

CHRONIC SUBSTANCE USE, MOOD DISORDER AND PSYCHOSIS

MENTAL HEALTH AND SUBSTANCE USE

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Abstract

Co-occurring bipolar disorder and substance use disorder pose a serious health risk to affected individuals. Patients with dual diagnoses may experience substantial challenges during treatment for their mental illness and recovery from substance use. Early diagnosis and intervention can significantly improve the potential outcomes for patients with a dual diagnosis. The changes made in this area within the Diagnostic and Statistical Manual of Mental Disorders guide health clinicians managing bipolar disorder complicated by a substance use disorder to lower the health risks throughout the age spectrum.

Policy Statement

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Statement of Learning Need

Health professionals need to be alert to the possibility of a dual diagnosis of bipolar disorder and substance use disorder to be able to provide each patient with the most appropriate and individualized treatment options.

Course Purpose

To provide health clinicians with knowledge about diagnosing a comorbid condition and the new criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) that help guide treatment for bipolar disorder and substance use disorder.

Target Audience

Advanced Practice Registered Nurses, Registered Nurses, and other Interdisciplinary Health Team Members.

Disclosures

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Self-Assessment of Knowledge Pre-Test:

- 1. A clinician who is evaluating a patient's mental health may use the term "dual diagnosis" to describe a person who**
 - a. exhibits "drug dependence" and "drug addiction."
 - b. has a mental health disorder and a substance use disorder.
 - c. exhibits high and low bipolar symptoms.
 - d. is diagnosed with cyclothymia and bipolar type I or II.

- 2. Switching is the term used to describe a patient with bipolar disorder who**
 - a. transitions between "drug dependence" and "drug addiction."
 - b. changes medications to treat a disorder.
 - c. discontinues a medication that triggers a manic episode.
 - d. transitions between high and low ends of the spectrum of bipolar symptoms.

- 3. The practice of self-medication is especially dangerous for a person who has not been diagnosed with bipolar disorder because**
 - a. this person may believe his or her emotional highs and lows are normal.
 - b. in these cases, substance use disorder always precedes bipolar disorder.
 - c. this "substance abuse" is more serious than "substance dependence."
 - d. a maladaptive pattern is unique to people who self-medicate.

- 4. Which of the following may be a causative factor that contributes to substance use when a mood disorder such as bipolar disorder is present?**
 - a. The maladaptive pattern
 - b. The self-medicating theory
 - c. Switching
 - d. The presence of cyclothymia

- 5. True or False: It is vitally important that a clinician determines which condition came first, the patient's bipolar disorder or substance use disorder, before treating a comorbid patient.**
 - a. True
 - b. False

Introduction

A person with bipolar disorder is at higher risk of developing problems with drugs, alcohol, or tobacco. The term dual diagnosis is used to describe a person who has been diagnosed with a mental health disorder and a substance use disorder or addiction. The incidence of bipolar disorder and substance use disorder is high, with many people affected with bipolar disorder turning to drugs or alcohol. Substance use when it becomes severe can lead to a mental health disorder, as the chronic use of alcohol or drugs can cause changes in the brain that affect a person's cognition and ability to make decisions and to perform independent activities of daily life. The individual with chronic substance use typically reaches a point of being unable to stop using by choice despite the negative consequences that have happened as a result of substance use.

DSM-5 Criteria: Comorbid Bipolar and Substance Use Disorder

The DSM-5 included changes in the diagnosis of a substance use disorder that impacted treatment options for individuals also diagnosed with bipolar disorder. The DSM-IV had defined "drug abuse" and "dependence" as separate conditions, although both situations could develop in a person with bipolar disorder. In the DSM-IV, *drug dependence* was a term used interchangeably with *drug addiction*, in which a person was understood to have a physiological craving for a drug that was often uncontrollable. Drug dependence was also considered a mental illness because a person with drug dependency experienced actual changes in the brain that affected an ability to function. The affected person was unable to stop using a substance even if a desire existed to stop. Also, in DSM-IV, "substance abuse" referred to the repeated use of drugs or alcohol in potentially harmful ways, even when negative consequences resulted.¹

Under DSM-5, clinicians may refer to a larger diagnostic category of *substance use disorders*, which becomes classified as either mild, moderate, or severe in intensity.^{1,2} DSM-5 classifications refer to a specific type of substance use; a condition may be classified as an alcohol use disorder, tobacco use disorder, hallucinogen use disorder, or cannabis use disorder.²

Whether a person is diagnosed with a substance use disorder depends on the impact the substance has on the person's life, such as how it affects behavior, level of impairment, and the risks associated with the substance use.

Although bipolar disorder and substance use disorders may be seen together, one condition does not necessarily precede or cause the other. While at times it may be obvious that one condition led to the development of the other, the clinician does not necessarily need to spend significant time trying to determine which condition came first. Often, in patients with co-occurring bipolar and substance use disorders, it can be extremely difficult to determine if the symptoms are associated with the bipolar disorder, the substance use, or from both conditions.³⁻⁵ A patient with bipolar disorder may eventually develop a substance use disorder because of severe mood changes and anxiety leading the person to choose a type of substance to self-medicate. A patient may not be able to relay information about when symptoms started or at what point drug or alcohol use started.

Substance use can lead to symptoms of other types of mental illness that can also compound the situation. For example, psychosis has been associated with amphetamine, cocaine, and marijuana use. Determining which condition is the primary disorder typically involves getting the person into a state of sobriety for a period of time. After a period of abstinence, the clinician may be better able to determine what symptoms the patient continues to have related to the mental illness.

Often overlapping symptoms will exist of a substance use and bipolar disorder. The individual will need to undergo a time of abstinence before symptoms associated with an underlying mental illness are recognized rather than the substance use itself.³⁻⁵ There is a high incidence of comorbid bipolar and substance use disorder and one meta-analysis reviewed inpatient and outpatient encounters involving patients diagnosed with bipolar disorder that sought treatment. The highest prevalence of substance use in persons with bipolar disorder was identified as alcohol use at 42%. Comorbid bipolar disorder and cannabis use was 20% and other drug use was 17%.⁶ Males

reportedly had a higher lifetime risk of substance use than females. Comorbid bipolar disorder and substance use was also associated with younger age of onset and generally resulted in hospitalizations more than non-users.⁶

Patients with bipolar disorder are also more likely to develop other psychological conditions as a result of substance use, including increased anxiety, rapid cycling as a result of bipolar disorder, greater numbers of hospitalizations, and more suicide attempts.⁷

Neurobiological Pathways

Bipolar disorder and substance use disorders share some common neurobiological pathways that are responsible for some of the behavioral manifestations that occur with both disorders.⁸ In other words, a person with bipolar disorder may have some of the same behaviors as when intoxicated or using drugs, such as impulsivity, grandiosity, or rapid speech. When dopamine levels are altered because of a substance use disorder, the affected person may also experience more symptoms of mental illness, which could be another reason why the two conditions are often seen together.

Dopamine is responsible for many functions, including communicating information in the brain, providing feelings of pleasure and enjoyment, and controlling a person's levels of motivation.⁸ During a period of mania, a patient with bipolar disorder may experience increased euphoria and excitability, exaggerated by the effects of substance use. The individual may seek to have that same feeling repeated again during manic stages and may continue to use drugs or alcohol to obtain it.

The dopamine hypothesis of bipolar disorder began in the 1970s and focused on mania, amphetamine use and its effect on bipolar disorder, and the use of antidopaminergic drugs to treat mania.⁹ Dopaminergic function was believed to affect the symptoms of bipolar disorder but did not explain how hyper- or hypodopaminergia led to cyclical changes in dopaminergic

neurotransmission.⁹ Faulty homeostatic mechanisms leading to hyperdopaminergia in the manic phase of bipolar disorder are suggested to eventually lead to an excessive reduction in dopaminergic function, or a hypodopaminergic state and depression, and then a switch back to a faulty regulatory response to hypodopaminergia and cycle back into mania. Normalisation of dopaminergic function through medication treatment of a bipolar disorder will result in remission and euthymia.⁹

Genetics

Bipolar disorder and substance use disorders may share some overlapping genes causing a person who has already been diagnosed with bipolar disorder to be more likely to develop a substance use disorder.¹⁰⁻¹² Genetic factors may increase a person's attraction to certain types of drugs or to alcohol, making it more likely that the affected person will first start using drugs. Genes may also affect how a person responds to stress or the likelihood of the person to take risks in some areas when compared to other people. When these genes are present in a person with bipolar disorder, the person may also be more likely to start using drugs or alcohol as a response to stress or to try new experiences and then develop a substance use disorder.

The National Institute on Drug Abuse (NIDA) has published statistics on an individual's risk related to genetic makeup to develop an alcohol, tobacco, or other drug use problem. The NIDA has reported on studies that included identical twins, fraternal twins, adoptees, and siblings, suggesting that "as much as half of a person's risk of becoming addicted to nicotine, alcohol, or other drugs depends on his or her genetic makeup."¹³

Cannabis Use and Psychosis

Cannabis use has been reported to correlate with an increased risk of psychosis. Research has indicated that there is an estimated 45% increase in risk of any psychotic outcome in cannabis users compared with those who never used.¹⁴ Specifically, cannabis use by age 15 years correlated with an increased risk of schizophreniform disorder at age 26 years and first-time

cannabis use in an older cohort of subjects (age 18 years) showed less symptoms of psychosis than those 15 years who were first-time cannabis users. The risk of psychosis in high risk groups is undergoing continued research relative to individuals with a genetic predisposition to psychosis.¹⁴

Some researchers have identified a risk genotype - Val/Val as having a higher risk associated with psychosis. The exact mechanism behind the association between genotype and cannabis induced psychosis is not entirely clear but researchers agree that cannabis is an important factor affecting mental health outcomes. Other significant factors include gender and family history of psychosis. Some researchers have identified genotypes in healthy individuals corresponding to substance use and the increased risk of hallucinations, paranoia, and delusions, and they have suggested moderating the use of cannabis and its effect on psychosis and cognition based on genotype and outcomes.¹⁴⁻¹⁶

To understand the interplay of genes and the potential effect of cannabis on the brain, it is important to know the effect that dopamine has on the development of psychosis. The D2 receptor gene (*DRD2*) has been associated with symptoms of psychosis; dopaminergic agonists and stimulants are known to worsen psychosis. On the other hand, dopamine receptor (D2/D3) antagonism is known to help reduce symptoms of psychosis. Substance use, including cannabis, as mentioned previously is linked to reward mechanisms, in which dopamine plays a central role.¹⁴⁻¹⁶ A significant interaction exists between dopamine and cannabis use. Substances that affect the core reward system - dopamine cell activation and dopamine release in the brain - facilitate reward behaviors.¹⁴⁻¹⁶

Dopamine levels in the cortex, striatum, and the mesolimbic pathway are known to increase with the use of cannabis. Gene-environment and the effect of cannabis on the brain interact and may lead to psychosis. More research is needed to fully understand the effect of substance use on the brain neuroreceptors affected by alcohol and drug use, such as cannabis use and its correlation with symptoms of psychosis.¹⁴⁻¹⁶ Current studies are reportedly difficult to replicate, including age differences related to the

assessment of psychotic symptoms and the differences between ethnic groups. Psychosis may not be solely associated with genetic variables but may also be a condition of the type and amount of drug use, mixing of drug types, such as methamphetamine combined with cannabis and alcohol use. However, the studies clearly indicate there is a correlation between drug use with psychosis as compared to subjects who never used.¹⁴⁻¹⁶ Some studies have correlated cannabis use to the onset of schizophrenia and symptoms of psychosis such as hallucinations and paranoia, using the DSM-5 diagnostic criteria.

First time cannabis use and lifetime cannabis use has been found to be more common in males. In individuals who started using cannabis early in life (before age 20), male gender, and whites there was a correlation with symptoms of psychosis using the DSM for diagnostic criteria. Studies indicate that drug-induced psychosis may be genetically linked and gene-environment interactions have a role in psychosis since it modulates dopamine function. There is increased vulnerability in individuals exposed to cannabis use early in life to develop psychosis. Researchers also suggest a link between the effect of environmental stress upon psychotic symptoms.¹⁴⁻¹⁶ The strength of these research findings will depend upon future studies and an ability to replicate study outcomes. Prior researchers have suggested that future studies examine the relationship between age of onset of prodromal symptoms of psychosis, duration of untreated psychosis, age at first presentation of DSM symptoms, genotype testing, and cannabis data collection, with the goal of enhancing clinical knowledge of the effects of substances upon mood and thought. Clinicians should be prepared to education patients on the effect of cannabis on genetically vulnerable individuals.

Emotions and Energy

Depending on the type of drug used, a person taking it may feel euphoric, giddy, dizzy, and accepted by others. The person using substances may feel more energy and be able to stay awake for longer periods when taking a drug such as a stimulant. This is in contrast to the depressed and sad

feelings a person may experience during a depressive episode when struggling with getting out of bed and performing daily activities.^{17,18}

Alcohol use also temporarily makes a person feel happy and content with decreased inhibition, which can help with social activities or with performing tasks that may otherwise be difficult to complete due to fear. The individual with bipolar disorder may drink alcohol to feel less inhibited and to overcome some of the depressing feelings that occur during mood episodes. Patients who experience *mixed episodes* are also at risk of developing problems with substance use. Because mixed episodes cause symptoms of depression and mania at about the same time, the affected person may feel even more confused and may struggle with feelings of hopelessness or guilt.^{17,18}

Episodes of struggling with symptoms of racing thoughts, being extremely distracted and unfocused, and a mixed mood often lead a person to self-medicate with drugs or alcohol in an attempt to calm and to combat some of these symptoms. Ultimately, however, the person finds that the effects of drugs and alcohol are only temporary, and the person is left with many of the same feelings and effects as before.

Mood Disorder and Self-Medicating

Bipolar disorder can cause painful symptoms with emotions that are difficult to tolerate. An affected person may experience highs, such as very elevated moods and feelings of joyfulness and happiness (mania or hypomania), but then later experience lows or crushing depression that diminish a person's energy and strength. A person may feel worse when remembering prior levels of higher motivation, happiness, and energy characteristic of the manic phase and may become perplexed and feel as though they have failed somehow. Turning to drugs or alcohol as a form of self-medication to offset some of the painful feelings of bipolar disorder and the psychic pain felt is not an uncommon behavior.

The pleasant effects of drugs or alcohol provide a numbing effect to some of the pain a person may be experiencing. This process of self-medication may be done to forget, albeit temporarily, some of the difficult feelings and

emotions associated with bipolar disorder that can otherwise be unavoidable. The practice of self-medication is especially dangerous when a person has not been diagnosed with bipolar disorder. The affected person may believe that the highs and lows of felt emotions and behavior are normal and that everyone feels the same way. Individuals with bipolar disorder may struggle with managing their own behavior and feelings and may not understand their behavior changes coinciding with the phases of bipolarity and switches of mood.¹⁹ Instead of seeking treatment through medication and therapy, the patient may instead self-medicate to try to control difficult or painful feelings.

Because bipolar disorder causes changes in the levels of some neurotransmitters in the brain, the affected patient may turn to drugs or alcohol as a method of regulating and normalizing feelings and emotions.¹⁹ The effects are not permanent, and chronic drug or alcohol use ultimately changes how the body excretes and controls neurotransmitters, leading to instability and potentially erratic behavior. When the effects of the drug or the alcohol wear off, the person is left with the same symptoms as before, as well as further problems due to substance use.

Patients with comorbid bipolar disorder and substance use disorder have more mixed manias and rapid cycles, poorer remission of symptoms, higher risk of suicidal thought and attempt, and less treatment adherence.¹⁹ An earlier age of onset of comorbid bipolar and substance use may in and of itself become the cause of pathology and of a poorer, more damaging outcome. Use of alcohol and drugs have been found to increase in patients during manic phases due to elevated mood and disinhibition.

Types of Substance Use and Mood Disorder

Since co-occurring mood and substance use disorders often worsen clinical symptoms, a person may be more likely to self-medicate to improve feelings of wellbeing. Researchers have studied the connection between mood disorders and substance use to determine whether comorbidities have cause-and-effect relationships. The self-medicating theory has been seen as

one type of causative factor that may contribute to substance use when a mood disorder is present. It is interesting to note, however, that self-medication may not completely explain substance use in patients who have bipolar disorder. Stokes, *et al.* (2017) noted that many patients who have bipolar disorder do not change their pattern of alcohol use during a manic or depressive episode and that the patterns of substance use in these patients and people who do not have bipolar disorder are quite similar.²⁰

Further studies have pointed out that self-medication directly impacts a person's risk of developing a substance use disorder when a mood disorder is present. Participants who were diagnosed with mood disorders and who used drugs (either illicit or prescription) or alcohol to self-medicate for affective symptoms had an increased risk of developing a substance use disorder by seven-fold.²¹ Stimulant drug use, such as cocaine and amphetamines, as well as other illicit or prescription drugs, such as opioid medications, place a patient at high risk of addiction because of the qualities of these substances that cause a person to crave them. Although stimulant drugs have been reported to be used less often in comparison to alcohol or cannabis, they can be highly dangerous for the patient who uses them to self-medicate.²¹ Bipolar disorder and substance use increases the risk for suicide, delays recovery from symptoms of bipolar disorder, decreases patient adherence to medication, and causes functional impairment.

Cannabis Use and Bipolar Disorder

Cannabis often provides a calming effect that some patients with bipolar disorder try to achieve by getting high while experiencing mania. Because manic episodes can lead a person to feel out of control, anxious, or irritable, the affected person may enjoy the pleasant and calming feelings obtained from smoking cannabis.²² Some experts would say that smoking cannabis does not lead to a substance use problem, and its availability for purchase, as well as the rising legal availability in varied jurisdictions for recreational purposes, may seem to support this theory. On the other hand, other researchers believe that cannabis can be dangerous and cause a substance use disorder, especially when it is used as a form of self-medication among some patients with a bipolar disorder.

Cannabis is often a precursor drug that is used early on, possibly because it may seem harmless. However, cannabis is a depressant and when used in excessive amounts, it can be harmful. Furthermore, it may serve as a gateway drug to open the door to use of other substances, either when it no longer provides as much relief as a form of self-medication, or when the user wants to experience other kinds of drugs.

Alcohol Use and Bipolar Disorder

Because of its widespread availability and legal use for people over 21 years of age in the U.S., alcohol may also be used regularly to combat uncomfortable feelings associated with bipolar disorder as a source of self-medication. Alcohol use disorder is common in patients who have bipolar disorder, and it is likely that patients who have bipolar disorder are particularly susceptible to developing alcohol use disorder.²¹⁻²³

Alcohol is a central nervous system depressant and initially produces feelings of slight dizziness, happiness, and a sense of calm. For many people, alcohol decreases feelings of inhibition so that they feel that some shortcomings can be overcome, such as being shy or feeling insecure. The effects of alcohol can be felt by having even one drink, although for someone who ingests large amounts of alcohol on a regular basis, the level of tolerance is usually much higher.²¹⁻²³ The person then must drink more to achieve the same effects when this tolerance develops.

Although alcohol use may initially increase activity, the person will feel tired after a period of time. Too much alcohol results in a cognitive dulling and headache, which often develops after an intoxicated person has fallen asleep and later wakes up. A hangover may last for several hours and occurs as the result of the effects of alcohol consumption on the body. The person may have a headache, nausea, sensitivity to light, and dry mouth; some people also experience heart palpitations and anxiety during this time. Further, the affected person often feels psychologically much worse while experiencing a hangover than when intoxicated. The initial physical effects may make a person feel a lack of desire to drink again, but after a period of time the

alcohol consumption generally starts again after the side effect has subsided.

For the person who struggles with alcoholism, regular consumption of alcohol occurs because of cravings for it. The individual may develop a compulsion to use alcohol, and feel a physiological need to have it. There is an inability to control how much of an alcoholic beverage is consumed at one given time.

Among the high rates of patients with bipolar disorder, alcohol ranks as one of the most frequently used substances.²¹⁻²³ It can be dangerous because it is relatively easy to access for many people and does not necessarily have to be regulated when a person drinks at home alone. Also, alcohol is often included in parties or social gatherings and it may be difficult to abstain from drinking when everyone else in the room is not. The social acceptance of alcohol and its availability make recovery from an alcohol use disorder extremely difficult, even for a person who does not already suffer from comorbid mental illness. When the two conditions are combined, the person can struggle with potentially disastrous effects and may have a difficult time going through recovery.

Stimulant Use and Bipolar Disorder

Stimulants, while less commonly used when compared to alcohol or cannabis, may still cause problems for some patients who use them and who simultaneously suffer from bipolar disorder.^{24,25} Normally, stimulants are taken because they increase energy, and help keep a person awake and able to maintain focus and attention. A person struggling with bipolar disorder may take stimulants during the depressive phase of the condition, as use of these types of drugs may help a person to feel more awake and may reduce lethargy.

The depressive phase of bipolar disorder can be terribly difficult to cope with for a patient. Instead of feeling the energy and motivation associated with mania, the person may feel extremely hopeless and sad, and may desperately want to achieve a normal state once again. A patient may turn

to stimulants as an artificial means of boosting energy and avoiding the despair associated with depression.²⁶ Drugs such as cocaine, amphetamines, and crystal meth are all stimulants that will produce euphoria and a high that leads to excess energy and wakefulness, but as with other types of drugs or alcohol, these substances can also be dangerous.

Many people who use stimulants find that they do not achieve the same effects as they once did early in the time of use. While they may be euphoric and happy initially, after a period of time, the pleasant feelings are less and less pronounced. Instead, a person may experience greater feelings of irritability and could feel intense paranoia.²⁷ When a stimulant use disorder develops, the person also tends to have greater bouts of depression after the drug wears off, leaving the person to feel much worse than before.²⁷ By this point, the person may have developed such a craving to the drug that use is aimed at alleviating the physical craving rather than for the pleasurable effects of the drug. Unfortunately, in an attempt to combat negative feelings of depression, stimulant use causes further problems that require the affected person to work harder to overcome the drug use.

Self-medicating to “Help Treatment Along”

While it is not uncommon for patients with bipolar disorder to use drugs or alcohol as a form of self-medication to manage difficult moods and symptoms, the results can be dangerous.^{29,30} Patients may try to self-medicate, even when they already have prescriptions for medications for the treatment of their bipolar symptoms; they may continue to use drugs and alcohol if they believe that their prescription medications are not effective or to “help treatment along”. Alternatively, some patients do not take prescribed medications or do not seek help from a health clinician for the treatment of bipolar symptoms and instead self-medicate with drugs and alcohol on their own.

Because of the frequent connection between a substance use disorder and bipolar disorder, and the fact that it often develops when patients try to self-medicate for their problems, clinicians may have a difficult time managing both conditions and to help patients to stay on track with treatment. It may be difficult to diagnose bipolar disorder in a patient with a co-occurring

substance use disorder if mood symptoms have not been evaluated by a mental health professional; a substance use can cause many similar symptoms and can exacerbate symptoms of bipolar disorder.^{29,30} The difficulties continue and increase when the patient seeks to take charge of matters by self-medicating and, instead, complicates treatment by developing another condition that eventually needs to be medically managed.

Substance-Induced Mood Disorder and Psychosis

As previously stated, a person with bipolar disorder does not necessarily suffer from episodes of mania or depression at a constant pace; instead, a person may more likely have long periods of normal behavior and emotions that are punctuated by manic or depressive episodes. These mood changes and associated symptoms may occur after some form of a trigger — an event or item that sets off an episode — causes the person to develop symptoms of the illness.

Triggers can take many forms and may be related to environmental factors, physical illness, or relational issues. Some examples include lack of sleep, changes in the family, such as with a birth or death of a family member, exciting events, such as a vacation or an anniversary, conflict with others, and increased amounts of daily stress. Drug and alcohol use can also be triggers that cause changes in mood and that lead to manic or depressive episodes.²⁹⁻³³

Some patients use substances as forms of self-medication in order to feel a sense of control over their mental illness or to help regulate their emotions and behavior. However, substance use may be a trigger for further episodes of mania or depression, which can only worsen the situation. For example, a patient may drink alcohol to the point of intoxication when experiencing symptoms of mania because the patient wants to feel calm or wants to self-treat insomnia. The alcohol use, or its effects when symptoms of withdrawal develop, may trigger further episodes of mania, so instead of solving the symptoms of bipolar disorder, the affected person only perpetuates it.

Some prescription medications may also act as mood triggers and require careful monitoring in order to prevent a relapse into a mood episode. With some drugs, discontinuing use typically causes the patient to return to normal for a period of time but symptoms can then return after using some other types of drugs or by returning to substance use again.

Medication-induced Mania

Medication-triggered mania may occur from the use of prescription drugs, illicit drugs or alcohol. Patients who take medications for the treatment of bipolar disorder may experience more episodes of mood dysregulation due to an opposite effect, referred to as *switching*. Switching is the term used when a patient transitions between high (mania) and low (depression) ends of the spectrum of bipolar disorder symptoms.²⁹⁻³³ A patient with a bipolar disorder may switch between depression and hypomania or mania very rapidly.

The risk for switching appears to be greatest during the acute phase of antidepressant treatment, less so during maintenance treatment, and the risk of switching may depend on the specific drug that is used. Switching may be more likely to occur if a patient with bipolar disorder has not yet been diagnosed or if the patient is having a drug reaction. The reaction of a drug that causes a switch in symptoms may perpetuate a diagnosis of bipolar disorder.²⁹⁻³³ Switching may occur with the use of some types of antidepressants, as well as with the use of drugs or alcohol if the patient has a concurrent substance use disorder.

As mentioned above, medication-induced mania may occur when a person takes an antidepressant to treat depressive symptoms the person experiences due to a bipolar disorder. In these cases, the antidepressant is the trigger of an episode of mania as it treats the patient's depression, or when it causes a patient to experience a mood swing in the opposite direction of depression. The evidence that antidepressants may induce mania is mixed.³⁴ Mania associated with antidepressant use has been found in patients with bipolar disorder. However, the research on antidepressants and the risk of mania has also found that the rates of switching associated

with antidepressants was close to the rate of spontaneous switching and close to the rate of switching seen in placebo-treated patients. There is also some evidence that specific antidepressants - tricyclic and tetracyclic antidepressants, serotonin norepinephrine reuptake inhibitors (SNRIs) - are more likely to cause switching but there is no conclusive evidence that any particular drug has a higher risk of causing switching.³⁴

Antidepressants are a controversial treatment for patients who have bipolar disorder even though they are often prescribed. When a patient is prescribed antidepressants for treatment of bipolar disorder, the patient must be monitored carefully to ensure that symptoms of mania do not occur as a result of the prescribed drug.³⁵ Medication-induced depression can also occur in people with bipolar disorder. The most common substances that have been shown to lead to triggered episodes of depression include corticosteroids, digoxin, interferon-alpha, and some types of anticonvulsants.³⁶ Long-term use and higher doses of steroids are more likely to cause depression. Anticonvulsant use may not only trigger depression but has been shown to increase the risk of suicidality among some patients.

Cannabis and Mania

Cannabis is the most commonly used federally classified illicit drug among persons diagnosed with bipolar disorder.³⁷ It has often been shown to act as a trigger for mood changes and its use is associated with decreased adherence to medication regimens and increased severity of symptoms. The substance found in cannabis that causes its psychedelic effects is tetrahydrocannabinol, referred to as THC; high levels of use of this substance may increase the risk of psychosis, and its use can increase the severity of mania symptoms in bipolar patients.³⁸

Alcohol and Other Substance-induced Mania

Alcohol also serves as a mood trigger for some symptoms associated with mania. An alcohol use disorder and addiction have been shown to increase a bipolar patient's difficulties with impulsivity and to increase risk-taking

behaviors that are often seen as part of manic behavior. Patients with bipolar disorder who use cocaine may also have tremendous difficulty with triggering symptoms because of this type of substance use.³⁹⁻⁴²

Other medications and substances that have been known to trigger manic behavior and moods include stimulants, such as cocaine, amphetamines, and ecstasy, corticosteroids, thyroid replacement medications, cold medications that contain pseudoephedrine, and caffeine. As mentioned, antidepressants are some of the most well-known drugs whose associated effects can cause mania.³⁹⁻⁴²

With some substances, discontinuing use typically causes a patient to return to normal for a period of time but symptoms may return if the drug is used again. Symptoms may also be caused by another type of drug that a person may take as an alternative.

Identifying a Substance-Induced Mood Disorder

A comprehensive physical and mental exam is important for identifying whether a patient is suffering from a substance-triggered mood disorder. A physical exam can identify whether a patient is suffering from physical complaints from medical conditions that are unrelated to mental illness and bipolar disorder or if they are side effects of medications. For example, a patient may struggle with fatigue as a side effect of a medication, but this does not necessarily result in a medication-triggered episode of depression. Additionally, both the physical and mental exams will help the clinician to identify the onset of symptoms of either mania or depression in relation to starting or stopping certain substances. The clinician can then determine if the mood swings and triggered behaviors ended after discontinuing the substance. This requires careful monitoring of the patient.³⁹⁻⁴²

In most cases, discontinuing a medication that triggers bipolar disorder episodes is enough to stop the changes from occurring. There are times, however, when a patient needs to be on a medication and cannot discontinue it, even though manic or depressive symptoms have developed from its use. In these cases, the clinician may need to change the type of medication the patient takes that may still provide the therapeutic effects

without triggering the episodes. The clinician may also alter the drug dosages and times of administration to lessen the effects.³⁹⁻⁴² Finally, there are some situations in which the patient may need to be monitored closely and treated for episodes of mania and depression separately because the triggering substance cannot be changed.

Case Study: Episode of Cannabis-induced Bipolar Disorder

The following case study was obtained from a PubMed search and describes a case of a 27-year-old man with a history of cannabis use disorder and bipolar I disorder. The authors reported that while the patient was treated with lithium, he was sent to emergency department by his community psychiatrist in a decompensated manic episode.

The patient's bipolar disorder had been reportedly well controlled after a manic episode 7 years prior. Lithium had been slowly tapered from 900 to 600 mg daily to reduce the potential for side effects. He was evaluated a few months later during an office visit with symptoms of decreased sleep, increased activity and talkativeness, and aggression, and was admitted to hospital for a 72 h assessment. The patient had coinciding daily vomiting and fluctuating periumbilical abdominal pain over the preceding 3 weeks. Fever, hematemesis, bilious emesis, hematochezia, melena or abnormal bowel movements were not reported, however diarrhea was problematic the week prior to admission. The patient reported nausea for 4 weeks before the vomiting started and this was a new occurrence. He reported use of "every over-the-counter antiemetic medication", especially dimenhydrinate, but the nausea persisted. The daily routine of every 2–3 hour hot baths and showers was reported to be the only intervention that allowed symptomatic relief.

It was discovered that the patient's cannabis use started at 13 years of age, which turned into chronic, daily use that increased in frequency and amount of cannabis use in the weeks leading up to admission. The patient denied continuing consumption of cannabis, despite significant cravings, as well as other substance use, including alcohol.

The authors stated that the patient received a physical assessment, and his abdomen was tender on palpation of the peri-umbilicus. A complete blood count (CBC) was significant for mild neutrophilia and the metabolic panel was unremarkable. The patient's vital signs were within normal limits. The lithium level was subtherapeutic at <0.20 mmol/L (therapeutic range of 0.50–1.50 mmol/L). The patient and his wife endorsed medication compliance, however, his community psychiatrist reported the patient the patient reported stopping lithium a weeks prior because he believed it was causing the vomiting.

Eventually, the patient was discharged after 3 days, as there was no reason to hold him in the hospital. He returned 3 days later reporting worsening psychiatric symptoms. Laboratory testing revealed a low serum amylase at 15 mmol/L (reference range 20–110 mmol/L), and lipase was unremarkable. Liver enzymes were mildly elevated and the patient's abdomen continued to be tender; an abdominal X-ray was done, which was normal. A urine drug screen was positive for cannabinoids.

The patient was assessed as being manic, having insomnia and psychotic symptoms. After transfer to the acute care psychiatric unit in the hospital, three subsequent urine cannabinoid screens were done and returned positive. Cyclic vomiting syndrome (CVS), a syndrome characterised by idiopathic cyclic episodes of vomiting, and cannabinoid hyperemesis were included in the differential diagnosis. The gastrointestinal symptoms were not attributed to lithium dosing because resolution of the patient's symptoms in hospital occurred despite lithium dose increase. Because of a long history of cannabis use, vomiting that resolved with cannabis cessation, abdominal pain and symptomatic relief with extended, compulsive bathing, a diagnosis of cannabis hyperemesis was made.

While in hospital the patient was trialed on titrations of clonazepam (1–4 mg daily), quetiapine (50–700 mg nightly), methotrimeprazine (5–20 mg nightly) and zopiclone (7.5–22.5 mg nightly). Lithium increased to 900 mg and then titrated to 1950 mg to reach therapeutic serum levels for acute mania. A therapeutic lithium level of 1.01 was reached.

The authors reported that the “patient’s insight into his illness was initially poor; he often stated that he had come into hospital for his gastrointestinal concerns. He intermittently experienced cramping suprapubic pain that consistently resolved with lorazepam and psychotherapeutic intervention. He also experienced mild gastric reflux and was treated with pantoprazole. He vomited twice while in hospital. He initially had mild constipation, which resolved with daily sennosides. After 25 days of inpatient care, his manic symptoms subsided and his gastrointestinal symptoms largely resolved.” Eventually, the patient discharged home and his community psychiatrist took over care.

Discharge recommendations included cannabis abstinence, however the patient disagreed and stated that cannabis helped his gastrointestinal symptoms and identified with his alcohol consumption as being the cause of gastrointestinal symptoms. The patient also stated that repetitive bathing was a cleanse performed as an expression of his spirituality. Personal and family reasons caused him to want to reduce cannabis intake. A chemical dependency specialist was consulted. The patient eventually agreed to attend an addictions treatment group to work towards decreasing cannabis use. Three weeks following discharge he reportedly continued to abstain.

Discussion

The authors stated that the pathophysiology of cannabis hyperemesis remains uncertain. They pointed out that “cannabinoids act on the CB1 and CB2 receptors in the central and enteric nervous systems”. Further, the authors indicated that cannabinoid receptors involved in the hypothalamic–pituitary–adrenal axis respond abnormally due to long-term toxicity from chronic use, and this toxicity may increase corticotropin-releasing hormone levels, which has been proposed as a precipitating factor in a related condition called cyclical vomiting syndrome (CVS). They also raised another hypothesis that implicates enteric CB1 receptor activation causing decreased gastric motility, and vomiting. Central CB1 receptors involved in thermoregulation are thought to account for the symptomatic improvement with hot water bathing in either scenario. Compulsive bathing is not typically

found in other hyperemetic syndromes and has been previously described as pathognomonic of cannabis hyperemesis.

The authors raised the fact that lifetime prevalence of cannabis use among people with bipolar I disorder has been estimated as 30–64%, and suggested that cannabis hyperemesis may impact prognosis in some people with a bipolar disorder. Periodic vomiting may lead to reduced drug absorption of psychotropic medication. Patients may continue to use cannabis, despite recurrences of cannabis hyperemesis, therefore the management of drug use becomes a crucial consideration to prevent mood destabilisation. The authors suggested that in this case the increased use of cannabis and onset of vomiting resulted in the sharp decline of lithium level leading to psychiatric decompensation. The likelihood of lithium causing the patient's gastrointestinal symptoms was low, as the gut symptoms greatly improved despite lithium dose increase.

Cannabis hyperemesis may significantly increase the risk of manic episodes in patients with bipolar I disorder, and the authors suggested that further investigation is needed in order to better manage patient outcomes.

Learning points from this case for clinicians to observe included:

"1) Cannabinoid hyperemesis syndrome (CH) is an uncommon, but important, diagnosis in patients with unexplained vomiting. 2) CH is characterised by cyclic vomiting, chronic cannabis use, abdominal pain, symptomatic relief with hot water bathing and resolution with cessation of use. 3) CH may result in mood destabilisation in patients who have bipolar I disorder, by reducing serum levels of medications." Management of a substance use disorder is an important consideration in patients who have concurrent bipolar I disorder and cannabis hyperemesis.

Summary

Bipolar disorder and substance use disorders are often seen together as comorbid conditions. This relationship may occur because bipolar disorder and substance use disorders share common neurobiological pathways and current studies suggest a genetic correlation exists. They also are used

together to evoke certain feeling or emotions. Individuals may turn to drugs or alcohol as a form of self-medication to offset some of the painful feelings of bipolar disorder and the psychic pain felt.

The use of prescription and illicit drugs may act as triggers for mood changes. Whether a patient is prescribed medications for the treatment of bipolar disorder symptoms or uses drugs or alcohol and those substances trigger mood changes, drug use can greatly impact the patient with a bipolar disorder. The challenges of finding treatment methods that do not trigger mood changes can be difficult for some clinicians who care for these patients. Furthermore, it is challenging to help a patient with bipolar disorder undergo treatment when the patient is using substances that act as mood triggers. All potential factors must be accounted for when considering the best course of treatment for patients with a comorbid bipolar disorder and substance use disorder.

Self-Assessment of Knowledge Post Test:

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- 1. A clinician who is evaluating a patient's mental health may use the term "dual diagnosis" to describe a person who**
 - a. exhibits "drug dependence" and "drug addiction."
 - b. has a mental health disorder and a substance use disorder.
 - c. exhibits high and low bipolar symptoms.
 - d. is diagnosed with cyclothymia and bipolar type I or II.

- 2. Switching is the term used to describe a patient with bipolar disorder who**
 - a. transitions between "drug dependence" and "drug addiction."
 - b. changes medications to treat a disorder.
 - c. discontinues a medication that triggers a manic episode.
 - d. transitions between high and low ends of the spectrum of bipolar symptoms.

- 3. The practice of self-medication is especially dangerous for a person who has not been diagnosed with bipolar disorder because**
 - a. this person may believe his or her emotional highs and lows are normal.
 - b. in these cases, substance use disorder always precedes bipolar disorder.
 - c. this "substance abuse" is more serious than "substance dependence."
 - d. a maladaptive pattern is unique to people who self-medicate.

- 4. Which of the following may be a causative factor that contributes to substance use when a mood disorder such as bipolar disorder is present?**
 - a. The maladaptive pattern
 - b. The self-medicating theory
 - c. Switching
 - d. The presence of cyclothymia

5. True or False: It is vitally important that a clinician determines which condition came first, the patient's bipolar disorder or substance use disorder, before treating a comorbid patient.

- a. True
- b. False

6. Stimulant drug usage, such as cocaine and amphetamines, place a patient at high risk for substance use disorder because

- a. "substance addiction" is more serious than "substance dependence."
- b. they are used more often when alcohol or marijuana.
- c. they can be highly dangerous when using to self-medicate.
- d. substance addiction always precedes bipolar disorder.

7. It may be difficult to diagnose bipolar disorder in a patient with a co-occurring substance use disorder

- a. if the patient has not been evaluated for mood disorder symptom.
- b. as substance use can cause many symptoms that are similar to bipolar disorder.
- c. as substance use can exacerbate symptoms of bipolar disorder.
- d. All of the above

8. True or False: Smoking marijuana does not lead to a substance use disorder.

- a. True
- b. False

9. The risk for switching appears to be greatest during

- a. evaluation for mood disorder symptom.
- b. maintenance treatment for depression.
- c. the acute phase of antidepressant treatment.
- d. the phase when a patient does not have symptoms.

10. Antidepressants are a controversial treatment for patients who have bipolar disorder because

- a. the evidence is mixed on whether antidepressants induce mania.
- b. antidepressants definitively induce mania.
- c. antidepressants are chemically addictive.

- d. antidepressants work rapidly, causing abrupt changes in mood.
- 11. When a patient is prescribed antidepressants for treatment of bipolar disorder, there is a risk of “switching,” so the patient must be monitored carefully for symptoms of _____ as a consequence of switching.**
- a. depression
 - b. addiction
 - c. mania
 - d. adherence
- 12. Long-term use and higher doses of _____ are more likely to cause depression.**
- a. tricyclic antidepressants
 - b. steroids
 - c. SNRIs
 - d. anticonvulsants
- 13. _____ is the most commonly used drug among persons diagnosed with bipolar disorder.**
- a. Amphetamines
 - b. Ecstasy
 - c. Cocaine
 - d. Cannabis
- 14. A patient who intakes high levels of tetrahydrocannabinol (“THC”) (the substance found in cannabis that causes its psychedelic effects) may**
- a. increase the risk of psychosis
 - b. cause mania symptoms in bipolar patients to be more severe.
 - c. trigger mood changes in patients with bipolar disorder.
 - d. All of the above
- 15. In cases where a patient needs a medication to treat depression but the medication triggers manic bipolar disorder episodes,**
- a. the clinician may need to change the type of drug used.
 - b. the only option is to discontinue use of the trigger medication.
 - c. the patient must decide whether to treat the manic or depressive episodes.

- d. the best option for the patient is self-medication because the patient is in the best position to identify the type of episode.

CORRECT ANSWERS:

1. A clinician who is evaluating a patient's mental health may use the term "dual diagnosis" to describe a person who

- b. has a mental health disorder and a substance use disorder.

"The term dual diagnosis is used to describe a person who has been diagnosed with a mental health disorder and a substance use disorder."

2. Switching is the term used to describe a patient with bipolar disorder who

- d. transitions between high and low ends of the spectrum of bipolar symptoms.

"Switching is the term used when a patient transitions between high (mania) and low (depression) ends of the spectrum of bipolar disorder symptoms. A patient with a bipolar disorder may switch between depression and hypomania or mania very rapidly. The risk for switching appears to be greatest during the acute phase of antidepressant treatment, less so during maintenance treatment, and the risk of switching may depend on the specific drug that is used."

3. The practice of self-medication is especially dangerous for a person who has not been diagnosed with bipolar disorder because

- a. this person may believe his or her emotional highs and lows are normal.

"The practice of self-medication is especially dangerous when a person has not been diagnosed with bipolar disorder. The affected person may believe that the highs and lows of felt emotions and behavior are normal and that everyone feels the same way."

4. Which of the following may be a causative factor that contributes to substance use when a mood disorder such as bipolar disorder is present?

- b. The self-medicating theory

"The self-medicating theory has been seen as one type of causative factor that may contribute to substance use when a mood disorder such as bipolar disorder is present."

5. True or False: It is vitally important that a clinician determines which condition came first, the patient's bipolar disorder or substance use disorder, before treating a comorbid patient.

b. False

"Although bipolar disorder and substance use disorders are often seen together as comorbid conditions, one condition does not necessarily precede or cause the other. In fact, while at times it may be obvious that one condition led to the development of the other, such as a patient with bipolar disorder eventually developing a substance use disorder because of mood changes associated with the first illness, the clinician does not necessarily need to spend significant time trying to determine which condition came first."

6. Stimulant drug usage, such as cocaine and amphetamines, place a patient at high risk for substance use disorder because

c. they can be highly dangerous when using to self-medicate.

"Stimulant drug use, such as cocaine and amphetamines, as well as other illicit or prescription drugs, such as opioid medications, place a patient at high risk of addiction because of the qualities of these substances that cause a person to crave them. Although stimulant drugs have been reported to be used less often in comparison to alcohol or cannabis, they can be highly dangerous for the patient who uses them to self-medicate."

7. It may be difficult to diagnose bipolar disorder in a patient with a co-occurring substance use disorder

- a. if the patient has not been evaluated for mood disorder symptom.
- b. as substance use can cause many symptoms that are similar to bipolar disorder.
- c. as substance use can exacerbate symptoms of bipolar disorder.
- d. All of the above [correct answer]

"It may be difficult to diagnose bipolar disorder in a patient with a co-occurring substance use disorder if he or she has not been seen for mood disorder symptoms, as substance use can cause many similar symptoms and can exacerbate symptoms of bipolar disorder."

8. True or False: Smoking marijuana does not lead to a substance use disorder.

b. False

"Some experts would say that smoking cannabis does not lead to a substance use problem, and its availability for purchase, as well as the rising legal availability in varied jurisdictions for recreational purposes, may seem to support this theory."

9. The risk for switching appears to be greatest during

c. the acute phase of antidepressant treatment.

"The risk for switching appears to be greatest during the acute phase of antidepressant treatment, less so during maintenance treatment, and the risk of switching may depend on the specific drug that is used."

10. Antidepressants are a controversial treatment for patients who have bipolar disorder because

a. the evidence is mixed on whether antidepressants induce mania.

"The evidence that antidepressants may induce mania is mixed... the research on antidepressants and the risk of mania has also found that the rates of switching associated with antidepressants was close to the rate of spontaneous switching and close to the rate of switching seen in placebo-treated patients."

11. When a patient is prescribed antidepressants for treatment of bipolar disorder, there is a risk of "switching," so the patient must be monitored carefully for symptoms of _____ as a consequence of switching.

c. mania

"When a patient is prescribed antidepressants for treatment of bipolar disorder, the patient must be monitored carefully to ensure that symptoms of mania do not occur as a result of the prescribed drug."

12. Long-term use and higher doses of _____ are more likely to cause depression.

b. steroids

"The most common substances that have been shown to lead to triggered episodes of depression include corticosteroids, digoxin, interferon-alpha, and some types of anticonvulsants. Long-term use and higher doses of steroids are more likely to cause depression."

13. _____ is the most commonly used drug among persons diagnosed with bipolar disorder.

d. Cannabis

"The highest prevalence of substance use in persons with bipolar disorder was identified as alcohol use at 42%. Comorbid bipolar disorder and cannabis use was 20% and other illicit drug use was 17%."

14. A patient who intakes high levels of tetrahydrocannabinol ("THC") (the substance found in cannabis that causes its psychedelic effects) may

- a. increase the risk of psychosis
- b. cause mania symptoms in bipolar patients to be more severe.
- c. trigger mood changes in patients with bipolar disorder.
- d. All of the above [correct answer]

"Cannabis ... has often been shown to act as a trigger for mood changes.... The substance found in cannabis that causes its psychedelic effects is tetrahydrocannabinol, referred to as THC; high levels of use of this substance may increase the risk of psychosis, and its use can increase the severity of mania symptoms in bipolar patients."

15. In cases where a patient needs a medication to treat depression but the medication triggers manic bipolar disorder episodes,

- a. the clinician may need to change the type of drug used.

"In most cases, discontinuing a medication that triggers bipolar disorder episodes is enough to stop the changes from occurring. There are times,

however, when a patient needs to be on a medication and cannot discontinue it, even though manic or depressive symptoms have developed from its use... the clinician may need to change the type of medication the patient takes...

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