Mini Review

CLINICAL INVESTIGATION

Melatonin as a treatment for mental illness

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Abstract

Primary despair has been linked to disrupted circadian rhythms, which could be the fundamental cause of disorder. Because of half complete sleep wake and body temperature patterns, the pathophysiology for depression exists. Rhythm regulation is a brand-new therapy method. The treatment involves modulating melatonin secretion, which peaks at night and is a key regulator of circadian rhythms. Melatonin may play a role in the development of mood disorders. In depressive individuals, the metabolite 6-sulfatoxymelatonin in urine had a substantial adjustment for melatonin secretion sooner or later in the acute phase of disease. Exogenous melatonin, as well as agonism of specific melatonin receptors inside the suprachiasmatic nucleus, can alter the time cycle for melatonin release. Seasonal affective difficulties are characterised as affective problems that include primary depression, bipolar disorders, and changes in the number of neural systems. The addition of the traditional monoaminergic hypothesis provided a comprehensive explanation for the pathophysiology of these issues, such as the strong correlation between cardiac rhythms and the temper law, which has been recommended in light of several medical and preclinical studies. The unusual hypotheses on the pathological mechanism that underpins depressed problems, with a special emphasis on changes in melatonin secretion and the accompanying adjustments in organic rhythms that express temper issues.

Keywords: Melatonin • Metabolite • 6-Sulfatoxymelatonin Bipolar disorder • Organic rhythms • Circadian rhythms • Pathophysiology • Rhythm-regulation • Melatonin metabolite

Submitted: 25 August 2021; Accepted: 12 September 2021; Published online: 18 September 2021

Introduction

The rhythm of melatonin production and secretion is entrained to a circadian duration in large part due to the use of light and darkness in the environment. The Suprachiasmatic Nucleus (SCN) sends a message to the pineal gland *via* a multisynaptic channel, and it is responsible for melatonin's dependable cardiac rhythm, which is distinguished by a gradual upward push next after the time of day and a height in the middle of the night (approximately 3:00 am-4:00 am). The pineal gland is innervated by norepinephrine secretion, which is released at night by postganglionic sympathetic neurons [1]. The pineal gland's sympathetic nerve activity is inextricably tied to the environment's light and dark cycle. Melatonin production is influenced by tryptophan availability as well as several dietary factors such as folate status and diet, as well as a coenzyme involved in tryptophan decarboxylation that can stimulate melatonin generation. Melatonin activates two specific receptors, MT1 and MT2, which belong to the seven-transmembrane superfamily of G-protein coupled receptors. The soluble guanylyl cyclase pathway is likely inhibited by the MT2 receptor, and melatonin receptors can activate a variety of 2D messenger cascades depending on the tissues and species [2]. The MT1 and MT2 receptors can be found in a variety of tissues, including the retina, ovary, testis, and kidney. The Dim Light Melatonin Onset (DLMO) is the maximal and normal circadian melatonin segment producer. The DLMO indicates when one's organic night begins, and it's useful for determining circadian misalignment and segment type because it's the interporal clock moment when the ascending segment of melatonin reaches 20 pg/ml.

In the use of a circadian feature dysregulation, some affective issues such as Major Depressive Disorder (MDD), Bipolar Disorder (BD) and Seasonal Affective Disorder (SAD) are noticed. Some changes in biochemical (melatonin and cortisol profiles), actigraphic (sleep/wake patterns), and circadian clock makers can occur during an acute temper episode during the euthymic period. Similarly, in the classic monoaminergic hypotheses, which have been proposed for a long time to provide information about the pathophysiology for mood spectrum disorders and a strong relationship between circadian rhythms, improper regulation of melatonin secretion, and the law, which has been cautioned

with a small number of preclinical and scientific findings [3]. Melatonin helps to stimulate circadian rhythms in a variety of organic functions, including as activity/rest, sleep/wake frame temperature, coronary heart rate, and endocrine rhythms. The study discusses the affective issues that arise as a result of circadian dysfunction, which can theoretically be remedied by adjusting the circadian machine that administers melatonin. These statistics on the efficacy of treating mood issues are so inconsistent.

Melatonin

Melatonin (N-acetyl-5-methoxytryptamine) is an indolamine hormone discovered in early 1958 and described. Aaron Lerner, a dermatologist, discovered a light-skin factor in bovine pineal gland extracts. Because of the ability of stellate amphibian melanophores to contract, it is referred to as melatonin [4].

It is produced in a unique fashion that is a spinoff of the amino acid tryptophan using the parenchymal cells of the pineal gland, resulting in an unanticipated secretion in the blood vascular system and the cerebrospinal fluid. The retina, intestines, skin, platelets, and bone marrow are the secondary pathways [5].

For the synthesis, there are three separate enzymatic steps:

- N-acetylation of l-tryptophan to serotonin with the help of the enzyme Serotonin N-Acetyltransferase (SNAT) to obtain the product N-acetylserotonin
- Using the enzyme Hydroxyindole-o-Methyltransferase, the synthesis process for converting N-acetylserotonin to melatonin (HIOMT)

For the main synthesis of melatonin, the physiological law of SNAT, with the sharp increase in interest at night, is brought to the fore.

Melatonin has four main ways of displaying its effect:

- Binding to melatonin receptors in the plasma membrane
- Binding to intracellular proteins such as calmodulin
- Binding to an orphan nuclear protein

Melatonin and Psychiatric Disorders

Anxiety and melatonin

According to several studies, if melatonin is administered in excess, the exploratory conduct of hysteria in rats should be increased or the warfare conduct pattern should be extruded. Melatonin is said to initiate sleep and maintain peaceful wakefulness, according to research on its effects on sleep. Melatonin shortage LPS induced tension, according to studies, suggesting that melatonin could be utilised as an adjuvant anti-tension treatment [6-8]. In the clinic, Hasen and his colleagues have successfully used melatonin to alleviate tension and insomnia.

Depression and melatonin

Melatonin and depression have been linked in recent studies. The norepinephrine hormone regulates melatonin production and secretion. Melatonin levels are a good indicator of norepinephrine activity in the brain. Melatonin secretion is the index for the activity of norepinephrine in depressed individuals, and it was discovered that people suffering from major depressive illness have a high serum of melatonin. After the pharmacological treatment, this can be treated.

Melatonin has been demonstrated to be ineffective in pregnancies caused by an aberrant reaction during the tail suspension test. Women with breast cancer who received oral melatonin at a dose of 6 mg after surgery in the afternoon may experience significantly less anxiety, ache, and sleep issues than those who did not receive melatonin medication [9].

Schizophrenia and melatonin

Melatonin has been used to treat schizophrenia since 1920, when it was discovered using a method of extracting the pineal body for the treatment of a group of "dementia praecox" patients. Since then, there has been an increase in interest in conducting research to determine the relationship between melatonin and psychiatry. Scientists attempted to relate melatonin to schizophrenia in 1996, and as a result, he stated that hallucinations and delusions are the main positive symptoms of schizophrenia, and he discovered that the structure of melatonin is quite similar to hallucinogenic harmala alkaloids [10].

Melatonin levels are used to distinguish the clinical subtypes of schizophrenia. In the paranoid subtype of schizophrenia, lower levels of melatonin have been recorded than in ideal subjects, implying that melatonin has a low concentration in the paranoid subtype.

Conclusion

The relationship between melatonin and mental diseases is still unknown, despite the fact that melatonin was discovered 50 years ago and is extensively used, and there are few studies on melatonin treatment of mental problems. The results of investigations demonstrate that biochemical measurements of melatonin can be used to treat mental disorders. This also demonstrates that there are no major side effects and that it may be widely utilised in clinical practise to treat mental problems. On the other side, melatonin therapy reaction estimation will be more standardised and effective. In the coming year, there may be some advancements in the treatment of mental problems with the use of technology.

References

1. Emet M, Ozcan H, Ozel L, et al. A Review of Melatonin, its receptors and drugs. *Eurasian J Med* 48: 135-141 (2016).
2. Zlotos DP, Jockers R, Cecon E, et al. MT1 and MT2 melatonin receptors: ligands, models, oligomers, and therapeutic potential. *J med chem* 57: 3161-3185 (2014).
3. Hardeland R, Poeggeler B, Srinivasan V, et al. Melatonergic drugs in clinical practice. *Arzneimittel forschung* 58: 1-10 (2008).
4. Yang C, Liu Q, Chen Y. Melatonin delays ovarian aging in mice by slowing down the exhaustion of ovarian reserve. *Commun Biol* 4: 534-539 (2021).
5. Sutherland JM, Frost ER, Ford EA, et al. Janus kinase JAK1 maintains the ovarian reserve of primordial follicles in the mouse ovary. *Mol Hum Reprod* 1: 533-542 (2018).
6. Mao K, Luo P, Geng W. An integrative transcriptomic and metabolomic study revealed that melatonin plays a protective role in chronic Lung Inflammation by reducing Necroptosis. *Front Immunol* 12: 66-78 (2021).
7. Yang Z, Li C, Wang Y, et al. Melatonin attenuates chronic pain related myocardial ischemic susceptibility through inhibiting RIP3-MLKL/CaMKII dependent necroptosis. *J Mol Cell Cardiol* 24: 185-194 (2018).
8. Coughlin SS, Callie EE, Teras LR, et al. Diabetes mellitus as a predictor of cancer mortality in a large cohort of US adults. *Am J Epidemiol* 159: 1160-1167 (2004).
9. Lu CC, Chu PY, Hsia SM, et al. Insulin induction instigates cell proliferation and metastasis in human colorectal cancer cells. *Inter J Onco* 50: 736-744 (2017).
10. Akam A, Yeatman T, Lu L, et al. Expression of insulin-like growth factor-1 receptor in human colorectal cancer. *Hum Pathol* 30: 1128-1133 (1999).