In This Issue

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

Sensory and Sleep Problems in Autism

The locus coeruleus–norepinephrine system helps regulate arousal, which evidence suggests may be altered in autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). Using pupillometry during a visuospatial task, **Bast *et al.*** (pages 11–20) found slower reaction times in children with ASD, but not in children with ADHD, compared with typically developing children. Arousal, as measured by pupil dilation, was associated with task performance and was altered in the ASD group. These data provide insight into the links between locus coeruleus–norepinephrine activity and atypical arousal regulation in children with ASD.

Sensory and sleep problems are common in children with ASD. In this functional magnetic resonance imaging (fMRI) study, **Linke *et al.*** (pages 21–31) report that sleep problems are associated with heightened sensory sensitivity and increased thalamocortical connectivity in young children with ASD, compared with typically developing children. These findings support a model of early neurodevelopmental disturbances of thalamocortical connectivity in ASD.

School Environment and the Brain

Children's school environment influences their development, but little is actually known about the impact of the school environment on the developing brain. Here, **Rakesh *et al.*** (pages 32–41) found that school environment is associated with resting-state functional brain connectivity in systems involved in higher-order cognitive and language processing. Importantly, the connectivity of some of these functional systems was associated with good mental health. No associations were found between school environment and brain gray or white matter structure. These findings highlight neural mechanisms through which positive school environments may promote mental health.

Developing Brain-Based Biomarkers

Major depressive disorder (MDD) is a heterogeneous syndrome that may involve abnormalities across several specific brain circuits. Using an individualized functional imaging approach in patients with MDD, **Zhao *et al.*** (pages 42–51) identified a brain-based biomarker for dysphoric symptoms, which involved the default, dorsal attention, and limbic networks. Changes in this imaging biomarker tracked improvement of dysphoric symptoms following antidepressant treatment. Identification of replicable, robust brain-based biomarkers may assist in diagnosis and form the basis for developing much-needed personalized therapeutics.

Common treatment interventions in ADHD have variable remission rates in clinical settings, likely due in part to ADHD's high heterogeneity. Here, **Voetterl *et al.*** (pages 52–60) used electroencephalography data to develop a biomarker based on individual alpha peak frequency (iAPF), a brain rhythm. The biomarker was then used to predict treatment outcome in boys with ADHD. A faster iAPF was associated with better response to methylphenidate treatment, while neurofeedback treatment worked better for those with a slower iAPF. These findings suggest that an iAPF-based treatment stratification biomarker may be capable of differentially informing stratification to ADHD treatments.

Memory in Schizophrenia

Relational episodic memory encoding is impaired in schizophrenia, but the neural basis of these deficits is not well understood. Analyzing task fMRI data, **Roes *et al.*** (pages 61–70) found that participants with schizophrenia exhibited weakened anticorrelation between a language/attention network and the default mode network compared with healthy control participants, a pattern that predicted poorer memory retrieval performance. These findings indicate that abnormalities in the brain's representation of language may limit the effectiveness of semantic encoding strategies in schizophrenia.

Memory-based predictions, which rely on drawing from past experiences, may be impaired in schizophrenia. Here, **Williams *et al.*** (pages 71–78) analyzed fMRI data to examine the ability of people with schizophrenia to use memories of previously learned object sequences to predict upcoming objects in the sequence. In people with schizophrenia, the prediction effect was reduced relative to healthy individuals and was related to disrupted object/sequence representations in the dorsolateral prefrontal cortex. These findings suggest that people with schizophrenia are able to learn sequences but may have deficits in their ability to use these memories to predict future events.

Cerebellar and Hippocampal Alterations

22q11.2 deletion syndrome (22q11DS) is a genetic condition with an increased risk of schizophrenia. The cerebellum is a brain region that has been linked to psychosis. Here, **Schmitt *et al.*** (pages 79–90) found reduced cerebellar volumes in individuals with 22q11DS compared with typically developing controls, particularly in regions involved in cognition (superior posterior lobule). The superior posterior lobule was associated with cortical thickness in brain regions previously implicated in 22q11DS, and further, exploratory analyses indicated that this region may be associated with psychosis in 22q11DS.

The hippocampus is implicated in virtually every major psychiatric disorder. Here, **Jiang *et al.*** (pages 91–101) identified both common and specific abnormalities in hippocampal subfields across 4 disorders: schizophrenia, bipolar disorder, MDD, and obsessive-compulsive disorder. The authors also

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identified 2 factors of hippocampal subfields that represented deficits across diagnoses. These data provide categorical and dimensional insights into hippocampal subfield deficits across 4 major neuropsychiatric disorders.

Threat Neurocircuitry Predicts Symptom Changes

Many symptoms and neural mechanisms are shared across anxiety and depressive disorders, and both diagnostic categories have been associated with disruptions in threat neurocircuitry. Using a dimensional model and longitudinal data from young adult participants, **Peng *et al.*** (pages 102–110) found that greater neural responses to threat, particularly in the ventromedial prefrontal cortex, were associated with development of fears prospectively. In addition, change in neural responses during fear extinction recall were associated with changes in general distress. These results provide insight into how changes in symptom dimensions may be related to threat neurocircuitry.

Characterizing Psychiatric Risk

Characterization of risk states for the development of psychiatric disorders is important for early intervention. Using a multimethodological approach in a community-based sample, **Berhe *et al.*** (pages 111–120) report that young adults at risk for anxiety and depression show reduced affective well-being and blunted amygdala habituation to negative stimuli, compared with healthy people at no known risk. These data identify daily-life and neural affective markers of psychiatric risk in the community, and highlight the potential significance of amygdala habituation measures for affective experience in real-world environments.

ZNF804A and Dopamine Receptor Availability

Variation in *ZNF804A* has been identified as a risk factor for schizophrenia in genome-wide association studies, but the mechanisms underlying this risk are unknown. Using positron emission tomography with 2 different radioligands, **Hegarty *et al.*** (pages 121–128) report that the *ZNF804A* risk allele was associated with lower levels of D_2/D_3 receptor, but not D_1 receptor, availability in the striatum of healthy individuals. These data suggest a link between *ZNF804A* genotype and dopaminergic function that may be specific to D_2/D_3 receptor subtype.