Shining light on neuromodulator function with iTango, a new reporting system of ligand-receptor interactions

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Video Abstract

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Abstract

Ever wonder why missing your morning train is sometimes annoying but other times a welcome opportunity to grab some coffee? You can thank proteins called neuromodulators for that. These proteins determine your mood and the cellular activity that produces your response. Exactly how neuromodulators do this has remained a mystery because it's been impossible to witness their effects at precise moments in time. But a technological tweak made by researchers at the Max Planck Florida Institute for Neuroscience has revealed neuromodulator function like never before. That could pave the way toward improved understanding of the diversity of human behaviors. Researchers have typically relied on sensors that change gene expression to watch neuromodulators at work. When a neuromodulator binds to a receptor fitted with this type of sensor, it drives the expression of a fluorescent protein. This tiny beacon thus labels cells influenced by the neuromodulator. The problem with these sensors is that scientists couldn't use them to link a neuromodulator's effects to a specific behavior because they couldn't pinpoint when the sensors were activated. The researchers overcame this limitation by adding an external, light-controlled switch to existing sensors. With this switch, they could restrict the sensor's activation and its reporting of the neuromodulator's effects to events that occurred when they were shining blue light. The researchers demonstrated the advantages of the improved sensor system by using it to identify the cells involved in reward-based learning. This form of learning depends on the well-known neuromodulator dopamine, which is released in anticipation of rewards like food or praise. The scientists expressed the dopamine sensor in the brains of mice trained to walk on a ball with various textures; when the mice stopped on a specific texture, they got a drink of water. Thirsty mice were motivated to find the water-associated texture to receive their refreshing reward. So when the researchers paired blue light with water delivery during learning, they could see the cells that transformed the dopamine reward signal into puzzle-solving behavior because they expressed the marker. The scientists also made improved sensors for other neuromodulators like serotonin. This arsenal of improved sensors will likely provide considerable insight into how neuromodulators shape behavior, including in addiction and mood disorders.