News Release

Title

Large Timescale Interrogation of Neuronal Function by Fiberless Optogenetics Using Lanthanide Micro-particles

Key Points

○ To achieve behavioral control experiment using optogenetics, insersion and tethering of optical fiber to the experimental animal was unavoidable. In order to solve various problems caused by this, we developed fiber-less optogenetics which does not use optical fiber.

○To manipulate nerve activity with near infrared light, lanthanide microparticles which convert near infrared light to visible light with high efficiency by up-conversion reaction were used. By injecting lanthanide microparticles into the brain and irradiating near infrared light from outside the body, visible light was emitted in the deep tissue. We manipulated the nerve activity by that light and showed that it is possible to control behavior of individual animals.

○ It was possible to manipulate for 8 weeks after the injection of the lanthanide microparticles, and it was shown that the usual behavioral experiment can be sufficiently performed by one injection.

Summary

The research group of Professor Akihiro Yamanaka, Associate Professor Yamashita Takayuki of Research Institute of Environmental Medicine, Nagoya University, collaborated with the Japan Science and Technology Agency (CREST, PRESTO), Tohoku University, Tokyo institute of Technology, developed fiber-less optogenetics. We have developed a technology to manipulate nerve activity without fiber optics insertion.

Optogenetics that manipulates functions of target neurons with high temporal and spatial resolution using light requires the expression of opsin that manipulates nerve activity by sensing light of a specific wavelength. These opsins sense visible light (400 - 600 nm) which is low tissue permeability, it was unavoidable to insert and tethering fiber optics to deliver visible light to deep tissue. Insertion and tethering of fiber optics caused tissue damage and behavioral restriction. Thereby limiting the type of behavioral experiments or affecting experimental results.

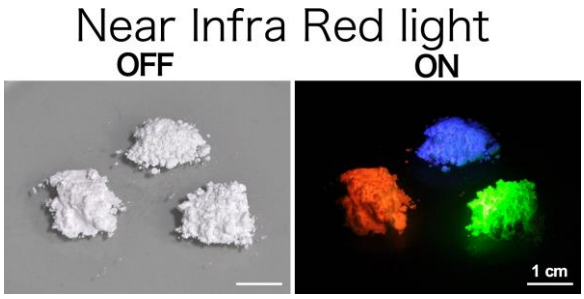
Therefore, in order to solve these various problems caused by insertion and tethering of fiber optics, we developed fiber-less optogenetics using near-infrared light which has high tissue-permeability. In order to manipulate nerve activity with near infrared light, we used lanthanide microparticles that convert near infrared light to visible light with high efficiency by up-conversion reaction. The up-conversion reaction is a reaction of converting light of long wavelength into light of short wavelength, and near infrared light (967 nm) is converted into visible light (540 nm) by a combination of rare earth element, lanthanide. By microinjecting

these lanthanide microparticles in the brain and irradiating near infrared light from outside the body, visible light is emitted in the deep tissue, the nerve activity is manipulated by the light, and behavior control of animals can be performed. Behavioral control is possible for 8 weeks after the injection of lanthanide microparticles and it has been shown that long-term behavioral experiments can be sufficiently performed by single injection.

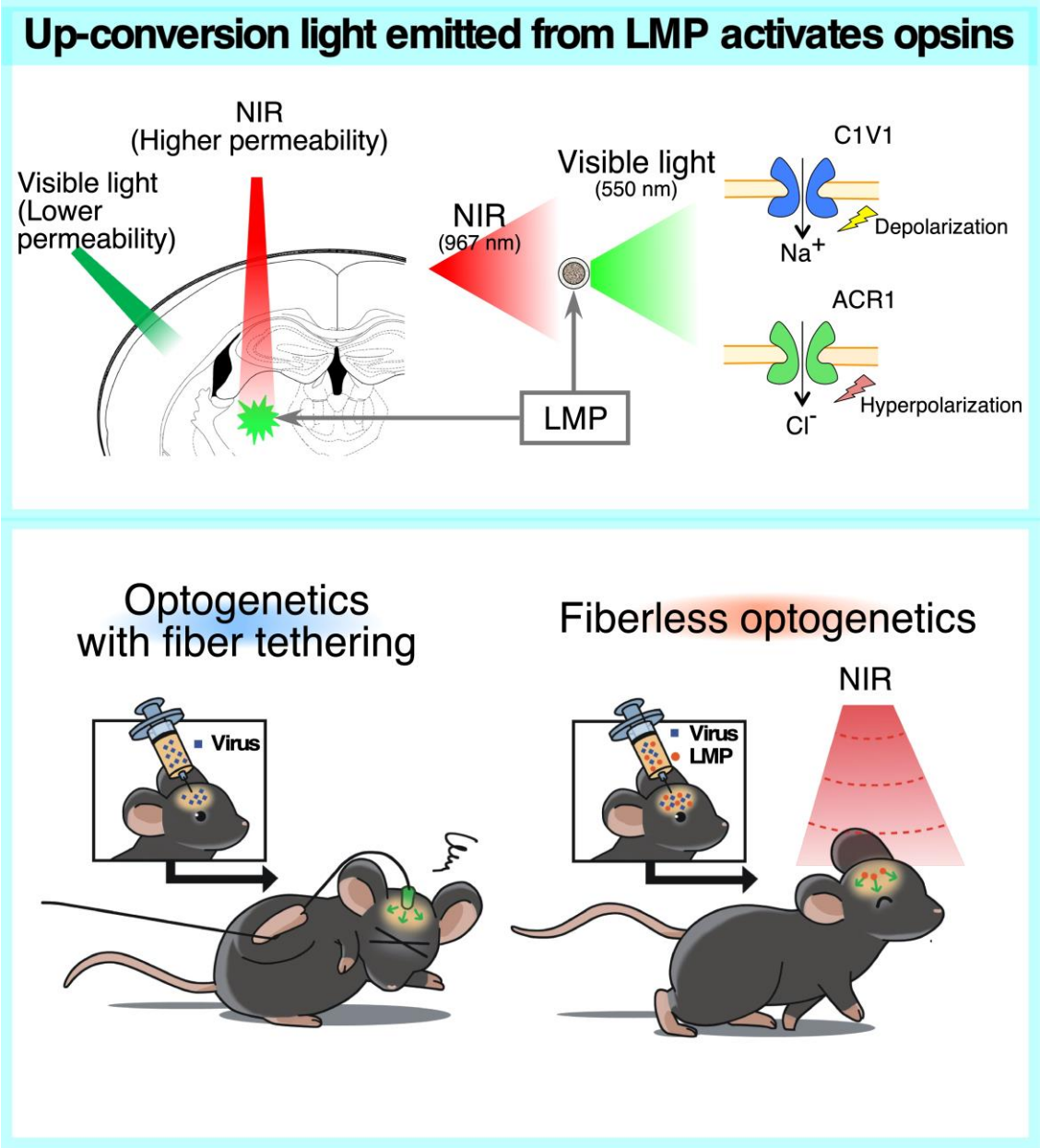
Research Background

Optogenetics that manipulates specific cell functions with high temporal and spatial resolution using visible light with low tissue permeability. So for light delivery to deep tissue, it was unavoidable insertion and tethering of fiber optics to experimental animal. Due to insertion and tethering of fiber optics, tissue damage and behavioral restriction are inevitable. Thereby limiting the type of behavioral experiments, or the experimental results included effects of tissue damage.

Research Results



Lanthanide microparticles (LMP, upper figure) that convert near-infrared light to visible light (red, blue, green) by up-conversion reaction were used. A channel rhodopsin mutant C1V1, which activates nerve activity by green light, was expressed in the striatal neurons, which is a brain region involved in motor control, and a lanthanide particle emitting green light was injected in a very small amount into the same region. By illuminating near-infrared light from the outside of the body of the mouse, green up-conversion luminescence was emitted from the lanthanide microparticles in the brain, and the striatal nerve cells were activated. As a result, the spontaneous behavior of mice increased. In addition, anion channel rhodopsin (ACR1), a molecule that suppresses nerve activity by green light, was expressed in the striatal nerve and suppression of neuronal activity was performed, and coordinated movement of mice were suppressed. From these results, neural activity manipulation became possible without inserting fiber optics (below figure). Since behavior control was possible for 8 weeks from the injection of lanthanide microparticles, it was confirmed that the study of neural circuit function can be performed for a long time.



Research Summary and Future Perspective

Improvement to further deep nerve cell activity manipulation eliminates the need for optical fiber insertion in many experiments using optogenetics. This increases applicable behavioral experiments, and elucidation of neural circuit function accelerates.

Publication

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Large Timescale Interrogation of Neuronal Function by Fiberless Optogenetics Using Lanthanide Micro-particles
Cell Reports, published online on January 22, 2019.
DOI: 10.1016/j.celrep.2019.01.001

Japanese ver.
https://www.med.nagoya-u.ac.jp/medical_J/research/pdf/Cell_R_20190123.pdf