New studies of the 'natural history' of schizophrenia raise hope for new treatments

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Emerging evidence on the development, "prodromal" characteristics, and long-term course of schizophrenia provide reasons for optimism for developing new treatments and preventive approaches for this devastating disorder, according to the special March/April issue of Harvard Review of Psychiatry.

"This special issue of the *Harvard Review of Psychiatry* brings together global experts in the epidemiology, neurobiology, and treatment of schizophrenia to reevaluate the natural history of the illness, and to elaborate priorities for new interventions," according to an introduction by guest editor Dr. Joshua L. Roffman of Massachusetts General Hospital and Harvard Medical School.

New Insights into Neurobiology, Early Treatment, and More

The eight papers in the special issue highlight key areas of progress toward understanding the development and course of schizophrenia—a condition for which the last major treatment breakthrough occurred decades ago. Specific advances that are highlighted include:

- The contributions of *altered genetics and brain connectivity* to the biology of schizophrenia. While the idea that schizophrenia is a disease of "disconnectivity" is not new, it has recently been validated by modern genetic and brain imaging techniques.

Connectome-based studies may inform the development of new approaches to schizophrenia treatment.
- A renewed focus on the *schizophrenia "prodrome"*—a critical early period with opportunities for early detection and intervention. This line of research has enabled identification of young people at "clinical high risk," with the potential to develop interventions to prevent or delay development of schizophrenia.
- The identification of risks faced by *offspring of parents with schizophrenia*—including increased rates not only of psychotic disorders, but also depression/anxiety and other mental health conditions. Research suggests that children at "familial high risk" can be identified early, with important implications for predicting later risk.

Other articles highlight new approaches to understanding how this complex and variable condition unfolds over time:

- Recommended approaches to studying the *long-term course of schizophrenia*—including a new analysis suggesting that the symptoms and impaired cognition (thinking) may be more stable than previously thought.
- The potential for electroencephalography (EEG) to show genetically mediated patterns of brain electrical activity, or *"electrophysiological endophenotypes,"* in patients with schizophrenia.
- Updated evidence suggesting that *dysfunctional voice processing* may explain the auditory and verbal hallucinations ("hearing voices") that occur in schizophrenia.

The special issue also presents updates on new directions in treatment. One promising therapy for patients early in the course of psychosis is *"cognitive remediation"*—a psychological treatment to improve thinking skills, that may be especially helpful during the prodromal period.

Another paper highlights *emerging treatment and preventive approaches*. Recent evidence suggests possible benefits of some "repurposed" treatments and supplements, such as B-vitamins and omega-3 fatty acids.

Dr. Roffman likens the "new natural history" of schizophrenia to a "gut renovation"—while the core concepts remain the same, scientists' understanding of the long-term clinical course and related neurobiology is undergoing transformative change. He concludes, "The critical reappraisal of the natural history of schizophrenia, and the related insights around new intervention strategies...provide every reason to be optimistic."

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