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Deep brain stimulation realized with the help of nanoparticles

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Video Abstract

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Abstract

Light-responsive proteins have revolutionized our understanding of the brain. By introducing the genes encoding these proteins into neurons and then exciting the cells using lasers – a technique known as optogenetics – individual cells can be rapidly turned on or off, enabling exquisitely sensitive investigations of brain function. But a fundamental limitation of the method is that light doesn’t travel very far through brain tissue, which has hampered the study of more buried – and often vital – structures. Now, researchers at the RIKEN Center for Brain Science have developed a way to extend the reach of optogenetics by nearly an order of magnitude, providing new possibilities for deep-brain stimulation. The team accomplished this using a special type of nanoparticle known as an upconversion nanoparticle, so named for its ability to transform – or “upconvert” – near-infrared light into visible output. Near-infrared light penetrates deeply into brain tissue, but it’s not transmitted at the right wavelength to activate lightresponsive proteins. The nanoparticles bridge this gap by transforming near-infrared wavelengths into visible light, which can be picked up by the proteins. In this way, the particles can effectively expand the optogenetic range. The scientists injected the nanoparticles into different brain regions in mice and then applied transcranial near-infrared stimulation, providing a minimally invasive way to manipulate brain activity. They found that the nanoparticles largely remained at the site of injection, which gave a high level of control in targeting specific areas. The team also altered the particles to make them emit different wavelengths of light. By changing whether the particles emitted green versus blue light, for example, they could selectively activate or inhibit neighboring neurons that contained different types of light-responsive proteins. Using this method, the group successfully stimulated dopamine release, silenced seizure activity, triggered memory recall, and modified fear responses in living animals. The particles’ outer coatings were also modified to improve their biocompatibility, thereby enhancing their safety. Although much testing is still needed before the technology can be used in human brains, the use of upconverting nanoparticles should allow researchers to safely explore nearly the entire mouse brain, opening the door to greater understanding of brain function and health.