

## News Release

### Orexin Neurons as a Core Motivational System in the Brain

#### Key Points

- Increasing the activity of orexin neurons boosted motivation to work for a reward.
- During reward-seeking behavior, orexin neurons adjusted their activity depending on the situation. Their activity rose when a reward was expected, dropped after the reward was received, stayed high when the expected reward did not appear, and became stronger when more effort was required.
- When the function of orexin neurons was reduced—either with drugs or by suppressing their activity during the reward-prediction phase—motivation decreased.

#### Summary

A research team led by Hiroyuki Mizoguchi, Ph.D., Associate Professor at Nagoya University, and Kiyofumi Yamada, Ph.D., Professor Emeritus (currently Visiting Professor at Fujita Health University), has demonstrated that reward prediction is encoded by orexin neuron activity during motivated behavior.

#### Research Background

Orexin neurons play a central role in many essential functions, including wakefulness, sleep, appetite, and energy balance. Over the nearly 30 years since their discovery, they have also been linked to more complex behaviors such as stress resilience, attention, and motivation. People with narcolepsy, a condition caused by the loss of orexin signaling, often show difficulties in reward-based decision making, suggesting that orexin contributes to emotional and motivational processes as well.

Although many studies have used mice, rats are better suited for examining complex behaviors like motivation because of their superior learning abilities. However, it has been technically challenging to precisely control or monitor specific neurons in rats.

In this study, we used genetically engineered rats that allow selective control of orexin neurons. By combining this with advanced techniques that can track and manipulate neuronal activity with high precision, we investigated how orexin neurons support motivated behavior—specifically, how their activity changes while animals work toward a reward and how they help initiate and sustain motivated actions.

#### Research Results

In this study, animals performed a task in which they had to press a button

several times to earn a food reward. By increasing the amount of effort required and measuring how consistently and quickly the task was completed, we assessed their motivation. When orexin neurons were activated, motivation increased; when these neurons were removed, motivation dropped.

Real-time monitoring of orexin neurons revealed clear activity patterns during motivated behavior. Their activity rose when a reward was expected, decreased after the reward was received, stayed high when the expected reward did not appear, and became stronger when more effort was required. These patterns suggest that orexin neurons help estimate the likelihood of receiving a reward and adjust the level of effort accordingly.

When orexin activity was suppressed during the reward-prediction phase, motivation declined. Together, these findings show that orexin neurons play a key role in linking “expectation” to “action,” and that proper orexin function is essential for initiating and sustaining motivated behavior.

### Research Summary and Future Perspective

Our study shows that orexin neurons play a key role in generating motivation and supporting goal-directed actions. Their activity changed noticeably when a reward was anticipated, and these changes influenced how much effort the animals were willing to invest. This suggests that orexin neurons help estimate “how much effort is needed to obtain a reward” and drive the behavior required to achieve it.

Looking ahead, it will be important to identify the brain circuits that send signals to orexin neurons and those that receive their output. Understanding these pathways may offer new insights into motivational difficulties, such as trouble getting started, difficulty sustaining effort, or, in some cases, excessive drive.

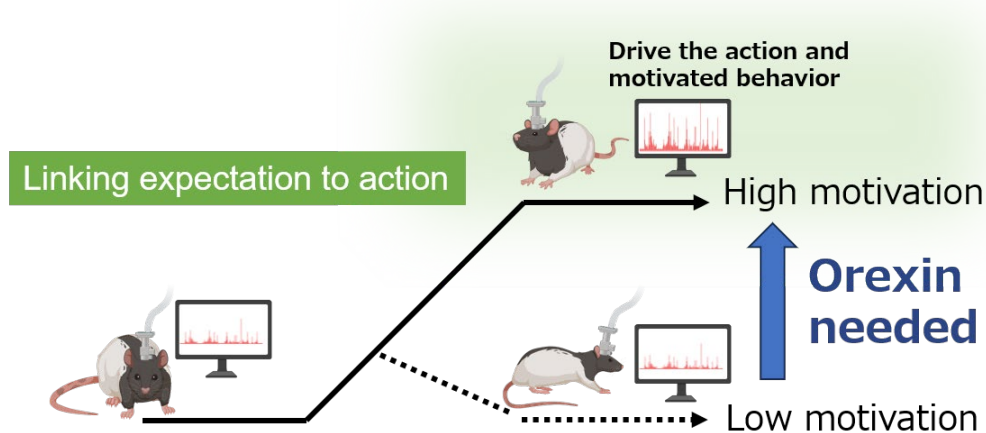


Figure. Reward prediction is encoded by orexin neuron activity during motivated behavior

## **Publication**

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