In This Issue

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

Review: Multimodal Neuroimaging to Personalize rTMS

Repetitive transcranial magnetic stimulation (rTMS) is used as a treatment for major depressive disorder, but clinical effectiveness remains limited. The high inter- and intraindividual variability in clinical response could potentially be addressed through personalized rTMS treatment. Multimodal neuroimaging techniques such as magnetic resonance imaging (MRI) and electroencephalography (EEG) can provide insight into individual brain characteristics that could be used to guide treatment. In this review, **Klooster *et al.*** (pages 536–545) provide an overview of a range of potential approaches by which multimodal neuroimaging could aid in the personalization of certain rTMS parameters, including coil positioning, stimulation intensity, frequency, and timing.

EEG Connectivity: A Fundamental Guide and Checklist

EEG is a method through which brain activity and the connections between areas of the brain can be measured. However, the ways in which EEG is measured and analyzed can vary significantly across research studies, making it difficult to compare results across studies and reach a more integrated level of understanding. In this review, **Miljevic *et al.*** (pages 546–554) present recommendations and a novel checklist to facilitate the standardization of research methods and quality assessment specifically for EEG brain connectivity studies.

Individual Variability in the Error-Related Negativity

Research on neural indices of performance monitoring, which may be a transdiagnostic marker of psychopathology, typically examines group and interindividual differences in mean scores across subjects. Intraindividual variability, however, is less understood. Using EEG, **Clayson *et al.*** (pages 555–565) report that intraindividual variability in the error-related negativity was considerable and common across all groups, which included psychiatrically healthy individuals as well as participants with major depressive disorder, generalized anxiety disorder, or obsessive-compulsive disorder. These data suggest that fixed intraindividual variability should not be assumed for error-related negativity studies in healthy or clinical populations.

Atypical Theta Oscillations in Autism

Cognitive control, which is disrupted in autism spectrum disorder (ASD), is linked to task-related theta oscillations. Using EEG, **Buzzell *et al.*** (pages 566–575) report that young children with ASD showed reductions in error-related mediofrontal theta patterns while completing a cognitive task, compared with typically developing children. These reductions in late theta oscillations predicted poorer academic and social outcomes in children with ASD, suggesting a potential target for early interventions.

Functional Connectivity in Prairie Voles

Like humans, prairie voles form long-term bonds, and the expression of this prosocial behavior differs between vole populations. Using functional MRI, **Ortiz *et al.*** (pages 576–587) assessed the functional connectivity of the prosocial and olfactory core regions of the brain and the differences associated with culturally distinct patterns of prosocial behavior and aggression in voles. The authors found that these differences in social behavior are related to differences across vole species in global connectivity in the prosocial core, and that the degree of connectivity between the olfactory and prosocial cores influences the differential expression of male social behavior.

Prairie voles have been studied to advance our knowledge of the neural circuits involved in prosocial behavior. Here, **Ortiz *et al.*** (pages 588–597) used diffusion-weighted imaging and resting-state functional MRI to demonstrate that brain architecture and functional connectivity differs between male prairie voles that display different levels of prosocial behavior, suggesting that higher-order brain structure may be important in the expression of prosocial behavior.

Glutamate System: Metabolism and Availability

Alterations in glutamatergic function are implicated in cognitive dysfunction and numerous neuropsychiatric diseases, but the development of novel therapeutics is hampered by a lack of relevant biomarkers. Using ^{1}H-magnetic resonance spectroscopy, **Miller *et al.*** (pages 598–606) developed a novel biomarker of neuronal glutamate metabolism, supported by use of modeling and simulations. The authors then used this biomarker to show that treatment with BNC375, an α7 nicotinic acetylcholine receptor positive allosteric modulator, increases glutamate metabolism in male rhesus macaques. This platform may support the clinical evaluation of pharmacologic agents that modulate glutamatergic neurotransmission.

The $mGlu_5$ receptor (mGluR5), part of the metabotropic glutamate family of G protein–coupled receptors, is implicated as playing an important role in stress disorders, and is commonly quantified with one of two positron emission tomography tracers, [^{11}C]ABP688 or [^{18}F]FPEB. In this work, **Glorie *et al.*** (pages 607–615) provide evidence in wild-type mice for a common binding site, and in a direct comparison, both radioligands showed decreased mGluR5 availability in *Sapap3* knockout mice, a model of obsessive-compulsive behavior. However, [^{11}C]ABP688 showed greater sensitivity, suggesting that its use to quantify mGluR5 may be preferable.

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Subcortical Volume and Genetics

Subcortical brain structures play a key role in the pathological processes underlying late-onset neurodegenerative diseases, the alterations of which may be present long before clinical symptoms. Using large population-based cohorts, **Le Grand *et al.*** (pages 616–628) found decreasing heritability of subcortical volumes with increasing age and identified common genetic variants associated with smaller subcortical volumes across the whole adult lifespan. Further, the authors also provide preliminary evidence for the biological pathways that may be involved and the potential clinical significance of these findings related to cognitive performance and neurodegenerative diseases.