

Melatonin and Exercise Work Against Alzheimer's in Mice

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2 Oct 2012 --- The combination of two neuroprotective therapies, voluntary physical exercise, and the daily intake of melatonin has been shown to have a synergistic effect against brain deterioration in rodents with three different mutations of Alzheimer's disease.

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Daily voluntary exercise and daily intake of melatonin, both of which are known for the effects they have in regulating circadian rhythm, show a synergistic effect against brain deterioration in the 3xTg-AD mouse, which has three mutations of Alzheimer's disease.

"For years we have known that the combination of different anti-aging therapies such as physical exercise, a Mediterranean diet, and not smoking adds years to one's life," Coral Sanfeliu, from the IIBB, explains to SINC. "Now it seems that melatonin, the sleep hormone, also has important anti-aging effects".

The experts analysed the combined effect of sport and melatonin in 3xTg-AD mice which were experiencing an initial phase of Alzheimer's and presented learning difficulties and changes in behaviour such as anxiety and apathy.

The mice were divided into one control group and three other groups which would undergo different treatments: exercise –unrestricted use of a running wheel–, melatonin –a dose equivalent to 10 mg per kg of body weight–, and a combination of melatonin and voluntary physical exercise. In addition, a reference group of mice were included which presented no mutations of the disease.

"After six months, the state of the mice undergoing treatment was closer to that of the mice with no mutations than to their own initial pathological state. From this we can say that the disease has significantly regressed," Sanfeliu states.

The results, which were published in the journal *Neurobiology of Aging*, show a general

improvement in behaviour, learning, and memory with the three treatments.

These procedures also protected the brain tissue from oxidative stress and provided good levels of protection from excesses of amyloid beta peptide and hyperphosphorylated TAU protein caused by the mutations. In the case of the mitochondria, the combined effect resulted in an increase in the analysed indicators of improved performance which were not observed independently.

“Transferring treatments which are effective in animals to human patients is not always consistent, given that in humans the disease develops over several years, so that when memory loss begins to surface, the brain is already very deteriorated,” the IIBB expert points out.

However, several clinical studies have found signs of physical and mental benefits in sufferers of Alzheimer’s resulting from both treatments. The authors maintain that, until an effective pharmacological treatment is found, adopting healthy living habits is essential for reducing the risk of the disease appearing, as well as reducing the severity of its effects.

The use of melatonin, a hormone synthesized from the neurotransmitter serotonin, has positive effects which can be used for treating humans. With the approval of melatonin as a medication in the European Union in 2007, clinical testing on this molecule has been increasing. It has advocates as well as detractors, and the scientific evidence has not yet been able to unite the differing views.

According to the Natural Medicines Comprehensive Database, melatonin is probably effective in sleeping disorders in children with autism and mental retardation and in blind people; and possibly effective in case of jet-lag, sunburns and preoperative anxiety.

“However, other studies which use melatonin as medication show its high level of effectiveness,” Darío Acuña-Castroviejo explains to SINC. He has been studying melatonin for several years at the Health Sciences Technology Park of the University of Granada.

The expert points out that international consensus already exists, promoted by the British Association for Psychopharmacology –also published in the Journal of Psychopharmacology in 2010–, which has melatonin as the first choice treatment for insomnia in patients above the age of 55. This consensus is now being transferred to cases of insomnia in children.

Its use in treating neurodegenerative diseases is acquiring increasing scientific support in lateral amyotrophic sclerosis, in Alzheimer’s, and Duchenne muscular dystrophy.

“Even though many more studies and clinical tests are still required to assess the doses of melatonin which will be effective for a wide range of diseases, the antioxidant and anti-inflammatory properties of melatonin mean that its use is highly recommended for diseases which feature oxidative stress and inflammation,” Acuña-Castroviejo states.

This is the case for diseases such as epilepsy, chronic fatigue, fibromyalgia, and even the aging process itself, where data is available pointing to the benefits of melatonin, though said data is not definitive.

- *Full bibliographic information: García-Mesa Y, Giménez-Llort L, López LC, Venegas C, Cristòfol R, Escames G, Acuña-Castroviejo D, Sanfeliu C. “Melatonin plus physical exercise are highly neuroprotective in the 3xTg-AD mouse”. Neurobiol Aging 2012 Jun; 33(6):1124.e13-29.*