In This Issue

Volume 77, Number 2, January 15, 2015

A brief summary of the articles appearing in this issue of *Biological Psychiatry.*

Molecular and Synaptic Mechanisms of L-DOPA-Induced Dyskinesia

L-DOPA-induced dyskinesia (LID) is a common motor complication of current pharmacotherapy for Parkinson's disease. **Ruiz-DeDiego *et al.*** (pages 95–105) used transgenic and knockout mouse models to investigate the role of DREAM (downstream regulatory element antagonistic modulator), a calcium-binding protein, in LID. They report that DREAM decreases dyskinesia in hemiparkinsonian mice without affecting L-DOPA's therapeutic effect and reduces FosB, dynorphin-B, and phosphoacetylated histone H3 expression induced by L-DOPA in denervated striatal neurons. These data suggest that activation of DREAM through novel therapeutic approaches may effectively alleviate LID.

The synaptic processes underlying LID are largely unknown. Using electrophysiology in mouse slices, **Cerovic *et al.*** (pages 106–115) provide evidence of a central role for extracellular signal-regulated kinase (ERK)-dependent and Ras-GRF1-dependent signaling in corticostriatal plasticity. Their findings indicate that the Ras-ERK cascade, a molecular pathway that has been implicated in LID, controls synaptic functions in the striatum in a complex manner, providing a better understanding of LID at the cellular level.

Altered Event-Related Potentials in Psychotic Disorders

Schizophrenia is associated with social impairments and marked impairment in face processing, which is associated with the N170 and N250 event-related potentials, but the findings in schizophrenia have been inconsistent across studies. **McCleery *et al.*** (pages 116–126) conducted a meta-analysis and found strong support for reduced amplitude in N170 and N250 in schizophrenia patients compared with controls. Effect sizes for the two waveforms were comparable, providing clear electroencephalographic evidence of abnormal cortical face processing in schizophrenia.

Ethridge *et al.* (pages 127–136) assessed event-related potential amplitude measurements and event-related oscillations during an auditory oddball task in a sample of schizophrenia and psychotic bipolar disorder families. N1 and P3b showed evidence as genetic risk markers specific to schizophrenia while P2 was specific to psychotic bipolar disorder. N2 was significant for psychosis in general. These data highlight the shared and unique deficits across psychotic diagnostic groups and, combined with other related abnormalities, may provide insight into deficits underlying the neural architecture of psychosis.

Heritability and Risk for Schizophrenia: Structural Imaging Findings

Abnormalities of subcortical and limbic brain structures are commonly reported in neuroimaging studies of schizophrenia. Using structural magnetic resonance imaging (MRI), **Roalf *et al.*** (pages 137–146) report that subcortical and limbic volume and shape are heritable in multiplex-multigenerational families affected with schizophrenia, compared with healthy subjects. These results indicate that both volume and shape of subcortical and limbic structures are potential endophenotypic markers in schizophrenia and may aid in the identification of specific genetic targets that affect brain structure and function in schizophrenia.

Adolescents and young adults at risk for psychosis who progress to psychotic symptoms show a steeper rate of gray matter loss compared with non-converters and healthy controls, but the factors underlying this decline are unclear. **Cannon *et al.*** (pages 147–157) conducted a longitudinal, multi-site, MRI study of individuals at clinical high risk for psychosis and healthy controls. Individuals who converted showed a steeper rate of thinning in prefrontal cortex. This differential tissue loss was not explained by exposure to antipsychotic drugs but was correlated with levels of pro-inflammatory cytokines in plasma, suggesting that these brain changes may play a role in the pathophysiology of psychosis.

Copy Number Variants Overlap MicroRNAs in Schizophrenia

Warnica *et al.* (pages 158–166) investigated the role of microRNAs in the genetic risk for schizophrenia using high-resolution microarrays to detect copy number variants (CNVs) in adults with schizophrenia. Compared with a control population, the schizophrenia group was enriched for rare CNVs that disrupt microRNAs. These results demonstrate a genome-wide role for CNVs that overlap microRNAs in the genetic risk for schizophrenia and implicate a new pathogenetic mechanism for this complex disease.

Lower GAD65 Levels in Schizoaffective Disorder

Lower expression of the GABA-synthesizing enzyme GAD67 in the prefrontal cortex has been reported in subjects with schizophrenia and schizoaffective disorder, but whether GAD65 expression is also altered is unclear. **Glausier *et al.*** (pages 167–176) examined postmortem tissue from healthy comparison and schizophrenia or schizoaffective disorder subjects and report that both GAD65 mRNA and protein levels were lower, but only in subjects with schizoaffective disorder. These findings suggest disorder-specific differences may underlie their altered cortical GABA signaling.

Memory Consolidation and Prefrontal-Hippocampal Connectivity

The process of memory consolidation, which occurs during sleep, is disrupted in both schizophrenia and depression. **Genzel *et al.*** (pages 177–186) used functional MRI and polysomnography in healthy controls and patients with

ISSN: 0006-3223

depression or schizophrenia to investigate the underlying mechanisms. Both patient groups showed similar deficits in consolidation associated with hippocampal-prefrontal cortex connectivity. Other observed activation patterns were disease-specific, with an upregulation of subcortical regions in depression, and a recruitment of adjacent cortical areas in schizophrenia.

Impaired Goal-Directed Action in Schizophrenia

Schizophrenia is associated with deficits in decision-making, but whether this reflects a deficit in establishing the reward value of events or in integrating these values with action is unknown. **Morris *et al.*** (pages 187–195) assessed the contribution of reward value to goal-directed actions in people with schizophrenia. Compared to healthy adults, they found that people with schizophrenia failed to accurately integrate actions and values to guide choice, and functional MRI analyses revealed dysfunction in the corticostriatal circuit mediating goal-directed action.

Ventral Striatum Binding and Normal Body Mass Index

Dopamine D2/3 receptor availability is negatively correlated with body mass index (BMI) in obese individuals. Using positron emission tomography, **Caravaggio *et al.*** (pages 196–202) investigated the relationship between BMI and D2/3 receptor availability in the ventral striatum, a region important in motivation and reward, in healthy humans with normal BMI. They report a positive correlation between BMI and agonist, but not antagonist, ventral striatum binding, which advances understanding of the dopaminergic correlates of healthy-weight individuals.