Melatonin, Mitochondria and Successful Aging

Idowu Abimbola John*

Department of Physiology, Lagos State University College of Medicine, Nigeria

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*Corresponding author: Idowu Abimbola John, Department of Physiology, Lagos State University College of Medicine, 1-5 Oba Akinjobi Way GRA, Ikeja, Lagos, Nigeria

Abstract

Although melatonin has been shown to be involved in the aging process and as a therapeutic target during normal aging, it is yet to be widely accepted as a therapeutic target for age related vulnerabilities. With more evidences being unraveled from different studies, important lifestyle changes that will optimize its normal synthesis could be beneficial for the human population.

Introduction

Aaron Lerner and colleagues discovered melatonin in 1958 and the chemical structure was described in 1959 as N-acetyl-5-methoxytryptamine [1]. Melatonin is endogenously produced majorly in the pineal gland especially at night. Melatonin is one of the strongest antioxidants known; it scavenges hydroxyl and peroxyl radicals [2,3]. Melatonin has a strong relationship with aging, the loss of melatonin in old age may contribute to the severity and incidence of neurodegenerative diseases such as Alzheimer’s disease [4]. Armstrong and Redman in 1991 suggested that melatonin might have beneficial effects in aging because of its association with the circadian timing system [5]. At advanced age melatonin is lost and leads to disturbances in the circadian pacemaker, which causes internal desynchronization and deterioration of health. Hence, melatonin has been used to treat jet lag symptoms as well as phase shift the circadian clock [6]. This is also validated by the presence of melatonin receptors on the suprachiasmatic nucleus [7]. Although, melatonin has been used to treat jet lag and insomnia, it is yet to be widely accepted as a therapeutic target for successful ageing despite the convincing evidences. In here, it is suggested that lifestyle be adjusted to allow body to maximize the natural synthesis of melatonin.

Mitochondria, Mitochondrial Biology and Implication in Aging

The mitochondria produce ATP through oxidative phosphorylation by the respiratory chain complexes I, II, III, and IV and ATP synthase, V [8]. The proton gradient across the inner mitochondrial membrane is used for ATP production via ATP synthase, Complex V [8,9]. The mitochondria play an important role in the aging process; respiratory chain dysfunction, formation of reactive oxygen species, damage of mitochondrial proteins or lipids and mitochondrial DNA damage [10-13]. In relation to increasing age, there is a direct correlation of reactive oxygen species and oxidative damage of DNA, proteins and lipids [14]. Mitochondrial defects associated with aging have been observed in skeletal muscle and the brain, which are high-energy demanding tissues, which depend on oxidative phosphorylation [15].

Implication on Successful Aging

Melatonin plays a significant role in modulating organelle, cell and system function. Among compounds that have been tested as a therapeutic agent for age related vulnerabilities, melatonin has been shown to be the most potent. It has been used as a therapeutic target in cardiovascular, reproductive, neurodegenerative, sleep, memory and microbial studies. Recently, it was discovered that melatonin is able to regulate mitochondria membrane potential to optimize ATP production in middle age and old mitochondria isolated from cortical neurons in mice [16]. Despite the implication of melatonin in many age-related abnormalities, it is presently not widely accepted as a therapeutic agent for successful aging. Successful aging in this context meaning growing older without vulnerability to age related disease or loss of normal function. While this is due partly to the lack of longevity studies in humans, it is important to recommend on the basis of supporting evidences from animal experiments, that the natural production of melatonin in the human body should be optimized.

This can be achieved by sleeping in dark rooms at night. This is because melatonin synthesis is sensitive to light, which is why melatonin levels are at the highest levels at night. Alongside this, the circadian rhythm should not be altered for too long unnecessarily. Melatonin levels in the blood are at the peak between 2:00am and 4:00am in the morning. In order to gain the maximum benefit from this important therapeutic molecule, it is believed that sleep occurring between 11:00pm and 5:00am will aid this process.
Hence, adjusting the sleep time at night in a dark room to create the appropriate conditions for the body to maximally synthesize and release melatonin could help human population age successfully.

References