

NEUROPROTECTION: A NEW STRATEGY IN THE TREATMENT OF SCHIZOPHRENIA

AUTHORS Jeffrey A. Lieberman, MD
Peter F. Buckley, MD
Diana O. Perkins, MD, MPH

SECTION EDITOR David L. Ginsberg, MD

ABSTRACT

Intervention in the progression of schizophrenia is an effort not just to deter psychosis but also to protect the brain from physiologic deterioration. Neurodegeneration is believed to result from neurochemical dysregulation during the onset of schizophrenia. Deterioration accrued over recurring psychotic episodes causes cumulative loss of cell processes, loss of gray matter volume, and apoptosis. Neurodegeneration ultimately results in persistent symptomology and functional impairment. Functional decline occurs early in the course of schizophrenia, and the symptoms that emerge during the prodromal stage may derail the normal adolescent neurodevelopment. Both first-episode psychosis and the prodrome may be opportunities to forestall neurodegeneration. Unfortunately, people with schizophrenia often experience a long duration of untreated psychosis. Treatment of first-episode psychosis with antipsychotic agents shows robust response. However, early-stage patients have very high rates of medication noncompliance. Treatment in the prodrome may offer the best chance to delay the onset of illness, mitigate its severity after onset, or even prevent onset of symptoms entirely. Nonpharmacologic treatments during the prodrome, such as education, treatment for substance use, and cognitive-behavioral therapy, are low-risk interventions that are potentially beneficial. Pharmacologic interventions during the prodrome are also effective in delaying onset of illness, but carry the risk of adversely affecting patients who are false positives for prodromal schizophrenia.

In this Expert Roundtable Supplement, Jeffrey A. Lieberman, MD, provides an overview of the neurobiological basis of neurodegeneration and the concept of neuroprotection. Next, Peter F. Buckley, MD, reviews the importance of first-episode psychosis, including duration of untreated illness and medication adherence. Finally, Diana O. Perkins, MD, MPH, reviews treatment strategies for prodromal schizophrenia.

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CNS Spectrums' editorial mission is to address relevant neuropsychiatric topics, including the prevalence of comorbid diseases among patients, and original research and reports that emphasize the profound diagnostic and physiologic connections made within the neurologic and psychiatric fields. The journal's goal is to serve as a resource to psychiatrists and neurologists seeking to understand and treat disturbances of cognition, emotion, and behavior as a direct consequence of central nervous system disease, illness, or trauma.

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This activity has been peer reviewed and approved by Eric Hollander, MD, Chair and Professor of Psychiatry at the Mount Sinai School of Medicine. Review Date: September 11, 2007

Statement of Need and Purpose

Schizophrenia is a chronic mental disorder characterized by psychosis, delusional behavior, and hallucinations. Research has demonstrated that the prognosis for schizophrenia is affected by the amount of time between the initial onset of psychotic symptoms and adequate pharmacologic treatment. Research has unveiled biological markers that correlate with schizophrenia symptoms and support the importance of early intervention for patients with schizophrenia. Neuroimaging studies have demonstrated that there is a neurodegenerative syndrome associated with the cognitive decline that accompanies first-episode psychosis and that loss of gray matter is most significant during early psychosis. In order to achieve a full neuroprotective effect, symptoms must be treated early and to full remission. Both conventional and atypical antipsychotics are effective for treating the symptoms of schizophrenia later in the course of illness, although atypicals appear to have a more significant neuroprotective effect at the time of initial psychosis. Patients who discontinue pharmacologic treatment run a higher risk of relapse with each episode. Managing medication side effects, as well as use of psychosocial interventions, can improve treatment adherence. Given the overall burden of schizophrenia, new efforts at early detection and early treatment with effective antipsychotics are essential. Clinicians must be vigilant in looking for symptoms of schizophrenia and aggressive in treating the disorder once the patient has been diagnosed.

Target Audience

This activity is designed to meet the educational needs of psychiatrists.

Goal of the Activity

To educate physicians on the model of schizophrenia as a limited neurodegenerative disease. Progression of this disease may be prevented by early intervention with antipsychotic treatment and other adjunctive therapies.

Learning Objectives

- Recognize the latest evidence of neurodegeneration associated with cognitive decline in schizophrenia.
- Explain the benefits and risks of pharmacologic treatments.
- Describe the impact of relapse and the need for compliance in limiting the burden of illness in patients with schizophrenia.

Faculty Disclosures

Jeffrey A. Lieberman, MD, is a consultant to Eli Lilly and Pfizer; is on the advisory boards of AstraZeneca, Eli Lilly, GlaxoSmithKline, Lundbeck, Organon, and Pfizer; receives grant/research support from Acadia, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Merck, Organon, and Pfizer; and is a patent holder for Repligen. He receives no financial compensation or salary support for participation as a consultant or member of an advisory board.

Peter F. Buckley, MD, is a consultant to Abbott, Alamo, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer, Merck, Roche, Solvay, and Wyeth; receives grant/research support from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Janssen, National Institute of Mental Health, Pfizer, Solvay, and Wyeth; and receives honoraria/expenses from Abbott, Alamo, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Janssen, and Pfizer.

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Peer Reviewers

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Eric Hollander, MD, reports no financial, academic, or other support that may pose a conflict of interest.

Minimum Hardware/Software Requirements

Macintosh: PowerPC processor, Mac OS 8.6, 9.0.4, 9.1, or Mac OS X, 64MB of RAM, 24MB of available hard-disk space, and Safari 1.x or 2.x.

Windows PC: Intel Pentium processor, Microsoft Windows 95 OSR 2.0, Windows 98 and 98 SE, Windows Millennium Edition, Windows NT 4.0 with Service Pack 5, Windows 2000, or Windows XP, 64MB of RAM, 24MB of available hard-disk space, and Internet Explorer 6.x and newer or Firefox 1.x and newer.

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For editorial inquiries, please contact Deborah Hughes at dh@mbldcommunications.com. For bulk reprints, please contact Christopher Naccari at cdn@mbldcommunications.com.

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NEUROPROTECTION: A NEW STRATEGY IN THE TREATMENT OF SCHIZOPHRENIA

To Receive Credit for this Activity

Listen to this PsychCast™, reflect on the information presented, and complete the CME posttest, evaluation, and answer form provided on the following page as directed and return it to **CME Director, CNS Spectrums**, 333 Hudson Street, 7th Floor, New York, NY 10013; or fax it to 212-328-0600. This quiz is also available at psychcast.mblcommunications.com/cme. Release date: November 15, 2007. Termination date: November 15, 2009. All psychiatrists may participate in the CME program. The estimated time to complete this activity is 1 hour. Early submission of this posttest is encouraged. Please submit this posttest by November 1, 2009 to be eligible for credit.

To obtain credit, you should score 70% or better.

CME QUESTIONS

1. **The natural history of schizophrenia indicates that:**
 - A. Patients suffer a limited neuroprogressive disorder that may benefit from neuroprotective intervention in the prodromal, onset, or clinical deterioration stages
 - B. Patients progress to a clinical deterioration stage involving subsequent relapses and increasing symptoms after a first-episode psychotic event
 - C. Patients would benefit greatly from identification of genotypic or phenotypic prodromal markers because prophylactic neuroprotection strategies fit the course of the disease
 - D. All of the above
2. **Symptoms in initial prodrome of schizophrenia include:**
 - A. Perceptual abnormalities
 - B. Development of odd beliefs
 - C. Dysphoric mood
 - D. All of the above
3. **Available information on the efficacy of antipsychotics in first-episode schizophrenia suggests that:**
 - A. Most patients respond reasonably well to any agent, especially when it is prescribed in very low doses
 - B. All drugs have FDA indications in this patient group
 - C. More studies are required in this patient group
 - D. All of the above
4. **Patients in their first episode of psychosis are prone to discontinue medications because:**
 - A. They do not think they have an illness
 - B. The medications only work in 10% of patients
 - C. They experience side effects
 - D. A and C
5. **Adverse effects of atypical antipsychotics when used in first-episode schizophrenia are:**
 - A. Extrapyramidal side effects
 - B. Endocrine effects
 - C. Weight gain
 - D. All of the above
6. **For most patients, decline in function associated with the development of schizophrenia occurs primarily:**
 - A. During the initial prodromal stage
 - B. After psychosis emerges
 - C. After treatment is initiated
 - D. After chronic symptoms have developed
7. **Investigations into the mechanism producing changes in brain structure and volume in schizophrenia found:**
 - A. That there is dramatic gray matter volume loss during the periods of deterioration
 - B. Massive amounts of cell loss similar to Alzheimer's
 - C. A loss of cells in specific populations of cell types and a loss of cell processes
 - D. A and C
8. **Preliminary clinical trials indicate that in patients with prodromal symptoms, psychosis may be prevented with:**
 - A. Antipsychotic treatment
 - B. Cognitive-behavioral psychotherapy
 - C. Both A and B
 - D. Neither A nor B



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ANSWER FORM

Expert Roundtable PsychCast™ – Neuroprotection: A New Strategy in the Treatment of Schizophrenia

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To receive credit, you should score 70% or better (participants will receive certification for their records in approximately 4–6 weeks). Early submission of this posttest is encouraged. Please submit this test by November 1, 2009, to be eligible for credit. If you have any questions about this, or any of our other CME materials, please E-mail CME@mblcommunications.com

Please circle your answers

1. A B C D 2. A B C D 3. A B C D 4. A B C D 5. A B C D 6. A B C D 7. A B C D 8. A B C D

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