

## What Is the Relationship between Schizophrenia and Substance Abuse?

**We asked Alan I. Green, M.D., Center Director of the Commonwealth Research Center and Associate Professor of Psychiatry at Harvard Medical School.**

About 50% of people with schizophrenia also have a history of substance abuse or dependence, including alcoholism — a rate three times higher than average. This common combination of problems is sometimes called dual diagnosis. Alcohol, marijuana, and cocaine (in that order) are the substances most commonly involved. Schizophrenic patients who abuse substances are more likely to relapse into psychosis, require hospitalization, neglect antipsychotic medications and other treatments, commit acts of violence, and kill themselves.

Why do people with schizophrenia have such a high rate of substance abuse?

They may be trying to override the neurological side effects of antipsychotic drugs, which can make coordinated movements difficult. They may also be attempting to medicate themselves for their symptoms, especially the so-called negative symptoms, which include a lack of motivation and an inability to experience pleasure. There is some evidence that because of inadequate functioning in certain brain circuits, schizophrenic patients suffer from what may be called a reward deficiency syndrome. These circuits, sometimes called the brain reward system, are responsible for the ability to get pleasure out of everyday life. The system uses the neurotransmitter dopamine, and its malfunctioning is apparently the cause of at least some schizophrenic symptoms, both positive (chiefly hallucinations and delusions) and negative. Alcohol, marijuana, and cocaine may facilitate dopamine transmission in these circuits, producing a short-lived sense of well-being. The price is a long-term

deterioration in functioning and a generally poor outcome.

To cope with the problem of dual diagnosis, many individual and group programs for the treatment of schizophrenia have been modified to include methods used in drug abuse treatment. But there is now also some evidence that a change in medications may help. The newer "atypical" antipsychotic drug clozapine seems to lower the rate of substance abuse; preliminary data that require confirmation suggest that this effect includes alcohol, cannabis, and cocaine use. As noted above, alcohol and other substances may offer relief from persistent negative symptoms or from the side effects of antipsychotic medications, especially their uncomfortable effects on body movements. Clozapine has little effect on body movements, and it apparently relieves some negative symptoms more effectively than older drugs do. But it may also have a more direct effect on substance abuse. It acts on many kinds of brain receptors, including those for the neurotransmitters norepinephrine and serotonin as well as dopamine. These complex actions may move brain reward circuits closer to normal functioning and thus reduce the presumed reward deficits that lead to substance abuse. Further study is needed to clarify this point and to determine whether other novel antipsychotic medications (such as risperidone, olanzapine, and quetiapine) have similar effects.

If further studies confirm that clozapine or other new antipsychotic drugs are able to limit dual-diagnosis substance abuse, the overall outlook for patients with schizophrenia may dramatically improve. This could be especially important in the early stages of the illness. There is evidence that the outcome of schizophrenia is improved if psychotic symptoms (especially hallucinations and delusions) are treated and controlled as early as possible. But when substance abuse continues, patients are more likely to relapse into a psychotic state, and long-term deterioration may be more likely. Thus the use of novel antipsychotic drugs at an early stage offers special promise of improved long-run prospects for those with schizophrenia. This is now an active area of research.

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