Developing Nanoprobes to Detect Neurotransmitters in the Brain

2023-03-05

Researchers synthesize fluorescent molecularly imprinted polymer nanoparticles to sense small neurotransmitter molecules and understand how they govern brain activity.

Neurons perform numerous complex tasks by communicating with each other via small messenger molecules called neurotransmitters. Accurately detecting them is crucial to understanding the functioning of our brain. To this end, researchers at the Shibaura Institute of Technology have demonstrated that fluorescent nanoparticles imprinted with the molecular structure of a target neurotransmitter, immobilized on glass beads at a controlled surface density, can detect specific neurotransmitters based on their expansion during interaction with the target transmitters.

The animal brain consists of tens of billions of neurons or nerve cells that perform complex tasks like processing emotions, learning, and making judgments by communicating with each other via neurotransmitters. These small signaling molecules diffuse – move from high to low concentration regions – between neurons, acting as chemical messengers. Scientists believe that this diffusive motion might be at the heart of the brain's superior function. Therefore, they have aimed to understand the role of specific neurotransmitters by detecting their release in the brain using amperometric and microdialysis methods. However, these methods provide insufficient information, necessitating better sensing techniques.

To this end, scientists developed an optical imaging method wherein protein probes change their fluorescence intensity upon detecting a specific neurotransmitter. Recently, a group of researchers from Shibaura Institute of Technology in Japan led by Professor Yasuo Yoshimi has taken this idea forward. They have successfully synthesized fluorescent molecularly imprinted polymeric nanoparticles (fMIP-NPs) that serve as probes to detect specific neurotransmitters–serotonin, dopamine, and acetylcholine. Notably, developing such probes has been considered difficult so far. Their groundbreaking work, published in Volume 13,

Issue 1 of the journal Nanomaterials on 3 January 2023 involves contributions from Mr. Yuto Katsumata, Mr. Naoya Osawa, Mr. Neo Ogishita, and Mr.Ryota Kadoya.

Prof. Yoshimi briefly explains the fundamentals of fMIP-NP synthesis. “It involves multiple steps. First, the target neurotransmitter to be detected is fixed on a glass beads surface. Next, monomers (building blocks of polymers) with different functions – detection, cross-linking, and fluorescence – polymerize around the beads, enveloping the neurotransmitter. The resulting polymer is then washed out to obtain a nanoparticle with the neurotransmitter structure imprinted as a cavity. It will fit only the target neurotransmitter, just like only a particular key can open a lock. Hence, fMIP-NPs can detect their corresponding neurotransmitters in the brain.”

When the target neurotransmitters fit inside the cavity, the fMIP-NPs swell and get bigger. The researchers suggest that this increases the distance between the fluorescent monomers that, in turn, reduces their interactions, including self-quenching that suppresses fluorescence, with each other. As a result, the fluorescence intensity is enhanced, indicating the presence of the neurotransmitters. The researchers improved their selectivity of the detection by adjusting the neurotransmitter density on the surface of the glass beads during fMIP-NP synthesis.

Additionally, the choice of material for fixing the neurotransmitters was found to play a crucial role in the detection specificity. The researchers found that blended silane is better than pure silane for attaching the neurotransmitters, serotonin and dopamine, to the glass bead surface. The fMIP-NPs synthesized using blended silane specifically detected serotonin and dopamine. In contrast, those synthesized using pure silane resulted in non-specific fMIP-NPs that responded to non-target neurotransmitters, identifying them incorrectly as serotonin and dopamine. Likewise, poly([2-(methacryloyloxy)ethyl] trimethylammonium chloride (METMAC)-co-methacrylamide) but not METMAC homopolymer was found to be an effective dummy template of the neurotransmitter acetylcholine. While the former produced fMIP-NPs that selectively detected acetylcholine, the latter led to unresponsive nanoparticles.

These results demonstrate the feasibility of fMIP-NPs in the selective detection of

neurotransmitters released in our brain. “Imaging the brain with this new technique could reveal the relationship between neurotransmitter diffusion and brain activity. This, in turn, can help us treat neurological diseases and even create advanced computers that mimics human brain functions,” said Professor Yoshimi, who is enthusiastic about the innovative research.

Read the original article on Shibaura Institute of Technology.