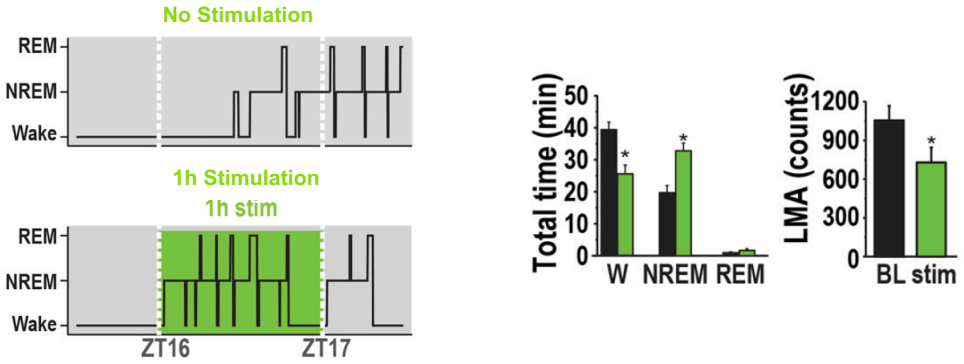
Transgenic Archaerhodopsin-3 mice as Type 2 Narcolepsy model mice

Background

Narcolepsy, a sleep disorder, is a sudden onset of sleep with excessive daytime sleepiness. It is said that around 1 in 2,000 have narcolepsy. The main symptoms of narcolepsy are a sudden onset of sleep, a sudden loss of muscle tone (cataplexy), and hallucinations of sleep paralysis and falling asleep. Narcolepsy is a chronic neurodegenerative disease caused by a deficiency of orexin/hypocretin-producing neurons in the lateral hypothalamus. There are types 1 and 2 of narcolepsy, and people with type 2 narcolepsy do not have symptoms of cataplexy. To understand the mechanisms by which disease occurs, it is important to have model mice that exhibit similar symptoms in both types. In the case of type 1 narcolepsy, the model mice in which the orexin neurons were ablated are used, but there was no model mouse of type 2 narcolepsy. To understand the mechanisms by which type 2 narcolepsy, it is important to have model animals of type 2 narcolepsy that exhibit similar symptoms.

Technology Overview

Researchers created a transgenic mice line to control the activity of the orexin neurons in the hypothalamus by exposure to light. This mice express a light-sensitive proton pump called archarhodopsin-3 exclusively in orexin neurons. Archarhodopsin-3 enables block neural activity by sensing green light. When green light was applied into the hypothalamus, activity of orexin neurons was suppressed, and as a result, mice started sleep. In addition, transgenic mice that express a large amount of the archarhodopsin-3 protein in orexin neurons showed abnormality of circadian rhythm, metabolic and sleep disturbances without illumination of green light onto the hypothalamus. This mice showed an increase in REM sleep which is seen in patients with narcolepsy, but no cataplexy-like symptoms characteristic of narcolepsy type. It is noteworthy that no loss of orexin neurons was observed in this mouse. Since there is no loss of orexin neurons in this model mice, it can be said that it succeeded in making a model mouse of type 2 narcolepsy.



Green light stimulation (1 h) significantly increased in non-REM (NREM) sleep (left) and concomitantly reduced in both wake and locomotor activity (LMA) during photoillumination (right).

Benefits

To understand the mechanisms by which type 2 narcolepsy, it is important to have model animals that exhibit similar symptoms, but there was no model mouse of type 2 narcolepsy. This study may help to understand mechanisms, and better treatments for type 2 narcolepsy.

Applications

This model mice contribute to the development of drugs that improve the symptoms of type 2 narcolepsy by screening various drugs using these new model mice for type 2 narcolepsy.

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