Press Release

2022.6.1 | International Institute for Integrative Sleep Medicine (WPI-IIIS)

Lessons on how to sleep: what we can learn from worms

Researchers from the University of Tsukuba identify how a single neuron can turn on and off to regulate the transition from wakefulness to sleep in worms

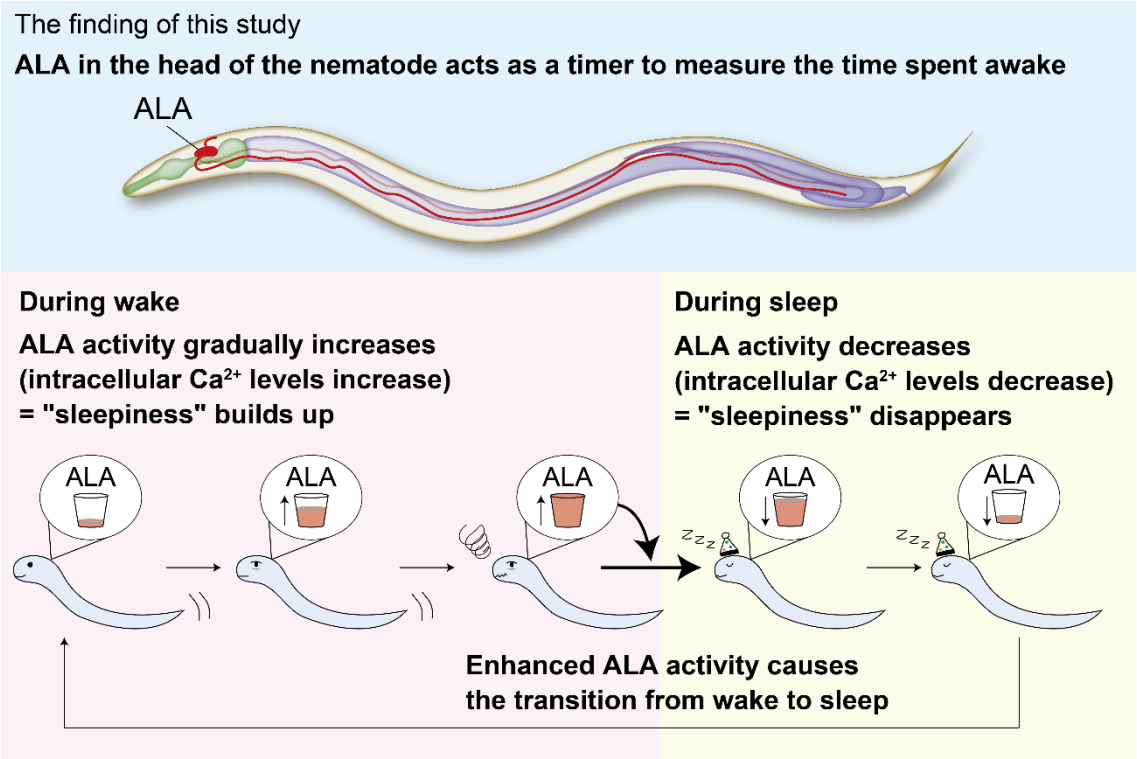
Tsukuba, Japan – Sleep regulation in a worm is not as different from sleep regulation in mammals, including humans, as you may think. Therefore, knowing how worms switch between being asleep and being awake can tell us a lot of useful information about sleep patterns in humans and what cells regulate them.

In a paper published in *iScience* in May 2022, researchers from the University of Tsukuba used the model organism *Caenorhabditis elegans*, a transparent worm, to reveal how "sleepiness" is encoded in the nervous system. *C. elegans* is one of the simplest organisms with a nervous system.

"Our sleep is homeostatically regulated. In other words, the more we stay awake, the more we subsequently sleep. How the preceding amount of wakefulness affects the subsequent amount of sleep still remains a great mystery. *C. elegans* also exhibits alternating cycles of wake and sleep that are homeostatically regulated," explains Professor Yu Hayashi, lead author of the study. Thus, we expected that studies using *C. elegans* might give us hints regarding the molecular and cellular mechanisms underlying the homeostatic regulation of sleep".

The researchers suspected that a single interneuron called ALA is a key player in the process. Intracellular calcium ion currents are essential in neurons; they act as little messengers telling the cell what to do depending on the external circumstances. The research team used a special imaging technique that allowed the visualization of calcium ions in the ALA neuron while the worms were asleep and while they were awake. "This study revealed that the interneuron ALA is crucial for homeostatic regulation of sleep," explains Professor Hayashi,

confirming their initial hypothesis. “We observed that intracellular calcium gradually increased in the ALA neuron during wakefulness and rapidly decayed upon transitions to sleep bouts. In addition, we also found that artificial activation of ALA can cause an immediate transition to sleep. Thus, ALA seems to act as a timer that measures the amount of time spent awake, and when it reaches a certain level it will force the animal to fall asleep. We also found that this function of ALA requires a protein called CEH-17, which is highly conserved in mammals.”



These findings shine light on the mechanisms in charge of the switch between sleep and wakefulness in worms. The next steps could involve studying similar mechanisms in mammals, such as mice and also humans. In addition, the knowledge that CEH-17 plays such a vital role in sleep is highly relevant to sleep dysregulation, and may contribute to the design of new treatments for insomnia and other sleep disturbances.

####

The article, “Intracellular Ca2+ dynamics in the ALA neuron reflect sleep pressure and regulate sleep in *Caenorhabditis elegans*,” was published in *iScience* at DOI: 10.1016/j.isci.2022.104452.

Funding: This work was supported by the JSPS KAKENHI under grant 317 numbers JP21J21778 (to S.M.), JP21H00414 and JP2121H04961 (to Y.H.), CREST, JST under grant 318 number JPMJCR1655, AMED under grant number JP21zf0175005 and the MEXTWPI program (to 319 M.Y. and Y.H.), the Asahi Glass Foundation, the Astellas Foundation for Research on Metabolic 320 Disorders, and the Daiichi Sankyo Foundation of LifeScience (to Y.H.)

Summary: *Caenorhabditis elegans* is a worm that has been used for decades as a model organism. Researchers from the University of Tsukuba have found that a specific neuron, called ALA, and the amount of calcium it contains are essential for the homeostatic regulation of sleep in *C. elegans*. ALA was found to contain more calcium ions when the worms were awake for a long time, and less when they slept. Considering that the molecules involved in sleep regulation are widely conserved, these results may translate to other animals, including humans.

Tweets

Tweet #1: Worms teach us how the brain can measure the time spent awake and force animals to sleep

Tweet #2: Researchers found a highly conserved molecule that is required for homeostatic regulation of sleep in worms

Keywords

Primary Keyword: Life Sciences

Additional Keywords: Neurons, Sleep, Physiology, Calcium, C. elegans

---

Bibliographic information

Miyazaki S, Kawano T, Yanagisawa M, Hayashi Y (2022)

“Intracellular Ca2+ dynamics in the ALA neuron reflect sleep pressure and regulate sleep in Caenorhabditis elegans” published in ***iScience*** at DOI: 10.1016/j.isci.2022.104452.

Media Contact

Alliance and Communication Unit, International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba, Japan

E-mail: wpi-iiis-alliance@ml.cc.tsukuba.ac.jp