In This Issue

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

Special Issue: Neural Organoids to Study Psychiatric Disease: The Pros and Cons

The emergence and rapid advances of human brain organoid technology provide unprecedented opportunities for investigation of potential disease mechanisms and development of targeted or even personalized treatments for various psychiatric disorders. In this review**, Zhang *et al.*** (pages 594–605) summarize recent advances for generating regionalized organoids from human pluripotent stem cells resembling distinct brain compartments. The authors highlight recent progress, discuss limitations, and propose potential improvements in using patient-derived or genetically engineered brain region–specific organoids for investigating psychiatric disorders.

Human brain organoids have emerged as a powerful tool to interrogate cellular pathologies associated with neuropsychiatric disorders. **Urenda *et al.*** (pages 606–615) highlight recent advancements in brain organoid generation and the current state of psychiatric disorder modeling with this system. The authors describe clinical neuroimaging studies that have found aberrant functional and morphological connectivity between brain structures, with an emphasis on axes that may be modeled with the current array of regional brain organoids. The authors close by offering a future perspective on the importance of using interdisciplinary strategies to establish next-generation, multiregional organoids to model macroscale circuit dysfunction.

Human brain organoids are 3-dimensional cell aggregates that are generated from pluripotent stem cells and recapitulate features of the early developing human brain. However, current brain organoid systems lack functional vasculature and other non-neuronal cells that are indispensable for oxygen and nutrient supply. Attempts to utilize intracerebral transplantation approaches have demonstrated successful vascularization of brain organoids and robust maturation. In this review, **Wang *et al.*** (pages 616–621) summarize recent progress in the field, discuss ethical considerations, and highlight possible applications for organoid engraftment strategies.

In this review, **Wang *et al.*** (pages 622–631) describe the current state of stem cell–based organoid modeling across severe neurodevelopmental disorders caused by various classes of genetic mutations, structural and copy number variants, somatic mosaic mutations, and gene-environment interactions. In addition, the authors detail a range of new techniques to add further sophistications and improve physiological relevance and therapeutic opportunities.

In this review, **Levy and Paşca** (pages 632–641) provide an overview of human stem cell–derived models of the nervous system and their application to understanding neuropsychiatric disorders. The authors describe how stem cells can be used to model disease-relevant brain regions and circuits in organoids and assembloids both in vitro and in vivo. They discuss key findings from recently developed disease models, model limitations, and future directions of the field aimed at understanding and treating neuropsychiatric conditions.

Here, **Seah *et al.*** (pages 642–650) review and discuss methods and insights from context-specific modeling of genetically and environmentally regulated expression using human induced pluripotent stem cell models. These new multiplex approaches hold promise to uncover gene-by-environment interactions mediating disorder risk, which will ultimately improve our ability to diagnose and treat psychiatric disorders.

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