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A Functional Application of the Gut-Brain Axis: A Proposed Nutrition Intervention for the
Treatment of Depression

by

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An undergraduate honors thesis submitted in partial fulfillment of the requirements for the

degree of

Bachelor of Science degree

in

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Portland State University

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Abstract

In the last 10 years, research on the human microbiome has grown exponentially due to the increasing understanding of its effects on human health. The gut-brain axis has become one area of focus, linking gut health and mental disorders. This review of the literature will examine the connection between depression and gut health, primarily mediated by the gut microflora. Due to the complex nature of studying the gut-brain axis and the heterogeneity of depression, recent studies have faced some difficulty in finding significant results based on isolated nutrients, foods, supplements, or probiotics. This proposal seeks to build on prior research to produce an inclusive whole food-based nutrition intervention that potentially will have a more significant impact on depressive disorders. This research will be combining well studied probiotics with a beneficial dietary pattern in the hopes of creating a protocol that yields a more pronounced reduction on depressive symptoms, which could be used in a clinical trial or as an adjuvant treatment.

Keywords: *Gut-Brain Axis, Depression, Mental Health, Gut Microbiome, Probiotics, Prebiotics, Psychobiotics, Mediterranean Diet, Dietary Patterns, Nutrition Intervention*

Introduction

Depression Significance and Diagnostic Criteria

Depression is one of the most common mental disorders globally and a leading cause of disability affecting more than 300 million people worldwide (Kessler & Bromet, 2013; World Health Organization, 2018). Depression greatly reduces quality of life and can have major personal, professional, and social consequences. It also has the capability to bring on suicidal thoughts and potentially lead to death (Popa & Ladea, 2012). According to the Diagnostic and Statistical Manual of Mental Disorders (5th ed.), the myriad of depressive disorders share common diagnostic criteria including: “the presence of sad, empty, or irritable mood, accompanied by somatic and cognitive changes that significantly affect the individual’s capacity to function” (American Psychiatric Association, 2013). The different types of depressive disorders primarily differ because of timing, duration, or presumed etiology (American Psychiatric Association, 2013). It is understood that depression can stem from biological, social, and environmental factors. The present research seeks to address possible biological and environmental origins of depression.

Depression as an Inflammatory Disease

Current pharmacological treatments for depression involve the use of medications that primarily function to adjust neurotransmitter activity, but these treatments can cause severe side effects and withdrawal symptoms (National Institute of Mental Health, 2018; Wallace & Milev, 2017). A recent study examining the efficacy on antidepressants found them to be much less clinically significant than previously thought (Moncrieff & Kirsch, 2005). The common notion that depression stems solely from neurochemical imbalances has more recently been reconsidered and depression is now hypothesized to be an inflammatory disease (Berk et al.,

2013). Common biomarkers of depression include elevations of pro-inflammatory cytokines including interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor - alpha (TNF- α), and c-reactive protein (CRP) (Dowlati et al., 2010; Gururajan, Clarke, Dinan, & Cryan, 2016). It's also common to see evidence of stress-related physiology, such as elevated cortisol levels (Connor & Leonard, 1998). Brain-related biomarkers of depression include lowered levels of dopamine, serotonin Gamma-Aminobutyric Acid (GABA), and various neurotrophic factors, especially brain-derived neurotrophic factor (BDNF) (Strawbridge, Young, & Cleare, 2017; Gururajan et al., 2016). All these biomarkers suggest depression to be highly correlated to inflammation, stress, immune dysfunction, and a hyperactive hypothalamus-pituitary-adrenal (HPA) axis (Sandhu et al., 2017).

Study Aims

Berk et al. (2013) have examined the many possible sources of inflammation that may be influencing depression. Sources of inflammation can stem from biological, social, and environmental factors which helps explain the heterogeneity of depression. Research has shown a strong correlation between depression and gastrointestinal dysfunction, shown in the comorbidity of depression with many gastrointestinal disorders and related inflammatory responses (Mangiola et al., 2016). This has led to an increased interest in studies surrounding nutritional psychiatry, neurogastroenterology, and the gut-brain-axis (Logan & Katzman, 2005). This paper will be examining the role of dietary patterns and gut microflora as mediators of depression to culminate a nutrition intervention that may potentially prevent or treat depression.

Gut-Brain Axis

The Gut-Brain Axis as a Mediator of Depression

In the last decade, a growing field of research has emerged looking into the bidirectional connection between the central nervous system (CNS) and the gastrointestinal (GI) tract, which is now known as the gut-brain axis. The cross talk between the GI tract and the CNS is mediated through the autonomic and enteric nervous systems, immune system, and endocrine system (Sandhu et al., 2017). The human GI tract is also home to over 100 trillion bacteria which make up the gut microbiome. This microbiome is a very influential part of the gut-brain axis and has a significant impact on human health by maintaining the intestinal barrier, supporting immune function, metabolizing nutrients, producing short chain fatty acids (SCFAs), and producing neurochemicals, such as 90% of the bodies serotonin (Mangiola et al., 2016; Sandhu et al., 2017). The importance of nutrition and maintaining a healthy gut microbiome has been well established, but the role these play in psychiatric disorders is emerging in research with promising findings. The gut microbiome may modulate cognitive functioning and behavior through possible mechanisms involving the immune system, HPA axis, inflammation, and the production of neurochemicals and neurohormones (Sandhu et al., 2017). Maintenance of a healthy gut microbiome has the potential to modulate levels of anti-inflammatory cytokines, reduce oxidative stress, and increase BDNF, GABA, and serotonin, all of which have negative correlations with depression (Logan & Katzman, 2005).

The Gut-Microbiome - An Ecosystem Within Us

The gut microflora is unique to every individual and is influenced by several factors including genetics, lifestyle, birthing method, antibiotic history, and dietary patterns (Sandhu et al., 2017). It is well established which bacteria are beneficial versus harmful, and the balance

between positive and negative species is essential to host health. An unbalanced microflora is known as dysbiosis and is directly correlated to a plethora of disorders and diseases, one of which being depression. Although everyone's microbiome is distinct, similar populations share certain species, quantities, and diversity (Sandhu et al., 2017). Healthy individuals are primarily populated by the phyla Firmicutes and Bacteroidetes, which contain many beneficial species including the well-known *Bifidobacterium* and *Lactobacillus* (Johnson et al., 2012). Individuals with depressive disorders have shown to have an abundance of Enterobacteriaceae (phyla containing mostly pathogenic species), and lower levels of *Bifidobacterium* and *Lactobacillus* (gram positive beneficial bacteria) when compared to healthy subjects (Aizawa et al., 2016; Jiang et al., 2015; Sandhu et al., 2017). In a study by Zheng et al. (2016), fecal microflora from patients with major depressive disorder (MDD) were transplanted into germ free mice. This induced depressive-like behaviors and caused metabolic dysfunction when compared to mice who received fecal microflora transplants from healthy subjects (Zheng et al., 2016). There have been numerous other demonstrations that depression may stem from negative alterations in gut microflora.

From Probiotics to Psychobiotics

Probiotics are defined as “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host” (Hill et al., 2014, p. 506). Probiotics have been prescribed by doctors for many gut-related disorders, but as the understanding of the gut-brain axis has evolved a new era of probiotics has been termed “psychobiotics” for their influence on the CNS, cognition, and behavior (Dinan, Stanton, & Cryan, 2013). In a systematic review on the effects of probiotics on the CNS, it was found that probiotics can improve CNS functioning possibly through increasing BDNF levels, enhancing serum tryptophan, and decreasing pro-

inflammatory cytokines (Wang, Lee, Braun, Enck, 2016). In a study on Ulcerative Colitis, probiotics were found to diminish inflammation by decreasing IL-6 and TNF-a concentrations, both of which are inflammatory biomarkers of depression (Hegazy & El-Bedewy, 2010). Akkashah et al. (2015), found that probiotic treatment to patients with MDD significantly reduced signs of oxidative stress and CRP levels, other inflammatory biomarkers of depression. A growing body of research is examining the efficacy of specific probiotic strains for the treatment of depression, those with promising results are summarized and presented in Table 1. These studies focus on increasing the quantity and diversity of beneficial gut bacteria, primarily using *Bifidobacteria* and *Lactobacillus* supplementation, to bring dysbiotic microflora back to a healthy status.

Table 1. Probiotics for Depression

This table provides a list of probiotic strains with corresponding evidence in preclinical and clinical studies for the treatment of depressive disorders or associated risk factors. Clinical diagnosis, method of probiotic treatment, and depression scales may differ between studies due to the heterogeneity of depression.

Probiotic Strain	Authors	Study Design	Overview
<i>B. bifidum</i>	Akkashah et al. (2016)	Randomized double-blind placebo controlled	Probiotic formula (<i>L. acidophilus</i> , <i>L. casei</i> , <i>B. bifidum</i>) administered to 20 patients with MDD over 8 weeks significantly decreased scores on Beck Depression Inventory
	Steenbergen et al. (2015)	Triple-blind, placebo controlled, randomized, pre and post intervention assessment	20 healthy participants were administered a probiotic formulation of <i>B. Bifidum</i> , <i>B. lactis</i> , <i>L. acidophilus</i> , <i>L. brevis</i> , <i>L. casei</i> , <i>L. salvarius</i> , and <i>L. lactis</i> for a 4-week period. Leiden Index of Depression Sensitivity Scale was used to measure cognitive reactivity to sad mood (a precursor for depression) and the probiotic formulation showed significant reductions on scale.
<i>B. infantis</i>	Desbonnet et al. (2010)	Preclinical animal study	<i>B. Infantis</i> proved to be nearly as effective as citalopram (a common antidepressant) in

			normalizing forced swim test behaviors in a rat maternal separation model, which is a reliable marker of antidepressant activity.
<i>B. lactis</i>	Steenbergen et al. (2015)	Triple-blind, placebo controlled, randomized, pre and post intervention assessment	20 healthy participants were administered a probiotic formulation of <i>B. Bifidum</i> , <i>B. lactis</i> , <i>L. acidophilus</i> , <i>L. brevis</i> , <i>L. casei</i> , <i>L. salvarius</i> , and <i>L. lactis</i> for a 4-week period. Leiden Index of Depression Sensitivity Scale was used to measure cognitive reactivity to sad mood (a precursor for depression) and the probiotic formulation showed significant reductions on scale.
<i>B. longum</i>	Messaoudi et al. (2011)	Randomized double-blind placebo controlled	The probiotic formula of <i>L. helveticus</i> and <i>B. longum</i> reduced anxiety and in preclinical rats and had beneficial psychological effects (including depression reduction) in 26 human volunteers.
	Pinto-Sanchez et al. (2017)	Randomized double-blind placebo controlled pilot study	Pilot study found that <i>B. longum</i> reduces depression and increases quality of life in 22 patients with IBS compared to controls.
<i>L. acidophilus</i>	Akkasheh et al. (2016)	Randomized double-blind placebo controlled	Probiotic formula (<i>L. acidophilus</i> , <i>L. casei</i> , <i>B. bifidum</i>) administered to 20 patients with MDD over 8 weeks significantly decreased scores on Beck Depression Inventory
	Steenbergen et al. (2015)	Triple-blind, placebo controlled, randomized, pre and post intervention assessment	20 healthy participants were administered a probiotic formulation of <i>B. Bifidum</i> , <i>B. lactis</i> , <i>L. acidophilus</i> , <i>L. brevis</i> , <i>L. casei</i> , <i>L. salvarius</i> , and <i>L. lactis</i> for a 4-week period. Leiden Index of Depression Sensitivity Scale was used to measure cognitive reactivity to sad mood (a precursor for depression) and the probiotic formulation showed significant reductions on scale.
<i>L. brevis</i>	Steenbergen et al. (2015)	Triple-blind, placebo controlled, randomized, pre and post intervention	20 healthy participants were administered a probiotic formulation of <i>B. Bifidum</i> , <i>B. lactis</i> , <i>L. acidophilus</i> , <i>L. brevis</i> , <i>L. casei</i> , <i>L. salvarius</i> , and <i>L. lactis</i> for a 4-week period. Leiden Index of Depression Sensitivity Scale was used to measure cognitive reactivity to sad mood (a

		assessment	precursor for depression) and the probiotic formulation showed significant reductions on scale.
<i>L. casei</i>	Akkasheh et al. (2016)	Randomized double-blind placebo controlled	Probiotic formula (<i>L. acidophilus</i> , <i>L. casei</i> , <i>B. bifidum</i>) administered to 20 patients with MDD over 8 weeks significantly decreased scores on Beck Depression Inventory
	Steenbergen et al. (2015)	Triple-blind, placebo controlled, randomized, pre and post intervention assessment	20 healthy participants were administered a probiotic formulation of <i>B. Bifidum</i> , <i>B. lactis</i> , <i>L. acidophilus</i> , <i>L. brevis</i> , <i>L. casei</i> , <i>L. salvarius</i> , and <i>L. lactis</i> for a 4-week period. Leiden Index of Depression Sensitivity Scale was used to measure cognitive reactivity to sad mood (a precursor for depression) and the probiotic formulation showed significant reductions on scale.
<i>L. helveticus</i>	Messaoudi et al. (2011)	Randomized double-blind placebo controlled	The probiotic formula of <i>L. helveticus</i> and <i>B. longum</i> reduced anxiety and in preclinical rats and had beneficial psychological effects (including depression reduction) in 26 human volunteers.
<i>L. plantarum</i>	Liu et al. (2016)	Preclinical animal study	<i>L. plantarum</i> effectively decreased serum IL-6 levels and improved depressive behaviors in mice with early life stress
<i>L. reuteri</i>	Ma, Forsythe, & Bienenstock (2004)	Preclinical study	<i>L. Reuteri</i> directly inhibited IL-8 and TNF-alpha, promoting an anti-inflammatory effect on human epithelial cells.
<i>L. rhamnosus</i>	Slykerman et al. (2017)	Randomized double-blind placebo controlled	Study showed a significant reduction of depressive and anxiety postpartum symptoms in 212 women compared to placebo group.
<i>L. salivarius</i>	Steenbergen et al. (2015)	Triple-blind, placebo controlled, randomized, pre and post intervention assessment	20 healthy participants were administered a probiotic formulation of <i>B. Bifidum</i> , <i>B. lactis</i> , <i>L. acidophilus</i> , <i>L. brevis</i> , <i>L. casei</i> , <i>L. salvarius</i> , and <i>L. lactis</i> for a 4-week period. Leiden Index of Depression Sensitivity Scale was used to measure cognitive reactivity to sad mood (a precursor for depression) and the probiotic formulation showed significant reductions on scale.

Research Significance and Recommendations

Based on the results of these articles, it's reasonable to conjecture that a combination of these beneficial probiotic species may be a promising option for the prevention and treatment of depression. An important thing to mention is that few of these studies have large sample sizes, control for diet and prebiotic consumption, use modes of transmission beside capsulized probiotics, or analyze the stool to confirm the probiotics were able to colonize in the lower GI tract. The efficacy of probiotics relies on their ability to survive through the stomach and adhere permanently to the epithelium of the large intestine. Their ability to do so depends on how the cultures were administered, the presence of prebiotics, and the quantity and quality of the probiotic culture (Johnson et al., 2012). Although these studies have found clinically relevant and promising results, it is possible that these findings could be improved if more measures are taken to ensure the colonization of probiotic species in the GI tract.

The Role of Nutrition

The Importance of Diet and Prebiotics

The most effective way to rapidly improve the gut microbiome and promote the colonization and growth of beneficial species is through diet (Singh et al., 2017). Although the use of probiotic supplements has demonstrated potential effectiveness in promoting the integrity of the microbiome and improving depressive symptoms, research suggests that the influence of a healthy diet and consumption of probiotic foods and drinks may be more influential (Walker et al, 2011). The probiotic research presented in Table 1 primarily establishes what specific species show the most promise in influencing mood and depressive symptoms. These “psychobiotic” species include *B. bifidum*, *B. infantis*, *B. lactis*, *B. longum*, *L. acidophilus*, *L. brevis*, *L. casei*, *L. helveticus*, *L. plantarum*, *L. reuteri*, *L. rhamnosus*, and *L. salivarius*. These species can be found

in a variety of fermented foods and drinks including fermented dairy products, sauerkraut, kimchi, kombucha, etc. Another main way diet supports microbiome health is from the presence of prebiotics, specific nondigestible foodstuffs, that feed beneficial bacteria which then outcompete harmful species (Singh et al, 2017). Prebiotics include fructooligosaccharides, galactooligosaccharides, lactulose, cereal fibers, resistant starches, lactosucrose, soybean, and oligosaccharides (Johnson et al., 2012). To see more significant clinical results for treating depression the consumption of probiotics, prebiotics, and quality of diet must be established to improve the gut microbiome and feed these psychobiotic species.

Dietary Patterns

A fundamental approach to achieving optimal function of the gut-brain axis is through specific nutritional interventions focused on dietary patterns. While some research has focused on the use of specific vitamins, minerals, and other supplements to promote gut and brain health, results are mixed (Wallace & Milev, 2017). This has led many to propose that, rather than focusing on isolated nutrients, examining diet patterns as a whole may be more impactful when studying mental health, especially depression (Del Chierico, Vernocchi, Dallapiccola, & Putignani, 2014). There is a growing body of research that supports the Mediterranean diet as an effective prevention or treatment plan for depression as they are inversely related (Psaltopoulou et al., 2013; Sanchez-Villegas et al., 2007; Sandhu et al., 2017). Correspondingly, there is a strong correlation between the Western diet (high in refined carbohydrates, animal protein and fat) and depression, along with the comorbidity of many other metabolic disorders (Jacka et al, 2010; Psaltopoulou et al., 2013). Studies continue to evaluate the possible antidepressant properties of the Mediterranean dietary pattern, one of which may be the positive impact it has on the gut microbiome (Sanchez-Villegas et al., 2007). Research has compared the influence of

dietary patterns on gut microflora and found that Western diets limit microflora density and show a reduction in amounts of *Bifidobacteria* and *Lactobacillus* and an increase in Enterobacteria (Singh et al., 2017). On the other hand, the Mediterranean diet increases microflora diversity and promotes the growth of *Bifidobacteria* and *Lactobacillus* (see figure 1.) (Singh et al., 2017).

Figure 1. Western diet vs. Mediterranean diet effects on microflora (Singh et al., 2017).

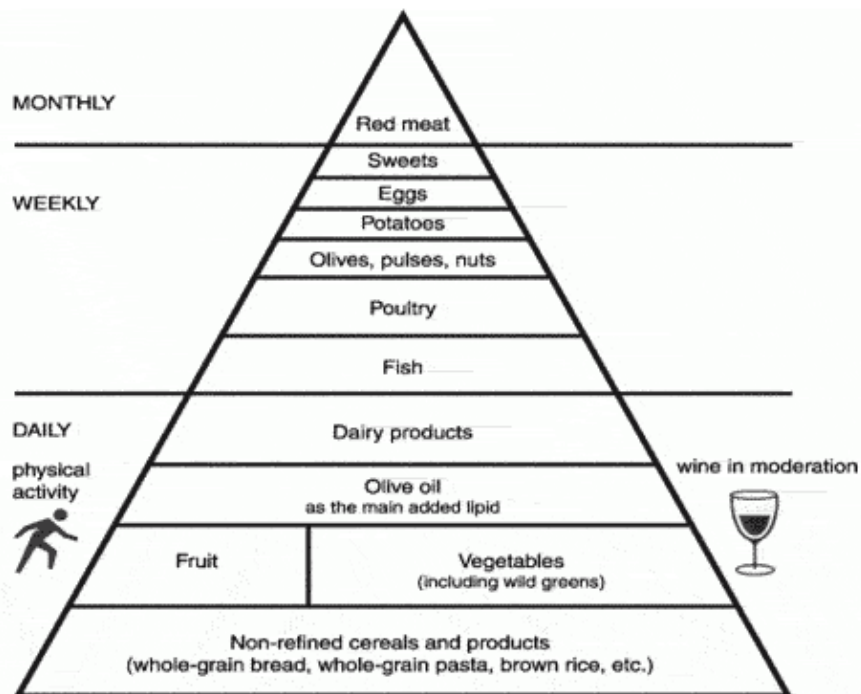


The Mediterranean Diet and the Gut Microbiome

The Mediterranean Diet: What is it?

The Mediterranean diet has come to be known as one of the healthiest and most beneficial ways of eating. The Mediterranean diet is an eating pattern characterized by daily intake of unrefined grains, vegetables, fruit, olive oil, and dairy, with a moderate intake of fish, poultry, eggs, sweets, and legumes, and rarely red meat. (see figure 2).

Figure 2. The Mediterranean Diet food pyramid (Trichopoulou, 2004).



Mediterranean Diet Carbohydrates (Prebiotics)

In a study done by Filippis et al. (2016), the microbiomes of 153 volunteers were analyzed in relation to their adherence to a Mediterranean diet. The results of the study found that dietary patterns closest to that of the Mediterranean diet were associated with healthier microbiome profiles compared to those consuming a Western diet (Filippis et al., 2016). A large portion of the Mediterranean diet is composed of fruits, vegetables, and foods high in fiber, which provide the variety of prebiotics that promote beneficial gut bacteria. Prebiotics, such as fructooligosaccharides, oligosaccharides, cereal fibers, and resistant starches found in the Mediterranean diet, are often indigestible carbohydrates that can only be broken down by beneficial species such as *Bifidobacterium* and *Lactobacillus*. The consumption of these prebiotics allows beneficial gut microbes to produce SCFA, such as butyrate, that directly support digestive function and produce anti-inflammatory effects (Singh et al., 2017). Prebiotic consumption is associated with reductions of pro-inflammatory cytokine IL-6, increases in the

anti-inflammatory cytokine IL-10, and other positive metabolic markers while also increasing microflora density and diversity (Martinez et al., 2013; Singh et al., 2017).

Mediterranean Diet Proteins

Aside from its high content of beneficial carbohydrates, the Mediterranean dietary pattern also emphasizes a reduced consumption of meat and promotes the ingestion of healthy fats. Meat intake and fat quality have also shown to influence the composition of the gut microbiome and may add to the success of the Mediterranean diet in reducing depression. Plant protein rich diets increase microflora diversity and can increase beneficial microbes, but diets with high consumption of animal-based protein produce an opposite effect. Diets high in animal-based protein increase counts of *Bacteroides*, *Alistipes*, and *Bilophila*, which increase protein fermentation that lead to toxic metabolites. These metabolites are associated with the development of cancer, irritable bowel disease, and cardiovascular disease (Singh et al. 2017; Sandhu et al., 2017). De Filippo et al. (2010), found that an animal protein rich diet produces fewer SCFA's, which protect the gut membrane and reduce inflammation. Diets high in animal protein and low in prebiotic foods promote the colonization of harmful species, which degrades the health of the gut microflora.

Mediterranean Diet Fats

Other nutrient components of the Mediterranean diet may also serve as protective agents against depression. The emphasis on healthy mono- and polyunsaturated fat (PUFA) consumption in the Mediterranean diet increases omega-3 levels which may play a major role in inflammatory responses (Simopoulos, 2002). The ratio of omega-6 to omega-3 PUFA consumption is understood to be of importance when it comes to human health. A high ratio of omega-6/omega-3 has been highly correlated to inflammatory diseases, especially in Western

cultures where the average PUFA ratio is 16-1 when it is recommended to be 2-1 or 1-1 (Simopoulos, 2002). The Mediterranean diet supports a high consumption of fish and olive oil (both high in omega-3) which has shown to decrease pro-inflammatory markers such as IL-6, CRP, and TNF- α (Bountziouka et al., 2009). Studies have shown that a lack of dietary omega-3 is correlated with depression, and populations with a higher PUFA ratio have higher prevalence of major depressive disorders (Bountziouka et al., 2009).

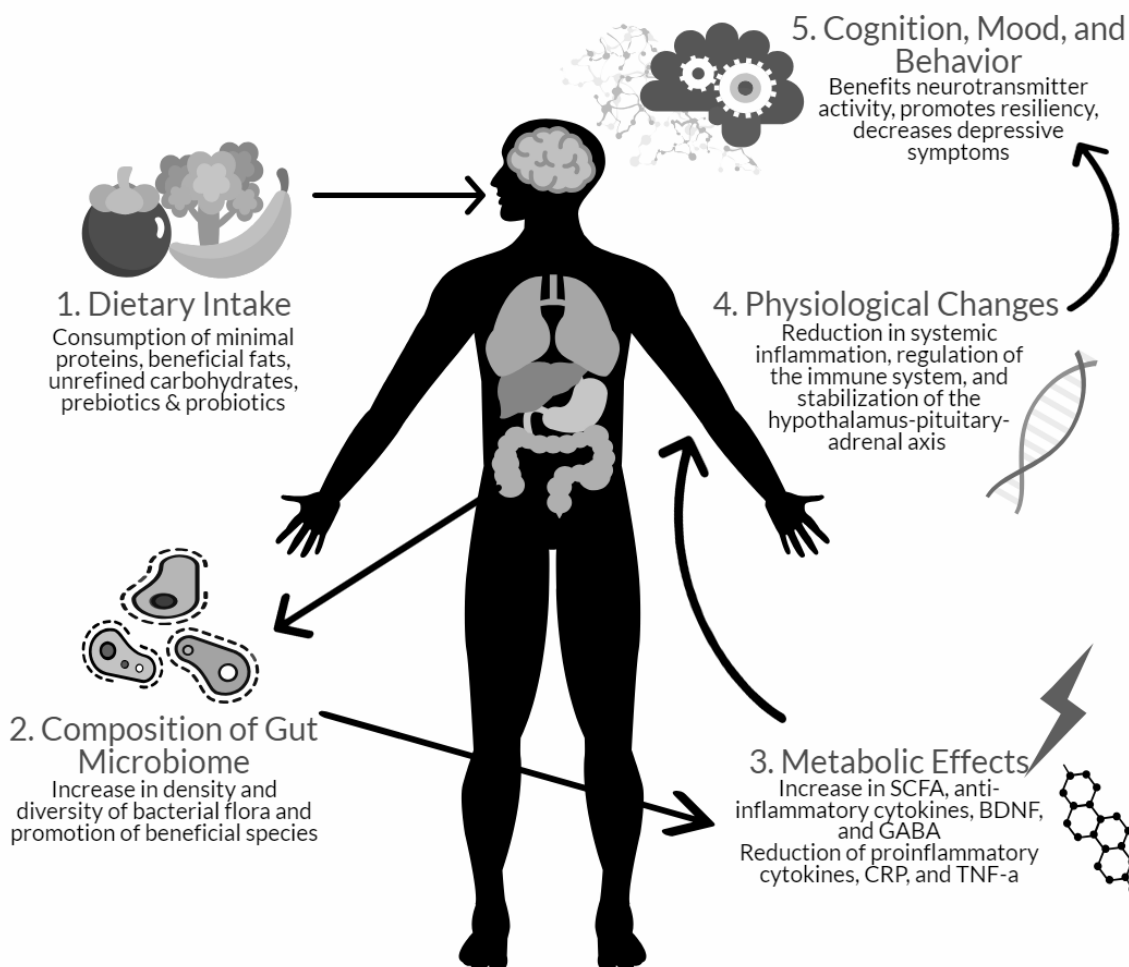
Conclusions

Summary of Research

As the understanding of the gut-brain axis evolves, research continues to find connections between depression, gut microflora, and the Mediterranean diet. Studies continue to search for isolated solutions from probiotics and nutritional aspects, but it is apparent the success from recent research stems from a cumulative effect that diet has on the microflora, and that the microflora has on the brain. As depression is now seen as an inflammatory disease, it is crucial to pinpoint the root of this inflammation and find functional ways to reduce it. As the GI tract is the body's largest immune organ, the idea that gut inflammation can be the underlying cause of some depressive disorders is not unlikely. The culmination of this research has uncovered the mechanisms by which diet can improve gut microflora, and in turn may decrease depressive symptoms. Figure 3 presents a simplified version of the mechanistic actions of this nutrition intervention. Essentially, what we eat influences the composition of our gut microbiota and thus what metabolites are produced. When eating a healthy diet rich in probiotics and prebiotics we feed the beneficial microbes in our gut and they return the favor by producing anti-inflammatory metabolites, energy, and beneficial neurochemicals. These metabolites then reduce systemic inflammation by regulating the immune system and calming the HPA axis, which helps bring the

body back into homeostasis and reduces depressive symptoms. The beneficial neurochemicals produced by the microflora are able to pass the blood-brain barrier and regulate levels of BDNF, GABA, dopamine, and serotonin in the brain, also thus reducing depressive symptoms.

Figure 3. Influence of proposed nutrition intervention on gut microbiome and cognitive functioning.



Proposed Nutrition Intervention

Through this research, a nutrition intervention based on a Mediterranean dietary model with an emphasis on the consumption of probiotic and prebiotic foods may successfully prevent/treat depressive disorders. The outline of this intervention is presented in Figure 4.

Figure 4. Nutrition Intervention proposal for the prevention/ treatment of depression.

Nutrition Intervention for Depression

Foods/Drinks to consume

Daily:

Unrefined grains

Prebiotic grains to include:

- Whole grain wheat
- Whole grain cereals
- Oats
- Rice (cooked and cooled)

Any Vegetables

Prebiotic Vegetables to include in diet are:

- Artichoke
- Asparagus
- Endive
- Jerusalem artichoke
- Garlic
- Onion
- Parsnip
- Leek
- Radishes
- Carrots
- Tomatoes
- Jicama
- Yams
- Spinach
- Potatoes (cooked and cooled)

Any Fruits

Prebiotic fruits include:

- Green bananas
- Apples
- Blueberries

Any Legumes and Seeds

Prebiotics include:

- Chia seeds
- Flax seeds
- legumes in general

Healthy Fats

- Olive oil
- Avocado oil
- Coconut oil

Probiotic foods

- Kimchi
- Sauerkraut
- Kefir
- Tempeh
- Kombucha
- Pickled foods
- Miso
- Olives
- Probiotic enriched dairy (or dairy alternatives)

Probiotic Species (in foods or supplements)

- *B.bifidum*
- *B. infantis*
- *B. lactis*
- *B. longum*
- *L. acidophilus*
- *L. brevis*
- *L. casei*
- *L. helveticus*
- *L. plantarum*
- *L. reuteri*
- *L. rhamnosus*
- *L. salivarius*

Water

2 liters is recommended

Moderately:

Fish and seafood

At least twice a week

Dairy Products

Preferably containing probiotics and less sugar

Poultry/ Eggs

Antibiotic- free

Rarely:

Red meat

Antibiotic free and preferably grass fed/sustainable

Sweets

This includes refined grains and anything high in sugar

This nutrition intervention is not all inclusive, but a recommendation based on the present research. This intervention is a non-harmful, holistic, accessible, and potentially effective way to prevent or manage depressive symptoms. For depressed populations who have a history of antibiotic use, poor dietary habits, or other inflammatory or GI problems (such as eczema or IBS) this nutrition intervention could serve as an extremely beneficial solution. This intervention is not meant to replace current depression treatments and individuals should always consult their physician before making any large scale dietary changes. This recommendation is meant to be a supplemental, holistic way to potentially address depression and more research is needed to support its efficacy in clinical trials.

Future Perspectives

In the future, research on this topic must approach it from a more functional direction by implementing larger scale nutrition interventions and probiotic treatments to modulate depression. Present research focused on isolated nutrients and single probiotic strains continues to show promise but lacks large sample sizes and high significance. No single nutrient or single probiotic strain is going to solve the depression epidemic. Dietary habits need to be controlled, effective methods to promote probiotic colonization need to be used, and stool samples must be analyzed to produce more conclusive results. Diet, microflora, and mood are clearly interrelated, and more research is necessary to reveal the mystery of this connection. As projects such as the Human Microbiome Project (National Institute of Health) make advancements in uncovering the complex world of our microbiomes, more studies need to solidify the best practices for ensuring colonization of beneficial microbes in the GI tract and how nutrition affects the ecosystem in our gut. Research on the gut microbiome and the influence of nutrition expands beyond depression to a variety of other psychiatric disorders, as well as numerous metabolic disorders. As this field of

research grows, it is very clear the ecosystems within our bodies may play a much larger role in our mental health than previously understood.

Limitations

One of the main limitations of this research is the heterogeneity of depression and how this causes many discrepancies among current research. There are a multitude of diagnoses for depressive disorders and a similar plethora of scales to measure them. The present research only addresses depression from an inflammatory perspective that focuses on inflammation stemming from the gut. This does not account for possible other roots of inflammation but may serve as a way to promote anti-inflammatory responses systemically. This nutrition intervention may not be applicable among all people due to the personalized nature of the gut microbiome. Some research has supported a personalized nutrition intervention based off individual microbiomes and genetics. The present approach supports a general dietary plan that can be modified by individuals and is based off the healthiest dietary model currently acknowledged by science.

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