Proceedings of the 2nd International Conference on Biological Engineering and Medical Science (ICBioMed 2022), Part II
DOI: 10.54254/2753-8818/4/20220576

Links between Serotonin and Depression

Betty Li

Guanghua Cambridge International School, Shanghai, China.

bettyli54@stu.cuz.edu.cn

Abstract. Serotonin is a common neurotransmitter linked closely with the feeling-good effects, while the dysregulation of serotonin could lead to the major depressive disorder which affect 350 million people's lifetime all over the world. The synthesis of serotonin is stimulated by its precursor tryptophan. It is an important type of amino acid found in dietary protein. Furthermore, low level of serotonin could lead to lack of melatonin. This indicates the various symptoms caused by depression.

Keywords: serotonin, depression.

1. Introduction

Depression is considered as a serious health threat. It is categorized as a prevalent psychiatric disorder that affects approximately 350 million people's lifetimes from worldwide, among which women have the twice risk of the first attack as men [1, 2]. Moreover, it is counted that one out of five people are affected by major depressive disorder (MDD) which even cause disability [3]. MDD is mainly qualified by manifestations of cognitive and mental domains. This wide range of types of problems makes it difficult to cure [4]. Unfortunately, there is no completely effective treatments for depression until now. In the last century, it is claimed that patients suffering from depression are prone to showing a deficiency of serotonin circuits. Moreover, impairing serotonin receptors or the secretion pathways can lead to the dysfunction of brains that showed as the symptoms of depression on animal models. Thus, further studies are in need. Research targeting serotonin is promising to give people a therapeutic targets or early diagnostic markers that may promote studies on depression.

Furthermore, the causality of how depression is formed has been explored deeply. It is noticeable that, as a chronic mental disorder, a number of studies on the correlation between depression and neuroscience have been done to illustrate part of the mechanism, while the whole mechanism is still waiting to be explored. Here we provide a number of common symptoms and the resulting mechanisms which related to serotonin.

2. Synthesis of serotonin

Depression is caused by the low level of serotonin (a type of neurotransmitter) which cause the "feel-good" effect. The mechanism of the conversion from tryptophan to the serotonin helps to explain the dysregulation of serotonin.

Tryptophan, the sole precursor of serotonin (5-hydroxytryptophan), is one of the important types of amino acid found in dietary proteins which is consist of nuts, cheese, and egg whites [5, 6]. The level of

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tryptophan in our brain is tightly linked with the rate of serotonin synthesis, which is mostly determined by the CAA ratio and the proportion of diets. Low level of tryptophan could cause depression.

Firstly, tryptophan is transported to the brain and cross the blood-brain barrier. Tryptophan is unique comparing to other amino acids as it circulates in the bloodstream. Most of it bounds with the plasma albumin while only about 10% of circulating tryptophan is mobile.[7] The free tryptophan owns the access for transporting across the blood-brain barrier (BBB), which is an obstacle for the serotonin production. However, the affinity between the tryptophan and BBB is higher than with the albumin so the strong natural attraction force causes the high possibility of the dissociation of albumin-bound tryptophan near the BBB to the brain. It is even concluded by researchers that 75% of the tryptophan would be able to cross the BBB [8]. After taken up into the brain, the synthesis of serotonin is worked by mainly two steps in the CNS: hydroxylation and decarboxylation [9].

Hydroxylation occurs at first. Tryptophan is hydroxylated by enzyme tryptophan hydrolase type2 to the L-5-hydroxytryptophan with the cofactors like tetrahydrobiopterin and the oxygen molecules. This process will add a hydroxyl group to the carbon-5 of the tryptophan. It also produces dihydrobiopterin from tetrahydrobiopterin. Dihydrobiopterin could be recycled back to the tetrahydrobiopterin by the oxidation of NADPH using the enzyme DHB reductase.

In this case, the rate of the serotonin synthesis is mainly affected by the availability of tryptophan in the brain as the tryptophan hydrolases are commonly 75% saturated by the substrate. Tetrahydrobiopterin and oxygen, as the cofactors of tryptophan hydrolases, also influence the levels of serotonin [10].

Subsequently, decarboxylation occurs. The dimeric enzyme L-aromatic acid decarboxylase (AAAD) catalyzes the conversion of L-5-hydroxytryptophan to the serotonin which is the 5-hydroxytryptamine(5-HT) by removing the carboxyl group to form the 5-hydroxytryptophan and carbon dioxide. The co-factor of this decarboxylation is pyridoxal phosphate which is the active form of vitamin B6.

3. Synthesis of melatonin

Synthesis of serotonin is linked with the production of melatonin. Serotonin is a precursor of melatonin. This part clarifies the production of melatonin after the 5-HT being produced. The lack of serotonin could also lead to the symptoms of lacking melatonin.

Melatonin, or N-acetyl-5-methyltryptamine, is a hormone produced by serotonin which control human's circadian rhythms and with sleep. The production of N-acetyl-5-methyltryptamine also requires two main steps. After the 5-HT is produced, the serotonin N-acetyl transferase acts on the 5-HT by the donation of acetyl group from acetyl-CoA. The acetyl group then attaches to the nitrogen group of the 5-HT to produce N-acetyl-serotonin. This is also called normelatonin. Coenzyme A and hydrogen ions are produced as the byproducts.

The N-acetyl-serotonin is next convert into the N-acetyl-5-methoxytryptamine which is also called melatonin. In this process, normelatonin is converted by the donation of a methyl bond from S-adenyosyl-methionine (SAM) utilizing the enzyme N-acetyl serotonin O-methyl transferase. The methyl group of SAM is added to the hydroxyl group of the N-acetyl-serotonin and leaves the S-adenyosyl-homocysteine, while it can be recycled by the activated methyl cycle.

4. Symptoms of depression

Major depressive disorder is a psychology-related illness that can be seen in many people recently, especially in people who are highly stressed. Moreover, the prevalence is that the diseases now have impacts on the younger generation that many teenagers are now suffering from depression. The scientists believed that both genetic and environmental factors are the causality, while the family and school interventions seem to be more important. MDD has a variety of symptoms influencing somatic, cognitive, affective, and social behaviors in human body. [11] These symptoms occur nearly every day in people's life. The most common symptom of major depressive disorder is the feeling of sadness, tearfulness, emptiness, or hopelessness. For young children suffering depression, they tend to refuse to go to school and become underweight. Thus, parents and elder people are responsible for being aware of the changes of the psychological status on the surrounding children.

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It is noticed that as people grow up to teenagers, the revealed symptoms are becoming more extreme, which includes using excessive recreational drugs or alcohol. After growing up to older age, memory difficulties, and changes in the personality of these elder patients occur. Physical aches also stimulate their suicidal thinking, especially in older men.

Due to the chain reaction of the production of serotonin and melatonin, lack of serotonin is tightly related to the melatonin deficiency. MDD often occurs with the symptoms of excessive daytime sleepiness, nocturnal awakening, and insomnia. These are the consequences of low level of melatonin being produced.

However, melatonin is accessible. People are able to gain melatonin in some of their daily food such as eggs and fish. Preferable dietary sources also contain mushrooms, cereals, and germinated legumes [12].

5. Conclusion

The impacts of depression on people are serious. Most commonly, it affects people's social aspects. And the factors that cause depression are also well-analyzed in the paragraphs above. The low level of serotonin produced could increase the chance of getting depression. This should be noticed by people, and they have to digest suitable amount of products such as nuts and egg whites in their daily life to sustain enough tryptophan every day. Apart from that, lack of serotonin would lead to low level of melatonin. This brings many side effects to people such as insomnia. Indeed, accumulation of pressures is also a significant factor contributing to depression. This article hopes that more and more people could realize the severity of depression and try to care more about both their biological and psychological health.

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