EDITORIAL

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Mental health horizons

From organoids to population-level studies, mental health research has begun to crack long-standing mysteries. Longitudinal investigations into brain and cognitive development among adolescents, such as the forthcoming 10,000-person ABCD project, will help to mature the field.

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Mental health disorders and neuropsychiatric disease negatively affect the lives of a staggering number of people. Although estimates vary from country to country, data compiled by the World Health Organization's World Mental Health surveys suggest that the global lifetime prevalence of any mental health disorder might range between 20% and 35%, with a one-year prevalence for serious mental illness of 1–7%, depending on the country. In Europe and the United Kingdom, as much as one-third of the adult population may be mildly-to-severely affected by at least one disorder in any given year. In the United States, 2014 statistics from the National Institute of Mental Health (NIMH) show that serious mental illnesses (defined as clinically diagnosed disorders that cause major functional impairment sufficient to substantially interfere with everyday life activities) affect approximately 10 million adults, or more than 4% of the adult population. These US numbers do not even include those individuals experiencing the negative mental-health effects of substance-abuse disorders such as alcohol or drug dependencies, or those with undiagnosed conditions.

Basic, translational and clinical research that promises to transform our understanding, diagnosis and treatment of mental health disorders is urgently needed. This month, *Nature Medicine* and *Nature Neuroscience* present joint focus issues containing Commentaries, Perspectives and Reviews that summarize key findings and explore important issues faced by the neuropsychiatric disease research community. On page 1220, Quadrato *et al.* discuss the potential advantages and limitations of three-dimensional human brain-organoid cultures as a platform to model neuropsychiatric disease. Yun *et al.* (page 1239) discuss the role of hippocampal adult neurogenesis in neuropsychiatric disorders and its potential therapeutic implications. At the human-population level, Owen and O'Donovan highlight the clinical implications of genetic pleiotropy on neuropsychiatric disease pathogenesis and diagnosis (page 1214).

Among the many problems that confront the neuropsychiatric disease research community today, the lack of a detailed account of how the human brain and cognitive abilities mature during the dynamic and vulnerable period of adolescence still remains a key gap in our scientific knowledge. As outlined in the Perspective by Oscar Marin in this issue (page 1229), whereas the majority of neuropsychiatric disorders are diagnosed on the basis of a cluster of specific symptoms observed in adult individuals, it is becoming increasingly clear that some of the biological processes that contribute to the pathophysiology of mental health disorders occur during critical windows of late childhood to early-adolescent development. Indeed, recent NIMH statistics also note that as many as 13% of US adolescents between the ages of 8 and 15 have been diagnosed with a mental disorder within the previous year. In addition, recent experimental evidence suggests that genetic loci associated with neuropsychiatric disorders such as schizophrenia harbor individual genes that, when manipulated in model systems, can cause dysregulation of neurodevelopmental processes, including neural-precursor migration and synaptic pruning. However, what distinguishes adolescents at risk for the development of mental health disorders from others who remain mentally healthy remains unknown.

This could soon change. In late September, the NIH announced the initiation of participant recruitment for the Adolescent Brain Cognitive Development (ABCD) study, in conjunction with the first round of funding recipients for this project. The initiative aims to provide the largest, most diverse sampling done to date of longitudinal brain development during adolescence. Coordinating research across eight NIH centers and departments and 19 academic-research sites, along with the help of numerous public, private and charter elementary schools, ABCD seeks to enroll 10,000 students between the ages of 9 and 10 years across different socioeconomic backgrounds to participate in the decade-long study. It will require an extraordinary amount of public participation and commitment to accomplish these aims—not only to ensure that the initial 10,000 participants are recruited, but also that they are retained for the full duration of the study.

Participants will undergo magnetic resonance imaging (MRI)-based brain scans every other year to chart the course of structural and functional brain development between the ages of 10 and 20. In parallel, investigators will track cognitive development with a standardized set of games and puzzles, as well as acquire biospecimens from participants and their family members for genetic analysis. Numerous other environmental and behavioral factors that are thought to affect brain development will be monitored, including physical activity and sleep patterns. The ABCD study is especially interested in determining how the use or abuse of chemical substances (including caffeine, nicotine, alcohol or marijuana) can affect developmental outcomes, both at the level of brain-structure function and neurocognitive maturation. As a result, ABCD investigators could also be in a position to examine how genetic or environmental factors might influence risk for substance use or abuse.

Given the prevalence of mental health disorders among both adolescents and adults, the data collected as part of the ABCD study might represent a unique resource for the development of biomarkers to diagnose or identify more accurately individuals who are at risk for the development of neuropsychiatric disorders such as depression, schizophrenia or anxiety disorders. As discussed by Horga and Abi-Dargham on page 1248 of this issue, the development of neuroimaging-based biomarkers for psychiatric disease faces many challenges, but the scale, standardization of methods and open-data policy of ABCD should give researchers many of the tools needed to make progress in this endeavor. Efforts such as the ABCD initiative offer reasons to be optimistic that, one day, it might be possible to identify individuals at risk for neuropsychiatric disease during early course pathogenesis, and hopefully, to initiate therapeutic interventions and support systems to help steer their developmental trajectories back on track.