Here begins our new MIRAI
MOONSHOT RESEARCH & DEVELOPMENT PROGRAM

R&D Theme

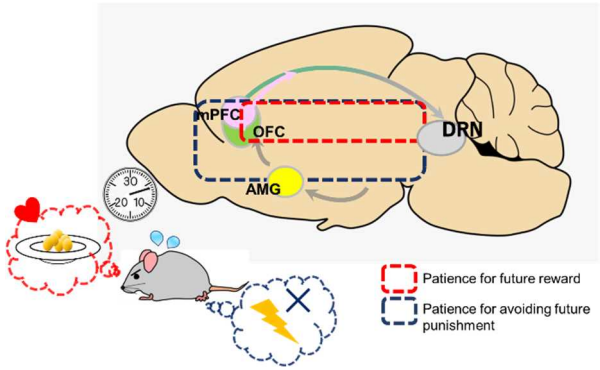
Serotonin subsystem for optimism and pessimism: Optogenetics

Progress until FY2022

1. Outline of the project

In this research topic, we directly control neural activity of behaving mice from the outside. Using genetically modified mouse, we use the latest technology called optogenetics, which manipulates neural activity by light, to explore optimism and optimism in the mind. In the experiment, we examine how mice's behavior and neural activity in serotonin projection sites are affected, when light stimulus manipulates serotonergic neural activity while mice are working hard to achieve their future goals.

Our hypotheses: Different neural circuits including serotonin neurons contribute to patience behavior for reward acquisition and punishment avoidance

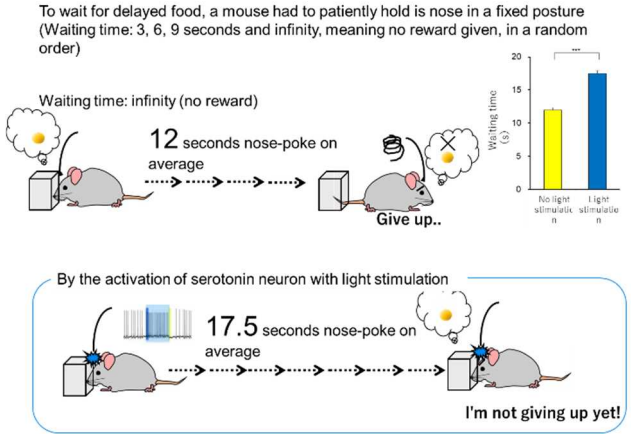


In this study, we focus on the dorsal raphe nucleus (DRN), which is the nucleus origin of serotonergic neurons, and the medial prefrontal cortex, orbitofrontal cortex, and amygdala, which are the projection sites of serotonergic neurons. These brain regions are known as the neural substrates that organize action selection and decision-making based on sensory input and are important for generating our mind. We will verify our original hypothesis with the latest technology and clarify the serotonergic neural mechanism that produces "I'm sure things will go well".

2. Outcome so far

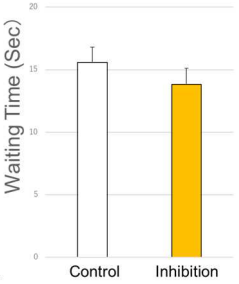
2.1 Behavioral changes by serotonergic manipulation of DRN

In our previous research, when it was predicted that mice would be able to obtain rewards in the future by waiting without getting impatient, optogenetic activation of serotonin neurons during waiting for reward enabled them to wait longer (be patient) (Miyazaki et al., Curr Biol 2014).



We also found that serotonin, which promotes patience, works differently in medial prefrontal cortex and orbitofrontal cortex (Miyazaki et. al., Sci Adv 2020).

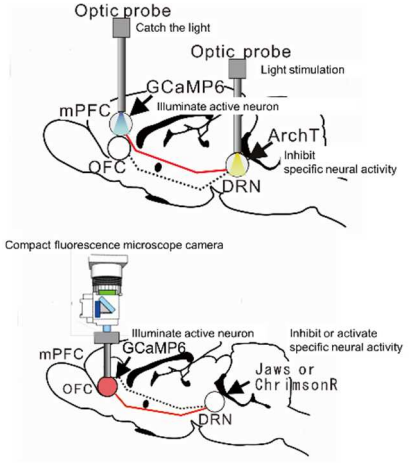
We also confirmed optogenetic inhibition of serotonin neurons during waiting for delayed reward shortened the waiting time (easily gave up).



3. Future plans

2.2 Changes in neural activity by serotonin manipulation (excitation/inhibition)

In parallel with these experiments, we will investigate how serotonin neurons in DRN affects neural activity of serotonin projection sites to understand at the network level.



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