In This Issue

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

Special Issue: Techniques for Translational Neuroscience

Understanding brain connectivity will help to identify the changes in neural circuitry that underlie behavioral dysfunction. In this special issue, **Snyder and Bauer** (pages 510–521) review the mapping of brain activity and neural connectivity in rodents using optogenetics in conjunction with either functional magnetic resonance imaging (fMRI) or optical intrinsic signal imaging. The authors also discuss implementation strategies for brain connectivity mapping in humans using transcranial magnetic stimulation for both basic and clinical applications. They conclude with a discussion on how mapping studies in animals can be utilized to influence preclinical imaging studies as well as clinical practice.

Functional neuroimaging in animals is a crucial translational tool to further our understanding of neuropsychiatric disease, but awake animal imaging has challenging constraints. In this review, **Sumiyoshi *et al.*** (pages 522–532) discuss the physiological basis of and the influence of anesthetics on neurovascular coupling. They discuss the use of anesthetics in fMRI and focus on a specific anesthetic protocol developed in their lab. They conclude with a discussion of their recent work examining the physiological basis of resting-state fMRI using this anesthetic regimen and the future directions of animal neuroimaging research.

A detailed understanding of complex brain networks from the cellular to the macroscopic scale could be gained by combining fMRI with new powerful imaging and microscopy techniques in awake, behaving mice. Here, **Desjardins *et al.*** (pages 533–542) demonstrate the feasibility of fMRI in awake mice implanted with chronic transparent "cranial windows" compatible with two-photon microscopy of single vessels and optical imaging. This study provides proof-of-principle for conducting multiscale and multimodal imaging in awake mice.

Individual differences are heterogeneous across the cortex in the human brain, but interindividual variability in the nonhuman primate brain is not well understood. Here, **Xu *et al.*** (pages 543–553) leveraged an open resource with awake and anesthetized fMRI datasets to examine individual differences in the functional brain organization of rhesus monkeys. They found that primary sensory and motor cortices showed lower variability than the high-order association regions in the awake state, whereas the anesthetized state showed a distinct pattern, with lower variability in medial frontal cortex, precuneus and somatomotor regions and higher variability in the lateral ventral frontal and insular cortices. These data reflect what is also observed in the human brain, suggesting a potential evolutionary source of functional variability.

Optogenetic fMRI is a promising approach for testing circuit-level hypotheses derived from clinical neuroimaging studies. However, this approach assumes that functional connectivity alterations are important components of depression pathophysiology and are reliable predictors of behavior. **Grosenick *et al.*** (pages 554–566) showed that connectivity–symptom correlations are robustly significant, and they defined methods for improving generalization to new data. Further, the authors reviewed recent optogenetic fMRI advances and illustrate an approach to formulating hypotheses about subtype-specific circuit mechanisms and then testing them in animal models.

Dissecting Heterogeneity of Autism With Normative Modeling

The high heterogeneity of autism spectrum disorder (ASD) has proven a barrier to the identification of neuroimaging biomarkers. To avoid the limitation of a case-control approach, **Zabihi *et al.*** (pages 567–578) used a normative modeling approach to estimate typical cortical thickness development and then mapped the deviation of each individual ASD participant. Despite few group-level differences, they found that the ASD cohort showed highly individualized patterns of cortical alterations that were widespread and correlated with severity of repetitive behaviors. These data highlight that case-control group-level comparisons may disguise significant variation in heterogenous disorders such as ASD.

Brain Iron Imaging in Cocaine Use Disorder

Brain iron is required for neural processes involved in addiction and can be lethal to cells if unbound, especially in excess. Using an advanced iron MRI method called magnetic field correlation imaging, **Adisetiyo *et al.*** (pages 579–588) demonstrate that, compared with healthy control subjects, individuals with cocaine use disorder have elevated iron in the globus pallidus internal segment and lack the age-related gradual iron deposition within the globus pallidus and striatum that is seen in normal aging. These data suggest that brain iron homeostasis is dysregulated in reward-related regions of the brain in cocaine use disorder.

Machine Learning for Alcoholism, HIV, and Their Comorbidity

Alcohol use disorder (AUD) and human immunodeficiency virus (HIV), both of which are associated with structural brain deficits, are commonly comorbid. Here, **Adeli *et al.*** (pages 589–599) used a machine learning approach to test whether MRIs can be used to predict diagnosis and cognitive measures in individuals with AUD, HIV, or AUD+HIV. After first identifying diagnostic patterns, their analysis predicted diagnostic classification and cognitive performance of individuals with AUD, HIV, and AUD+HIV relative to control patterns. Further, the patterns suggested an exacerbated effect of AUD+HIV comorbidity. This data-driven approach provides a novel means of delineating a constellation of brain regions that are predictive of diagnosis at an individual level.