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In This Issue

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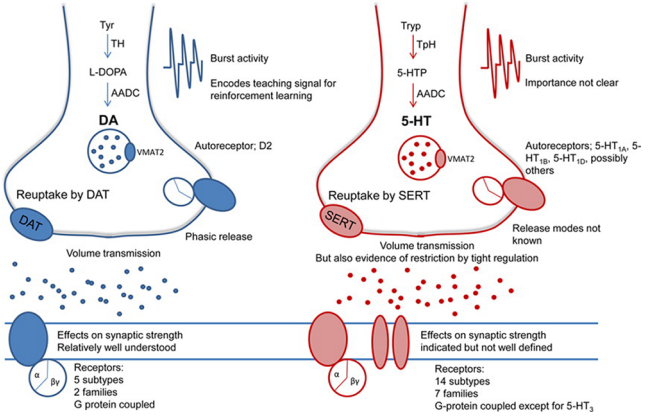
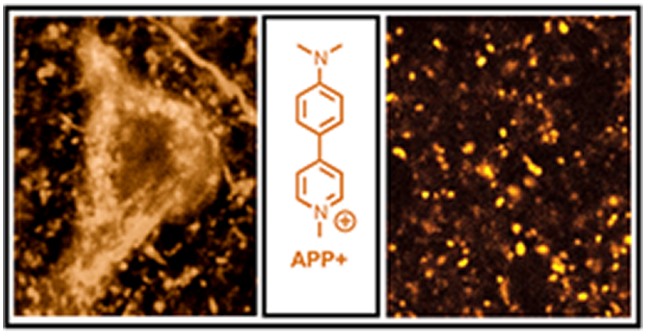
UNDERSTANDING SEROTONIN SIGNALING VIA FAST-SCAN CYCLIC VOLTAMMETRY



Selective serotonin-reuptake inhibitors (SSRIs) are currently the most widely prescribed antidepressant and antianxiety medications. However, SSRI use is also associated with side effects. Therefore, a clearer understanding of serotonin neurotransmitter signaling as it pertains to mechanisms of action of SSRIs is of great importance. In the current issue, two papers make contributions in this regard.

Wood and Hashemi (DOI: 10.1021/cn4000378) describe the acute effects of the SSRI escitalopram (ESCIT) on serotonin kinetics using fast scan cyclic voltammetry (FSCV) in anesthetized mice. They found that ESCIT inhibited uptake of serotonin, as expected. Moreover, serotonin release was increased acutely, a finding that relied on fast serotonin measurements. Also in the current issue, Katie Jennings (DOI: 10.1021/cn4000605) reviews current understanding of dopamine neurobiology achieved through the use of FSCV. Comparing and contrasting the neurobiology of the dopamine and serotonin systems, the author provides insight on the field and suggests future avenues of study.

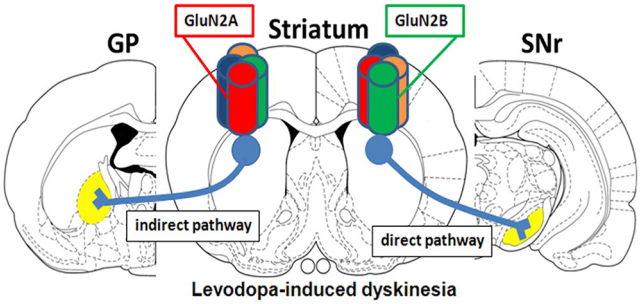
DEVELOPING NEW FLUORESCENT NEUROTRANSMITTER PROBES



Monitoring chemical neurotransmission in the brain with spatial resolution at the level of individual synapses has been a long-standing challenge. David Sulzer, Dalibor Sames, and colleagues (DOI: 10.1021/cn4000956) express their views on recent advances toward this goal. Also in the current issue, these authors (DOI: 10.1021/cn400038u) describe the development of a new class of imaging probes called "fluorescent false neurotransmitters" (FFNs) for optical imaging of neurotransmitter signaling.

The authors describe a fluorescent pyridinium dye, APP+, for studying the functions of dopamine transporters (DAT), norepinephrine transporters (NET), and serotonin transporters (SERT). DAT and NET accumulate APP+ in catecholaminergic neurons; however, only a small change occurs in the fluorescence signal during stimulated release, and this appears to limit the suitability of APP+ for use as a FFN.

REGULATION OF STRIATAL DOPAMINE DYNAMICS



Dopamine (DA) systems play major roles in a number of important brain functions, and DA dysfunction is implicated in several disorders, notably Parkinson's disease and schizophrenia. As a result, the development of drugs modulating DA concentrations or targeting DA transporters (DAT), particularly in specific brain regions, is of high therapeutic value. In the current issue, four independent papers contribute toward our understanding of the regulation of dopamine dynamics.

Abnormal involuntary movements, known as dyskinesias, are a major complication of long-term pharmacotherapy of Parkinson's disease with the dopamine precursor, L-DOPA. Mabrouk et al. (DOI: 10.1021/cn400016d) elucidate reciprocal functions of two NMDA receptor subunits, GluN2A and GluN2B, on different striatal pathways in a model of L-DOPA-induced dyskinesia.

Serotonin $(5\text{-HT})_{1A}$ receptor agonists have been shown to diminish dyskinesia while maintaining L-DOPA's effectiveness thus far; however, their clinical translation has been variable. Now, Dupre et al. (DOI: 10.1021/cn300234z) show that combined 5-HT_{1A} and D1 receptor stimulation in hemiparkinsonian rats leads to antidyskinetic and pro-rotational effects with concurrent increases in striatonigral GABA activity.

In a separate paper, Spanos et al. (DOI: 10.1021/cn4000499) use fast-scan cyclic voltammetry to study H_2O_2 dynamics in vivo, and to demonstrate directly a precise physiological interaction between H_2O_2 and DA in the striatum. Also in the current issue, Taylor et al. (DOI: 10.1021/cn400078n) use FSCV to study DA microdomains in the striatum. These authors show differential effects of DAT

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inhibition on dopamine signaling in "fast" versus "slow" domains in the dorsal striatum. The findings suggest that dopamine diffusion is restricted to microdomains and shed important light on new aspects of striatal dopaminergic neurochemistry.

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