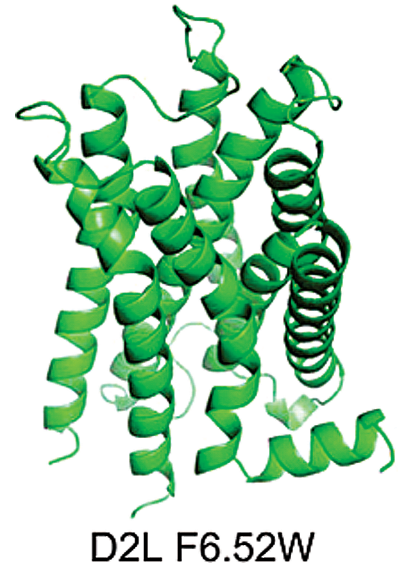
Modifying the Dopamine Receptor

G-protein-coupled receptors (GPCRs) are involved in myriad activities in neuroscience including the regulation of the autonomic nervous system, the regulation of mood and behavior, and the perception of smell and sight. Among the GPCRs, receptors for the neurotransmitter dopamine are associated with diverse processes such as cognition, learning, motivation, the perception of pleasure, and the coordination of movement. Currently, targets of GPCRs represent almost half the market for drugs and, therefore, are a major focus area in biomedical research.

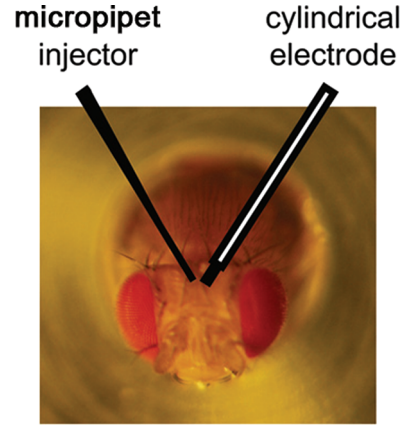
Within the past decade, scientists have realized the potential for studying neurotransmission by using engineered GPCRs that are activated by synthetic ligands but not by endogenous ones. Now, Tschammer et al. (DOI: 10.1021/cn900001b) present the first receptor activated solely by a synthetic ligand (RASSL) for the dopamine receptor family of GPCRs but not activated by dopamine. The orthogonal ligand−receptor pair described by the authors provides a novel tool for researchers to investigate GCPRs in specific milieus and is a step in engineering ligand−receptor pairs with novel function.



Doping Flies

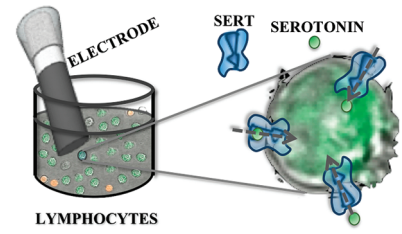
The neurotransmission of dopamine has been implicated in addiction-reinforcing mechanisms of abuse of many drugs. Electrochemical techniques have been employed extensively for monitoring *in vivo* dopamine changes in the brains of model organisms including rats, mice, and primates.

Now, Makos et al. (DOI: 10.1021/cn900017w) investigate the effects of several drugs on the central nervous system of the model fruit fly, *Drosophila melanogaster*. Using recently developed microanalytical tools, the authors carried out measurements of dopamine neurotransmission. Specifically, they used a small carbon fiber to make a microelectrode that was then placed in the brain of the fly to measure the concentration of various chemical compounds. The results indicate that the rate at which nerve cells take up dopamine is decreased by administering psychostimulants. This observation is similar to what is noticed in mammals. The authors conclude that it might be possible to use fruit flies as model organisms for extensive studies on the cellular and molecular mechanisms of human drug addiction.



A Better Way To Measure Serotonin

The serotonin transporter (SERT) controls serotonin neurotransmitter signaling in the central nervous system. It is the target of drugs commonly used to treat anxiety and depression and of drugs of abuse like cocaine and Ecstasy. A common genetic variant in the promoter region of this gene is associated with differences in anxiety-related personality traits and susceptibility to depression in humans. However, mechanistic details have been lacking.



© 2010 American Chemical Society

DOI: 10.1021/cn9000395 | *ACS Chem. Neurosci.* (2010), *1*, 2–3

It has been known that the SERT gene is also natively expressed in peripheral lymphocytes. Now, using a very sensitive electrochemical technique combined with fouling-resistant boron-doped diamond microelectrodes, Singh et al. (DOI: 10.1021/cn900012y) find differences in serotonin uptake associated with a similar gene variant in peripheral blood lymphocytes of rhesus monkeys. These results suggest that peripheral lymphocytes can be used as markers to study central nervous system function in primates.

© 2010 American Chemical Society

DOI: 10.1021/cn9000395 | *ACS Chem. Neurosci.* (2010), *1*, 2–3