Melatonin and serotonin in psychiatric and brain disorders

Melatonin is well known as a treatment for jet lag, being naturally released by the brain when we close our eyes to go to sleep. However, recent research shows that melatonin is released by many, if not all, cells in all areas of the brain and body. For example, melatonin is very highly produced in the gut, where it prevents the gut from becoming 'leaky' and therefore prevents gut bacteria and tiny partially digested bits of food from triggering an immune response. Emerging evidence suggests that targeting melatonin synthesis in different brain and body cells, including the gut and immune system, may have significant benefits for a host of currently very poorly treated medical conditions, including Alzheimer's disease, Parkinson's disease and multiple sclerosis as well as a wide array of psychiatric conditions, such as bipolar disorder.

All of these disorders are associated with increased levels of depression, with this being due to the overlaps in the biological changes underlying these different medical conditions, which overlap with the changes occurring in depression. As such, depression is part of the biological changes that occur in these medical conditions, and not a psychological reaction to them. Most people are aware that decreased serotonin occurs during depression, with antidepressants classically thought to have their effects by increasing levels of serotonin availability. However, serotonin is broken down into N-acetylserotonin, which is then broken down into melatonin. As such, many of the benefits of antidepressants in increasing serotonin is actually *via* making serotonin available for melatonin production, both in the brain and body.

The latest edition of the journal, Current Pharmaceutical Design, looks at the role of melatonin production in many cell types, especially in brain and immune cells, but also in the placenta. Medications targeting the production of melatonin in different cell types are relevant to many medical conditions, including psychiatric, that are currently poorly treated. This edition of the journal looks at the role of melatonin in the treatment of many conditions, including glioblastoma, the most common brain cancer in adults, which has very poor survival rates. Melatonin is well-proven to kill brain cancers, as well as decrease their proliferation and spread. Recent work shows that melatonin is produced by brain cells, although this may be altered in brain cancers. It is proposed that the immediate precursor of melatonin, N-acetylserotonin, is not converted into melatonin around brain cancers, with the increased levels of N-acetylserotonin acting to increase the proliferation of some brain cancers. As such, the ratio of N-acetylserotonin to melatonin may be an important pharmaceutical target, whereby pharmaceuticals may target a relative increase in melatonin production in cells immediately surrounding brain cancer cells. Similar processes are thought to be relevant in bipolar disorder, with an increase in the N-acetylserotoin to melatonin ratio, being proposed to underlie the manic phase of bipolar disorder, which is the defining feature of a bipolar disorder diagnosis. However, generally an increase in both N-acetylserotonin and melatonin are useful, with an increase in both being proposed to be relevant to Alzheimer's disease and multiple sclerosis. Melatonin is also very highly produced in the placenta, with a decrease in melatonin linked to many bad pregnancy outcomes, including preeclampsia and maternal stress effects in the developing foetus.

Overall, the article contained in this edition of Current Pharmaceutical Design, provide novel treatment targets for what are still very poorly managed and treated medical conditions. It is likely that targeting melatonin will significant treatment improvements, with minimal side-effects, given that melatonin is a completely natural substance that all of us produce everyday.

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