Melatonin is synthesized in the pineal gland of the brain from the amino acid tryptophan, shown in Figure 1. Light cycles regulate melatonin synthesis and release, which is responsible for the circadian and seasonal signal within the human brain. Suprachiasmatic nuclei, located above the optic chiasma, expresses a series of genes that reacts via light input. Secretion of melatonin lowers body temperature, regulates immune function, reproductive functions, and has antioxidant properties.

Melatonin Synthesis

The amino acid tryptophan is absorbed by the pineal gland mitochondria forming serotonin [5]. During periods of darkness, the pineal gland receives a signal from post ganglionic fibers that results in noradrenaline production and increased cyclic AMP. This cascade of reactions triggers the conversion of serotonin to N-acetylserotonin (NAS), followed by ASMT catalyzing the conversion of NAS to melatonin, as shown in Figure 1. Once melatonin is produced, it is secreted into the bloodstream and cerebrospinal fluid by pinealocytes.

What Goes Wrong?

Autism spectrum disorders (ASD) can cause biochemical impairment of melatonin syntheses. Individuals with ASD have elevated blood serotonin and NAS levels as well as low ASMT activity [4]. Disregulation of melatonin production can cause a variety of sleeping disorders, as shown in Figure 5. In some forms of autism, the inactive form of melatonin (NAS) is not converted into the active form of melatonin because of an underproduction of ASMT, steps shown in Figure 1. This failure of signaling conversion causes low melatonin synthesis, these individuals would experience restlessness. Over 80% of children with ASD experience sleep problems.

Current Research

There are several uses for melatonin immediate release including poor circadian rhythms, seasonal affective and bipolar disorders. Melatonin prolonged release and similar drugs are being developed for therapies that consider the suprachiasmatic nuclei disorders and its function.

References