



Is there a relationship between childhood ADHD and later drug abuse? See page 2.

Research Report Series

from the director:

Comorbidity is a topic that our stakeholders—patients, family members, health care professionals, and others—frequently ask about. It is also a topic about which we have insufficient information, so it remains a research priority for NIDA. This Research Report provides information on the state of the science in this area. Although a variety of diseases commonly co-occur with drug abuse and addiction (e.g., HIV, hepatitis C, cancer, cardiovascular disease), this report focuses only on the comorbidity of drug use disorders and other mental illnesses.*

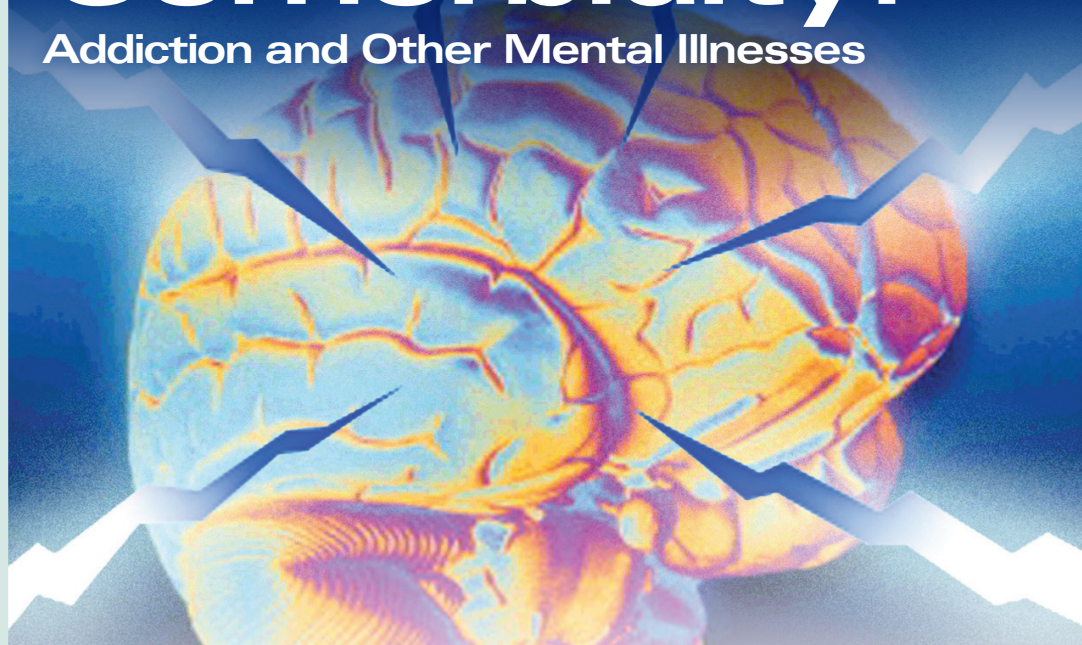
To help explain this comorbidity, we need to first recognize that drug addiction is a mental illness. It is a complex brain disease characterized by compulsive, at times uncontrollable drug craving, seeking, and use despite devastating consequences—behaviors that stem from drug-induced changes in brain structure and function. These changes occur in some of the same brain areas that are disrupted in other mental disorders, such as depression, anxiety, or schizophrenia. It is therefore not surprising that population surveys show a high rate of co-occurrence, or comorbidity, between drug addiction and other mental illnesses. While we cannot always prove a connection or causality, we do know that certain mental disorders are established risk factors for subsequent drug abuse—and vice versa.

It is often difficult to disentangle the overlapping symptoms of drug addiction and other mental illnesses, making diagnosis and treatment complex. Correct diagnosis is critical to ensuring appropriate and effective treatment. Ignorance of or failure to treat a comorbid disorder can jeopardize a patient's chance of recovery. We hope that our enhanced understanding of the common genetic, environmental, and neural bases of these disorders—and the dissemination of this information—will lead to improved treatments for comorbidity and will diminish the social stigma that makes patients reluctant to seek the treatment they need.

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse

Comorbidity:

Addiction and Other Mental Illnesses



What Is Comorbidity?

When two disorders or illnesses occur in the same person, simultaneously or sequentially, they are described as comorbid. Comorbidity also implies interactions between the illnesses that affect the course and prognosis of both.

continued inside

*Since the focus of this report is on comorbid drug use disorders and other mental illnesses, the terms “mental illness” and “mental disorders” will refer here to disorders other than substance use disorders, such as depression, schizophrenia, anxiety, and mania. The terms “dual diagnosis,” “mentally ill chemical abuser,” and “co-occurrence” are also used to refer to drug use disorders that are comorbid with other mental illnesses.



Childhood ADHD and Later Drug Problems

Numerous studies have documented an increased risk for drug use disorders in youth with untreated ADHD, although some suggest that only a subset of these individuals are vulnerable: those with comorbid conduct disorders. Given this linkage, it is important to determine whether effective treatment of ADHD could prevent subsequent drug abuse and associated behavioral problems. Treatment of childhood ADHD with stimulant medications such as methylphenidate or amphetamine reduces the impulsive behavior, fidgeting, and inability to concentrate that characterize ADHD. Yet, some physicians and parents have expressed concern that treating childhood ADHD with stimulants might increase a child's vulnerability to drug abuse later in life. Recent reviews of long-term studies of children with ADHD who were treated with stimulant medications (e.g., Adderall, Ritalin, Concerta) found no evidence for this increase. However, most of these studies have methodological limitations, including small sample sizes and nonrandomized study designs, indicating that more research is needed, particularly with adolescents.

Is Drug Addiction a Mental Illness?

Yes, because addiction changes the brain in fundamental ways, disturbing a person's normal hierarchy of needs and desires and substituting new priorities connected with procuring and using the drug. The resulting compulsive behaviors that override the ability to control impulses despite the consequences are similar to hallmarks of other mental illnesses.

In fact, the DSM, which is the definitive resource of diagnostic criteria for all mental disorders,

Addiction changes the brain, disturbing the normal hierarchy of needs and desires.

includes criteria for *drug use disorders*, distinguishing between two types: drug abuse and drug dependence. *Drug dependence* is synonymous with addiction. By comparison, the criteria for *drug abuse* hinge on the harmful consequences of repeated use but do not include the compulsive use, tolerance (i.e., needing higher doses to achieve the same effect), or withdrawal (i.e., symptoms that occur when use is stopped) that can be signs of addiction.

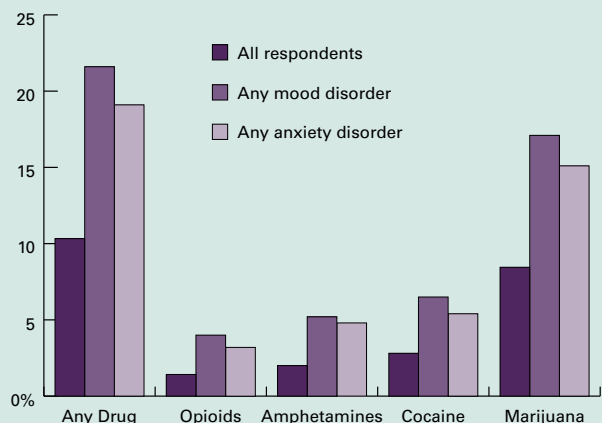
How Common Are Comorbid Drug Use and Other Mental Disorders?

Many people who regularly abuse drugs are also diagnosed with mental disorders and vice versa. The high prevalence of this comorbidity has been documented in multiple national population surveys since the 1980s. Data show that persons diagnosed with mood or anxiety disorders are about twice as likely to suffer also from a drug use disorder (abuse or dependence) compared with respondents in general. The same is true for those diagnosed with an antisocial syndrome, such as antisocial personality or conduct disorder. Similarly, persons diagnosed with drug disorders are roughly twice as likely to suffer also from mood and anxiety disorders (see page 3, "Overlapping Conditions— Shared Vulnerability").

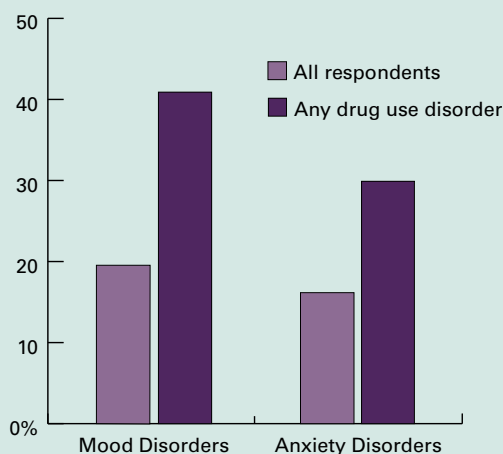
Gender is also a factor in the specific patterns of observed comorbidities. For example, the overall rates of abuse and dependence for most drugs tend to be higher among males than females. Further, males are more likely to suffer from antisocial personality disorder, while women have higher rates of mood and anxiety disorders, all of which are risk factors for substance abuse.

Overlapping Conditions—Shared Vulnerability

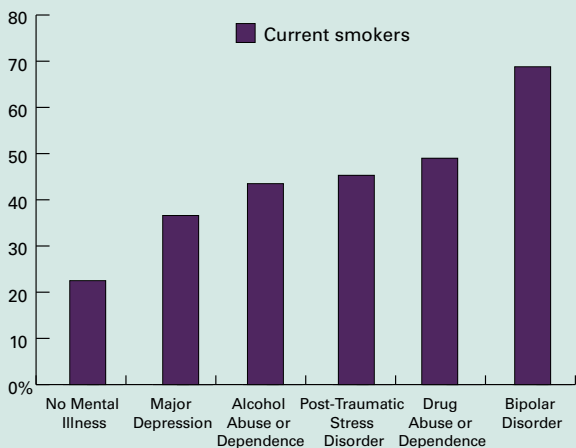
High Prevalence of Drug Abuse and Dependence Among Individuals With Mood and Anxiety Disorders



Higher Prevalence of Mental Disorders Among Patients With Drug Use Disorders



Higher Prevalence of Smoking Among Patients With Mental Disorders



Because mood disorders increase vulnerability to drug abuse and addiction, the diagnosis and treatment of the mood disorder can reduce the risk of subsequent drug use. Because the inverse may also be true, the diagnosis and treatment of drug use disorders may reduce the risk of developing other mental illnesses and, if they do occur, lessen their severity or make them more amenable to effective treatment. Finally, because more than 40 percent of the cigarettes smoked in this country are smoked by individuals with a psychiatric disorder, such as major depressive disorder, alcoholism, post-traumatic stress disorder (PTSD), schizophrenia, or bipolar disorder, smoking by patients with mental illness contributes greatly to their increased morbidity and mortality.

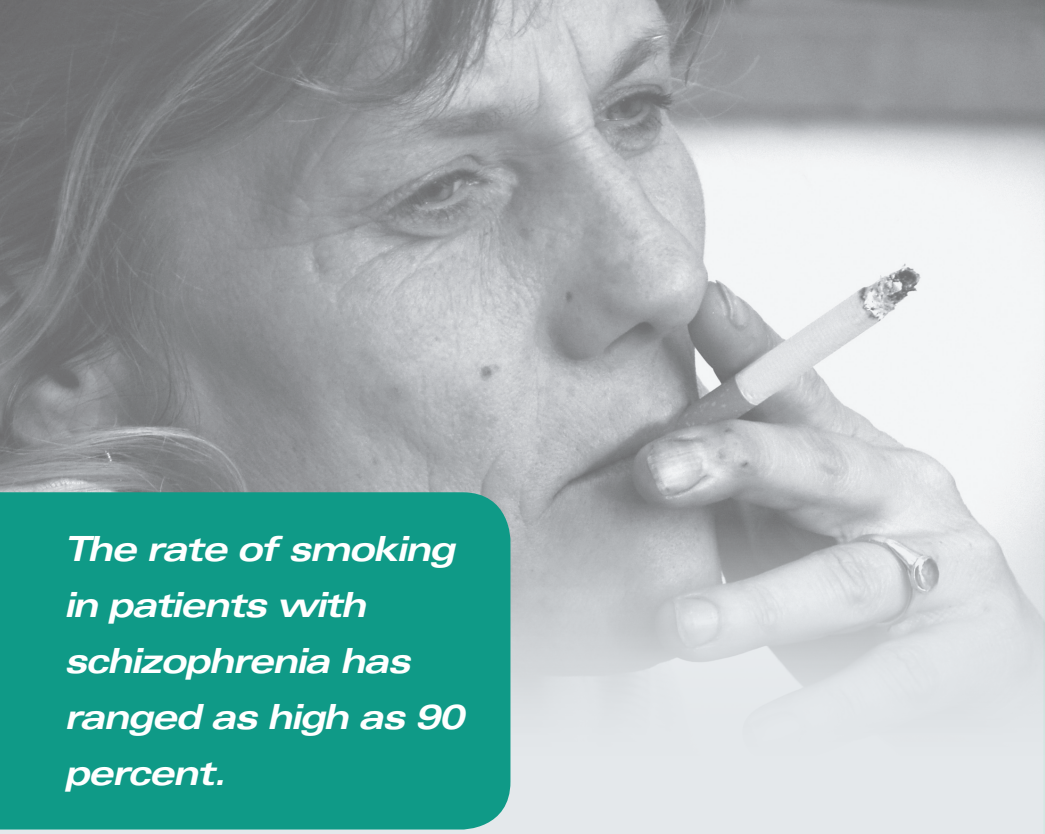
Why Do Drug Use Disorders Often Co-Occur With Other Mental Illnesses?

The high prevalence of comorbidity between drug use disorders and other mental illnesses does not mean that one caused the other, even if one appeared first. In fact, establishing causality or directionality is difficult for several reasons. Diagnosis of a mental disorder may not occur until symptoms have progressed to a specified level (per DSM); however, subclinical symptoms may also prompt drug use, and imperfect recollections of when drug use or abuse started can create confusion as to which came first. Still, three scenarios deserve consideration:

1. Drugs of abuse can cause abusers to experience one or more symptoms of another mental illness. The increased risk of psychosis in some marijuana abusers has been offered as evidence for this possibility.
2. Mental illnesses can lead to drug abuse. Individuals with overt, mild, or even subclinical mental disorders may abuse drugs as a form of self-medication. For example, the use of tobacco products by patients with schizophrenia is believed to lessen the symptoms of the disease and improve cognition (see page 4, “Smoking and Schizophrenia: Self-Medication or Shared Brain Circuitry?”).
3. Both drug use disorders and other mental illnesses are caused by overlapping factors such as underlying brain deficits, genetic vulnerabilities, and/or early exposure to stress or trauma.

All three scenarios probably contribute, in varying degrees, to how and whether specific comorbidities manifest themselves.

Data in top two graphs reprinted from the National Epidemiologic Survey on Alcohol and Related Conditions (Conway et al., 2006). Data in bottom graph from the 1989 U.S. National Health Interview Survey (Lasser et al., 2000).



The rate of smoking in patients with schizophrenia has ranged as high as 90 percent.

Smoking and Schizophrenia: Self-Medication or Shared Brain Circuitry?

Patients with schizophrenia have higher rates of alcohol, tobacco, and other drug abuse than the general population. Based on nationally representative survey data, 41 percent of respondents with past-month mental illnesses are current smokers, which is about double the rate of those with no mental illness. In clinical samples, the rate of smoking in patients with schizophrenia has ranged as high as 90 percent.

Various self-medication hypotheses have been proposed to explain the strong association between schizophrenia and smoking, although none have yet been confirmed. Most of these relate to the nicotine contained in tobacco products: Nicotine may help compensate for some of the cognitive impairments produced by the disorder and may counteract psychotic symptoms or alleviate unpleasant side effects of antipsychotic medications. Nicotine or smoking behavior may also help people with schizophrenia deal with the anxiety and social stigma of their disease.

Research on how both nicotine and schizophrenia affect the brain has generated other possible explanations for the high rate of smoking among people with schizophrenia. The presence of abnormalities in particular circuits of the brain may predispose individuals to schizophrenia, increase the rewarding effects of drugs like nicotine, or reduce an individual's ability to quit smoking. The involvement of common mechanisms is consistent with the observation that both nicotine and the medication clozapine (which also acts at nicotine receptors, among others) can improve attention and working memory in an animal model of schizophrenia. Clozapine is effective in treating individuals with schizophrenia. It also reduces their smoking levels. Understanding how and why patients with schizophrenia use nicotine is likely to help us develop new treatments for both schizophrenia and nicotine dependence.

Common Factors

Overlapping Genetic Vulnerabilities. A particularly active area of comorbidity research involves the search for *genes* that might predispose individuals to develop both addiction and other mental illnesses, or to have a greater risk of a second disorder occurring after the first appears. It is estimated that 40–60 percent of an individual's vulnerability to addiction is attributable to genetics; most of this vulnerability arises from complex interactions among multiple genes and from genetic interactions with environmental influences. In some instances, a gene product may act directly, as when a protein influences how a person responds to a drug (e.g., whether the drug experience is pleasurable or not) or how long a drug remains in the body. But genes can also act indirectly by altering how an individual responds to stress or by increasing the likelihood of risk-taking and novelty-seeking behaviors, which could influence the development of drug use disorders and other mental illnesses. Several regions of the human genome have been linked to increased risk of both drug use disorders and mental illness, including associations with greater vulnerability to adolescent drug dependence and conduct disorders.

Involvement of Similar Brain Regions.

Some areas of the brain are affected by both drug use disorders and other mental illnesses. For example, the circuits in the brain that use the neurotransmitter dopamine—a chemical that carries messages from one neuron to another—are typically affected by addictive substances and may also be involved in depression, schizophrenia, and other psychiatric disorders.

Indeed, some antidepressants and essentially all antipsychotic medications directly target the regulation of dopamine in this system, whereas others may have indirect effects. Importantly, dopamine pathways have also been implicated in the way in which stress can increase vulnerability to drug addiction. Stress is also a known risk factor for a range of mental disorders and therefore provides one likely common neurobiological link between the disease processes of addiction and those of other mental disorders.

The overlap of brain areas involved in both drug use disorders and other mental illnesses suggests that brain changes stemming from one may affect the other. For example, drug abuse that precedes the first symptoms of a mental illness may produce changes in brain structure and function that kindle an underlying propensity to develop that mental illness. If the mental disorder develops first, associated changes in brain activity may increase the vulnerability to abusing substances by enhancing their positive effects, reducing awareness of their negative effects, or alleviating the unpleasant effects associated with the mental disorder or the medication used to treat it.

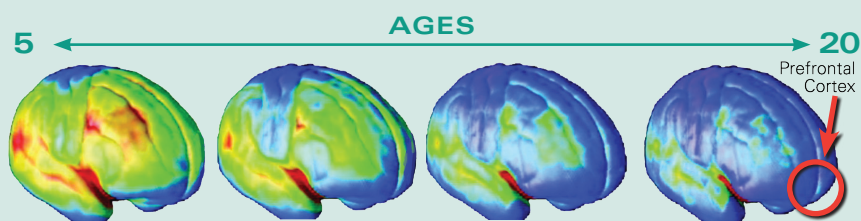
The Influence of Developmental Stage
Adolescence—A Vulnerable Time. Although drug abuse and addiction can happen at any time during a person's life, drug use typically starts in adolescence, a period when the first signs of mental illness commonly appear. It is therefore not surprising that comorbid disorders can already

be seen among youth. Significant changes in the brain occur during adolescence, which may enhance vulnerability to drug use and the development of addiction and other mental disorders. Drugs of abuse affect brain circuits involved in learning and memory, reward, decisionmaking, and behavioral control, all of which are still maturing into early adulthood. Thus, understanding the long-term impact of early drug exposure is a critical area of comorbidity research.

Early Occurrence Increases Later Risk. Strong evidence has emerged showing early drug use to be a risk factor for later substance abuse problems; additional findings suggest that it may also be a risk factor for the later occurrence of other mental illnesses. However, this link is not necessarily a simple one and may hinge upon genetic vulnerability, psychosocial experiences, and/or general environmental influences. A 2005 study highlights this complexity,

The brain continues to develop into adulthood and undergoes dramatic changes during adolescence.

One of the brain areas still maturing during adolescence is the prefrontal cortex—the part of the brain that enables us to assess situations, make sound decisions, and keep our emotions and desires under control. The fact that this critical part of an adolescent's brain is still a work in progress puts them at increased risk for poor decisions (such as trying drugs or continuing abuse). Thus, introducing drugs while the brain is still developing may have profound and long-lasting consequences.



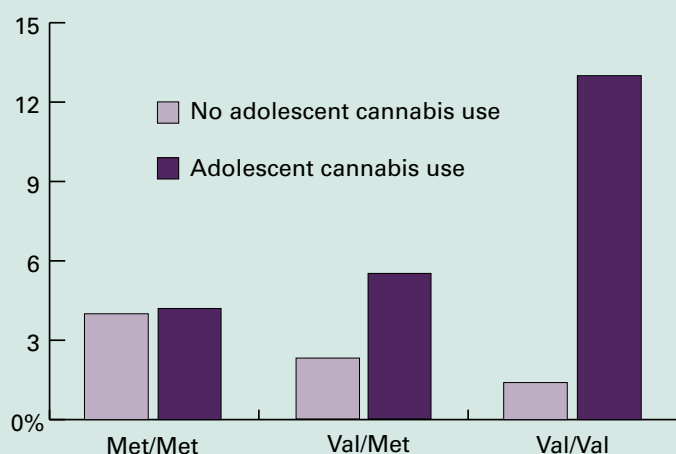
Blue represents maturing of brain areas.



The high rate of comorbidity between drug abuse and addiction and other mental disorders argues for a comprehensive approach to intervention that identifies and evaluates each disorder concurrently, providing treatment as needed.

The Influence of Adolescent Marijuana Use on Adult Psychosis Is Affected by Genetic Variables

Percentage of Individuals Meeting Diagnostic Criteria for Schizophreniform Disorder at Age 26



Source: Caspi A, Moffitt TE, Cannon M, et al., 2005.

The above figure shows that variations in a gene can affect the likelihood of developing psychosis in adulthood following exposure to cannabis in adolescence. The catechol-*O*-methyltransferase gene regulates an enzyme that breaks down dopamine, a brain chemical involved in schizophrenia. It comes in two forms: Met and Val. Individuals with one or two copies of the Val variant have a higher risk of developing schizophrenic-type disorders if they used cannabis during adolescence (dark bars). Those with only the Met variant were unaffected by cannabis use. These findings hint at the complexity of factors that contribute to comorbid conditions.

with the finding that frequent marijuana use during adolescence can increase the risk of psychosis in adulthood, but only in individuals who carry a particular gene variant (see sidebar, “The Influence of Adolescent Marijuana Use on Adult Psychosis Is Affected by Genetic Variables”).

It is also true that having a mental disorder in childhood or adolescence can increase the risk of later drug abuse problems, as frequently occurs with conduct disorder and untreated attention-deficit hyperactivity disorder (ADHD). This presents a challenge when treating children with ADHD, since effective treatment often involves prescribing stimulant medications with abuse potential. This issue has generated strong interest from the research community, and although the results are not yet conclusive, most studies suggest that ADHD medications do not increase the risk of drug abuse among children with ADHD (see page 2, “Childhood ADHD and Later Drug Problems”).

Regardless of how comorbidity develops, it is common in youth as well as adults. Given the high prevalence of comorbid mental disorders and their likely adverse impact on substance abuse treatment outcomes, drug abuse programs for adolescents should include screening and, as needed, treatment for comorbid mental disorders.

How Can Comorbidity Be Diagnosed?

The high rate of comorbidity between drug use disorders and other mental illnesses argues for a comprehensive approach to intervention that identifies and evaluates each disorder concurrently, providing treatment as needed. The needed approach calls for broad assessment tools that are less likely to result in a missed diagnosis. Accordingly, patients entering treatment for psychiatric illnesses should also be screened for substance use disorders and vice versa. Accurate diagnosis is complicated, however, by the similarities between drug-related symptoms such as withdrawal and those of potentially comorbid mental disorders. Thus, when people who abuse drugs enter treatment, it may be necessary to observe them after a period of abstinence in order to distinguish between the effects of substance intoxication or withdrawal and the symptoms of comorbid mental disorders. This practice would allow for a more accurate diagnosis and more targeted treatment.

How Should Comorbid Conditions Be Treated?

A fundamental principle emerging from scientific research is the need to treat comorbid conditions concurrently—which can be a difficult proposition (see page

9, “Barriers to Comprehensive Treatment of Comorbidity”). Patients who have both a drug use disorder and another mental illness often exhibit symptoms that are more persistent, severe, and resistant to treatment compared with patients who have either disorder alone. Nevertheless, steady progress is being made through research on new and existing treatment options for comorbidity and through health services research on implementation of appropriate screening and treatment within a variety of settings, including criminal justice systems.



Medications

Effective medications exist for treating opioid, alcohol, and nicotine addiction and for alleviating the symptoms of many other mental disorders, yet most have not been well studied in comorbid populations. Some medications may benefit multiple problems. For example, evidence suggests that bupropion (trade names: Wellbutrin, Zyban), approved for treating depression and nicotine dependence, might also help reduce craving and use of the drug methamphetamine. Clearly, more research is needed to fully understand and assess the actions of combined or dually effective medications.



Behavioral Therapies

Behavioral treatment (alone or in combination with medications) is the cornerstone to successful outcomes for many individuals with drug use disorders or other mental illnesses. And while behavior therapies continue to be evaluated for use in comorbid populations, several strategies have shown promise for treating specific comorbid conditions (see page 8, “Examples of Promising Behavioral Therapies for Patients With Comorbid Conditions”).

Most clinicians and researchers agree that broad spectrum diagnosis and concurrent therapy will lead to more positive outcomes for patients with comorbid conditions. Preliminary findings support this notion, but research is needed to identify the most effective therapies (especially studies focused on adolescents).

Examples of Promising Behavioral Therapies for Patients with Comorbid Conditions

Adolescents

Multisystemic Therapy (MST)

MST targets key factors (attitudes, family, peer pressure, school and neighborhood culture) associated with serious antisocial behavior in children and adolescents who abuse drugs.

Brief Strategic Family Therapy (BSFT)

BSFT targets family interactions that are thought to maintain or exacerbate adolescent drug abuse and other co-occurring problem behaviors. These problem behaviors include conduct problems at home and at school, oppositional behavior, delinquency, associating with antisocial peers, aggressive and violent behavior, and risky sexual behaviors.

Cognitive-Behavioral Therapy (CBT)

CBT is designed to modify harmful beliefs and maladaptive behaviors. CBT is the most effective psychotherapy for children and adolescents with anxiety and mood disorders, and also shows strong efficacy for substance abusers. (CBT is also effective for adult populations suffering from drug use disorders and a range of other psychiatric problems.)



Adults

Therapeutic Communities (TCs)

TCs focus on the “resocialization” of the individual and use broad-based community programs as active components of treatment. TCs are particularly well suited to deal with criminal justice inmates, individuals with vocational deficits, women who need special protections from harsh social environments, vulnerable or neglected youth, and homeless individuals. In addition, some evidence suggests the utility of incorporating TCs for adolescents who have been in treatment for substance abuse and related problems.

Assertive Community Treatment (ACT)

ACT programs integrate the behavioral treatment of other severe mental disorders, such as schizophrenia, and co-occurring substance use disorders. ACT is differentiated from other forms of case management through factors such as a smaller caseload size, team management, outreach emphasis, a highly individualized approach, and an assertive approach to maintaining contact with patients.

Dialectical Behavior Therapy (DBT)

DBT is designed specifically to reduce self-harm behaviors (such as self-mutilation and suicidal attempts, thoughts, or urges) and drug abuse. It is one of the few treatments that is effective for individuals who meet the criteria for borderline personality disorder.

Exposure Therapy

Exposure therapy is a behavioral treatment for some anxiety disorders (phobias, PTSD) that involves repeated exposure to or confrontation with a feared situation, object, traumatic event, or memory. This exposure can be real, visualized, or simulated, and always is contained in a controlled therapeutic environment. The goal is to desensitize patients to the triggering stimuli and help them learn to cope, eventually reducing or even eliminating symptoms. Several studies suggest that exposure therapy may be helpful for individuals with comorbid PTSD and cocaine addiction, although retention in treatment is difficult.

Integrated Group Therapy (IGT)

IGT is a new treatment developed specifically for patients with bipolar disorder and drug addiction, designed to address both problems simultaneously.



Exposure to Traumatic Events Puts People at Higher Risk of Substance Use Disorders

Physically or emotionally traumatized people are at much higher risk of abusing licit, illicit, and prescription drugs. This linkage is of particular concern for returning veterans since nearly 1 in 5 military service members back from Iraq and Afghanistan have reported symptoms of post-traumatic stress disorder (PTSD) or major depression. Recent epidemiological studies suggest that as many as half of all veterans diagnosed with PTSD also have a co-occurring substance use disorder (SUD), which could pose an enormous challenge for our health care system. Many PTSD programs do not accept individuals with active SUDs, and traditional SUD clinics defer treatment of trauma-related issues. Nevertheless, there are treatments at different stages of clinical validation for comorbid PTSD and SUD; these include various combinations of psychosocial (e.g., exposure therapy) and pharmacologic (e.g., mood stabilizers, anxiolytics, and antidepressants) interventions. However, research is urgently needed to identify the best treatment strategies for addressing PTSD/SUD comorbidities, and to explore whether different treatments might be needed in response to civilian versus combat PTSD.



Barriers to Comprehensive Treatment of Comorbidity

Although research supports the need for comprehensive treatment to address comorbidity, provision of such treatment can be problematic for a number of reasons:

- In the United States, different treatment systems address drug use disorders and other mental illnesses separately. Physicians are most often the front line of treatment for mental disorders, whereas drug abuse treatment is provided in assorted venues by a mix of health care professionals with different backgrounds. Thus, neither system may have sufficiently broad expertise to address the full range of problems presented by patients. People also use these health care systems differently, depending on insurance coverage and social factors. For example, when suffering from substance abuse and mental illness comorbidities, women more often seek help from mental health practitioners, whereas men tend to seek help through substance abuse treatment channels.
- A lingering bias remains in some substance abuse treatment centers against using any medications, including those necessary to treat serious mental disorders such as depression. Additionally, many substance abuse treatment programs do not employ professionals qualified to prescribe, dispense, and monitor medications.
- Many of those needing treatment are in the criminal justice system. It is estimated that about 45 percent of offenders in State and local prisons and jails have a mental health problem comorbid with substance abuse or addiction. However, adequate treatment services for both drug use disorders and other mental illnesses are greatly lacking within these settings. While treatment provision may be burdensome for the criminal justice system, it offers an opportunity to positively affect the public's health and safety. Treatment of comorbid disorders can reduce not only associated medical complications, but also negative social outcomes by mitigating against a return to criminal behavior and reincarceration.

Glossary

Addiction: A chronic, relapsing disease characterized by compulsive drug seeking and use and by long-lasting changes in the brain.

Antisocial Personality Disorder: A disorder characterized by antisocial behaviors that involve pervasive disregard for and violation of the rights, feelings, and safety of others. These behaviors begin in early childhood (conduct disorder) or the early teenage years and continue into adulthood.

Anxiety Disorders: Varied disorders that involve excessive or inappropriate feelings of anxiety or worry. Examples are panic disorder, PTSD, social phobia, and others.

Attention-Deficit Hyperactivity Disorder (ADHD): A disorder that typically presents in early childhood, characterized by inattention, hyperactivity, and impulsivity.

Bipolar Disorder: A mood disorder characterized by alternating episodes of depression and mania or hypomania.

Comorbidity: The occurrence of two disorders or illnesses in the same person, either at the same time (co-occurring comorbid conditions) or with a time difference between the initial occurrence of one and the initial occurrence of the other (sequentially comorbid conditions).

Conduct Disorder: A repetitive and persistent pattern of behavior in children or adolescents in which the basic rights of others or major age-appropriate societal norms or rules are violated.

Depression: A disorder marked by sadness, inactivity, difficulty with thinking and concentration, significant increase or decrease in appetite and time spent sleeping, feelings of dejection and hopelessness, and, sometimes, suicidal thoughts or an attempt to commit suicide.

Dopamine: A brain chemical, classified as a neurotransmitter, found in regions of the brain that regulate movement, emotion, motivation, and pleasure.

Dual Diagnosis/Mentally Ill Chemical Abuser (MICA): Other terms used to describe the comorbidity of a drug use disorder and another mental illness.

Major Depressive Disorder: A mood disorder having a clinical course of one or more serious depression episodes that last 2 or more weeks. Episodes are characterized by a loss of interest or pleasure in almost all activities; disturbances in appetite, sleep, or psychomotor functioning; a decrease in energy; difficulties in thinking or making decisions; loss of self-esteem or feelings of guilt; and suicidal thoughts or attempts.

Mania: A mood disorder characterized by abnormally and persistently elevated, expansive, or irritable mood; mental and physical hyperactivity; and/or disorganization of behavior.

Mental Disorder: A mental condition marked primarily by sufficient disorganization of personality, mind, and emotions to seriously impair the normal psychological or behavioral functioning of the individual. Addiction is a mental disorder.

Neurotransmitter: A chemical produced by neurons to carry messages from one nerve cell to another.

Post-Traumatic Stress Disorder (PTSD): A disorder that develops after exposure to a highly stressful event (e.g., wartime combat, physical violence, or natural disaster). Symptoms include sleeping difficulties, hypervigilance, avoiding reminders of the event, and re-experiencing the trauma through flashbacks or recurrent nightmares.

Psychosis: A mental disorder (e.g., schizophrenia) characterized by delusional or disordered thinking detached from reality; symptoms often include hallucinations.

Schizophrenia: A psychotic disorder characterized by symptoms that fall into two categories: (1) positive symptoms, such as distortions in thoughts (delusions), perception (hallucinations), and language and thinking and (2) negative symptoms, such as flattened emotional responses and decreased goal-directed behavior.

Self-Medication: The use of a substance to lessen the negative effects of stress, anxiety, or other mental disorders (or side effects of their pharmacotherapy). Self-medication may lead to addiction and other drug- or alcohol-related problems.

References

- Biederman, J.; Monuteaux, M.C.; Spencer, T.; Wilens, T.E.; Macpherson, H.A.; and Faraone, S.V. Stimulant therapy and risk for subsequent substance use disorders in male adults with ADHD: A naturalistic controlled 10-year follow up study. *Am J Psychiatry* 165(5):597–603, 2008.
- Brady, K.T., and Verduin, M.L. Pharmacotherapy of comorbid mood, anxiety, and substance use disorders. *Subst Use Misuse* 40:2021–2041; 2043–2048, 2005.
- Caspi, A.; Moffitt, T.E.; Cannon, M.; McClay, J.; Murray, R.; Harrington, H.; Taylor, A.; Arseneault, L.; Williams, B.; Braithwaite, A.; Poulton, R.; and Craig, I.W. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: Longitudinal evidence of a gene x environment interaction. *Biol Psychiatry* 57(10):1117–1127, 2005.
- Compton, W.M.; Conway, K.P.; Stinson, F.S.; Colliver, J.D.; and Grant, B.F. Prevalence, correlates, and comorbidity of DSM-IV antisocial personality syndromes and alcohol and specific drug use disorders in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *J Clin Psychiatry* 66(6):677–685, 2005.
- Conway, K.P.; Compton, W.; Stinson, F.S.; and Grant, B.F. Lifetime comorbidity of DSM-IV mood and anxiety disorders and specific drug use disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *J Clin Psychiatry* 67(2):247–257, 2006.
- James, D.J., and Glaze, L.E. Mental health problems of prison and jail inmates. *Bureau of Justice Statistics Special Report*. U.S. Department of Justice, 2006 (available at <http://bjs.ojp.usdoj.gov/content/pub/pdf/mhppji.pdf>).
- Kessler, R.C. The epidemiology of dual diagnosis. *Biol Psychiatry* 56:730–737, 2004.
- Lasser, K.; Boyd, J.W.; Woolhandler, S.; Himmelstein, D.U.; McCormick, D.; and Bor, D.H. Smoking and mental illness: A population-based prevalence study. *JAMA* 284(20):2606–2610, 2000.
- Mannuzza, S.; Klein, R.G.; Truong, N.L.; Moulton, J.L. III; Roizen, E.R.; Howell, K.H.; and Castellanos, F.X. Age of methylphenidate treatment initiation in children with ADHD and later substance abuse: Prospective follow-up into adulthood. *Am J Psychiatry* 165(5):604–609, 2008.
- Negrete, J.C. Clinical aspects of substance abuse in persons with schizophrenia. *Can J Psychiatry* 48(1):14–21, 2003.
- Nestler, E.J., and Carlezon, W.A. Jr. The mesolimbic dopamine reward circuit in depression. *Biol Psychiatry* 59(12):1151–1159, 2006.
- Quello, S.B.; Brady, K.T.; and Sonne, S.C. Mood disorders and substance abuse disorders: A complex comorbidity. *Science & Practice Perspectives* 3(1):13–24, 2005.
- Rand Corporation. News Release, April 17, 2008: *One in five Iraq and Afghanistan veterans suffer from PTSD or major depression*. Retrieved July 19, 2010 from <http://www.rand.org/news/press/2008/04/17/>.
- Rand Corporation. Online Summary: [Invisible wounds of war—Psychological and cognitive injuries, their consequences, and services to assist recovery](#) (T. Tanielian and L. Jaycox, eds). Retrieved July 19, 2010 from <http://www.rand.org/pubs/monographs/MG720/>.
- Riggs, P.D. Treating adolescents for substance abuse and comorbid psychiatric disorders. *Sci Pract Perspect* 2(1):18–28, 2003.
- Saal, D.; Dong, Y.; Bonci, A.; and Malenka, R.C. Drugs of abuse and stress trigger a common synaptic adaptation in dopamine neurons. *Neuron* 37(4):577–582, 2003.
- Uhl, G.R., and Grow, R.W. The burden of complex genetics in brain disorders. *Arch Gen Psychiatry* 61(3):223–229, 2004.
- Volkow, N.D. The reality of comorbidity: Depression and drug abuse. *Biol Psychiatry* 56(10):714–717, 2004.
- Volkow, N.D., and Li, T.-K. Drug addiction: The neurobiology of behavior gone awry. *Nat Rev Neurosci* 5(12):963–970, 2004.
- Weiss, R.D.; Griffin, M.L.; Kolodziej, M.E.; Greenfield, S.F.; Najavits, L.M.; Daley, D.C.; Doreau, H.R.; and Hennen, J.A. A randomized trial of integrated group therapy versus group drug counseling for patients with bipolar disorder and substance dependence. *Am J Psychiatry* 164(1):100–107, 2007.
- Wilens, T.E.; Faraone, S.V.; Biederman, J.; and Gunawardene, S. Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature. *Pediatrics* 111(1):179–185, 2003.

Where Can I Get More Scientific Information on Comorbid Addiction and Other Mental Illnesses?

To learn more about drug use disorders and other mental illnesses, or to order materials on these topics free of charge in English or Spanish, visit the NIDA Web site at www.drugabuse.gov or contact the *DrugPubs* Research Dissemination Center at 877-NIDA-NIH (877-643-2644; TTY/TDD: 240-645-0228).



What's New on the NIDA Web Site

- Information on drugs of abuse
- Publications and communications (including *NIDA Notes* and *Addiction Science & Clinical Practice* journal)
- Calendar of events
- Links to NIDA organizational units
- Funding information (including program announcements and deadlines)
- International activities
- Links to related Web sites (access to Web sites of many other organizations in the field)

NIDA Web Sites

drugabuse.gov
backtoschool.drugabuse.gov
smoking.drugabuse.gov
hiv.drugabuse.gov
marijuana-info.org
clubdrugs.gov
steroidabuse.gov
teens.drugabuse.gov
inhalants.drugabuse.gov

Other Web Sites

Information on drug abuse and other mental illnesses is also available through these other Web sites:

- National Institute of Mental Health: www.nimh.nih.gov
- National Institute on Alcohol Abuse and Alcoholism: www.niaaa.nih.gov
- Substance Abuse and Mental Health Services Administration Health Information Network: www.samhsa.gov/shin

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NIH Publication Number 10-5771
Printed December 2008, Revised September 2010
Feel free to reprint this publication.