Goal9 Realization of a mentally healthy and dynamic society by increasing peace of mind and vitality by 2050.

Understanding the cognitively regulatory basis of food value that controls feeding behaviors

Here begins our new MIRAI

MOONSHOT
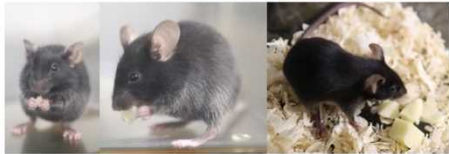RESEARCH & DEVELOPMENT PROGRAM

R&D Theme

Understanding the cognitively regulatory basis of food value that controls feeding behaviors

Progress until FY2022

1. Outline of the project

We developed a feeding behavioral task in mice that reproduces the food valance

Mouse eating cheese (eating with hands)

change observed in humans, and a behavioral task in which positive emotion is generated by feeding. Using these tasks, we tried to identify the brain regions/ neurons that generate positive and negative emotions in response to food valence, as well as the memory engrams that store food experience through comprehensive analyses of neural activity-dependent gene expression in the brain followed by computational analysis.
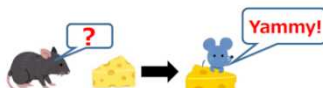
2. Outcome so far

Development of a mouse feeding behavior task modeled on the human food valence change

Mouse feeding behavioral tasks in this study

Neophobia (Even if it's their favorite cheese, they don't eat much at first.)

Sensory satiety task (Mice keep eating the same food and next time eat a different food)

Yammy!

Which do you like?

We have established mice feeding behavior tasks mimicking human behaviors, in which mice show food neophobia; mice eat more food the next time compared to the first time, even if the food is highly palatable (e.g., cheese), and sensory satiety; mice preferentially eat something else after keeping eating the same food. Interestingly, when the mice continued to be fed cheese

In the experimental box, if cheese is always placed in the white box, the mice will prefer to stay in the white box even if there is no cheese.

Black box   White box

after their normal food, they saved the amount of normal food they ate and tried to eat more cheese (food withholding task). Importantly, this task will allow us to evaluate the likes or dislikes of food in mice compared to normal food.
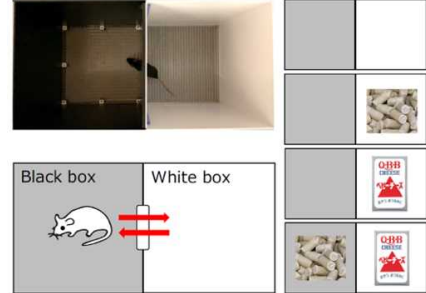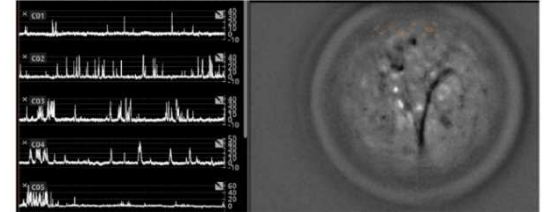
Generation of positive emotion by feeding cheese

We performed conditioned place preference tasks and found that mice stayed longer in the location (white box in the above figure) where they had fed cheese, indicating a preference for the white box. Therefore, we hypothesized that cheese is a highly preferred food for mice, and that generates positive emotions.

Identification and characterization of neurons that stores feeding experience (memory engrams)

Using the feeding behavior tasks, we comprehensively analyzed the brain regions showing increased neural activity after cheese intake by measuring the neural activity-dependent gene expression (c-fos) to identify brain regions involved in memory engrams. Significant gene expression was observed in a variety of brain regions including the medial prefrontal cortex (mPFC). Subsequent computation analysis established by us suggested neural networks involved in memory engrams encoding feeding experience.

We are trying Ca^{2+} live imaging to measure the neuronal activity of neurons in the mPFC.

The activation of brain regions observed after cheese intake is comparable to the neural activity after traumatic experiences such as fear conditioning, suggesting that

Live Ca^{2+} imaging of neuronal activity in the prefrontal cortex

emotional responses to the first experience of cheese are as strong as those to traumatic experiences. Thus, the first experience of feeding cheese is thought to generate strong memory associated with positive emotion. First cheese intake may be a big life event for the mouse.

3. Future plans

We are trying to understand the biological mechanisms for controlling food valence by identifying memory engrams and subsequent circuits analyses. We will also understand the mechanisms for generations of positive emotion by feeding highly preferred food. On the other hand, as research on human subjects, we will develop tasks that analyze changes in food valence that are homologous to the tasks in mice to understand the neural basis of food valence change using fMRI and other techniques. In the future, through collaboration between human and mouse research, we will understand the mechanism in the brain that changes food valence and try to achieve the goal of "increasing mental comfort and vitality" from the viewpoint of food.
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