The hormone of darkness: melatonin could hurt memory formation at night

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In a study with zebrafish (Danio rerio), Gregg W. Roman, assistant professor in the Department of Biology and Biochemistry at the University of Houston, has found that melatonin directly inhibits memory formation at night. He describes his team's findings in a paper titled "Melatonin Suppresses Nighttime Memory Formation in Zebrafish," appearing in Science, the world's leading journal of original scientific research. Credit: Thomas Shea

What do you do when a naturally occurring hormone in your body turns against you? What do you do when that same hormone – melatonin – is a popular supplement you take to help you sleep? A University of Houston professor and his team of researchers may have some answers.

Gregg W. Roman, assistant professor in the department of biology and biochemistry at UH, describes his team's findings in a paper titled "Melatonin Suppresses Nighttime Memory Formation in Zebrafish," appearing Nov. 16 in *Science*, the world's leading journal of original scientific research, global news and commentary.

Frequently called "the hormone of darkness," melatonin is a hormone the body produces that may regulate patterns of sleeping and awakening in humans. In almost all organisms tested, this antioxidant's natural levels are high during the night and low during the day. In addition to what the body produces naturally, many people also take melatonin supplements to fight jet lag, balance out seasonal affect disorder and regulate nighttime dementia.

Roman says, however, that melatonin could actually be hurting you at night, finding in a study with zebrafish (Danio rerio) that melatonin directly inhibits memory formation.

"This work is about the mechanism by which the biological clock controls the formation of new memories," Roman said. "We were interested in the circadian control – the day-night cycle control – of learning and memory formation. We found zebrafish are capable of learning very well during their active phase during the day, but learn very poorly at night during their sleep or quiet phase."

The experiments were performed using zebrafish for several reasons. They're small and breed in large numbers (thereby being less expensive to use), and they are diurnal, having the same activity rhythms as people. Zebrafish are most active during the day and less active at night, whereas many other vertebrate model systems, such as rodents, are nocturnal. Roman reasons that if you are interested in how the biological clock regulates cognitive function in humans, you should use a model system that reacts to the clock the same way people do.

More than two years worth of work, including the discovery that the ability to learn and remember was controlled by an endogenous (or internal) clock originating within the zebrafish, led Roman and his colleagues to hypothesize that melatonin may be responsible for poor learning and memory formation during the night. In order to test whether melatonin was involved in inhibiting nighttime learning and memory formation, they treated the zebrafish during the day with this hormone to see how the fish performed. Interestingly, melatonin

failed to affect learning, but dramatically inhibited the formation of new memories, with the melatonin-treated fish resembling fish trained during the night in a test for 24-hour memory.

“The next step was to inhibit melatonin signaling during the night with a melatonin receptor antagonist and test for effects on memory formation,” Roman said. “It was tremendous – the results were, excuse the expression, like night and day. We saw dramatic improvements in nighttime memory formation by inhibiting melatonin signaling, indicating that the reason the zebrafish did not form memories at night was because of the melatonin hormone.”

Next, with the pineal gland being the primary source of melatonin in fish and in people, Roman’s student Oliver Rawashdeh removed this gland from the fish and found they could now form memories at high levels even during the night. Removing this melatonin-producing gland allowed the researchers to alleviate the hormone’s negative side effects, further demonstrating that melatonin inhibits the formation of new memories during the night.

With these findings, Roman hopes to be able to retain the beneficial effects of melatonin’s antioxidant properties. Such benefits include fighting free radical damage to slow some forms of neurodegeneration, such as in Parkinson’s and Alzheimer’s diseases, and stopping DNA damage, which has potential to act as a preventative against cancer. And, since the positive antioxidant effect is direct and independent of receptor signaling, there is hope that removing the melatonin receptor signaling will combat only this hormone’s negative effects on cognitive function.

Additionally, Roman said that inhibiting melatonin signaling with receptor antagonists may help with a large number of nighttime cognitive tasks, helping such people as students studying for finals, airplane pilots, ER physicians and night-shift workers. Roman also thinks that a natural role of melatonin may be to facilitate the storage of memories made during the day and that more studies are required to understand the ultimate role melatonin has in memory formation.

“The value of melatonin as a supplement is largely due to its antioxidant properties,” Roman said. “The use of melatonin receptor antagonists will not affect this attribute, but may alleviate an important side effect on nighttime cognitive function.”

In other words, a ‘best of both worlds’ scenario could result, taking advantage of melatonin’s antioxidant benefits while improving nighttime memory formation that is now inhibited by it.

Roman’s team at UH for this breakthrough study includes Gregory M. Cahill, associate professor of biology and biochemistry, and two of their students and research assistants, Oliver Rawashdeh and Nancy Hernandez de Borsetti.

Source: University of Houston