R&D Theme

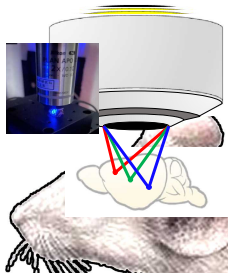
Optical manipulation of functional brain networks by optogenetics

Progress until FY2022

1. Outline of the project

In this R&D project, we use optogenetics, a technology to control neural activity with light, to induce changes in the brain function network artificially. By analyzing the changes in mouse behavior observed, we clarify how the functional brain network responds to changes in the "mind" and changes in behavior.

The elemental technology to be developed in this R&D project is a method of optical manipulation of the functional brain network by simultaneous optical stimulation of multiple brain points from the outside of the mouse cranium. For this purpose, we are constructing a holographic multi-point simultaneous cellular optical stimulation with a 3D measurement of brain shape and a 3D observation system.

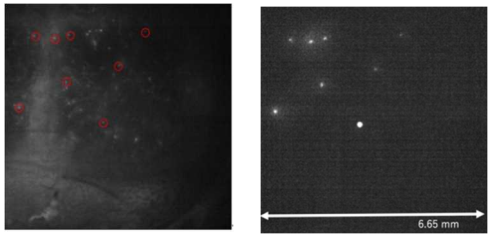


Overview of wide-field holographic microscopy covering the whole brain

2. Outcome so far

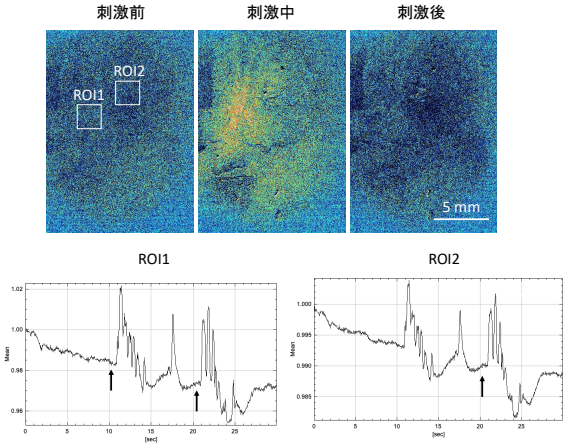
We have constructed a system that enables high-speed, three-dimensional observation of the brain by applying optical stimulation to precise areas based on brain geometry. Conventional optical light stimulation studies have been limited to small brain regions, but in this study, we constructed an experimental system that enables holographic light stimulation using a low-magnification objective lens to apply to the entire mouse cerebral cortex spanning 1 cm. Performance evaluation using fluorescent beads confirmed that the constructed system could cover a wide field of view of 6.6 mm and can also perform light illumination and fluorescent observation with a high spatial resolution of 20 μm.

Using this system, we also demonstrated that holographic light stimulation is possible through the skull by irradiating fluorescent beads applied to the skull of a mouse.



(Left) Fluorescent image of uniform illumination by LED light. Fluorescent images from individual fluorescent beads can be seen in the area circled in red. (Right) Multiple fluorescent beads were selected through the skull and simultaneously photostimulated using a hologram at the exact bead position. It can be seen that the beads were selectively and correctly photostimulated through the skull.

We also constructed a macro calcium imaging system for holographic optical stimulation of live mice using a low-magnification objective lens to detect the response to stimulation. We observed the reaction of the mouse cerebral cortex and confirmed that the system can detect the brain response to stimulation.



Visualization of the calcium response of the mouse brain to sensory stimulation by macro calcium imaging. Electrical stimulation was applied to the orbital nerve at the time of the arrow in the figure below.

3. Future plans

We will develop a technology to manipulate the mouse cortical neural network. Namely, we will construct a holographic multi-point simultaneous cellular photostimulation and 3D observation system that simultaneously stimulates multiple points in the mouse cortex.

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