducted by Gofman and Martin (2022), have shown that these diets can positively impact various aspects of brain health. The study mentioned that the ketogenic diet has been demonstrated to have neuroprotective effects, potentially benefiting conditions such as Alzheimer's disease, Parkinson's disease, and traumatic brain injury. The research also suggests that the ketogenic diet may enhance cognitive function and mood in healthy individuals. These findings indicate that the ketogenic diet, in addition to its traditional use in managing epilepsy and other neurological disorders, may have broader implications for maintaining and improving brain health across various populations. However, more research is needed to fully understand the mechanisms by which ketogenic diets exert their effects on the brain and to determine the optimal duration and intensity of ketogenic dietary interventions for different individuals and health conditions.

Research investigating the impact of fasting on brain health has shown promising results, suggesting that various fasting protocols may have beneficial effects on cognitive function and overall brain health. The study mentioned that fasting has been shown to promote neuroplasticity, reduce inflammation, and enhance the production of brain-derived neurotrophic factor (BDNF), a protein that supports the growth and survival of neurons. These findings suggest that fasting may have potential therapeutic benefits for various neurological conditions and cognitive impairments. However, more research is needed to understand the optimal fasting protocols, duration, and frequency for different individuals and health conditions, as well as to elucidate the underlying mechanisms by which fasting exerts its effects on brain health.

Psychobiotics: Future Directions and Conclusions

It is important to acknowledge that the microbiome is a complex and dynamic ecosystem that varies between individuals and changes over time as knowledge grows about what kind of microbial populations are beneficial for humans. This will pose challenges for the development of standardized psychobiotic interventions, as what may be beneficial for one individual may not be beneficial for another. The concept of personalized medicine, tailoring treatments based on individual genetic, microbiome, and other factors, may be relevant in the context of psychobiotics, as it could potentially lead to more effective and targeted interventions for mental health disorders. However, this approach also raises ethical considerations and the need for rigorous scientific evidence to support the efficacy and safety of personalized psychobiotic therapies.

Many studies mentioning the metabolic tests to shine an increase or decrease in the relative abundance of certain species/strains/genera/families found in a sample, or what we refer to as "microbiome signatures". As we are gradually understanding the role of the microbiome in the gut-brain axis, future efforts should be aimed at establishing causality between microbiome signatures and various mental health conditions. Moreover, the metabolic pathways underlying functions have already commenced. And it is worth mentioning that future research should focus on strain-targeting neuropsychiatric interventions, which have been conducted. Such human studies have shown promising results in the treatment of depression, anxiety, and other mental health conditions. Strain-specific interventions have the potential to provide more precise and effective treatments, as different strains may have different functions leading to enhance mood and cognitive performance. Ultimately, the goal of future research in this field is to develop a more nuanced understanding of the complex interactions between the microbiome, the gut-brain axis, and mental health, in order to develop more effective and personalized interventions for various psychiatric disorders and cognitive impairments.

Figure 2. Illustration of the relationship between the microbiome and the neurology of depression.

Strains the effect of a particular food, or mood is a complex and multifactorial phenomenon. The number of conversations between the brain and the microbiome, the gut-brain axis, is a rapidly growing field. The research is consistent. In such a case, we would not be surprised to see a significant number of studies on digestion and assimilation, the direct effects on the CNS, or whether it is moderating gut-brain axis pathways. The research is clear, dietary mood supplementation is a promising approach with the potential to influence gut-brain pathways. However, the exact mechanisms of action and the optimal dosages and formulations for different individuals remain to be fully elucidated. Future research should focus on conducting more rigorous, large-scale clinical trials to validate the efficacy and safety of these interventions, while also exploring the potential for personalized nutritional approaches tailored to individual gut microbiome profiles and specific mental health challenges. As our understanding of the complex interactions between the microbiome, the gut-brain axis, and mental health continues to grow, it may lead to the development of more effective and targeted nutritional interventions for various psychiatric disorders and cognitive impairments, ultimately offering new hope for improved mental health and well-being.

Perspectives, Future Directions and Conclusions

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