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Neurobiology

Visualizing the effects of sleep on neurons' maintenance

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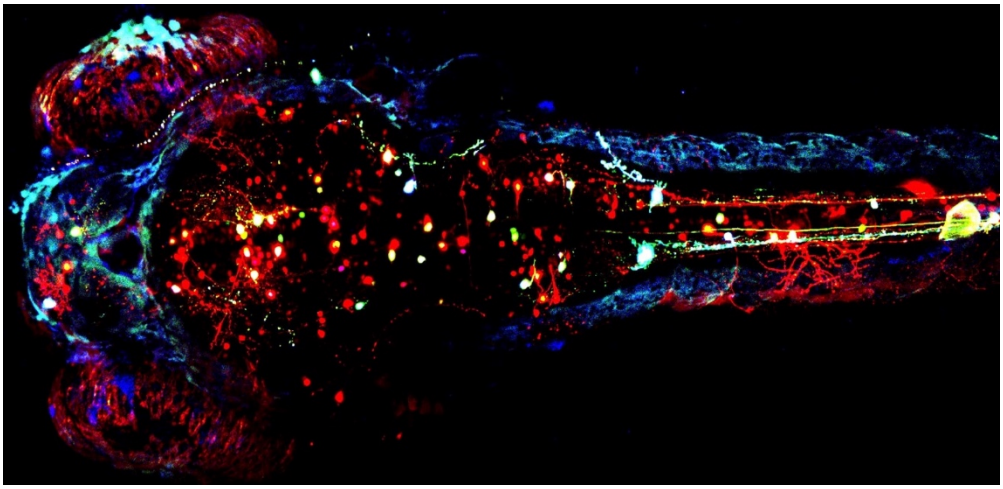
ABSTRACT

All animals sleep and the loss of sleep result in significant deficit to brain performance. Prolonging sleep deprivation could be fatal; however, why do we sleep is still largely an open question. Our research suggests that single neurons require sleep to maintain their DNA.



The transparent zebrafish enables the time-lapse imaging of single neurons and chromosomes in a live animal. Using multicolor fluorescent proteins (Brainbow), each neuron can be labeled independently in the zebrafish brain. Image credits: David Zada©

Why do we spend a third time of our lives sleeping? Why do all animals with a nervous system sleep? And how can we define sleep in all species? From jellyfish to mice to humans, all animals sleep despite the risk of predation and survival. Remarkably, the evolutionarily conserved role of sleep remains a mystery and is considered among the biggest unanswered questions in life sciences.

Much theoretical and experimental research was conducted in an attempt to explain the function of sleep. Indeed, sleep is essential for brain performance, and aids in vital processes, such as metabolic clearance, energy conservation, macromolecule synthesis, synaptic plasticity, learning, and memory consolidation. However, even animals with a basic nerve net require sleep, and sleep in local brain regions was observed in animals such as marine mammals. These observations suggest that sleep could be vital for the function of single neurons.

In our recent study, we used the tiny fish *Danio rerio*, also called "Zebrafish", to study the cellular mechanism of sleep in live animals. Zebrafish is a vertebrate with a conserved yet relatively simple brain compared to mammals, which sleeps during the night, as is the case in humans. Zebrafish are highly amenable for genetic manipulations, and their transparent brain gives a unique opportunity to

image live neurons within the brain in the context of physiological behaviors such as arousal and sleep. We developed 3D imaging techniques to image and quantify the movements of basic DNA structures – chromosomes – within single neurons during the day, night, and sleep manipulations. Surprisingly, sleep increases chromosome movements compared to wakefulness. These sleep-dependent increased movements appeared to be unique to neurons and were not detected in two other cell types.

Why do DNA structures increase their movements during sleep? How do the single neurons, the whole brain, and the entire animal benefit from sleep-dependent increased DNA movements? Analyzing single neurons, we showed that during wakefulness, when chromosome movements are low, DNA damage increases. This accumulation in DNA damage can be the result of chemical species containing oxygen, natural nuclear processes to expedite gene expression, and even neuronal activity. The accumulation of DNA damage eventually triggers sleep that increases the movements of the DNA, which is essential for efficient repair of the DNA damage. If sleep-dependent DNA movements are inhibited in single neurons, DNA damage keeps accumulating, which may lead to malfunctioning neuronal networks and possibly cell death. This could explain how sleep disturbances affect brain performance, aging, and various brain disorders.

Altogether, this work on zebrafish suggests that the role of sleep is to enable efficient nuclear maintenance in neurons. An intriguing allegory could be a city center. During the daytime rush hours, the roads accumulate potholes, wear, and tear. Although we can fix this damage during the day, the most convenient and efficient time to maintain and repair the roads is during low traffic nighttime hours.

These findings open new research capabilities and fields in neuroscience and sleep research. It shifts cell biology experiments into a live transparent, and behaving animal. Furthermore, this work links sleep behavior with processes at the levels of single cells and molecules. It suggests that quantification of chromosome movements can be used to define sleep in individual cells and that one of the functions of sleep is nuclear maintenance. However, further experiments should be performed in new organisms, ranging from cnidarian to mammals, in order to test whether these findings are conserved across all animal kingdom. Regardless, this work provides a possible explanation for why sleep is not a luxury - it is mandatory.