Diet and its Overlooked Role in Depression

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Abstract

This thesis explores the relationship between food and its impact on mood and risk of depression. Specific nutrients, food groups, and dietary patterns were examined for their impact on mood, including the risks of underconsumption and overconsumption. Potential mechanisms of how these food components may impact mood were also explored. Dietary patterns such as the Western diet and Mediterranean diet were examined for their impact on mood. Research on the influence of food on individuals diagnosed with depression as well as undiagnosed individuals was included. After reviewing the current literature, a Mediterranean-style diet is associated with a decreased risk of depression, while a Western-style diet is associated with an increased risk. Diets with adequate consumption of fruits, vegetables, and micronutrients are associated with a decreased risk of depression, while excess consumption of added sugar, refined grains, saturated fat, and alcohol is associated with an increased risk of depression. The effect of certain food components on mood such as dairy and protein vary depending on content and consumption.

Keywords: dopamine, serotonin, cortisol, autophagy, vegetables, protein, grains, fat, dairy, water, fiber, added sugar, alcohol, vitamins, minerals, Western diet, ketogenic diet, Mediterranean diet, intermittent fasting

Introduction

Can the consumption of certain foods lead to individuals experiencing depression? There may be some truth to the statement, 'you are what you eat,' as underconsumption, overconsumption, or an utter lack of consumption of food can impact mood in various ways. There is limited research on the impact of specific nutrients and food groups on mood, so this thesis explores potential mechanisms of certain foods and their impact on mood as well as potential impacts of overconsumption and underconsumption. There are a few main mechanisms of how food can affect mood: the hormonal response, the metabolic stress response, the effect on neurotransmitter production, and the effect on the gut microbiome. When certain foods are under or over consumed, some, or all, of these pathways can be affected which may impact mood in different ways. In addition to food affecting mood, this thesis also explores the impact of fasting on mood. Fasting can induce autophagy and its impact on mood is still being researched. Discovering the impact on mood that certain dietary patterns may have can lead to a better understanding of how a poor diet can lead to depression. Understanding the relationship between food and mood may lead to an alternative treatment for depression in the future: a change in diet.

Current Research

There is a substantial body of research that has focused on how mood can affect diet, and how diet can in turn affect mood (Flaskerud, 2015). Some specialized research looks at the role stress can play in the relationship between consumption of certain types of food and the

subsequent mood. Flaskerud suggests that there is a vicious cycle between mood and food, which starts with stress. Stress can lead to a depressed mood, which in turn can lead to overeating of comfort foods which are typically high in carbohydrates. Too many carbohydrates can cause surges and crashes in blood sugar, increasing in the stress response and instigating the cycle to start again (Flaskerud, 2015). Lemmens et al. (2011) researched high-protein diets and high-carbohydrate diets and their effects on level of cortisol, which is a stress hormone. High-protein diets were composed of 65 percent protein, 5 percent carbohydrates, and 30 percent fat (En% P/C/F 65/5/30) while high-carbohydrate diets were composed of 6 percent protein, 64 percent carbohydrates, and 30 percent fat (En% P/C/C 6/64/30). They concluded that diets high in carbohydrates, as opposed to diets high in protein and fat, were far more likely to increase cortisol levels, showing how carbohydrate-rich diets can increase stress more so than diets high in protein and fat.

Some research has consistently shown that there is a link between depressed mood and low heart rate variability (HRV), however recent research suggests that dietary behavior might explain this association (Young, Cousins, Watkins, & Benton, 2017). In their study, Young et al. concluded that a poor diet was most consistent with low HRV and depressed mood compared to diets that were defined as healthy.

There is also a growing field of research suggesting that gut bacteria influences mood, and that this gut bacteria is fueled by food that people consume. Borysenko says that the gut bacteria produce more neurotransmitters for the brain than the actual brain itself, so there could be a larger link between diet and mood than people have previously thought (Howes, 2016).

Li et al. (2017) conducted a meta-analysis of articles regarding dietary patterns and risk of depression. Their findings show that diets consisting of red and/or processed meat, refined grains, sweets, high-fat dairy products, butter, potatoes and high-fat gravy, and low intakes of fruits and vegetables are associated with an increased risk of depression (Li et al., 2017). While some components of food have been associated with increased risk of depression, there is not enough current research to explain which kinds of foods can lead to a depressed mood, as well as how much of the consumed food can significantly impact an individual's mood. There is already a link between high carbohydrate diets and depressed mood, however some foods high in carbohydrates can elevate mood depending on what else is in the food, such as foods high in L-glycine (Neubert, 2018). This thesis will serve to fill the gap in current research and explore which foods in particular and how much of them it takes to impact mood in a negative and positive way.

Methods

For this literary review, an exhaustive search for articles using keywords such as "food", "diet", "depression" and "mood" was done using the search engines OU Libraries, CINAHL Plus with FullText, and Google Scholar. Twenty-eight articles were identified. Articles were reviewed for dietary patterns as well as individual food components and their impact on mood. Articles were then reviewed for potential mechanisms of how foods may impact on mood. A relationship was formed between these food components and their effect on mood. After relationships between food components and dietary patterns on mood were established, dietary reference intakes were identified. Underconsumption of certain nutrients and food groups was

defined as falling below the recommendations (e.g. RDA, AMDR), and overconsumption of certain nutrients was defined as exceeding the recommendations.

Literature Review

Food Groups and Mood

Fruit and Vegetables. High fruit and vegetable intake may play a role in preventing depression. White, Horwath, and Conner (2013) conducted a study in which 281 young adults tracked their diet over 21 days. They found a positive correlation between high fruit and vegetable consumption (7-8 servings per day) and positive mood. Participants whose diets were high in fruits and vegetables reported feeling more calm, happy, and energetic than those whose diets were not high in fruits and vegetables. Fruit and vegetable intake was also predictive of positive mood the next day suggesting that healthy foods may have a sustained effect on mood. These findings were consistent with Tsai, Chang, & Chi (2012) who studied vegetarian diets and found a positive correlation with healthy mood states. **Potential Mechanism.** Phytochemicals in fruits and vegetables may be the reason for fruit and vegetables having a positive effect on mood due to their antioxidant properties. Fruits and vegetables are high in antioxidants such as vitamin C, vitamin E, and other carotenoids compounds (Li et al., 2017). Li et al. found that consumption of foods high in antioxidants is associated with a reduced level of oxidative stress. Oxidative stress can lead to neuronal damage, particularly neurons in the hippocampus, which is thought to contribute to depression.

Protein. Protein serves a vast array of essential functions in the human body, but too much or too little of it in the diet can negatively impact mood. A diet disproportionately high in protein

can lead to a decreased mood (Flaskerud, 2015), especially if the protein is from processed meats (Li et al., 2017). In addition, not consuming an adequate amount of protein may lead to a decrease in mood (Flaskerud, 2015). **Potential Mechanism.** Consuming protein is not only necessary for maintaining lean body mass, but it is also necessary for the production of chemical messengers. According to Rintamäki, Preedy, Watson, and Martin (2011), three main amino acids contribute to mood by acting as precursors to neurotransmitters. Tryptophan is a precursor to serotonin, tyrosine is a precursor to dopamine and noradrenaline, and glutamate is a precursor to gamma-aminobutyric acid (GABA). A deficiency in tryptophan can result in the underproduction of serotonin, which can in turn lead to overeating and depressive symptoms. A deficiency in tyrosine can lead to a lack of synthesis of dopamine and noradrenaline which are involved in mood regulation and sleep. GABA is involved in regulation of normal brain functions such as sleep and memory processes and plays a role in anxiety and depression. Therefore, an underconsumption of glutamate can lead to a decrease in GABA which can lead to anxiety and depression (Rintamäki et al., 2011). While it is important to consume a diet with adequate amounts of protein to avoid deficiencies, it is also important to consume a diet that is an appropriate balance of protein, fat, and carbohydrates. Tryptophan is necessary for the production of serotonin, yet Flaskerud (2015) says a meal composed primarily of protein may actually decrease serotonin synthesis. This is due to the idea that a protein-rich meal raises the blood level of many amino acids and tryptophan is one of the least common amino acids in dietary protein. The other amino acids from a protein-rich meal can be large neutral amino acids that outcompete tryptophan, resulting in reduced entry of tryptophan into the brain and reduced serotonin synthesis. Flaskerud says that while a protein-rich diet may decrease serotonin

synthesis, a diet with a larger proportion of carbohydrates to protein increases brain serotonin synthesis. This is because consuming foods high in carbohydrates can change amino acid levels in the blood. Carbohydrates increase blood glucose which stimulates the release of insulin and enables muscle tissues to take up most amino acids except for tryptophan, which is bound to albumin in the blood. As a result, Flaskerud explains that the ratio of tryptophan relative to other amino acids in the blood increases which enables tryptophan to bind to transporters, enter the brain in large amounts, and stimulate serotonin synthesis.

Grains. Diets high in grains are typically of more concern when they are high in refined grains. Li et al. (2017) found that a diet high in refined grains is associated with an increased risk of depression. This is because refined grains can lead to a quicker surge in blood sugar compared to whole grains. In addition, Lemmens et al. (2011) found that diets high in carbohydrates are associated with increased stress compared to diets high in protein or fat. **Potential Mechanism.** Refined grains are typically high in simple carbohydrates and low in fiber, which can cause a rapid increase in blood glucose, leading to an eventual sugar crash. This sugar crash leads to an increase in stress which is associated with an increased risk of depression (Flaskerud, 2015, Lemmens et al., 2011).

Dairy. Research on dairy and its impact on mood is largely inconclusive, though there may be an association between high-fat dairy products and depression. Li et al. (2017) found that diets high in high-fat dairy products such as butter were associated with an increased risk of depression, while diets high in low-fat dairy products were associated with a decreased risk of depression. **Potential Mechanism.** The mechanism behind high-fat dairy and depression is largely speculative, though it may be due to the contents in high-fat dairy products. High-fat

dairy products such as butter have higher amounts of saturated fat than low-fat dairy products, and saturated fat is believed to increase inflammation which is related to depression (Li et al., 2017).

Components of Food and Mood

Water. Inadequate water intake can have a variety of negative effects on health, including on mood. Pross et al. (2014) conducted a week-long study to assess the impact of water consumption on mood. Participants were divided into two groups according to their baseline water consumption: high-volume drinkers (> 2 L/day) and low-volume drinkers (<1.2 L/day). High-volume drinkers decreased their water intake to 1 L/day for the last 3 days while low-volume drinkers increased their intake to 2.5 L/day. The results showed that an increase in water intake had especially beneficial effects on moods of habitual low-volume drinkers, and a decrease in water intake had detrimental effects for habitual high-volume drinkers who experienced reduced feelings of calmness, satisfaction, and positive emotions. These results are consistent with the findings of Masento, Golightly, Field, Butler, and van Reekum (2014) who reviewed studies on dehydration and mood. Masento et al. discovered that dehydration decreased mood and could also have an effect on cognitive performance. In some studies of dehydrated individuals, cognitive performance remained unchanged while mood declined, and in other studies cognitive performance declined while mood declined. These findings highlight that mood states are sensitive to changes in hydration state and can occur whether cognitive performance declines or not. **Potential Mechanism.** According to Masento et al., when the body is in a state of dehydration, many substrates and neurotransmitters are influenced by circulating hormones involved in fluid imbalance such as vasopressin (antidiuretic hormone) and

angiotensin. Increased circulation of these hormones can cause metabolic stress and lead to increased levels of cortisol. In addition to hormones involved in fluid imbalance, serotonergic and dopaminergic systems can also be affected by dehydration. One of the roles of serotonergic and dopaminergic systems is to modify blood-brain barrier permeability. Sustained modification of these systems can lead to central nervous system dysfunction and decrease levels of serotonin and dopamine (Masento et al., 2014). These modulations are just two of the many that play a role in how dehydration can affect mood.

Dietary Fiber. Fiber is the nondigestible form of carbohydrates and lignin from plant sources. Dietary fiber can either be insoluble or soluble. Insoluble fiber does not dissolve in water and increases fecal bulk, while soluble fiber dissolves in water and can act as a prebiotic which has many effects on mood (see 'The Influence of Food on Gut Bacteria and Mood' below). Dietary fiber, both insoluble and soluble, has a plethora of actions within the body: it increases fecal bulk and reduces transit time of feces through the bowel, increases excretion of bile acid, estrogen, and fecal procarcinogens and carcinogens, lowers serum cholesterol, slows glucose absorption and improves insulin sensitivity, lowers blood pressure, promotes weight loss, inhibits lipid peroxidation, and produces anti-inflammatory effects (Farooqui, 2015). The role that fiber plays in affecting mood can be either direct or indirect. For example, fiber intake is associated with anti-inflammatory effects which can reduce stress and therefore improve mood, while a deficiency can lead to an increased risk of coronary heart disease, type II diabetes, obesity, and some cancers (Farooqui, 2015), all of which can cause stress and increase risk of depression.

Mechanism. Because fiber has antioxidant effects (Farooqui, 2015), it aids in reducing metabolic stress. Metabolic stress can lead to inflammation and an increase in cortisol, so the

antioxidant effects of fiber can reduce inflammation and stress and therefore decrease the resulting negative mood that comes with inflammation (Farooqui, 2015).

Sugars & Saturated Fat. Vermeulen et al. (2017) say a diet high in saturated fat and added sugar is linked to an increased risk of depression. **Potential Mechanism.** According to Li et al. (2017), diets high in added sugar and saturated fat are associated with higher levels of inflammation and subsequent brain atrophy, which are positively associated with depression.

Aspartame. Aspartame is a common artificial sweetener found in soft drinks and diets high in aspartame are associated with an increased risk of depression. **Potential Mechanism**. Aspartame can be metabolized into phenylalanine, aspartic acid, and methanol. Phenylalanine can then be naturally converted to tyrosine. According to Farooqui (2015), these amino acids are intimately involved in the production of neurotransmitters such as dopamine, norepinephrine and serotonin. In excess, phenylalanine can block the transport of important amino acids to the brain, contributing to a reduction in dopamine and serotonin that can then lead to chemical imbalances associated with depression, mood and emotional disorders, and anxiety.

Omega-3-Fatty Acids. Omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are high in seafood, and adequate intake of PUFAs are associated with a decreased risk of depression. Flaskerud reviewed clinical studies regarding PUFAs in depressed subjects and the studies demonstrated lower concentrations of omega-3 PUFAs in plasma or red blood cell membranes of depressed subjects. Additionally, Tsai, A., Chang, T., & Chi, S. (2012) found an association between adequate intakes of PUFAs and a decreased risk of depression in a 10-year prospective study. Li et al.

(2017) also found that high consumption of PUFAs are associated with a decreased risk of depression. **Potential Mechanism**. According to Li et al. (2017), PUFAs have anti-inflammatory properties to reduce stress. They may also contribute to brain functioning and serotonin neurotransmission. Li et al. also notes that there is evidence to suggest that adding PUFAs to antidepressants may improve mood in depression.

Alcohol. Alcohol is a depressant and the relationship is bidirectional (e.g. drinking can lead to depression, and depression can lead to drinking to cope). When it comes to consumption of alcohol, intensity opposed to frequency is a better predictor for the risk of depression. Excess alcohol intake is described as more than two drinks per day for men and one drink per day for women and is associated with an increased risk of depression (Awaworyi Churchill & Farrell, 2017). According to Awaworyi Churchill and Farrell, alcohol and depression presents two major conclusions: attempts to cope with depression may lead individuals to alcohol abuse and alcohol consumption can lead to depression due to its various psychological effects and impacts on mental health. Additionally, excess alcohol intake can lead to disruptions in jobs and relationships, which could increase the risk for depression. **Potential Mechanism.** Microglia are brain cells involved in neuroimmune signaling, and according to Walter, Vetreno, and Crews (2017), innate signaling molecules such as cytokines and chemokines are constitutively expressed in microglia. These cells are activated by both alcohol and stress. Therefore, alcohol may induce stress-related feelings through a mechanism that mocks the stress response. Additionally, alcohol may increase the risk of depression by increasing gut permeability. Walter et al. found that the combination of stress and alcohol increased blood endotoxin by increasing gut permeability, allowing bacterial leakage into peripheral circulation. Circulating endotoxins

are known to increase stress hormones, such as ACTH and corticosterone, as well as brain proinflammatory cytokines.

Micronutrients and Mood

Vitamins. Poor mood has been associated with deficiency of a number of key vitamins. For one, Li et al. (2017) and Harris et al. (2011) both found that inadequate intake of vitamin B9 (folate) is associated with an increased risk of depression. Harris et al. found that inadequate intake of vitamin B12 (cobalamin) is associated with an increased risk of depression while inadequate intake of vitamin D is associated with anxiety as well as depression. The team of researchers conducted a randomized, double-blind, placebo-controlled trial to test the use of multivitamins and their effect on mood. They found that supplementation with a multivitamin was effective in reducing depression, anxiety, and stress compared to a placebo. **Potential Mechanism.** Vitamins have various roles in the body and the mechanism of how they impact mood is still largely unclear. Vitamin D is shown to decrease inflammation and therefore reduce inflammation (Li et al., 2017), whereas a deficiency in folate may result in increased homocysteine concentrations and reduced availability of S-adenosylmethionine, which in turn are suggested to play a critical role in the pathophysiology of depression (Li et al., 2017).

Minerals. Acting as electrolytes, cofactors, and antioxidants are a few of the multitude of functions that minerals play. Minerals such as magnesium, zinc, selenium, and iron have been known to have an impact on mood (Harris et al., 2011, Tarleton et al., 2017). Magnesium is typically found in dark leafy greens and legumes, and inadequate intake is associated with an increased risk of depression (Tarleton et al., 2017, Rajizadeh et al., 2017). **Potential**

Mechanism of Magnesium. While association between magnesium and depression is well documented, the mechanism is largely hypothetical. Magnesium plays a role in many of the pathways, enzymes, hormones, and neurotransmitters involved in mood regulation (Tarleton et al., 2017). It is a calcium antagonist which regulates the flow of calcium into the neuron. In low magnesium states, high levels of calcium and glutamate may deregulate synaptic function, resulting in depression. Depression and magnesium are also both associated with systemic inflammation (Rajizadeh, Mozaffari-Khosravi, Yassini-Ardakani, & Dehghani, 2017). Rajizadeh et al. conducted a study over the course of two months in which participants with depression and low levels of magnesium were split into two groups: one group was given a 500 mg magnesium supplement to meet the recommended dietary allowance and the other group was given a placebo. This study indicated that daily consumption of 500 mg magnesium oxide tablets for individuals with depression and low levels of magnesium resulted in improvement in both the depression and the status of magnesium in their bodies. Rajuzadeh et al. also noted that magnesium supplementation increased expression of the BDNF gene to a similar effect of some antidepressants. Therefore, adequate magnesium intake may be an effective alternative in treating depression. Additionally, Li and colleagues (2017) found that adequate intake of dietary zinc and iron were associated with a decreased risk of depression. **Mechanism of zinc**. There are several proposed mechanisms for the inverse relationship between zinc and depression. According to Li and colleagues (2017) the hippocampus is susceptible to zinc deficiency. Zinc typically can inhibit the activation of N-methyl-D-aspartate (NMDA) receptors when consumed in adequate amounts. When levels of zinc are low, stress-related neurotoxicity occurs due to expression of NMDA receptors. Additionally, Li and colleagues explained that inadequate zinc

intake can influence brain derived neurotrophic factor (BDNF) activity. Levels of BDNF are typically decreased in patients with depression. Downregulation of BDNF decreases the neurogenesis signaling pathways and neuronal plasticity which can accompany depression. Furthermore, zinc can decrease metabolic stress and inflammation, which are known to increase risk of depression (Li et al., 2017). **Mechanism of Iron**. Iron is an essential trace element which is required for normal cellular function and DNA synthesis. One hypothetical mechanism for how adequate iron intake can decrease the risk of depression is that it plays a role in the oxygenation of brain parenchyma and the synthesis of neurotransmitters such as dopamine and serotonin (Li et al., 2017).

Dietary Patterns and Mood

Western Diet. According to Farooqui (2015), a high calorie diet, also known as the Western diet, "provides about 50% of total daily calories from refined carbohydrates, 35% calories from fat and refined oils, and 15% from proteins of animal origin". A Western diet typically contains high amounts of processed macronutrients, sodium, refined grains, and hydrogenated fats, while being low in fiber, fruits, and vegetables. Farooqui says long term consumption of a Western diet increases the risk of developing obesity and depression. Like alcohol and depression, the relationship between diabetes and depression is bidirectional. Patients with depression have an increased risk of developing type two diabetes, and patients with diabetes have a significantly increased risk of developing depression (Farooqui, 2015). Additionally, Tsai et al., (2012) and Li et al., (2017) found that a Western diet of processed or fried foods, refined grains, sugary products and beer was associated with an increased risk of depression. **Potential Mechanism**. There are many potential mechanisms for how a Western diet can increase risk of depression and

they are mostly related to the high prevalence of added sugar and saturated fat. For one, a Western diet with excess sugar and saturated fat can increase cortisol which increases risk for depression (Vermeulen et al., 2017, Li et al., 2017). Additionally, Farooqui (2015) explained that a Western diet can induce metabolic imbalances due to changes in cortisol, glucose, insulin. Metabolic imbalance is associated with higher levels of low-grade inflammation and subsequent brain atrophy which are associated with an increased risk of depression (Li et al., 2017). Li et al. also explained that a Western diet with high sugar intake is associated with an increased risk of depression due to altered endorphin levels and oxidative stress.

Mediterranean Diet. According to Tsai et al. (2012), a Mediterranean diet is associated with adequate intakes of fruits, nuts, vegetables, cereals, legumes, fish, and other important sources of nutrients, and is associated with a decreased risk of depression. **Potential Mechanism.** A Mediterranean diet is low in added sugar, saturated fat, and refined grains; all of which are associated with an increased risk of depression due to subsequent stress and metabolic imbalance (Vermeulen et al., 2017, Li et al., 2017). Aside from lacking components that may contribute to depression, this diet is high in components that are associated with a decreased risk like fruits, vegetables, fish, and whole grains. Fruits and vegetables are high in antioxidants which can decrease oxidative stress, and fish are high in PUFAs which have antiinflammatory properties (Li et al., 2017). Additionally, diets high in whole grains can produce neuroprotective effects which can influence the onset and development of metabolic and neurological disorders including obesity and depression (Farooqui, 2015).

Ketogenic Diet. The ketogenic diet and its proposed health benefits has been controversial, though recent research suggests it may be an effective diet in improving mood. The diet is

defined as a high fat, low protein, low carbohydrate diet. According to Arab, Mehrabani, Moradi, and Amani (2019), it reproduces the metabolic state of fasting and can exert a beneficial impact on negative mood. **Potential Mechanism.** Arab et al. concluded that a ketogenic diet could stabilize blood-glucose level and also reduce hunger, showing that this diet can play a role as mood stabilizer and antidepressant. A stable blood glucose level can prevent the cycle between blood sugar spikes and stress by keeping blood sugar levels stable (Flaskerud, 2015).

Intermittent Fasting. Intermittent fasting (IF) is a dietary pattern that is based on time intervals and is defined as periods of fasting followed by a feeding window. Periods of fasting can vary and there are different types of intermittent fasting. The 16:8 pattern allows an eight-hour feeding window each day, the 20:4 pattern allows a four-hour window, and alternate day fasting (ADF) allows eating every other day. The goal of intermittent fasting is to reach a calorie deficit so large that it cannot be overcome during feeding times. This diet is often used to achieve weight loss and is associated with many positive outcomes such as decreased body fat, increased lean body mass, increased insulin sensitivity, increased vigilance, and a decreased risk of depression (Jia & Le, 2015, Fond et al., 2013, Hussin et al., 2013). **Potential Mechanism.** Intermittent fasting leads to a multitude of metabolic effects, most of which are due to a lack of food components that are associated with an increased risk of depression. Without food components like added sugar and saturated fat, less metabolic stress is accrued resulting in a decreased risk of depression (Li et al., 2017). One side effect, however, is thought to be responsible for a majority of the benefits seen with IF: autophagy. Autophagy is a mechanism in which the body recycles old proteins, cell parts, and cells and is induced when caloric needs are not met by food. This recycling is associated with a decreased risk of depression for a few

reasons. For one, Jia and Le (2015) explained that autophagy has antidepressant effects. Antidepressants are commonly used in the treatment of patients with depression, and the underlying mechanisms are also related to inducing autophagy. Jie and Le explained that the neuronal autophagy signaling network is implicated in the mechanisms of some antidepressants. Additionally, Mattson et al. (2017) found that autophagy and intermittent fasting can reduce inflammation and therefore decrease stress and the risk of depression.

The Influence of Food on Gut Bacteria and Mood

Probiotics directly introduce beneficial bacteria such as Lactobacilli and Bifidobacteria into the gut. Prebiotics (e.g., galacto-oligosaccharides) support the growth of such bacteria. Gut bacteria are affected by the consumption of certain foods and have many functions: they enhance fecal bulk, produce vitamins endogenously, and produce hormones and neurotransmitters (Sarkar et al., 2016).

Probiotics. Sarkar et al. (2016) explained that Bifidobacteria and Lactobacilli do not possess pro-inflammatory lipopolysaccharide chains, so their establishment in the gut does not trigger immunological reactions. Sarkar et al. also reviewed a study that concluded consumption of probiotics decreased risk of depression in a healthy sample of participants. The study was a randomized and double-blind design in which healthy male and female volunteers consumed either a mixture of probiotics or a placebo over 30 days. After the 30-day period, participants completed a range of self-report measures on mood and distress, and urine samples were collected to evaluate cortisol levels. Participants that consumed probiotics showed significant declines in self-reported negative mood and distress compared to the control group. Participants

also had decreased urinary cortisol compared to the control group, which is suggestive of reduced stress.

Prebiotics. According to Sarkar et al., (2016) prebiotics also can reduce cortisol and the risk of depression. The team of researchers reviewed the first human study to examine the psychophysiological effects of prebiotics in which healthy male and female participants consumed either prebiotics or a placebo. In comparison to the control group, participants who consumed B-GOS (a prebiotic) showed a reduced waking-cortisol response, which is a biomarker of emotional disturbances such as depression. Additionally, participants completed an emotional dot-probe to measure anxiety and depression. Consumption of prebiotics, specifically B-GOS, was associated with reduced attention and reactivity to negative emotions. Reduced attention to negative stimuli may suggest a neurocognitive mechanism through which psychobiotics improve mood (Sarkar et al., 2016).

Gut Bacteria and the Brain. The mechanisms through which gut bacteria exert their effects on mood remain poorly understood. There are some studies that provide potential mechanisms for humans, though the majority of research is based on rodent models. **Hormones.** Both probiotics and prebiotics increase production of short-chain fatty acids (SCFAs), though prebiotics may have a greater effect. SCFAs interact with enteroendocrine cells and catalyse the release of gut hormones such as cholecystokinin, peptide YY, and glucagon-like peptide- 1 (Sarkar et al., 2016). SCFAs and gut hormones enter circulation and can migrate into the central nervous system. **Neurotransmitters.** Both probiotics and prebiotics enhance neurotransmitter production in the gut. These neurotransmitters include dopamine, serotonin, noradrenaline, and GABA, which likely modulate neurotransmission in the enteric nervous system (Sarkar et al.,

2016). **Potential Mechanism.** The microbiome appears to play a substantial role in generating metabolites that enter circulation and exert a range of consequences outside the gut. Though the mechanism is largely unknown as to how probiotics and prebiotics can improve mood, Sarkar et al. (2016) reviewed a study in which the impact of the microbiome of germ-free mice and normally colonized mice was studied. Germ-free mice had 40% greater plasma tryptophan than normally colonized mice, but the normal mice had nearly three times greater plasma serotonin levels than the germ-free mice. This suggests that gut bacteria affect the metabolism of tryptophan into serotonin in gut cells.

Dietary Recommendations and Risk of Depression				
Food Group	Recommendation for Men and Women		Depression Risk due to Underconsumption	Depression Risk due to Overconsumption
Vegetables	2.5 c-eq/day		Increased	N/A
Fruits	2 c-eq/day		Increased	N/A
Grains	6 oz-eq/day		N/A	Increased*
Dairy	3 c-eq/day		N/A	Increased*
Protein Foods	5.5 oz-eq/day		N/A	Increased*
Oils	27 g/day		N/A	Increased
Nutrient	Men	Women	Depression Risk due to Underconsumption	Depression Risk due to Overconsumption
Carbohydrates	130 g/day	130 g/day	N/A	Increased
Fats	10-35% kcal	10-35% kcal	N/A	Increased
Protein	56 g/day	46 g/day	N/A	Depends
Fiber	34 g/day	28 g/day	Increased	N/A
Water	3.7 L/day	2.7 L/day	Increased	None
Added Sugar	<10% kcal	<10% kcal	None	Increased
Saturated Fat	<10% kcal	<10% kcak	None	Increased
Sodium	<2300 mg	<2300 mg	None	N/A
Alcohol	N/A	N/A	None	Increased

Recommendations are based on a 2000 kcal diet for men and women ages 19-30. **N/A** means there not enough evidence to suggest an increased or decreased risk of depression. **None** means there is no known risk of depression.

*Excess grains are associated with an increased risk if they are refined grains, excess dairy is associated with an increased risk if it is high-fat dairy, excess protein foods are associated with an increased risk if they are red meat.

https://health.gov/our-work/food-nutrition/2015-2020-dietary-guidelines

Discussion

A Western-style diet that is high in refined grains, added sugar, and processed foods is associated with an increased risk of depression (Li et al., 2017), while a Mediterranean-style diet that is high in whole grains, fruits, and vegetables is associated with a decreased risk (Tsai et al., 2012). Food components that are associated with an increased risk of depression when consumed in excess include saturated fat, red meat, added sugar, refined grains (Li et al., 2017).

These food components can increase metabolic stress and lead to inflammation which is associated with an increased risk of depression (Li et al., 2017). Alcohol consumed in excess is defined as more than two drinks per day for men and 1 drink per day for women and is associated with an increased risk of depression (Awaworyi et al., 2017). Food components that are associated with a decreased risk of depression when consumed in adequate amounts include fruits, vegetables (White et al., 2013), whole grains, water, fiber, vitamins (Tsai et al., 2012), and minerals (Harris et al., 2011, Tarleton et al., 2017). Fruits, vegetables, fiber, and vitamins are known to decrease inflammation and therefore decrease the risk of depression (Li et al., 2017). Fasting is found to induce autophagy which can decrease metabolic stress and decrease risk of depression (Jia, Le, 2015). The role that the gut microbiome plays in depression has to do with the production of neurotransmitters by gut bacteria and the conversion of tryptophan into serotonin in gut cells (Sarkar et al., 2016).

Conclusion

The type of dietary pattern and its associated risk of depression depends on the contents of the diet. A healthy dietary pattern that includes adequate intake of the major food groups and micronutrients while limiting nutrients of concern (e.g. added sugar, sodium, alcohol) is associated with a decreased risk of depression. Some dietary patterns that are disproportionately high in one food group (e.g. Western diet) are associated with an increased risk of depression, while others like the ketogenic diet and intermittent fasting are associated with a decreased risk of depression. These findings add to the evidence of the role of dietary patterns in the prevention

and management of depression. Further studies are required to confirm the causal relationship between dietary patterns and the risk of depression including experimental studies that isolate single nutrients and identify their associated risk of depression. Given more research is done and causal relationships are established, a healthy diet that includes foods and dietary patterns that are shown to decrease the risk of depression may be considered as viable treatment options for depression.

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Bibliography

Anderson, S., Cryan, J., & Dinan, T. (2017). *The psychobiotic revolution : mood, food, and the new science of the gut-brain connection*. Washington, DC: National Geographic Partners.

Arab, A., Mehrabani, S., Moradi, S., & Amani, R. (2019). The association between diet and mood: A systematic review of current literature. Psychiatry Research, 271, 428–437. https://doi.org/10.1016/j.psychres.2018.12.014

Awaworyi Churchill, S., & Farrell, L. (2017). Alcohol and depression: Evidence from the 2014 health survey for England. Drug and Alcohol Dependence, 180, 86–92. https://doi.org/10.1016/j.drugalcdep.2017.08.006

Farooqui, A. (2015). High Calorie Diet and the Human Brain Metabolic Consequences of Long-Term Consumption (1st ed. 2015.). https://doi.org/10.1007/978-3-319-15254-7

Flaskerud, J. (2015). Mood and Food. *Issues in Mental Health Nursing*, *36*(4), 307–310. https://doi.org/10.3109/01612840.2014.962677

Fond, G., Macgregor, A., Leboyer, M., & Michalsen, A. (2013). Fasting in mood disorders: neurobiology and effectiveness. A review of the literature. Psychiatry Research, 209(3), 253–258. https://doi.org/10.1016/j.psychres.2012.12.018

Harris, E., Kirk, J., Rowsell, R., Vitetta, L., Sali, A., Scholey, A., & Pipingas, A. (2011). The effect of multivitamin supplementation on mood and stress in healthy older men. Human Psychopharmacology-Clinical And Experimental, 26(8), 560–567. https://doi.org/10.1002/hup.1245

Howes, R. (2016). Food and Mood. *Psychotherapy Networker*, *40*(6). Retrieved from http://search.proquest.com/docview/1867912866/

Hussin, N., Shahar, S., Teng, N., Ngah, W., & Das, S. (2013). Efficacy of Fasting and Calorie Restriction (FCR) on mood and depression among ageing men. The Journal of Nutrition, Health & Aging, 17(8), 674–680. https://doi.org/10.1007/s12603-013-0344-9

Jia, J., & Le, W. (2015). Molecular network of neuronal autophagy in the pathophysiology and treatment of depression. Neuroscience Bulletin, 31(4), 427–434. https://doi.org/10.1007/s12264-015-1548-2

Lemmens, S., Born, J., Martens, E., Martens, M., Westerterp-Plantenga, M., & Tomé, D. (2011). Influence of Consumption of a High-Protein vs. High-Carbohydrate Meal on the Physiological Cortisol and Psychological Mood Response in Men and Women. *PLoS ONE*, *6*(2), e16826. https://doi.org/10.1371/journal.pone.0016826

Li, Y., Lv, M., Wei, Y., Sun, L., Zhang, J., Zhang, H., & Li, B. (2017). Dietary patterns and depression risk: A meta-analysis. *Psychiatry Research*, *253*, 373–382. https://doi.org/10.1016/j.psychres.2017.04.020

Li, Z., Li, B., Song, X., & Zhang, D. (2017). Dietary zinc and iron intake and risk of depression: A meta-analysis. Psychiatry Research, 251, 41–47. https://doi.org/10.1016/j.psychres.2017.02.006

Masento, N., Golightly, M., Field, D., Butler, L., & van Reekum, C. (2014). Effects of hydration status on cognitive performance and mood. 111(10), 1841–1852. https://doi.org/10.1017/S0007114513004455

Mattson, M., Longo, V., & Harvie, M. (2017). Impact of intermittent fasting on health and disease processes. Ageing Research Reviews, 39, 46–58. https://doi.org/10.1016/j.arr.2016.10.005

Neubert, C. (2018). MOOD FOOD. *Natural Solutions*, (202), 26–27. Retrieved from http://search.proquest.com/docview/2036982986/

Opie, R., Itsiopoulos, C., Parletta, N., Sanchez-Villegas, A., Akbaraly, T., Ruusunen, A., & Jacka, F. (2017). Dietary recommendations for the prevention of depression. Nutritional Neuroscience, 20(3), 161–171. https://doi.org/10.1179/1476830515Y.0000000043

Privitera, G., King-Shepard, Q., Cuifolo, K., & Doraiswamy, P. (2019). Differential food intake and food choice by depression and body mass index levels following a mood manipulation in a buffet-style setting. Journal of Health Psychology, 24(2), 199–208. https://doi.org/10.1177/1359105316650508

Pross, N., Demazières, A., Girard, N., Barnouin, R., Metzger, D., Klein, A., … Guelinckx, I. (2014). Effects of changes in water intake on mood of high and low drinkers. PLoS ONE, 9(4), e94754. https://doi.org/10.1371/journal.pone.0094754

Rajizadeh, A., Mozaffari-Khosravi, H., Yassini-Ardakani, M., & Dehghani, A. (2017). Effect of magnesium supplementation on depression status in depressed patients with magnesium deficiency: A randomized, double-blind, placebo-controlled trial. Nutrition, 35, 56–60. https://doi.org/10.1016/j.nut.2016.10.014

Rintamäki, R., Preedy, V., Watson, R., & Martin, C. (2011). Dietary Amino Acids and Mood. In Handbook of Behavior, Food and Nutrition (pp. 565–576). https://doi.org/10.1007/978-0-387-92271-3_37

Sarkar, A., Lehto, S., Harty, S., Dinan, T., Cryan, J., & Burnet, P. (2016). Psychobiotics and the Manipulation of Bacteria–Gut–Brain Signals. Trends in Neurosciences, 39(11), 763–781. https://doi.org/10.1016/j.tins.2016.09.002

Tarleton, E., Littenberg, B., Maclean, C., Kennedy, A., & Daley, C. (2017). Role of magnesium supplementation in the treatment of depression: A randomized clinical trial. PloS One, 12(6), e0180067. https://doi.org/10.1371/journal.pone.0180067

Tsai, A., Chang, T., & Chi, S. (2012). Frequent consumption of vegetables predicts lower risk of depression in older Taiwanese - results of a prospective population-based study. Public Health Nutrition, 15(6), 1087–1092. https://doi.org/10.1017/S1368980011002977

Vermeulen, E., Stronks, K., Snijder, M., Schene, A., Lok, A., de Vries, J., … Nicolaou, M. (2017). A combined high-sugar and high-saturated-fat dietary pattern is associated with more depressive symptoms in a multi-ethnic population: the HELIUS (Healthy Life in an Urban Setting) study. 20(13), 2374–2382. https://doi.org/10.1017/S1368980017001550

Walter, T., Vetreno, R., & Crews, F. (2017). Alcohol and Stress Activation of Microglia and Neurons: Brain Regional Effects. Alcoholism: Clinical and Experimental Research, 41(12), 2066–2081. https://doi.org/10.1111/acer.13511

White, B., Horwath, C., & Conner, T. (2013). Many apples a day keep the blues away – Daily experiences of negative and positive affect and food consumption in young adults. British Journal of Health Psychology, 18(4), 782–798. https://doi.org/10.1111/bjhp.12021

Young, H., Cousins, A., Watkins, H., & Benton, D. (2017). Is the link between depressed mood and heart rate variability explained by disinhibited eating and diet? *Biological Psychology*, *123*, 94–102. https://doi.org/10.1016/j.biopsycho.2016.12.001