

Effect of the Nutritional Supplements in Mental Disorders – A Review

By

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requirements for the degree of
Bachelor of Pharmacy (Hons.)

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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing the degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

The thesis titled “Effect of Nutritional Supplements in Mental Disorders –A Review” submitted by Lamiya Alam Meem (14346023) of Summer 2014 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Hons.) on January 12, 2021

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Ethics Statement

This study does not involve any kind of animal trial or human trial.

Abstract:

Mental health is a major health issue worldwide. It is important to find the prevalence of mental disorders because it decreases quality of life, promote disability, and increase mortality. Furthermore, it can cause different social problems which decrease the productivity at work and increases suicidal or criminal behavior. Bipolar disorder, major depression, schizophrenia, and obsessive compulsive disorder (OCD) currently are the major mental disorders found around the world. Most antidepressants and other prescription drugs are used to cure mental disorders but they have several side effects which cause noncompliance, thus discourage patients to take medications. Studies have shown that general populations have shortage of daily supplements like vitamins, minerals, and omega-3 fatty acids and if they are administered with other medications they can effectively reduce the symptoms of mental disorder. The aim of this review is to emphasize which dietary supplements can aid in the treatment of the common mental disorders.

Keywords: Mental disorder; depression; nutritional supplements; antipsychotics drugs; antidepressant drug; omega 3 fatty acid.

Dedication

I dedicate my dissertation to my loving parents.

Acknowledgement

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List of Acronyms

EPA	Eicosapentaenoic Acid
DHA	Docosahexaenoic Acid
PTSD	Post-Traumatic Stress Disorder
ADHD	Attention Deficit Hyperactivity Disorder
AD	Alzheimer's Disease
LCPUFA	Long Chain Polyunsaturated Fatty Acids
OCD	Obsessive Compulsive Disorder
RDA	Recommended Dietary Allowance
AA	Arachidonic Acid
ASD	Autism Spectrum Disorder
POMS-B1	Profile of Moods States Bipolar Form
PPARs	Peroxisomal Proliferator-Enacted Receptor
ADD	Attention Deficit Disorder

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Chapter 1

Introduction

1.1 Mental disorder

Depression leads to mental disorder and is considered as one of the major concerns for disability. Globally, 264 million (0.25 billion) people are suffering from depression and women are more prone to be affected than men (WHO, 2020). There are several symptoms of depression like: sadness and sorrows, lack of interest in any topic, guilty feelings, sleep disturbance, anorexia, fatigueness and lack of concentration. There may be various physical complaints but there is no physical cause. Depression may come back and may sustain for a long time. This really hampers the daily lifestyle at work or at school. According to the studies depression may even leads to suicide (Wang et al., 2007; Stengel, 1959). There may be some different presentations regarding depression and are characterized by a single or combination of abnormal ideas, unrealistic thoughts / perceptions, undefined emotions, abnormal behaviour and abnormal relationships with others. There are different types of mental disorders like: depression, bipolar disorder, schizophrenia, psychosis, autism and dementia. Mental disorder is getting burdened day by day and affecting negatively the health and economic condition.

Prevention programmes have been shown to reduce depression, both for children (e.g. through protection and psychological support following physical and sexual abuse) and adults (e.g. through psychosocial assistance after disasters and conflicts). Mild to moderate depression can be reduced with talking therapies, such as cognitive behaviour therapy or psychotherapy. Antidepressants can be an effective form of treatment for moderate to severe depression but they should not be used for treating depression in children and are not the first line of treatment in adolescents, among whom they should be used with caution (Wang et al., 2007; Stengel, 1959).

Bipolar or mania disorder affects about 45 million people worldwide (WHO, 2019). It typically consists of both manic and depressive episodes separated by periods of normal mood. Manic episodes involve elevated or irritable mood, over-activity, rapid speech, inflated self-esteem and a decreased need for sleep. People who have manic attacks but do not experience depressive episodes are also classified as having bipolar disorder (Wang et al., 2007; Stengel, 1959).

20 million people worldwide are affected with schizophrenia. Schizophrenia is characterized by abnormal thought/perception, confusion and disorientation in language. There are some common and mostly occurred psychotic experiences which include hallucinations and delusions. Such kind of distinguishable mark may result in lack of access to health and in social services. These types of people are at high risk of being humiliated and may be subjected to human rights violations, such as long-term confinement in institutions (Wang et al., 2007; Stengel, 1959).

Worldwide, approximately 50 million people have dementia. Dementia is usually of a chronic or progressive nature in which there is deterioration in cognitive function (i.e. the ability to process thought) beyond what might be expected from normal ageing. It affects memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgement. The impairment in cognitive function is commonly accompanied, and occasionally preceded, by deterioration in emotional control, social behaviour, or motivation.

Dementia is caused by a variety of diseases and injuries that affect the brain, such as Alzheimer's disease or stroke. Though there is no treatment currently available to cure dementia or to alter its progressive course, many treatments are in various stages of clinical trials (Wang et al., 2007; Stengel, 1959).

Developmental disorder basically means the disability and pervasive developmental disorders like autism. The onset usually appears in childhood and may be sustained in adulthood. Cognitive functioning and adaptive behavior are one of the mental development areas which

may be defined as impaired skill. Lack in intelligence reduces the ability to adapt to the daily life demands (Wang et al., 2007; Stengel, 1959).

Symptoms of pervasive developmental disorders, such as autism, include impaired social behaviour, communication and language, and a narrow range of interests and activities that are both unique to the individual and are carried out repetitively. Developmental disorders often originate in infancy or early childhood. People with these disorders occasionally display some degree of intellectual disability (Wang et al., 2007; Stengel, 1959).

1.2 The need of new approaches in mental disorders

Most medicines that are used to treat mental disorders have several side effects which are the main cause of non-compliance. In some cases, this non-compliance becomes the reason for committing suicide or institutionalized.

Table 1: Some medicines and their side effects are listed in the table below –

Categories	Class	Generic name of the drug	Side effects
Antidepressant	Selective serotonin reuptake inhibitors (SSRIs)	Citalopram	<ul style="list-style-type: none"> ➤ Nausea and vomiting ➤ Weight gain ➤ Diarrhea ➤ Sleepiness ➤ Sexual problems ➤ Thoughts about suicide or dying
		Escitalopram oxalate	
		Fluoxetine	
		Fluvoxamine	
		Paroxetine HCI	
		Sertraline	
		Desvenlafaxine	

	Selective serotonin & norepinephrine inhibitors (SNRIs),	Desvenlafaxine Succinate	<ul style="list-style-type: none"> ➤ Attempts to commit suicide ➤ New or worsening depression ➤ New or worsening anxiety ➤ Feeling very agitated or restless ➤ Panic attacks ➤ Trouble sleeping (insomnia) ➤ New or worsening irritability ➤ Acting aggressively, being angry, or violent ➤ Acting on dangerous impulses ➤ An extreme increase in activity and talking (mania) ➤ Other unusual changes in
		Duloxetine	
		Levomilnacipran	
		Venlafaxine	
	Novel serotonergic	Vortioxetine	
		Vilazodone	
	Monoamine oxidase inhibitors (MAOIs)	Isocarboxazid	
		Phenelzine	
		Selegiline	
		Tranylcypromine	
	Tetracyclic antidepressants (noradrenergic and specific serotonergic antidepressants (NaSSAs))	Mirtazapine	
		L-methylfolate	
		Bupropion	

			behaviour or mood
Anti-anxiety	Selective serotonin reuptake inhibitors (SSRIs)	Citalopram	<ul style="list-style-type: none"> ➤ Risk of addiction ➤ Drowsiness, ➤ Poor concentration, ➤ Irritability
		Escitalopram oxalate	
		Fluoxetine	
		Fluvoxamine	
		Paroxetine HCl	
		Sertraline	
Anti-seizure		Gabapentin	<ul style="list-style-type: none"> ➤ Attempts to commit suicide ➤ Feeling very agitated or restless ➤ Panic attacks ➤ Insomnia
		Pregabalin	
Antipsychotics	Atypical Antipsychotic	Phenothiazines Thioxanthenes Butyrophenones Dibenzothiazepine	<ul style="list-style-type: none"> ➤ Sedation ➤ Weight gain ➤ Changes in blood sugar or cholesterol ➤ Drowsiness ➤ Rapid or irregular heartbeat ➤ Decrease in sexual interest or ability ➤ Skin rashes or skin sensitivity to the sun ➤ Muscle spasms
	Typical Antipsychotics	Clozapine Risperidone Olanzapine	

			<ul style="list-style-type: none"> ➤ Restlessness and pacing ➤ Slowing down of movement and speech
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Due to these increased side effects and according to several studies daily intake like vitamins, minerals and other related products used to boost the nutritional content of the diet. Studies have also revealed that patients extremely lack of nutrition when they suffer for extreme mental disorder. So further study is required determine the best suitable dose and supplements.

1.3 Aim of the study:

The aim of this review is to aid the search for most effective supplement that can be used with the conventional treatment of mental disorder.

1.4 Objective of the study:

The objective of the review is to–highlight the importance of nutritional supplements which has been reported to decrease the symptoms mental disorder. The other objective is to understand the mechanism of nutritional supplements to control mental disorder.

Chapter 2

Nutritional supplements and mental health:

2.1 Role of nutritional supplements in mental health

One of the mostly known polysaccharide is carbohydrate which exerts its diversified role in human. Mostly they affect the mood and the behavior. The release of insulin has been triggered due to consumption of carbohydrates (Gibson, 2007). A very effective hormone is insulin; produced by beta cell of pancreas and helps the blood sugar level to enter the cell through GLUT pathway where the glucose has been processed to make ATP the source of energy. It also helps the tryptophan to enter the brain. Tryptophan has role on neurotransmitters levels. Restricted intake of low carbohydrate may lead to depression. This is because carbohydrate rich food triggers the feeling of wellbeing which is basically promoted by brain chemicals like serotonin and tryptophan. Low glycemic index (GI) foods (whole grains, pasta, etc.) are more likely to provide sustained effect comparing the foods with high GI index like sweets (Gibson, 2007).

Proteins are building block of life and are made of amino acids. Among 20 amino acids 12 are manufactured in the body and remaining amino acids needs to be supplied through diet. Meat, milk and other dietary products have high quality protein. Plant proteins such as beans, peas, and grains may contain low in one or two essential amino acids. According to different studies low protein intake may effect the brain functioning and mental health. As most of the neurotransmitter are made up of amino acids, thus low protein intake can affect the function of brain. Dopamine and serotonin are two important neurotransmitters which are respectively made of tyrosine and tryptophan. So if there is any lack of these amino acids occurred in the body then they won't be able to produce dopamine and serotonin. Low level of these neurotransmitter's causes depression (Grantham-McGregor & Baker-Henningham, 2005).

Omega 3 fatty acids has the vast effect on mental disorders. Brain membranes are composed of fatty acids. According to different studies gray matter of brain is composed of 50%

polyunsaturated fatty acid among which 33% belong to the omega family. Majority of these fatty acid are supplied through diet. In an experiment of (Peet & Stoke, 2005) it was observed that omega-3 fatty acid especially alpha-linolenic acid (ALA) helps to develop the structure and function of the brain. Bruinsma and Taren of University of Arizona College of Public Health, Tucson, USA revealed that depression is co related with decreased level of plasma cholesterol. One important factor behind these are the quantity and ratio of omega-6 and omega-3 polyunsaturated fatty acids (PUFA) which alter the biochemical and biophysical properties of cell membranes (Peet & Stokes, 2005).

Deficiency of dietary omega-3 fatty can accelerate cerebral aging by preventing the renewal of membranes. However, the respective roles of the vascular component and the cerebral parenchyma have not yet been clearly resolved. In a coherent experiment which was carried out on *x-vivo* cultured brain cells and on *in vivo* brain cells, they found out that the nature of polyunsaturated fatty acids (in particular omega-3) determines the visual, cerebral, and intellectual abilities of infants (both premature and term).

According to a study reported in Neuropsychobiology, nine vitamins were ingested over 10 times of normal recommended dietary allowance (RDA) for one year showed improvement of mood in both men and women. This mood improvement was particularly associated with improved vitamin B2 and B6 status. Poor vitamin B1 was linked with poor mood in women and after 3 months of vitamin B1 supplementation showed an improvement of mood.

Thiamine is known to modulate cognitive performance particularly in the geriatric population (Lewis et al., 2013).

Clinical trials have indicated that vitamin B12 delays the onset of signs of dementia and blood abnormalities. Studies have revealed that people who has cognitive disorder can improve their condition with the supplementation with cobalamin which basically enhances cerebral functions as well as language functions.

It has been observed that depressed patient has 25% low blood folate levels than healthy patients. A controlled study has been reported to have shown that 500 mcg of folic acid

enhanced the effectiveness of antidepressant medication. Though it is not clear yet depression causes shortage of folate in the body or primary folate deficiency produces depression and its symptoms.

Many studies (e.g. Davidson et al., 2013) have showed that chromium has significant role in controlling depression.

Iodine plays a very important role in mental health as it ensures energy metabolism of the cerebral cell through thyroid hormone. During pregnancy, the dietary reduction of iodine induces severe cerebral dysfunction, eventually leading to cretinism.

Iron provides oxygen and produces energy in the cerebral parenchyma with the help of cytochrome oxidase. It also helps in the synthesis of myelin sheath and different neurotransmitter. Attention deficit disorder is found in children who have shortage of iron. Iron concentration is very important in fetus as it is directly linked with the IQ of the child. Infantile anemia can cause cognitive impairment as well. Research has also showed that women are more likely to depress compared to men and it is assumed to be linked with shortage of iron level in the body as the deficiency causes fatigue and depression (Kieling, 2011).

Lithium, a monovalent cation, was first discovered and defined by Johan August in 1817. Lithium is used in depression, schizoaffective disorder, aggression, impulse control disorder, eating disorders and in Attention deficit disorder (ADDs). Lithium is also considered as a mood stabilizing agent (Mauer, 2014).

Different five studies of Dr. David Benton of the University of Wales identified that low selenium intake is associated with depression and studies with selenium revealed that improved concentration of selenium can diminish anxiety and improves mood.

Zinc protects brain cells from free radicals and different studies showed that oral zinc can increase the effectiveness of antidepressant therapy (DiGirolamo & Ramirez-Zea, 2009).

Several studies have revealed the full genetic potential of the child for physical development and mental development may be compromised due to deficiency (even subclinical) of micronutrients. When children and adolescents with poor nutritional status are exposed to

alterations of mental and behavioral functions, they can be corrected by dietary measures, but only to certain extent. In aged people deficiency of antioxidants and micronutrients like trace elements, vitamins, and nonessential micronutrients such as polyphenols may not be able to protect against free radical which may initiate different brain diseases.

2.2 Mechanism of action of different nutritional supplements in different mental disorders

In the case of antidepressants, there are varieties of theories for the mechanism. One theory says that it may be because eicosapentaenoic acid gets converted into different chemicals of the brain like prostaglandins and leukotrienes (Vazquez et al., 2017).

According to another theory EPA and docosahexaenoic acid works by transmitting signals in the brain by activating peroxisomal proliferator-activated receptors (PPARs) and by inhibiting G-protein and protein kinase C and different ion channels (Firch, 2016).

Excess level of acetylcholine and vanadium is a major cause of depression and mania. A double-blind, placebo-controlled study showed that three grams of vitamin C can decrease the symptoms of mania by protecting the body from the damage that is caused due to excess vanadium. Taurine is an amino acid derived from cysteine which exerts a calming effect in the brain and also can control excess acetylcholine levels in the body. Studies have shown that shortage of amino acid increases the manic episodes of bipolar patients (Firch, 2016).

In schizophrenia, patients seem to have disturbed amino acid metabolism as well as lower serotonin level in the body. Different studies showed that high doses of glycine can reduce the symptoms of schizophrenia. According to double-blind, randomized, placebo-controlled and open-label clinical studies daily intake of approximately two grams of EPA with the existing treatment can effectively decrease the symptoms of schizophrenia (Firch, 2016).

Tryptophan supplements increase the serotonin levels which are a precursor of serotonin. According to different studies increased serotonin level will help to reduce the symptoms of OCD (Firch, 2016).

Methylphenidate is a CNS stimulant approved for treating narcolepsy and attention deficit hyperactivity disorder (ADHD). Methylphenidate inhibits dopamine and norepinephrine reuptake, increased dopaminergic and noradrenergic activity in the prefrontal cortex may explain its efficacy in ADHD (Firsch, 2016).

A lack of essential nutrients is known to contribute to the onset of poor mental health in people suffering from anxiety, depression, bipolar, schizophrenia, ADHD, etc. Generous intakes of the necessary nutrients will help our body's normal functioning, including the brain and enhance health in various ways. The rational use of these supplements, combined with a healthy diet, may contribute substantially to health promotion and disease prevention. A supplement will generally provide 100 percent of the daily recommended allowance for all vitamins and minerals. Among the three types of omega 3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) found in fish oil are vital for normal brain development and functioning.

Table 2: Effects of omega-3 fatty acid in mental disorder

Nutritional Medicine	Mental Disorders	Effect (Yes or No)	Reviewed Article
	Depression	Yes	Some studies showed that the depressive symptoms of most participants were improved with the combination of EPA and DHA (both are found in fish oil). By means of the analysis concluded the current purpose appears helpful and positive for the use of fish oil and omega-3 fatty acid within the medication, treatment and

Omega-3 fatty acids			management of depression (Lia et al., 2019).
	Bipolar disorder or Manic depression	Yes	It has beneficial effects on manic or bipolar disorder. 6 out of 10 patients' data has shown positive effects and supported that it has tremendous effect and potential treatment capacity on mania disorder (Rutkofsky et al., 2017; Saunders et al., 2016).
	Schizophrenia	Yes	The efficacy of intervention with omega-3 fatty acids could significantly reduce the severity of antipsychotic symptoms and relapse rates in first-episode schizophrenia (Xu et al., 2019).
	Dementia	Yes	Diminished levels of omega-3 fatty acid is related with age-related intellectual decay or dementia, for example, Alzheimer's infection (Cole et al., 2009).
	Developmental disorder	Yes	LCPUFA and DHA, are highly required to develop human brain. Nonetheless, the proof base for a useful impact of dietary LCPUFA on child's advancement is slender and has conflicting discoveries. Proof for a beneficial part of omega-3 fatty acid in cognitive functioning primarily comes from concentrations

			in certain patient groups or children with issues (ADHD, neurophysiologic Disorders, n-3 inadequacy (Osendarp, 2011)).
	Autism	Yes	Our meta-analysis showed significant positive treatment effects of omega-3 fatty acids compared to placebo not only on core symptoms of autism such as lethargy (social withdrawal) but also on other related secondary behavioral problems such as hyperactivity (Cheng et al., 2017).
	Post-traumatic stress disorder	Yes	This study showed a protective effect of omega-3 fatty acid against PTSD-induced short and long-term memory impairment, possibly through preventing alterations in oxidative stress biomarkers in the hippocampus of PTSD animals (Alquraan, 2019).
	Panic disorder	Yes	According to different studies, treatment with omega-3 polyunsaturated fatty acids may help to diminish indications in patients with clinical nervousness. Su and partners found that omega-3 PUFAs were related with a huge decrease in nervousness side effects contrasted

			and fake treatment controls (Ross, 2009).
	Attention deficit hyperactivity disorder	Yes	A later audit on omega-3 pills in 2017 demonstrated more noteworthy guarantee. Of the 16 examinations inspected, 13 indicated humble advantages in ADHD manifestations, including hyperactivity, impulsivity, consideration, visual learning, word perusing, and memory (Cassel, 2019).

Table -3: Effects of carbohydrates in mental disorder

Nutritional Medicine	Mental Disorders	Effect (Yes or No)	Reviewed Article
	Depression	Yes	When we eat carbs, our body makes more serotonin which is a feel good hormone. When we are depressed, Carbs attempt to undo the depressed mood (Wurtman & Wurtman, 1995).
	Bipolar or mania	No	Not found
	Schizophrenia	Yes	Schizophrenia is associated with addiction,

Carbohydrates			Obesity and diabetes. The common link drawn between eating, psychosis and mid-brain dopaminergic reward, logically, suggests that psychosis may be improved, by modifying carbohydrate consumption (Thornley et al., 2011).
	Dementia	Yes	A high carbohydrate and low protein diet tend to improve brain health in mice has sparked hopes. Carbohydrates could help ward off dementia (Robinson, 2016).
	Developmental disorder or autism	No	Not found
	Post-traumatic stress disorder	No	Not found
	Panic disorder	No	Not found

Table 4: Effects of amino acid in mental disorder

Nutritional Medicine	Mental Disorders	Effect (Yes or No)	Reviewed Article
Amino acid	Depression	Yes	The cascade depletion effect caused by inadequate or imbalanced amino acid precursors may result in worsening of depressive mood symptoms (Young et al., 1985).
	Bipolar or mania	Yes	Amino acids have beneficial effects on depressed mood, anxiety and insomnia in bipolar patients (Rao et al., 2008)
	Schizophrenia	Yes	Disturbance in amino acid levels has been linked to pathophysiology of schizophrenia (Saleem et al., 2017).
	Dementia	No	Not found
	Developmental disorder or autism	Low	Not sufficient
	Post-traumatic stress disorder	No	Not found
	Panic disorder	No	Not found

Table 5: Effects of B-complex in mental disorder

Nutritional Medicine	Mental Disorders	Effect (Yes or No)	Reviewed Article
B-complex	Depression	Yes	Low levels of vitamin B12 and other B vitamins may be linked to depression, but more research is needed (Wolffenbuttel, 2019) .
	Bipolar or mania	Yes	Vitamins B1, B6, and B12, in particular, have been shown to decrease the symptoms of bipolar disorder such as mood swings, depression, anxiety, fatigue, irritability, the inability to focus, and a loss of appetite (Patrick, 2017) .
	Schizophrenia	Yes	A review of worldwide studies has found that add-on treatment with high-dose B vitamins including B6, B8 and B12 can significantly reduce symptoms of schizophrenia more than standard treatments alone (Firth,2017) .
	Dementia	Yes	Large doses of B-complex vitamins could reduce the

			rate of brain shrinkage by half in elderly people with memory problems and slow the progression of dementia. Large doses of B-complex vitamins could reduce the rate of brain shrinkage by half in elderly people with memory problems and slow the progression of dementia (Szczechowiak, 2019).
	Developmental disorder or autism	Yes	Low serum vitamin B12 and folic acid was associated with Autism Spectrum disorder (ASD) (Mahruba, 2019).
	Post-traumatic stress disorder	No	Not found
	Panic disorder	No	Not found

Table 6: Effects of chromium in mental disorder

Nutritional Medicine	Mental Disorders	Effect (Yes or No)	Reviewed Article
Chromium	Depression	No	Not found
	Bipolar or mania	Yes	Early research suggests that taking 600–800 mcg of chromium chloride daily for up to 2 years can decrease the frequency of severe mood disturbances in people with bipolar disorder that is resistant to treatment (Bim Jumah, 2020) .
	Schizophrenia	No	Not found
	Dementia	No	Not found
	Developmental disorder or autism	No	Not found
	Post-traumatic stress disorder	No	Not found
	Panic disorder	No	Not found

Table 7: Effects of iodine in mental disorder

Nutritional Medicine	Mental Disorders	Effect (Yes or No)	Reviewed Article
Iodine	Depression	Yes	Low selenium and iodine levels may contribute to the development of anxiety and depression, independent of thyroid functions, in patients with euthyroid nodular goiter. In these patients, selenium and iodine replacement may be useful for the prevention of anxiety and depression, especially in deficient region (Turan, 2020).
	Bipolar or mania	No	Not found
	Schizophrenia	No	Not found
	Dementia	No	Not found
	Developmental disorder or autism	Yes	Children born with iodine deficiency often have mental retardation. Iodine deficiency in early postnatal life can result in degrees of intellectual dysfunction and autism. Iodine deficiency is the number one cause of intellectual disability worldwide (Corbier, 2012).

	Post-traumatic stress disorder	No	Not found
	Panic disorder	No	Not found

Table 8: Effects of iron in mental disorder

Nutritional Medicine	Mental Disorders	Effect (Yes or No)	Reviewed Article
Iron	Depression	Yes	The patients affected by iron deficiency anemia showed many mood and behavioral signs and symptoms similar to the depressed individuals (Shariatpanaahi, 2007).
	Bipolar or mania	Yes	Iron deficiency can cause mood swings, a key factor in the disease progression of bipolar disorder (Fishcher, 2020).
	Schizophrenia	Yes	In previous animal studies, induced iron deficiency has been reported to alter both dopaminergic and serotonergic transmission in the brain. This iron-dopamine interaction might therefore conceivably account for symptoms in

			patients with schizophrenia (Kim, 2018).
	Dementia	Yes	There is an imbalance in iron homeostasis in Alzheimer's disease (AD). Excessive iron contributes to the deposition of β -amyloid and the formation of neurofibrillary tangles, which in turn, promotes the development of AD (Liu, 2018).
	Developmental disorder or autism	No	Not found
	Post-traumatic stress disorder	No	Not found
	Panic disorder	No	Not found

Table 9: Effects of lithium in mental disorder

Nutritional Medicine	Mental Disorders	Effect (Yes or No)	Reviewed Article
Lithium	Depression	No	Not found
	Bipolar or mania	Yes	Lithium is used to treat mania that is part of bipolar disorder (Burdick, 2020).

	Schizophrenia	Yes	Lithium alone is an effective treatment for schizophrenia, schizophrenia-like psychoses and schizoaffective psychoses (Burdick, 2020).
	Dementia	Yes	Those who had bought lithium at least once had the 1.5-fold higher rate of dementia than the persons not taking lithium. However, those who continued treatment with lithium had the rate of dementia decreased to the same level as that for the general population (Rybakowski, 2018).
	Developmental disorder or autism	Yes	The mood-stabilizing drug lithium eases repetitive behaviors seen in mice missing SHANK3, an autism gene, according to a new study. The findings suggest lithium can be used as a treatment for autism, even though the drug has troublesome side effects, including tremors

			and impaired (Afjeh, 2019) .
	Post-traumatic stress disorder	No	Not found
	Panic disorder	Yes	Lithium limits the amount of norepinephrine that the body can process, which decreases the severity of the anxiety symptoms caused by the body's fear response (Brown & Gerbarg, 2005) .

Table 10: Effects of selenium in mental disorder

Nutritional Medicine	Mental Disorders	Effect (Yes or No)	Reviewed Article
Selenium	Depression	Yes	Selenium deprivation leads to depressed mood, and high dietary or supplementary selenium seems to improve mood (Ranjbar, 2013).
	Bipolar or mania	Yes	The positive effect of Selenium supplementation is appeared on mood, using the Profile of Moods States-Bipolar Form (Mortazavi et al., 2015).

	Schizophrenia	Yes	Selenium concentrations in plasma and red cells were found to be significantly lower in schizophrenic patients treated with clozapine as compared with all other groups (Ranjbar, 2013).
	Dementia	Yes	Many research has shown that oxidative stress plays a key role in the development of neurodegenerative Disorders, such as Alzheimer's and Parkinson's disease. As a result, antioxidant supplements like vitamin E and selenium have been proposed to prevent dementia (Mortazavi et al., 2015).
	Developmental disorder or autism	Yes	One study from Saudi Arabia suggested that selenium is lower in children with autism, and supplementation helps decrease the increased heavy metals (lead and mercury) found in those children (Ranjbar, 2013).

	Post-traumatic stress disorder	Yes	The study concludes that there is a reliable relationship between PTSD symptoms, their severity and oxidative stress. Supplements of selenium during a mission can reduce oxidative stress and minimize incidences of PTSD as well as its severity (Mortazavi et al., 2015).
	Panic disorder	No	Not found

Table 11: Effects of zinc in mental disorder

Nutritional Medicine	Mental Disorders	Effect (Yes or No)	Reviewed Article
Zinc	Depression	Yes	Patients in Zinc group received daily supplementation with 25 mg zinc adjunct to antidepressant to treat depressive patients (Ranjbar, 2013).
	Bipolar or mania	No	Not found
	Schizophrenia	Yes	A double-blind, placebo-controlled schizophrenia study showed that 220 mg of zinc sulfate TID, used as

			an adjuvant to 6 mg/day of risperidone, produced a statistically significant improvement of positive and negative symptoms and reduced aggressive behavior (Mortazavi et al., 2015).
	Dementia	No	Not found
	Developmental disorder or autism	No	Not found
	Post-traumatic stress disorder	No	Not found
	Panic disorder	No	Not found

Chapter 3

Conclusion

From the disorders' mechanism, it is observed that those who are suffering from mental disorders may have a lack of nutrition. By including the nutritional supplement with synthetic medicine, illness and disorder can be reduced. Though all the nutritional medicine did not show efficacy against all sorts of disorders but omega-3 fatty acid showed positive impact in almost all sorts of mental illnesses. Though more and more studies are required so that psychiatrists dealing with mental disorder patients should be aware of available nutritional therapies and their appropriate doses, and possible side effects. By the addition of nutritional medicine with conventional treatments results of noncompliance will be reduced. Like other therapies nutritional therapy should be supervised and doses should be adjusted as necessary to achieve optimal results.

Chapter 4

Future Studies:

Researchers have found and studies have shown that there are effects of nutritional supplement to improve mental disorders but no specific dose line has been developed which may be used by psychiatrists or physicians to prescribe a patient. Further studies are required to determine the dose so that a patient can take an accurate amount of dose for their treatment and avoid overdose related adverse effects.

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