Nutritional Neurosciences

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Nutrition and Psychiatric Disorders

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Nutritional Neurosciences

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In deep respect and with true love, I would like to dedicate this book to my best friend, forever and always, MYSELF.

Wael Mohamed
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To my mentor and colleague, the chair of the Department of Biochemistry and Molecular Genetics at the American University of Beirut, Professor Julnar Usta, whose honesty and knowledge touch the heart and mind of everyone working with her, I dedicate this humble work.

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Nutrition and Anxiety Disorders

Ramli Musa

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Abstract Food and anxiety are interrelated to each other in various relationships. Food may worsen the anxiety symptoms; hence, modification of food intake would certainly help in alleviating some of the anxiety symptoms at a certain degree. Certain foods, particularly organic in nature, are also effective in helping the patients to go through the treatment course and fasten the recovery process. It may not be the only key solution or main treatment, but modification in dietary intake would help the sufferers. In this chapter, we outline how anxiety and types of food are interrelated and different types of food could help or worsen the anxiety symptoms. Also, at the end of this chapter, we outline the effects of microbiome on human guts and anxiety symptoms.

Keywords Anxiety · Depression · Dietary · Panicogenic · Modification

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13.1 Introduction

13.1.1 What Are Anxiety Disorders?

Anxiety disorders are considered to be among common psychiatric disorders in our society that cause significant impact on an individual bearing the disease as well as causing burden on the country as a whole. The prevalence is ranging from 10 to 25%, and this is almost as common as depression. If we list down the common psychiatric disorders in our populations, anxiety and depression are the leading morbidity burden to the health system (Faravelli et al. 1989; Wittchen and Hoyer 2001).

It is reported by the National Health and Morbidity Survey (NHMS) in 2015 that there has been a triple increase of the prevalence of mental health issues in Malaysia from 10.7% in 1996 to 29.2% in 2016. Among the examples, disorders which are categorized under anxiety disorders are panic disorder, post-traumatic stress disorder (PTSD), generalized anxiety disorder (GAD), social phobia, and agoraphobia. It is mentioned that since mental disorders such as depression, dysthymia, and anxiety account for a big proportion of the world's disease problem, they place a large burden on the healthcare system. The global burden of mental disorders was updated by the WHO World Mental Health that poor mental health is very prevalent across the world, with depression and anxiety being the leading common psychiatric disorders (National Health and Morbidity Survey 2019).

Symptoms of anxiety disorders can be divided into emotional symptoms (feeling anxious, worries, fear) and also somatic symptoms such as palpitation, tremor, gastric problem, urinary frequency, loss of appetite, chest tightness, and shortness of breath. Bear in mind that most of the depression cases are also presented with symptoms of anxiety, and these two disorders (anxiety and depression) are closely related. In general, anxiety and depression share many common issues such as similar psychodynamic etiology (lack of serotonin and noradrenaline in the brain) and commonly coexist together. They also share similar treatment modality, that is, antidepressants. Antidepressants are indicated as first-line treatment for both disorders (Clemente-Suárez 2020).

Since anxiety and depression may affect appetite and cause weight loss, these illnesses would have some effects on patient dietary intake, and types of food could influence the symptoms.

13.1.2 How Does Anxiety Could Be Related to Nutrition?

Let us try to figure out the first question. The first question is this: Is there any correlation between food intake and anxiety? It is very clear that the answer is YES. They are interrelated based on various ways.

Firstly, anxiety disorders are commonly presented with gastrointestinal track (GIT) symptoms. Among the common GIT symptoms presented by anxiety are gastric pain, gastroesophageal reflux disease (GERD), and diarrhea. To my observation and as commonly reported, GERD is one of the common symptoms reported by patients with anxiety, and many of my anxiety patients meet gastroenterologists (medical specialists in stomach and gastric problem) but to no improvement although they were given medication. It is not uncommon also for many of them to go through some investigation procedures such as oesophagogastroduodenoscopy (OGDS) to investigate the possibility of having gastritis or ulcer. It does not stop there; they are also prescribed many expensive medicines, particularly the H1 antagonist drugs for gastric pain or complete antibiotic course for *Helicobacter pylori* bacteria. However, the symptoms will not resolve or will just partially resolve (Ünal et al. 2013).

Patients with anxiety disorders are commonly considered as potential for "doctor shopping." The illness itself may exhibit with multiple body or somatic complaints. Among the common physical symptoms are numbness, instability (ataxia), tinnitus, urinary frequency, diarrhea, and body weakness. Based on my observation, I have many patients presented to me who met various specialists before coming to see a psychiatrist. Among other specialists that they had met are cardiologist (for symptoms of palpitation, chest tightness), gastroenterologist (for gastric pain), ENT specialist (for tinnitus and instability), and urologist (for urinary frequency) (Clemente-Suárez 2020).

Second way of correlation is that some of the food may worsen the anxiety; among them are caffeine and spicy food. Food that contains high level of caffeine is considered panicogenic in nature or a panic stimulant (Buhiji et al. 2020).

Growing evidence suggests that there is a link between food and mental health. Recently, the relationship between food intake and mental well-being has been gaining considerable interest. Reports by El-Merabbi et al. from the study done on animals suggest that the food the people consume interacts not only with the enteric nervous system but also with the central nervous system via neural, neuroendocrine, neuroimmune, and humoral links (Sarris et al. 2016; El-Merahbi et al. 2015).

The etiology of anxiety is very complex, be it from the biological, psychological, and social factors involved in inducing the mental illness. Study done by Hjorth et al. (2021) using PET scan proved that serotonin and dopamine play a role in the development of anxiety and its severity. It is proven by the Global Burden of Disease Study, 2010, that 18.9% of all years lived with disability are attributed with mental disorders. It is mentioned that since mental disorders such as depression, dysthymia, and anxiety account for a big proportion of the world's disease problem, they place a large burden on the healthcare system. The global burden of mental disorders was updated by the WHO World Mental Health that poor mental health is very prevalent across the world, with depression and anxiety being the leading common psychiatric disorders (Addolorato et al. 1996).

Anxiety is mainly stimulated by sympathetic nervous system; hence, any food or drug (such as amphetamine) that may stimulate this system, could worsen the anxiety. One of the anxiety symptoms is the feeling of food caught in your throat.

Other anxiety symptoms are gastroesophageal reflux disease (GERD), regurgitation of food from stomach and from esophagus. Anxiety is strongly correlated with digestive system, heartburn, coughing, chest pain, problem swallowing, vomiting, sore throat, and hoarseness of voice (Butwicka et al. 2017).

Some foods can be a protective factor for not just anxiety, but also depression. In a study on the association of food groups with depression and anxiety disorders, Deborah Gibson-Smith found that lower depression and anxiety severity was associated with greater consumption of non-refined grains, fruits, and vegetables. Other types of food which have shown to be negatively associated with anxiety are fish and low-fat dairy. The mechanism is that these foods cause elevations of polyunsaturated fat/saturated fat ratios and have low trans fat.

13.1.3 Food and Brain Functions

It is well known that mood can affect the food choice of a person, using food as a comfort factor during stressful events, but there is also a mechanism that food triggers anxiety. Bad habits, such as poor nutrition, become one of the factors that create a biological basis for different pathologies and psychopathologies. People with nonoptimal nutrition profiles have been implicated with various underlying pathologies of behavioral health disorders due to insufficient nutrients essential in the neuroendocrine system. According to Sarris et al., nutrients which include tryptophan, vitamin B6, vitamin B12, folic acid, phenylalanine, tyrosine, histidine, choline, and glutamic acid are important for the development of neurotransmitters such as serotonin, dopamine, and norepinephrine, which are involved in mood, appetite, cognition, behavior (El-Merahbi et al. 2015), learning (El-Merahbi et al. 2015), and glucose homeostasis (El-Merahbi et al. 2015).

Lee and Choi (2017) also explained how the hypothalamic-pituitary-adrenal axis (HPA) controls the secretion of cortisol and causes changes to the neurological system. It plays an important role in regulating human's emotion and memory since the hippocampus that regulates these functions in the human brain is connected anatomically with the HPA axis.

Hassan et al. (2014) added that anxiety bio-mechanism is being linked to inflammation and oxidative stress. It has been consistently found to modulate the anxiety-related brain region such as in the anterior cingulate cortex, amygdala, and insula, which may have resulted from cytokine effects on the monoamine and glutamate. When there is increased circulating inflammatory cytokines, there is increase in oxidative stress and there will be generation of reactive oxygen species (ROS) as well as reactive nitrogen species. This can be linked with panic disorders. Dietary intake is one of the sources of production of reactive oxygen species.

Hassan et al. (2014) also noted that antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, when in the body, reduce molecules or nonenzymatic antioxidants. It also creates a defense mechanism that avoids the negative effects of ROS. However, in excessive concentration of

antioxidants, the cell reaches the antioxidative capacity and eventually leads to oxidative stress to the cell, damaging the cellular components.

It is stated by Bakhtiyari et al. that food and diet factors may be effective to regulate mental health during a lifetime from the adjustment of the risk of the brain changes. However, the mental disorders itself can affect the mood of the person, and this influences the habits of food intake, appetite, and choices of food that eventually creates an imperfect cycle by influencing the amount of nutrients, so this results in the exacerbation of the psychiatric illness itself.

13.1.4 Can Diet Modification or Healthy Diet Improve the Anxiety?

To answer whether diet modifiation could improve the anxiety, the answer is definitely yes. I strongly believe in the slogan of "we are what we eat." Many studies in the past mainly explored the associations between the effects of nutritious food and depression as compared to anxiety. These are among the modifications that we could adopt to improve the anxiety symptoms:

1. Food content: it is very important for anxiety sufferers to make some adjustment to the types of their diet. The main principle is healthy diet. Among the approaches in this strategy are putting more fiber in your food and including more grains, vegetables, and fruits in the daily dietary plan.
2. Second approach is to make some modifications in the diet habit; the slogan of "eat less but frequent" can be quite helpful in reducing the stomach discomfort among anxiety patients.

The underlying cause of anxiety is diminishing of serotonin and melatonin neurotransmitters in the brain. Hence, any food that could increase serotonin or melatonin would have a positive effect on anxiety. Among foods that were cited to improve mild-to-moderate anxiety were banana, plum, tomato, and pineapple (Feldman and Lee 1985).

The diets that are associated with lower anxiety levels are those with healthy diet patterns, the Mediterranean diet, ketogenic diets, and gluten-free diets (GFD) in specific groups of people. Clemente-Suárez (2020) have proven that people with existing anxiety had improved their anxiety state and anxiety traits after 6 weeks of nutritional recommendation interventions with healthy diet patterns. However, it is stated by Boerema et al. (2016) that they expect relapse of the symptoms after 6 weeks of nutritional intervention, but no relapse of symptoms will be seen only after 8 months of completing the nutritional intervention. It is postulated that good nutrition provides the anti-inflammatory effect to the subject, giving reason why 8 months is needed to observe the effect and also adherence to the intervention.

Food that is considered to improve diet quality and mood resembles food mostly from the Mediterranean diet. These diets focus on lean meats, fish, green leafy

vegetables, legumes, and nuts. Such food groups are rich in B-group vitamins, proving the possibility that there is a relationship between vitamin B intake and benefit to the brain health and mood. Sarris et al. (2016) stated that vitamin B is a cofactor in synthesizing and regulating the dopamine and serotonin neurotransmitters that help in clinical depression and anxiety, which are targeted by antidepressant medication. According to Sarris et al. and Scholey (2017), this has increased the acknowledgement that nutritional deficiency or suboptimal nutritional level heightens the risk for someone to have mood disorders and other psychiatric problems.

According to Ludwig (2020), a ketogenic diet with low amounts of carbohydrate consumption is good for weight mass optimization among people with psychiatric disorders for their possible anxiolytic effects. The diet is described as being low-carb high-fat (LCHF). By doing this, fat comprises >70% and sugar 5–15% of the daily food intake and the rest of the calories are supported with protein. There is my type of LCHF diet such as Atkins diet, modified Atkins, low glycemic index treatment diet, and medium-chain triglyceride ketogenic diet. Forte et al. (2016) in their writing suggested that for people adapting to a diet that induces ketosis, there is inhibition of glycolysis in the brain that reduces the excitation of the neuron by potentiation of GABA transmission via the steroid pathway. Nuss (2015) from their study done on animal subjects stated that there is reduction of anxiety level with infusions of GABA or GABA-A receptor agonists into the amygdala and there are anxiogenic effects upon infusion with GABA antagonists.

Gluten-free diet is also a good medium for people with intestinal disease such as celiac disease and also inflammatory bowel disease in terms of relieving the anxiety level. Since 1996, it has been proven by Addolorato et al. (1996) that people with inflammatory bowel disease and celiac disease are in a higher anxiety state compared to those healthy individuals. Butwicka et al. (2017) also proved that pediatric patients with celiac disease have a 1.4-fold higher anxiety level compared to the normal children. The study also concluded that malabsorption can be linked with brain function. So, there are various studies done across the years worldwide involving participants with IBD and celiac disease in the effects of gluten-free diet (GFD) in their anxiety level. Saadati et al. found that GFD reduces the somatic symptoms such as abdominal pain and bloating in IBD patients, which in turn reduces the anxiety level in Iran participants. The detailed effect of GFD on physiological symptoms remains unclear, but Van Hees et al. (2013) stated that the patients on GFD are linked with better psychological outcomes but only if the participants keep up with the GFD for more than 5 years. This might be due to the restoration of the intestinal lining, which improves the health of the patient as a whole, and this process takes years. The study also assumed that people with continuously untreated malabsorption disturbances can induce depressive symptoms. However, Rostami et al. (2022) reported that GFD, regardless of the duration, does not improve the anxiety level. It postulated that the anxiety symptoms might occur due to the diagnosis of the chronic disease itself, so GFD would not improve the anxiety symptom.

13.2 Food Improving Anxiety

Nguyen et al. (2017), in their study which has excluded people currently treated for anxiety and patients currently taking antidepressants, reported a positive association between consumption of fruits and vegetables, which acts as a protective factor, and anxiety. Same result was reported by Saghafian et al. (2018), Wu et al. (2018), Hodge et al. (2013), and Rienks et al. (2013). Study by Kose et al. (2021) showed that adolescents aged above 45 years old with lower consumption of fruits and vegetables have higher anxiety levels. Lee and Wan Muda on Malaysian adults proved that the intake of fruits and vegetables does not reach the recommendations.

As per Messamor and McNamara, it is suggested by the American Psychiatric Association for mentally ill persons to take at least 1 g of EPA and DHA daily in line with the American Heart Association. Martínez-Cengotitabengoa and González-Pinto mentioned that since 20% of the brain is composed of DHA, DHA constructs the cellular structure of the brain. All the omega-3 formulations give anti-inflammatory mechanisms helping to maintain the brain cells' stability linking to the proper function of neurotransmitters such as serotonin and dopamine.

Hassan et al. (2014) mentioned in their writing that fresh apples and a diet rich in sucrose and honey improve antioxidant status and have anxiolytic effects. Certain antioxidants such as vitamin C, vitamin E, carotenoids, thiol antioxidants for example glutathione, thioredoxin, and lipoic acid, natural flavonoids, melatonin and other compounds are good for improving defense mechanism against ROS.

It is mentioned in the Epidemics by Hippocrates that clean keto version is mostly based on healthy macronutrients such as minimally processed food, for example fat sources such as egg yolk and polyunsaturated fatty acids such as olive, canola, and grapeseed oil, oily fish, and nuts. Fish, meat, cheese, and egg whites are recommended for protein sources. Carbohydrates are limited to mostly unprocessed food and low glycemic index from green vegetables, brown rice, and others.

People adapting to the LCHF diet need a professional dietician's guidance. The previously mentioned divalent ions linked to anxiety can also be supplied in the LCHF menu, such that zinc can be gained through zinc-rich foods such as oysters and other seafood, magnesium can be found mostly in green leafy vegetables, while selenium is found in seafood, poultry, fish, and eggs, which are all favorable choices in LCHF diets.

Young et al. found that there is a significant relationship between vitamin B supplementation and stress level but not with anxiety and depression, so it is suggested that vitamin B supplementation is not worth it for people with anxiety and depression. The same study also exposed that most of the studies done in the previous years used excessive vitamin B supplementation exceeding the recommended daily intakes between 2 and 300 times.

13.3 Dietary Patterns Causing Anxiety

The dietary patterns associated with higher anxiety level include unhealthy diet patterns, diet with recurrent fluctuation of glycemic level, and vegetarian diet. A 1-month study done by Robert et al. during the first lockdown due to COVID-19 in 2019 showed that people stayed at home and adapted with new eating behavior. Some people adapted unhealthy dietary patterns with less fruits and vegetables and more processed meat and snacking, and some people adapted healthy dietary patterns which are more pasta or rice and less snacking. Results showed that people with unhealthy diets are associated with higher anxiety levels compared to those with healthy dietary patterns.

According to Firth et al., repeated fluctuation of blood glucose can increase the risk of developing anxiety. These include high intake of sugar and refined carbohydrates, lower fiber intake, irregular meals, and no caloric restriction. High dietary glycemic load and the resultant compensatory mechanism to reduce the plasma glucose trigger the secretion of autonomic counter-regulatory hormones including cortisol, adrenaline, growth hormone, and glucagon. Towler et al. found that these hormones may cause changes in anxiety, irritability, and hunger. This statement is supported by Lee and Choi (2017); the pathologies occur due to hypothalamic-pituitary-adrenal axis (HPA), which controls the secretion of cortisol and causes changes to the neurological system. The hippocampus, having an anatomical link with the HPA axis, plays a vital function in controlling human's emotion and memory.

In this situation, people with existing diabetes mellitus are vulnerable to develop anxiety due to poor glycemic control. Study done by Hendrieckx et al. suggested that there is a bidirectional relationship between diabetes mellitus and anxiety. In this context, patients with anxiety symptoms have higher risk of developing type 2 diabetes mellitus, and patients with type 2 diabetes mellitus have increased risk to develop anxiety disorders. A study done on Chinese individuals by Kose et al (2021) had shown that high-anxiety individuals aged under 45 years had significantly higher mean consumption of added simple sugars. High suger level has been associated with anxiety. However on other hand low sugar also could be related to anxiety. According to Seaquist et al., repeated low blood sugar levels are also associated with anxiety. In conclusion, moderate and well control of sugar is the best approach in anxiety control.

Woo, Kwok, and Celermajer stated that a vegetarian diet is well known due to the principle to have only vegetables and fruits in their diets, but people with this kind of diet may have insufficient essential nutrients such as vitamin B12, which eventually induces anxiety disorders. Lakin et al. also postulated that vegetarian diets also lack chain omega-3 fatty acids (EPA and DHA) that are a protective factor against anxiety. They concluded that this occurs due to the difference in bioavailability of certain nutrients such as iron, which is higher in animal sources than in plants. Therefore, people adapting vegetarian diets have limited absorption of iron from their diets.

13.4 Food Causing Anxiety

People take energy drinks to enhance alertness, physical ability, and cognitive enhancement. According to Bodenmann et al., in energy drinks, caffeine is the main component that causes GABA inhibition, phosphodiesterase modulation, ryanodine receptor activation, and A2 adenosine receptor antagonist. Caffeine presents naturally with different concentrations in many foods such as coffee, tea, and cocoa. Jin et al. stated that energy drinks have more caffeine than coffee and Coca-Cola and can cause attention problems, headache, anxiety, insomnia, overexcitement, and hyperactivity to the extent of causing death when taken excessively or being drunk with alcohol. Willson stated that it had also been used legally and safely as a mild stimulant before. However, caffeine consumption exceeding more than 1–1.5 g/day can cause caffeinism or caffeine poisoning. When this occurs, people consuming caffeine will experience anxiety, agitation, insomnia, gastrointestinal disorder, tremors, and mental disorders.

Richards and Smith also added that caffeine consumption can cause anxiety and increase the risk of relapse in secondary school children. Observational study done by Jahrami et al. on university students in Bahrain shows that students with higher caffeine intake have more anxiety-related symptoms such as headache, panic, feeling trapped or caught, worrying too much about things, anxiety, and psychological distress. Study done by Jin et al. on Korean adolescents stated that groups with higher caffeine intake are associated with higher anxiety levels.

Preservatives, flavoring agents, sweeteners, and coloring agents are commonly used as food additives in food manufacturing. Iwasaki et al. mentioned that antioxidants were added to food to avoid the degradation of food and fading of food's color. These antioxidants accumulate the reactive oxygen species (ROS) and stop ROS-induced oxidative DNA damage. However, mineral and trace elements are also found in many food and diet supplements such as iron and copper. When this ion interacts with antioxidants, the process produces ROS and causes DNA degradation in vitro. Study done by Bakhtiyari et al. (2013) proved that the level of anxiety level was obvious in people taking more processed food even after adjusting for the total calorie intake.

13.4.1 Relationships Between Caffeine and Anxiety

Based on the available evidence, the effects of caffeine to mental health are contradicting. Caffeine is said to be a mental stimulant. For this reason, it is considered as mental energy, whereby it causes increase in the level of arousal and better concentration to the extent of elevating the mood (Ferre 2008; Fredholm et al. 1999).

However, at a higher dose of caffeine, it could make the anxiety even worse. At this level, individuals would exhibit symptoms of restlessness, nervousness, panic,

insomnia, and agitation. In general, caffeine sounds good for depression as it is stimulating but not for anxiety. Based on one systematic review on the effects of caffeine on panic disorder patients, about half of the patients would experience the panic attack after consumption of caffeine. This clearly shows that caffeine could trigger the panic attack among these vulnerable individuals (Buhiji et al. 2020). Caffeine can be found naturally in beans of coffee, some fruits, and leaves. The consumers should be aware that many energy drinks and soda contain caffeine as it was added by the drink manufacturers.

13.4.2 Other Types of Food Related to Anxiety

Many studies have proven that high fiber intake such as vegetables and fruits could lower the anxiety symptoms. A study done by Deborah Gibson showed that the magnitude of ability in reducing anxiety is 0.7, which is considered a modest effect (Khan and Khan 2016).

13.5 New Food Dimension

In the recent studies on a new dimension, probiotics have been shown to have positive effects on anxiety. The effects are more apparent to be seen among healthy adults with minor A allele of rs16944. This led the scientists to further this new area of "psychobiotics" (Gualtieri et al. 2020).

Tea contains antioxidants but also contains a small amount of caffeine, which is a stimulant.

13.6 Anxiety, Stress, and Inflammation

In the recent studies, depression and anxiety happen due to abnormal response toward stress and inflammation. The fact that there was an increase in the number of people with depression and anxiety may be in part due to current lifestyle including dietary intake and social demand, which could lead to abnormal stress response. Anxious patients have been studied to have increased levels of proinflammatory cytokines compared to healthy individuals (O'Donovan et al. 2010). This inflammatory state is particularly of our concern as it may ultimately cause neuroinflammation, possibly affecting mental health. Moreover, anxiety patients may be associated with stress-induced interleukin (IL)-6 activity, which results in alteration in gene expression in monocytes as can be seen in anxiety-like behavior in mice according to the study made by Niraula et al. (2019). Plus, this population also has reduced level of microbiome-derived short-chain fatty acid

(SCFA), which is essential to prevent proinflammatory state ((Fukuda et al. 2011; Singh et al. 2010). Reduced SCFAs will also result in compromised intestinal barrier, thereby promoting microbial endotoxins to enter circulation and initiating an inappropriate immune response (Singh et al. 2010; Kelly et al. 2015).

Besides, stress often acts as a precipitator, which indirectly increases proinflammatory cytokine by dysregulating immune function as well as altering intestinal barrier permeability. The former acts as a preparation for human body to fight pathogen and helps in wound healing, while the latter is essential to increase water and sodium availability in the circulation. However, the diffusion of water and sodium into the circulation would also be accompanied by endotoxin and cause endotoxemia. This peripheral inflammation can actually induce central inflammation or neuroinflammation through the migration of activated immune cell into the brain as a result of endotoxemia. In short, stress-induced endotoxemia and increase in proinflammatory cytokine may cause neuroinflammation in brain, eventually affecting mental health.

13.7 Microbiome and Mental Health

Many points suggest that microbiome does influence mental health. First, patients with generalized anxiety disorder (GAD) have shown to have a different microbiome composition compared to healthy population. They have reduced amount of five genera, which include Faecalibacterium, *Eubacterium rectale*, Lachnospira, Butyricicoccus, and Sutterella, as compared to normal population in which 70% of them come from the two most prominent phyla Firmicutes and Bacteroides, while Proteobacteria, Actinobacteria, Fusobacteria, and Verrucomicrobia are present in reduced numbers (Jiang et al. 2018; Peirce and Alviña 2019). This change in composition of microbiome will lead to reduced short-chain fatty acid (SCFA) compounds and indirectly disrupt appropriate immune response because of impaired intestinal permeability, ultimately affecting normal brain function.

In view of recent studies that suggest that microbes play a significant role in stress response, intestinal barrier, and immune system, use of probiotics and prebiotic in an effort to improve microbiome has been done (de Vrese and Schrezenmeir 2008). Probiotics are live microorganisms to provide health benefit by altering gut microbiome, while prebiotics are dietary fiber ingested to feed and promote balanced gut microflora (de Vrese and Schrezenmeir 2008). Sudo et al. proved in their study that colonizing *Bifidobacterium infantis* strain in germ-free mice could reduce previously exaggerated response of HPA axis to normal level similar to what is seen in normal control. However, they concluded that more research still needs to be done to validate the result in humans (Sudo et al. 2004). Besides, Ait-Belgnaoui et al. stated that *Lactobacillus farciminis* administration could enhance intestinal barrier, thus preventing endotoxemia from occurring and causing neuroinflammation in the brain (Ait-Belgnaoui et al. 2014). Plus, those given *B. infantis* have more proper immune response compared to control by giving anti-inflammatory signals to

immune cells. To sum it up, prebiotic and probiotic may potentially be used to treat anxiety by improving the response to stress, intestinal barrier, and immune response.

To date, it has been recognized that physiological pathways involving inflammatory and stress responses likely play a significant role in the occurrence of anxiety and depression (Benatti et al. 2016; Bekhbat and Neigh 2018; Dantzer et al. 2011). Much research had found that microbiome does affect mental health through various mechanisms that alter the normal inflammatory and stress response, which ultimately causes increase in the level of proinflammatory cytokine compared to normal population. However, the evidence that stress-induced inflammatory response causes anxiety alone is still inconclusive as the analysis may be confounded with depression, which is a common comorbidity associated with anxiety, and due to the fact that HPA axis alteration occurs in temporary state (Peirce and Alviña 2019). Our culture and upbringing in this current era can lead to underdeveloped immune system later in life, eventually posing risk to mental health. One of them is wide consumption of fast food, which may contribute to poor microbiome health. Further research should be made on the role of probiotic, prebiotic, and other possible approaches that can improve microbiome health so that a more effective targeted treatment can be achieved.

13.8 Conclusion

There are close relationships between anxiety symptoms and food that we are taking. Some types of food may give good effects to anxiety, and in contrast some are detrimental. It depends on the ingredient of food. Anxiety patients are advisable to do some modifications in their diet, particularly to avoid food containing panicogenic ingredients such as caffeine.

However, those who exhibit severe symptoms of anxiety and depression which affect their daily function are advisable to seek a proper medical treatment, particularly treatment with antidepressants. With dietary modification alone, it is very unlikely that the person could easily be cured from the illness.

Nutritional psychiatry is the new emerging field focusing on diet intervention as adjunct to pharmacological therapy and psychotherapy in treating people with anxiety. This includes diet counseling, education, and food as intervention to anxiety disorders. The proposed mechanism of relationship between food and anxiety includes the development of neurotransmitters that are involved in emotion regulation such as serotonin and dopamine which are lower in people with anxiety. Other mechanisms are HPA axis regulation that produces cortisol which is the stress hormone, inflammation and oxidative stress that trigger anxiety, and also production of ROS.

Lifestyle changes need to be promoted to the community so that people can eat healthily together, avoiding the development of noncommunicable diseases that are now existing, becoming a big burden to Malaysian health care. The dietary pattern that should need to be promoted to reduce the exacerbation and induction of anxiety

includes healthy diet patterns, the Mediterranean diet, ketogenic diets, and gluten-free diets (GFD) in specific groups of people. They also need to avoid unhealthy diet patterns, diet with recurrent fluctuation of glycemic level, and vegetarian diet.

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