

# Clinical Aspects of Substance Abuse in Persons With Schizophrenia

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**Objective:** To review the current knowledge on the problem of psychoactive substance abuse by persons with schizophrenia, with particular attention to issues of direct relevance to clinical practice.

**Method:** The author examined the literature from the last 2 decades and data from studies in which he was involved.

**Results:** Schizophrenia sufferers show an elevated liability for substance abuse. Such comorbidity may derive from self-medication attempts, a common neuropathology for addiction and schizophrenia, the psychotogenic properties of certain drugs, or the influence of environmental factors. Among schizophrenia patients receiving treatment, substance misuse is associated with more severe symptoms and poorer therapeutic response. The presence of a chronic psychosis impedes treatment of the substance problem in traditional, nonpsychiatric addiction programs. Better outcomes are observed in integrated therapy services, where patients receive appropriate care for both conditions.

**Conclusion:** Dual-pathology patients need comprehensive care with appropriate pharmacotherapy and psychosocial interventions. This treatment can be best provided within the context of a continuing care psychiatric service.

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## Highlights

Schizophrenia sufferers show an elevated liability for substance abuse.

Among schizophrenia patients receiving treatment, substance misuse is associated with more severe symptoms and poorer therapeutic response.

Better outcomes are observed in integrated therapy services, where patients receive appropriate care for both conditions.

**Key Words:** *dual disorders, schizophrenia, self-medication, pharmacotherapy, integrated treatment*

It has been repeatedly confirmed that persons with schizophrenia have an abnormally high risk of developing substance use disorders (that is, abuse or dependence) during the course of their lives (1). The excessive probability revealed by the Epidemiological Catchment Area (ECA) study, a general-population household survey, is 3.6 times that for alcohol, 5 times that for cannabis, 6.5 times that for opiates, and 13 times that for cocaine (2).

It is also well known that persons with schizophrenia present rates of tobacco use (between 70% and 90%) that are well above those of the general population and also above the rates observed in persons with anxiety disorders or depression (although depression sufferers present the second-highest rates) (3).

## Risk of Occurrence

The highest rates of addiction comorbidity are found in clinical samples gathered from outreach programs and emergency or walk-in services attending to less stable, more severely afflicted subjects (4). However, it must be noted that substance abuse frequency is not evenly distributed across demographic categories within single samples of schizophrenia patients, nor is it evenly distributed among the different locations from which the data were gathered. Rather, the prevalence profile among these individuals follows closely the age and sex differences observed in the population at large: younger and male schizophrenia sufferers outrank older and female ones (1,5). Similarly, rates reported in the US are well in excess of rates found in German (6), French (7), British (8), or Canadian (9) samples, particularly in regard to cocaine abuse. It therefore seems that, as in the general population, the risk of addiction disorders occurring among persons with schizophrenia depends on environmental conditions such as drug availability and local drug culture. Most of the US data, for instance, pertain to patients seen in public facilities. These patients come mainly from within the Department of Veterans Affairs network, which may be catering to a population preselected for high risk of illegal substance misuse.

One interesting finding that emerged from a Montreal study of persons with chronic schizophrenia is that the prevalence of tobacco smoking, the most widespread drug problem in this particular population, covaries with prevalence of alcohol drinking (5). Of course, that is also the case in samples without psychosis (10). However, alcohol-abusing schizophrenia sufferers have been found to present nearly twice the rate of smoking (88.4 %) than do the single-diagnosis patients (49.5 %). This suggests that the early tobacco dependence manifested by persons with schizophrenia—it precedes alcohol abuse in nearly every case—can be considered as a precursor of a more general and indiscriminate addiction proclivity.

## Causation

An explanation for the excessive prevalence of substance abuse among persons with schizophrenia and the higher-than-expected rates of schizophrenic disorders in people with a lifetime history of addiction could be that the mere occurrence of one such disorder facilitates the development of the other. In other words, schizophrenia may play an etiological role in substance abuse, or substance abuse may lead to chronic psychosis.

Schizophrenia may lead to addiction through self-medication behaviour (11). This is a nonspecific explanation that applies equally well to most persisting psychological disturbances, including other Axis I categories and several personality disorders, all of which are associated with elevated rates of chemical addiction. This hypothesis has 2 basic premises. The

first is that substance use is perpetuated by the need to soothe or correct psychological deficits or distress. Such distress is believed to arise largely from primary self-regulation defects, or ego-function impairments, that manifest themselves as inability to tolerate negative affects, to maintain interpersonal relationships, to have a sense of personal identity, or to care for oneself. The second assumption is that substance use is not random; it is determined by a preference for drugs whose specific pharmacologic action best remedies particular individual ego-function defects. The self-medication construct thus defines addiction as the consequence of a negative reinforcement mechanism: the reward comes from impeding the occurrence of undesirable psychological states or, if they are inevitable, from decreasing the pain and discomfort they cause.

Such reinforcing benefits may indeed incline schizophrenia sufferers to use drugs. This is perhaps the most convincing explanation for the high rates of tobacco smoking among this population: nicotine is likely to decrease psychological lethargy and feelings of depletion, to ameliorate negative symptoms, and to enhance cognitive functions that are diminished by the illness. Nicotine may even decrease the severity of neuroleptic drug extrapyramidal side effects (EPSEs) (12). However, schizophrenia sufferers also present excess rates of cannabis and cocaine use. These substances are known to worsen delusional and hallucinatory symptoms—untoward effects that may be caused by the drugs' dopaminergic properties on the mesolimbic system. Of course, dopamine activation also occurs in the mesocortical projections and in the prefrontal cortex itself. This particular action potentially alleviates negative symptoms and may thus remedy what certain authors have described as “the reward-deficiency syndrome,” an anomaly believed to afflict persons with schizophrenia (13). It could therefore be postulated that the resulting lessened anhedonia, facilitated social interaction, and other such stimulating effects do constitute a reward powerful enough to counteract the aversive positive symptoms caused by these drugs. Surveys of clinical samples support this interpretation: when asked to describe their subjective experiences with each drug category, schizophrenia sufferers consistently report that cannabis and cocaine decrease “depression,” although they increase suspiciousness and distrust (14). Similarly, it is possible that activating dopaminergic function may diminish the negative mood correlates of neuroleptic-induced parkinsonism—a property that should additionally reinforce use of these drugs among schizophrenia patients receiving treatment.

Lately, however, widespread acceptance of the self-medication hypothesis is being challenged by the proponents of a “primary addiction” theory of comorbidity. This theory contends that individuals with schizophrenia suffer from a

nonspecific avidity for drugs that parallels their psychotic illness and may even be independent of it. According to this interpretation, the inclination of persons with dual pathology to abuse psychoactive substances is an additional symptom of the basic neuropathology underlying schizophrenia itself. In other words, both schizophrenia and substance abuse share a common pathophysiology. A review by Chambers and others details a wide range of neuroscience observations supporting the primary addiction theory (15). These authors conclude that some primary abnormalities in the hippocampal formation and in the frontal cortex exist in schizophrenia sufferers—abnormalities that facilitate the positive reinforcing effects of drug reward and reduce the individual's ability to inhibit drug-seeking behaviour. This preexisting neuropathology is thought to lead to brain responses that facilitate the rapid development of compulsive drug use patterns, providing a shortcut in the path to addiction, as it were. Goldstein and Volkow's report on brain-imaging studies observes that drug users experience abnormally high activation in the orbitofrontal cortex and the cingulate gyrus areas of the brain during craving and acute intoxication (16). The authors conclude that these anomalies represent the neurobiological basis of impaired inhibition, a major feature of addictive behaviour.

Another explanation for the excessive co-occurrence of addiction and schizophrenia is the possibility that drugs may trigger the clinical expression of the psychotic disease. This view is supported by epidemiologic and clinical findings demonstrating that drug use among youth is associated with a higher risk of developing psychosis in subsequent years (17,18); that two-thirds of subjects with first-episode schizophrenia and comorbid addiction used drugs in the premorbid or prodromal phases, prior to the appearance of the first positive symptoms (19); and that drug use by schizophrenia patients in remission is associated with a greater risk of early relapse (20).

However, incidence rates for schizophrenia have not increased in the last 30 years, whereas the prevalence of drug abuse has grown exponentially throughout the world. It therefore seems unlikely that drug abuse by itself suffices to cause the clinical manifestation of a schizophrenic disease.

Other causes of comorbidity are to be found in the high-risk social settings where many persons with schizophrenia are constrained to live. The variance in prevalence rates across demographic categories suggests that such external factors also play an important role in the causation of dual disorders. Access to drugs and the environmental prompting to which many schizophrenia sufferers are exposed cannot be ignored (21). This is especially the case in urban settings, where many schizophrenia patients live in conditions of high social pathology, homelessness, and transient accommodations; that is, in settings where drug circulation is particularly heavy.

## Phenomenology

It seems well established now that, when they coexist, both addiction and schizophrenia present a more problematic clinical picture with a less favourable outcome, compared with their occurrence in isolation. Substance-abusing schizophrenia sufferers fare more poorly than their nonabusing counterparts in just about every clinical parameter or measure. Similarly, when compared with addiction patients who do not suffer from psychosis, addiction patients with chronic psychosis are known to experience considerably more difficulties in terms of psychosocial consequences, access to treatment, and therapeutic response.

Some features that characterize the clinical picture of schizophrenia when it co-occurs with substance abuse are as follows:

1. Earlier outbreak of psychotic symptoms. This finding is consistent across many clinical surveys (1). On average, schizophrenia sufferers with a lifetime history of substance use disorders come to the attention of psychiatric services several years earlier than do those without such history. Of course, it is quite probable that toxic prompting accelerates the clinical manifestation of the psychotic illness. However, the significant association brought to light by these surveys could also be caused by a heightened proclivity to use drugs among individuals with more rapidly developing psychosis.
2. More severe productive symptoms. This is another undisputed finding recorded in a wide variety of studies. When compared with single-diagnosis schizophrenia patients, individuals with dual disorders are more likely to engage in violent behaviour (22). In fact, comorbid substance abuse explains most of the variance in violent occurrences between schizophrenia sufferers and control subjects without psychosis (23). Substance abuse is associated also with higher positive-symptom scores; particularly in regard to delusional and hallucinatory disturbances (24,25).
3. Poorer therapeutic response and less favourable course of illness. Several studies have shown that substance-abusing schizophrenia patients do not benefit from treatment as much as their nonabusing counterparts (1,26). Their remission rates are lower, their psychotic symptoms recur more readily, they require more inpatient treatment, their employment record is poorer, they tend to receive more welfare assistance, their housing and accommodations pattern is more unstable, and they make more visits to the emergency room. All this occurs in the context of a lesser observance of treatment programs, for they also tend to miss more clinic appointments and day-program sessions and to comply less with the prescribed pharmacotherapy (27).
4. Less severe negative symptoms? Some clinical research findings suggest this feature, but it is not as well established an

observation as are the previous ones. Some authors have found a negative linear correlation between amount of cannabis use and negative-symptom scores (28). A similar finding emerged in a clinical survey conducted by the present author, but the significant difference was seen only in patients aged 35 years or under. The negative-symptom ratings did not seem to be influenced by drug use status in the older subjects with chronic psychosis (29). Perhaps the greater severity of negative symptoms characteristic of the more advanced illness stages causes a “ceiling effect,” whereby the assessment instruments are no longer able to detect differences between older-aged comparison groups.

Other authors have reported that persons with schizophrenia who use drugs present a more functional premorbid personality and appear to have better interpersonal skills than do those in the nonusing comparison group (30). However, this observation was reported in a sample of patients who were mostly using cocaine—a group likely to have been preselected for better social efficacy, because cocaine is considerably more difficult to procure than alcohol, nicotine, or even cannabis.

The psychotic comorbidity confers some peculiar characteristics on the picture of addiction and has a significant negative impact on its clinical management:

1. Chaotic, polymorphous, and opportunistic substance abuse. In addition to the most frequently abused substances (nicotine, alcohol, and cannabis) (5), many persons with schizophrenia misuse drugs that are rather unknown outside the clientele of psychiatric services; for instance, the anticholinergic agents prescribed to treat EPSEs. They also resort to over-the-counter preparations such as cough and decongestant syrups, which contain codeine, other opioids, or sympathomimetic stimulants. Many of these patients can only afford to use drugs when they receive their monthly allowance or when they obtain them from someone else. This results in intermittent heavy binges, often with acute consequences that require immediate intervention (that is, emergency room visits). It is not uncommon for these patients to take whatever substance is available to them, without discrimination.

2. Limited motivation. Because of the rather deprived and simple existence they lead, many of these patients see little need to significantly change their habits. They do not readily see substance abuse as threatening their quality of life or as impeding their pursuit of personal goals (31).

3. Limited access to treatment. Patients with psychosis are often deemed ineligible for admission into addiction-treatment programs, most of which have no psychiatric resources or input. Even if accepted, however, these patients are not well served in time-limited programs that rely heavily on intensive and indiscriminate group interventions, because such

traditional addiction services are clearly unable to attend to the dual pathology. Conversely, most continuing care psychiatric services, where most of these patients are usually seen, do not adequately treat the addiction problem. In fact, the substance use disorder often remains totally untreated (32).

## Treatment Programs

It is now generally accepted that substance use disorders in those with chronic psychosis cannot be properly treated using a parallel approach, wherein each disorder is dealt with separately by 2 different care systems. There is a growing awareness of the need to integrate treatment within a single, comprehensive program that offers patients with dual disorders all the therapy they need from care providers who are properly qualified to attend to both the addiction and the psychiatric illness. Given the multiple and special needs of patients with chronic psychosis, it is rather obvious that such combined treatment programs can only be set up within psychiatric services, particularly services that offer long-term, continuing care (32,33).

This integrated approach has already been tested through randomized controlled studies (34,35) and found to be superior to standard treatments in most outcome measures: there is better participation and treatment retention, less drug and alcohol use, higher quality-of-life scores, more stable housing, and higher ratings in general levels of functioning.

The essential elements of a well-organized integrated therapy program include open-ended continuity of care; assertive case management; on-site addiction treatment, including specialized pharmacotherapy; psychiatric therapy that is mindful of the addiction comorbidity; supervised, safe housing; and occupational and work rehabilitation.

The better-designed programs provide the resources necessary to attend to dual-pathology patients through all the contingencies of their condition: acute detoxification and psychiatric stabilization inpatient services when necessary; longer-term residential rehabilitation for selected patients in a therapeutic community model, with adequate psychiatric monitoring and care; and continuing ambulatory treatment, the mainstay of the program. A dual-disorder program is best understood in terms of phases:

1. Engagement. the initial period, in which the main goal is to secure a stable and persisting affiliation with the program, regular attendance, compliance with the essential requirements, and a minimum degree of participation. This phase could last for months or years, and it is important to keep in sight the primary goals, even at the expense of tolerating the patient's initial lack of readiness to address the substance abuse problem. The following is an example of the therapy curriculum at this early stage:

- proactive case management
- in-depth assessment of psychiatric and addiction status
- fine-tuned psychiatric pharmacotherapy
- adapted health education
- positive reinforcement (rewards) for participation
- control over social support
- family intervention
- an accessible recreational or leisure management program
- contingencies

2. Persuasion. In this second phase, well-engaged patients are exposed to ongoing motivational therapies at different levels, both individually with the case manager and in “dual problem” group discussions. The goal at this point is to help patients better understand their particular substance abuse problems and set goals for therapy. Ideally, the work in this phase leads to the patient’s accepting addiction therapy. Some intervention modalities in this phase are as follows:

- continuing monitoring of the patient’s psychiatric and addiction condition, including longitudinal charting of crises and treatment events (for example, adapted health records, monthly Addiction Severity Index [ASI] scoring [36], timeline follow-back record [37], and urine toxicology screening)
- drug and mental illness education for patients and significant others
- social-skills training (38)
- systematic motivational enhancement work (39)

introduction of “maintenance and change” program tracks

3. Active addiction treatment. In this phase, the therapeutic activities involve patients who have opted for effecting the necessary changes in their alcohol and drug habits and see themselves as needing therapy for that specific purpose. To that end, the program could offer the following interventions:

- stabilization and detoxification
- optimized psychiatric and addiction pharmacotherapy
- continuous clinical and laboratory monitoring
- psychiatric case management, individual addiction counselling, and housing and social support control
- family intervention
- goal setting and a scaled goal-attainment reward program
- dual-diagnosis cognitive-behavioural therapy (CBT) sessions (40)
- dual-diagnosis social-skills training (41)
- peer support and 12-step program integration
- prevocational counselling and work placement support

4. Maintenance and relapse prevention phase. Both schizophrenia and addiction are chronic disorders that require continuous, open-ended treatment. Of course, treatment intensity and the frequency of contacts can be considerably scaled back once the patient has shown steady remission. However, the program must always provide the conditions for easy reentry into active care if patients are either lapsing or fully relapsed. In fact, the most likely treatment course is one of repeated interventions over time, and the occasional readmission should be seen as the norm. The following are examples of curriculum components in the program designed to help maintain change and avoid full relapse:

- continuing individual case management, with close monitoring of occupational and leisure activities and housing conditions
- appropriate long-term pharmacotherapy
- emergency plan to be observed by patients, next of kin, and program staff in case of relapse
- time-limited relapse prevention therapy sessions (that is, periodic reinforcement)
- open-ended, therapist-led support sessions
- continuing participation in a peer-support group

### Specific Pharmacotherapy Issues

Patients in treatment who have psychosis and who smoke tobacco or cannabis are exposed to the enzyme-induction properties of the smoke components and may experience an accelerated clearance of neuroleptic and antidepressant drugs (43). Therefore, the blood concentrations of these medications may not attain therapeutic levels at regular dosages. Conversely, they may increase rapidly following smoking cessation.

It is argued that neuroleptics with strong D<sub>2</sub> receptor-binding affinity may contribute to perpetuating substance abuse in persons with schizophrenia. Such a pharmacologic property does lead to receptor upregulation and supersensitivity (44), thus enhancing drug reward and positive reinforcement, and causes more severe EPSEs—another incentive to use drugs. It is therefore recommended that schizophrenia sufferers with dual diagnosis be treated with atypical neuroleptics (44). Several clinical-outcome reports support this view (13,45,46).

The use of opiate receptor agonists such as buprenorphine and methadone (47,48) is considered to be safe and useful in both detoxification and narcotic maintenance therapies for opiate addiction in schizophrenia patients. No untoward effects have been reported to date. The same can be said for opiate antagonist therapy (that is, naltrexone) in cases of opiate addiction and alcoholism. Disulfiram must be used with caution in persons with schizophrenia, for in addition to its prime target, acetaldehyde dehydrogenase, it inhibits dopamine beta-

hydroxylase, an enzyme involved in the conversion of dopamine and noradrenaline, and may thus increase delusional and hallucinatory activity (44). There is still not enough information on the performance of acamprosate in cases of comorbid alcoholism and schizophrenia and, in particular, on whether it has any negative interaction with antipsychotic therapy. This drug has undergone extensive trials in Europe and the US (49), but patients with psychosis appear to have been excluded from the samples studied so far. Bupropion and nicotine-replacement therapy (that is, the transdermal patch), used to achieve cessation of smoking, are apparently safe and effective in patients with chronic psychosis. Several trials have reported good results (50).

Another issue of considerable clinical importance is the decision to initiate a preventive course of pharmacotherapy in young people who have suffered brief, substance-induced psychotic episodes. Continuing neuroleptic treatment as a preventive measure has been recommended for persons who meet criteria for ultrahigh risk (51). It seems the right course if the brief psychotic outbreak occurs in a context of family history of schizophrenia and if the young person already presents other prodromal symptoms. However, other voices strongly advise caution, on the grounds that the reliability and specificity of the prodromal syndrome have not yet been satisfactorily established (52).

### Psychotherapy Issues

Motivational interviewing, CBT, relapse-prevention skills training, and the 12-step mutual-help programs are the most widely used approaches in the psychotherapy of addiction. All have been tried in dual-disorder treatment programs, but it is clear that some specific modifications are required to adapt those interventions to the particular conditions of the patient with psychosis.

The Alcoholics Anonymous (AA) program is the most heavily subscribed treatment resource. It is a significant component in the therapy curriculum for the vast majority of addiction-treatment centres in North America. It offers a time-honoured contribution to treatment success—one that is supported by empirical evidence (53). Most dual-disorder treatment services encourage or require their clients to become involved in this program, but as Noordsy and others have found (54), schizophrenia patients experience significant difficulties adjusting to it: few attend, despite efforts by referring clinicians, although attendance is better for patients with fewer negative symptoms. Most resent confrontation and the dismissal of their justification for drinking (that is, mental symptoms) as an attempt to “deny” alcoholism. Many are uncomfortable in large groups, feeling watched, different, and out of place among people who do not suffer from psychosis. Some are embarrassed by their own restlessness and their

inability to sit still through a long meeting. Most do not identify with the social loss stories of other group members (for example, loss of marriage, job, property, or driving permit), because they have seldom attained a similar status in life. Conversely, when self-help sessions are attended by peers and the experience of mental illness is part of the discussion agenda, patients with dual disorders appear to engage more readily and derive the expected benefits (55).

The main goal of motivational therapy is to help advance the process of change, to coach those who abuse substances into becoming more consciously aware of the nature and extent of the problems at hand, and to empower them to decide voluntarily to make the necessary effort and accept help. Such an approach is obviously more effective when the clients are able to recognize the costs and untoward consequences of not making the change, when they are capable of formulating goals for themselves, and when they can muster the necessary energy to pursue their goals. This is often not the case with persons who suffer chronic and severe mental illness. Dual-disorder motivational therapists must deal with individuals who often see nothing wrong with their drug practices and cannot perceive the advantage of quitting. Such patients have low levels of energy and a certain inability to become enthused with the idea of goal attainment (56). They may also be cognitively impaired. Despite all these limitations, evidence is accumulating to the effect that the motivation enhancement approach does yield positive results in this population and that it should be adopted (57,58).

### Conclusions

Chronic schizophrenia and substance abuse are significantly associated in terms of risk for occurrence and underlying neuropathology. This clinical reality cannot be overlooked; for it is both neglectful and self-defeating to treat one of these disorders while ignoring the other. Emerging evidence points to the significant advantage of treating both disorders jointly, in an integrated manner. Given that both illnesses follow a chronic and recurrent course, that their clinical management calls for a high level of psychiatric expertise, and that there is often a need to access hospital facilities within a continuing care model, integrated programs can be developed most adequately within psychiatric services that provide comprehensive and open-ended care.

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**Résumé : Aspects cliniques de l'abus de substances psychoactives chez les personnes souffrant de schizophrénie**

**Objectif :** Examiner les connaissances actuelles au sujet du problème d'abus de substances psychoactives chez les personnes souffrant de schizophrénie, en portant une attention particulière aux questions qui relèvent directement de la pratique clinique.

**Méthode :** L'auteur a examiné la documentation des vingt dernières années et des données d'études auxquelles il a participé.

**Résultats :** Les personnes souffrant de schizophrénie affichent un risque élevé d'abus de substances. Cette comorbidité peut découler de tentatives d'automédication, d'une neuropathologie commune à la toxicomanie et à la schizophrénie, des propriétés psychotogéniques de certains médicaments ou de l'influence de facteurs environnementaux. Parmi les patients schizophrènes qui reçoivent un traitement, l'abus de substances est associé à des symptômes plus graves et à une piètre réponse au traitement. La présence d'une psychose chronique empêche le traitement du problème d'abus de substances dans des programmes classiques non psychiatriques pour toxicomanie. On observe de meilleurs résultats dans des services thérapeutiques intégrés, où les patients reçoivent les soins appropriés pour les deux affections.

**Conclusion :** Les patients souffrant d'une double pathologie ont besoin de soins complets avec pharmacothérapie adéquate et interventions psychosociales. Ce traitement est mieux prodigué dans le cadre d'un service de soins psychiatriques continus.