R&D item

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

Progress until FY2023

1. Outline of the project

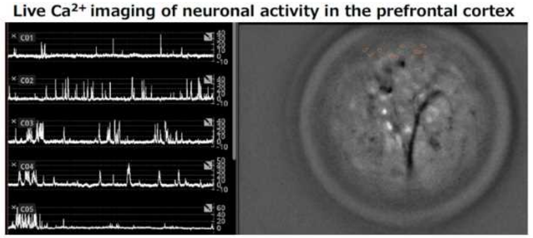
We developed a feeding behavioral task in which mice reproduce the food valance change observed in humans, and positive emotion is generated by feeding. We tried to identify the brain regions/neurons that generate positive and negative emotions in response to food valence, and the memory engrams that store food experience in the brain using these tasks. We discovered memory engram neurons that are active after feeding specific foods. Interestingly, we also established an experimental model in which the food valence with low preference increases in an experience-dependent manner. Additionally, we developed a video task to induce the sensory-specific satiety observed in mice and humans for human brain imaging using fMRI to understand the neural basis of food valence change in humans.

2. Outcome so far

Identification of Memory Engrams for Food Experience (Mouse Study)

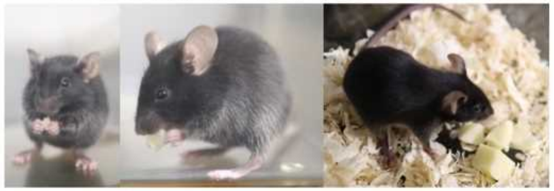
We analyzed the areas that increased neural activity after feeding novel food by analyzing neural activity-dependent gene expression. We suggested that food memory engrams are observed in several brain regions. Based on these findings, we performed Ca^{2+} imaging under free-moving conditions using a brain-mounted mini-microscope (left figure) by expressing calcium indicators in neurons using a virus. We found active neurons after feeding a specific food. Thus, we are identifying food memory engram neurons.

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



Mechanism of emotion generation after food experience (mouse research)

Mouse eating cheese (eating with hands)



To understand the mechanism for the generation of positive emotion by feeding highly palatable food, we established conditioned place preference tasks using cheese. We comprehensively analyzed brain regions activated following retrieval of this conditioned place preference memory and identified brain regions involved in the generation of positive emotions.

Brain regions that determine food valence (mouse study)

We tried to identify brain regions activated after feeding cheese, sweet chocolate, and bitter chocolate with high cocoa content for the first time. We found brain regions that are activated after feeding novel foods, only after feeding a highly palatable food, and only after feeding a less palatable food, respectively. These findings suggested that different neural circuits are activated in the brain depending on the novelty and/or food valence.

Establishment of a task to improve food valence (mouse research)

Conditioned taste aversion is, widely observed in animals, including humans, a phenomenon in which the experience of visceral discomfort after eating novel food first leads to avoidance of that food (like disliking a food after food poisoning). Referring to this task, we found that drinking a bitter solution with nicotine administration that generates positive emotions increases the preference for the bitter solution. Interestingly, this phenomenon was also observed when coffee was used as the bitter solution. Thus, we established a new task that evaluates food valence for bitter solutions.

Mechanisms of sensory-specific Satiety in humans and mice

Sensory-specific satiety is a phenomenon in which the food valence is devaluated with eating the same food. We established a mice model task of sensory-specific satiety in which mice are fed food A or B (cereal and refined food) for an hour and then ate more food B than food A when food A and B are given together. We are now trying to identify the brain regions involved in this sensory-specific satiety. Importantly, we developed a new movie task to induce sensory-specific satiety to perform brain imaging analysis such as fMRI for human research. We generated a movie that makes the subjects imagine eating snacks and conducted a questionnaire survey. Our results indicated that only snacks that the subjects imagined themselves eating induced sensory-specific satiety.

3. Future plans

We are trying to understand the biological mechanisms for controlling food valence by identifying memory engrams using chemical genetics and optogenetics. We will also understand the mechanisms for generations of positive emotion by feeding highly preferred food. Furthermore, we aim to understand the neural basis of the change in food valence using fMRI, using the newly developed movie that induces sensory-specific satiety in humans. Through these analyses, we try to understand the common neural basis of food valence change by comparing the results of human and mouse research.