

Volume 4, Number 2, February 2019

A brief summary of the articles appearing in this issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*.

Classification Accuracy in ADHD

Attention-deficit/hyperactivity disorder (ADHD) is a heterogeneous disorder, and yet some studies have reported high accuracy in diagnostic classification. Here, **Pulini et al.** (pages 108–120) assessed classification accuracy in neuroimaging studies of ADHD as a function of methodological factors that could bias results. Their data reveal that high accuracies are inflated by small sample size and circular analysis. Studies that met criteria for independence of feature selection, model construction, and test datasets showed unbiased classification accuracy of 60%–80%, suggesting that future ADHD neuroimaging studies should account for sample heterogeneity.

Neurochemistry and Network Disruption in Psychosis

Schizophrenia is characterized by brain dysconnectivity and cortical excitation/inhibition imbalance, but the relationship between these abnormalities is unclear. Using magnetic resonance spectroscopy and 7T functional magnetic resonance imaging (fMRI), **Overbeek et al.** (pages 121–130) report that patients with first-episode psychosis showed increased blood oxygen level-dependent (BOLD) response in the executive and default mode networks, relative to healthy control subjects (HCs). Patients showed a positive relationship between glutamate levels and BOLD response in the default mode network, which was opposite to that observed in HCs, and a positive correlation between gamma-aminobutyric acid and BOLD response that was not present in HCs. These data suggest a disrupted relationship between neurochemistry and functional brain networks in psychosis.

Electroencephalographic Abnormalities in Psychosis and Anxiety

The 40-Hz auditory steady-state response paradigm is used to assess gamma band function. Patients with schizophrenia display gamma band abnormalities, including reduced power and reduced phase-locking factor. In this study, **Roach et al.** (pages 131–139) introduce a novel measure for this paradigm, the phase-locking angle, to assess phase delay and report that patients with schizophrenia exhibit delayed 40-Hz phase-locking angle relative to HCs. The phase-locking angle measure was unrelated to phase-locking factor or power in either group, suggesting a potentially distinct pathophysiological mechanism from other measures of gamma oscillations.

Schizophrenia is associated with reduced *N*-methyl-D-aspartate (NMDA) receptor function. The use of ketamine, an NMDA receptor blocker, in healthy participants can reproduce some of the features of schizophrenia, including reduced auditory mismatch negativity. Here, **Rosch et al.** (pages

140–150) measured auditory event-related potentials in healthy volunteers exposed to ketamine. Using computational modeling, the authors found that localized disruption of synaptic transmission in cortical circuitry can explain ketamine-induced mismatch negativity changes. These results provide evidence that NMDA receptor hypofunction causes localized prefrontal disinhibition, which may play a pathological role in schizophrenia.

Internalizing disorders such as anxiety are difficult to diagnose and classify, and their underlying neurobiology is incompletely understood. Here, **MacNamara et al.** (pages 151–159) used a working memory task to investigate transdiagnostic associations between anxiety symptom dimensions and event-related potentials in a heterogeneous group of patients with internalizing disorders. Hypervigilance for negative stimuli was uniquely explained by social anxiety, whereas panic symptoms were associated with blunted processing of negative stimuli and reduced top-down control. These results reveal distinct associations between neural reactivity and symptom dimensions outside of traditional diagnostic boundaries.

Functional Networks in Late-Life Depression

Late-life depression is associated with alterations in intrinsic functional network connectivity, but the clinical significance of such findings is less clear. Using resting-state fMRI, **Gandelman et al.** (pages 160–170) report that older adults with depression exhibit decreased connectivity between the posterior cingulate cortex and frontal pole, relative to nondepressed older adults. In the depressed group, connectivity between cognitive control network regions was associated with depressive symptoms and cognitive performance, which suggests that regional connectivity differences contributing to depression vulnerability may be distinct from the relationship between connectivity and clinical symptoms.

Tracking Adolescent Neurodevelopment: PTSD and High Risk

Multiple structural and functional brain network abnormalities have been found in cross-sectional studies of pediatric posttraumatic stress disorder (PTSD), but longitudinal investigations have been lacking. Here, **Heyn et al.** (pages 171–179) report that relative to typically developing youths, youths with PTSD exhibited sustained gray matter volume abnormalities in prefrontal cortex regions, which were associated with atypical intrinsic connectivity with the amygdala and hippocampus over time. Further, the prefrontal volume abnormalities were associated with symptom severity. These

data indicate the presence of long-term altered structural and functional brain development in pediatric PTSD.

A family history of psychopathology has been associated with alterations in white matter microstructure in high-risk adolescents without current psychopathology, but whether these alterations persist is unknown. In this longitudinal structural MRI study, **Jones et al.** (pages 180–189) demonstrate that a greater degree of familial psychopathology is associated with altered white matter microstructure in adolescents with no psychopathology. However, except for persistent effects in the posterior limb of the internal capsule, the majority of these effects dissipated by late adolescence, providing insight into the neurodevelopmental trajectories of high-risk but resilient youths.

Personal Choice and Reward Processing

Reward processing is altered in many psychiatric disorders, including depression and schizophrenia. Personal choice is known to influence reward processing. **Romaniuk et al.** (pages 190–199) adapted an fMRI reward task to characterize the relationship between the value of choice and neural

activation in healthy individuals. The authors observed enhanced responses in brain regions associated with reward and motivation when subjects were anticipating personal choice and when receiving rewards that were actively earned versus passively received. Striatal response was diminished in participants with depressive symptoms. These data provide insight into the neurobiology of personal control and reward processing.

Impaired Goal-Directed Behaviors in OCD

An imbalance between goal-directed and habitual systems is hypothesized to underlie compulsive behaviors. Using a novel task, **Vaghi et al.** (pages 200–209) report that relative to HCs, patients with obsessive-compulsive disorder (OCD) showed increased response rates when outcomes were less contingent on responding, despite self-reports that reflected accurate understanding of the effectiveness of those actions. These data indicate a dissociation between actions and intact action-outcome knowledge in patients with OCD, suggesting that the goal-directed system may be deficient in OCD.