

# Role of Omega 3 Fatty acids, Vitamin D, Vitamin B12, Vitamin B6 and Folate in Mental wellbeing- A Short review of Literature

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## Abstract

Neuropsychiatric conditions have been linked to around 14 percent of the global disease burden, mainly due to the chronically debilitating nature of depression and other widespread mental disorders, alcohol and drug use disorders, and psychosis. The science and lay press have confirmed that vitamin D is an important factor that can have major health benefits in the prevention and treatment of many chronic diseases. Most people have inadequate vitamin D levels in this country. This is also relevant for people with depression and other mental illnesses as well. Inadequate food consumption, lifestyle or other factors are a major causes of Vitamin D deficiency. Successful diagnosis and treatment of insufficient levels of vitamin D in people with depression and other mental illnesses could be a simple and cost-effective therapy that could enhance the long-term health outcomes and quality of life of patients. It is now well known that omega-3 fatty acids are important for physical health, and there is growing evidence that omega-3 fatty acids may also be important for mental health. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the two major omega-3 fatty acids in fish oil, have essential biological roles within the CNS. DHA is a major structural component of neuronal membranes, and modifying the neuronal membrane fatty acid composition contributes to functional changes in the behaviour of phospholipid membrane-embedded receptors and other proteins. EPA has major physiological roles that can influence the behaviour of neurons. For innumerable aspects of brain functioning, adequate nutrition is needed. A modifiable risk factor for depression may be the poor quality of diet. The goal was to evaluate and synthesize the existing understanding of the role of nutrition in mental well-being. The risk of depression is increased by low omega-3 fatty acid status. Both fish oil and folic acid supplements have been successfully used to treat depression. The response to antidepressants is decreased by folate deficiency. Deficiencies in folate, vitamin B12, Vitamin D, Omega 3 fatty acids, Vitamin B6 tend to be more prevalent in depressed individuals than in nondepressed individuals. In this short review of Literature we have focused on role of Omega 3 Fatty acids, Vitamin D, Vitamin B12, Vitamin B6 and Folate in Mental wellbeing.

**Keywords :** Mental health, Vitamin B12, Vitamin D, Omega 3 Fatty acids, Folate, Vitamin B6

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## Introduction

Mental well-being is a core component of optimal health, and is a status that individuals can manage stress from daily living and make positive achievements pursuing public interest and contribution to the community. <sup>1</sup>

The World Health Organization (WHO) estimates that several hundred million people in the world suffer from a mental or behavioural disorder at the beginning of the new millennium. In addition, mental illnesses are the second leading cause of disability worldwide.<sup>2</sup> Mental disorders, which are the same as psychiatric disorders, are clusters of syndromes which disturb an individual's cognition, emotion regulation or behaviour. Common mental disorders include bipolar disorders (manic disorder, depression, and manic-depression), dementia, schizophrenia, and panic disorder.<sup>3</sup> Depression, the most common mental disorder, is one of the major global public health problems and projected to become the second leading cause of burden of disease by 2030.<sup>4,5</sup> Maintaining individual's mental health is important to improve personal life values, to reduce medical cost and other social expenses to deal with mental disorders, and to enhance national competitiveness. Several factors affecting the development of mental disorders include genetic factors, stress, diet, physical inactivity, drugs, and other environmental factors.<sup>6-8</sup> Among these factors, dietary factors may aggravate or ameliorate symptoms and the progression of the disorders although those are not major etiologies. Nutritional deficiencies, resulting from insufficient intake or absorption of nutrients critical to human health, are now a recognized risk factor for psychiatric disorders.<sup>9</sup> Nutritional factors having beneficial effect on mental health are polyunsaturated fatty acids (PUFAs), especially omega-3 FAs, phospholipids, cholesterol, niacin, folate, vitamin B6, vitamin B12, and vitamin D.<sup>10-13</sup>

### **Omega 3 fatty acids and mental health**

Omega-3 fatty acids play a critical role in the development and function of the central nervous system. Emerging research is establishing an association between omega-3 fatty acids (alpha-linolenic, eicosapentaenoic, docosahexaenoic) and major depressive disorder. Omega-3 PUFAs play fundamental roles in the development, functioning and aging of the brain. In humans, dietary deficiencies of omega-3 PUFAs, such as docosahexaenoic acid and eicosapentaenoic acid, have been associated with an increased risk of various mental disorders. Omega-3 fatty acids are long-chain, polyunsaturated fatty acids (PUFA) of plant and marine origin. Because these essential fatty acids cannot be synthesized by the human body, they must be derived

from dietary sources. Flaxseed, hemp, canola and walnut oils are all generally rich sources of the parent omega-3, alpha linolenic acid (ALA). Dietary ALA can be metabolized in the liver to the longer-chain omega-3 eicosapentaenoic (EPA) and docosahexaenoic acid (DHA). This conversion is limited in human beings, it is estimated that only 5–15% of ALA is ultimately converted to DHA.<sup>14</sup> Aging, illness and stress, as well as excessive amounts of omega-6 rich oils (corn, safflower, sunflower, cottonseed) can all compromise conversion.<sup>15</sup> They have long been investigated for their cardio protective and anti-inflammatory roles, which has lead to their increased use as dietary supplements.<sup>16</sup> A new application for omega-3 fatty acids has emerged recently, the treatment of certain forms of mental illness. Such a use is biologically plausible given that omega-3 fatty acids, in particular DHA, are abundant in the brain and are involved in, or modulate, the mechanism by which brain neurons communicate.<sup>17</sup> The role of omega 3 fatty acids in improving cognitive functions has been extensively studied in a variety of populations ranging from infants to the elderly, and from healthy individuals to patients with psychiatric, neurodegenerative or neurodevelopment disorders. For example, omega 3 fatty acids supplementation has been shown to improve depressive symptoms and verbal fluency in elderly with mild cognitive impairments. They have been shown to alter the functioning of neural systems utilising dopamine and serotonin, both of which are thought to play an important role in mental illness and are major targets of psychoactive medications.<sup>16,17</sup> Furthermore, animal models of mental illness have suggested that omega-3 fatty acids can affect brain processes such as those that control mood and anxiety.<sup>18-20</sup>

### **Vitamin D and mental Health**

Vitamin D deficiency is commonly defined as levels of 25-hydroxyvitamin D (25OHD) less than 25 nmol/L, insufficiency as between 25 and 50 nmol/L and sufficiency as greater than 50 nmol/L. Its RDA is 400 IU or 10 mg, it binds to the receptor of target cells and regulate through gene expression.<sup>21</sup> Poor diet, lack of sun exposure, decreased synthesis of vitamin D and decreased renal hydroxylation of 25(OH) D due to old age are the main cause of Vitamin D deficiency.<sup>22</sup>

Nearly 30 percent to 50 percent of people are estimated to have deficiency of vitamin D, and insufficiency and vitamin D deficiency are recognized as global health issues in the world.<sup>23</sup> Scientific findings about the role of vitamin D in healthy people and patients with numerous diseases increasingly accumulate in medical literature.<sup>24</sup> The fact that, taking into account recommended optimal values, about a third or more of adult population in societies with higher life standard had a deficiency of vitamin D, raises additional, widespread concern.<sup>25,26</sup> Vitamin D3 (cholecalciferol) is taken in the diet (fortified dairy products and fish oils) or is synthesized in the skin from 7-dehydrocholesterol by ultraviolet irradiation. It is transported in the blood by the vitamin D binding protein (DBP) to the liver. In the liver it is hydroxylated, resulting in the formation of 25 hydroxyvitamin D3 (25(OH)D3). This is then transported to the kidney by DBP. In the proximal renal tubule 25(OH)D3 is hydroxylated, resulting in the hormonally active form of vitamin D, 1,25-dihydroxyvitamin D3 (1,25(OH)2D3), which is responsible for most if not all of the biologic actions of vitamin D.<sup>27</sup> Vitamin D is crucial for several key physiological processes, including brain development, DNA repair, and regulation of many genes. Evidence indicates that prenatal and early postnatal vitamin D deficiency increases autism risk, probably through multiple effects, including impaired brain development and increased de-novo mutations.<sup>28</sup> Vitamin D receptors (VDR) were found in neurons and glial cells in brain areas responsible for the development of depression and suggesting a role of vitamin D for development of some mental disorders.<sup>29,30</sup> Vitamin D helps protect against oxidative stress, which is a key cause of DNA damage, and also aids in the repair of DNA damage once it occurs<sup>31,32</sup>

### **Vitamin B12 and Mental Health**

Vitamin B12 plays a crucial role in cell reproduction, normal erythropoiesis, nucleoprotein and myelin synthesis, normal growth, DNA synthesis, and one carbon metabolism.<sup>33</sup> Normal daily requirement is about 1 µg.<sup>34</sup> Vitamin B12 helps in synthesis of methionine from homocysteine and conversion of methylmalonylCoA to succinylCoA. Methionine is converted to SAM which donates its methyl group to myelin, membrane phospholipids and various neurotransmitters and free

THF is liberated from N5 methyl THF which is used in synthesis of purine, pyrimidine and nucleic acid.<sup>35</sup> An elevated level of Hcy as a neurotoxin was also shown to affect the redox signalling pathways in neurons through the generation of reactive oxygen species (ROS) and a decrease in endogenous antioxidants. If patterns of DNA methylation in redox-related genes can modulate cognitive impairment caused by vitamin B12 deficiency and hyperhomocysteinaemia is therefore of interest, low levels of vitamin B12 can cause serious cognitive dysfunction.<sup>36</sup> Psychiatric symptoms attributable to vitamin B<sub>12</sub> deficiency have been described for decades. The earlier studies are for the most part in accord with more recent ones, despite being diagnostically less precise in psychological and hematologic terms. These symptoms tend to fall into many clinically distinct categories: slow cerebration; confusion; memory changes; delirium, with or without hallucinations and/or delusions; depression; acute psychotic states; and more rarely) reversible manic and schizophreniform states.<sup>37</sup>

### **Folate and Mental Health**

Folate deficiency and insufficiency are common among patients with mood disorders and correlate with illness severity.<sup>38</sup> Folate deficiency may specifically affect central monoamine metabolism and aggravate depressive disorders.<sup>39</sup> There must be two reasons of folate deficiency, the biologically active form of folate, L-methylfolate, may act as a trimonoamine modulator and enhance the synthesis of three monoamines including dopamine, norepinephrine, and serotonin, and this has been reported to be involved in the efficacy of antidepressant. Patients with a methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism produce a less active form of the enzyme. The TT genotype is associated with major depression and bipolar disorder.<sup>40</sup> Dietary folate must be converted to L-methylfolate for use in the brain. Other potential explanation may be due to malnutrition or poor nutrition intake.

### **Vitamin B6 and Mental Health**

Vitamin B6 deficiency has been associated with neuropsychiatric conditions, including seizures, migraines, chronic pain and depression. In the control of mental function and mood, vitamin B6, containing three chemically distinct compounds, pyridoxal, pyridoxamine, and pyridoxine, is involved. Vitamin

B6 is also an important re-methylation cofactor for homocysteine, and deficiency is associated with an increase in levels of homocysteine in the blood. Homocysteine is a cerebrovascular disease risk factor and may also have a direct toxic impact on central nervous system neurons.<sup>41</sup>

### Conclusion

Nutrition deficiency leads to serious mental disorders, as body require adequate amount of nutrition for its proper functioning. Poor nutrition status in mental disorders leads to folate deficiency which appears to predominate in melancholic depression; anorexia and weight loss are common features of this type. In these settings, supplementation with folate or its derivative, methylfolate, may be found to play an important role in effective antidepressant treatment. Both folate and vitamin B12 deficiency may cause similar neurological depression, dementia, and a demyelinating myelopathy. Deficiency of omega 3 fatty acids, vitamin D, vitamin B12, folate, vitamin B6 are commonly seen in mental disorders, so adequate amount of nutrition and supplements should be given to reverse the cause of damage.

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