

Psychosis and catatonia after dancing with a dangerous partner

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How would you handle this case?

Answer the **challenge questions** throughout this article

Mr. D, age 23, presents with new-onset psychosis with auditory and visual hallucinations and catatonia 10 days after taking 2C-B, a designer drug. How would you treat him?

CASE Rigid, frightened, and mute

Mr. D, age 23, presents for evaluation immediately after discharge from another hospital, where he had been treated for altered mental status.

Ten days earlier, Mr. D's friends obtained 2C-B (2,5-dimethoxy-4-bromophenethylamine), from the "Darknet," an underground niche of the Internet. He ingested 20 mg of 2C-B in powder form. Although his friends recovered from a "safe trip," Mr. D decompensated rapidly over the next few days with persistent psychosis, experiencing both auditory and visual hallucinations. He is "acting strange" at work, and trying to find "hidden codes" in data. Mr. D also has persistent thought disorganization. He speaks of "connections" between people and things, and says that he is an alien in a spaceship. His friends and family report that he is talking rapidly and is sleeping only 2 or 3 hours each night. Mr. D abruptly quit his job as an analyst a few days after taking the drug.

Mr. D is a single, Ivy League-educated man and is described as hardworking and analytical. His family denies any recent mood changes or life stressors. They report that 1 month ago, Mr. D began smoking marijuana daily. He has no significant medical or psychiatric history, and no family history of psychiatric disorders.

What is your most likely diagnosis for Mr. D?

- a) delirium due to a general medical condition

- b) substance-induced psychotic disorder
- c) catatonia due to a general medical condition
- d) schizophrenia
- e) bipolar I disorder, currently manic, with psychosis

The authors' observations

Ring-substituted phenethylamines, commonly known as 2Cs, are designer drugs that are emerging as new substances of abuse.¹ 2C-B belongs to the phenethylamine subclass of monoamine alkaloids that includes more familiar drugs such as amphetamines, methamphetamines, and 3,4-methylenedioxy-methamphetamine (MDMA).² It was first synthesized in 1974 by Alexander Shulgin, later described in his book *Phenethylamines I Have Known and Loved: A Chemical Love Story*, and its hallucinogenic activity is reported to be similar to LSD, mescaline, and psilocybin.³ The literature is scant on the acute effects

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of 2C intoxication or long-term sequelae of 2C ingestion.¹ Most available information regarding the pharmacology of 2C-B comes from users who have reported their drug experiences on blogs, Web sites and forums, and in the media.⁴

2C-B usually is taken orally in powder or tablet form, in a dose of 10 to 50 mg.⁴ After an onset period of 20 to 90 minutes, the drug's effect reaches maximum effect in 15 to 30 minutes, then plateaus for 2 to 7 hours, and comes down within 1 to 2 hours.⁴ 2C-B is known to be orally active, and its hallucinogenic effects are mediated by its actions as a partial serotonin 5HT-2A and 5HT-2C receptor agonist.⁵ Entactogenic-stimulating effects have been reported at low doses (4 to 10 mg), whereas visual hallucinations with intense colors and object distortion have been reported at moderate doses (10 to 20 mg).⁴

2C-B, which users often take at parties or raves, appeared on the drug market in the mid 1980s and early 1990s under the names Nexus, Erox, Performax, Toonies, Bromo, Spectrum, and Venus and marketed as a replacement for MDMA after it became a Schedule I drug in the United States.^{4,6} Some users consume 2C-B in combination with other illicit drugs, including MDMA (called a "party pack") or LSD (referred to as a "banana split").⁶

According to the U.S. Drug Enforcement Agency, law enforcement authorities first seized 2C-B laboratories in California in 1986 and Arizona in 1992.⁶ Distribution of the drug has been sporadic since it became Schedule I in 1995, and it has been seized from several states, including Virginia, Nevada, Maine, Illinois, Missouri, South Dakota, and Kansas.⁶

Table 1

Changes in Mr. D's Bush-Francis Catatonia Rating Scale (BFCRS) scores

BFCRS score on presentation	BFCRS score after IV lorazepam, 2 mg
Excitement = 0	Excitement = 0
Immobility/stupor = 3	Immobility/stupor = 0
Mutism = 3	Mutism = 0
Staring = 0	Staring = 0
Posturing = 3	Posturing = 1
Grimacing = 0	Grimacing = 0
Echopraxia = 0	Echopraxia = 2
Stereotypy = 0	Stereotypy = 0
Mannerisms = 0	Mannerisms = 0
Verbigeration = 0	Verbigeration = 0
Rigidity = 2	Rigidity = 1
Negativism = 0	Negativism = 0
Waxy flexibility = 0	Waxy flexibility = 0
Withdrawal = 2	Withdrawal = 0
Impulsivity = 0	Impulsivity = 0
Automatic obedience = 0	Automatic obedience = 2
Mitgehen = 0	Mitgehen = 0
Gegenhalten = 3	Gegenhalten = 3
Ambitendency = 0	Ambitendency = 0
Grasp reflex = 0	Grasp reflex = 0
Perseveration = 0	Perseveration = 0
Combativeness = 0	Combativeness = 0
Autonomic abnormality = 1	Autonomic abnormality = 0
Total = 17	Total = 9

EXAMINATION Passive and mute

On examination, Mr. D is lying in bed with eyes closed and extremities extended in an odd, rigid posture. He is resistant to attempts at passive movement, is nonresponsive to verbal commands, and is mute. A review of vital signs shows tachycardia, 110 beats per minute, but the physical exam is otherwise unremarkable. His Bush-Francis Catatonia Rating Scale (BFCRS) score is 17, indicating a diagnosis of catatonia. Mini-Mental Status Examination cannot be completed because Mr. D is unable to participate.

Laboratory studies reveal an elevated creatinine kinase (CK) level of 356 U/L. Results of

Clinical Point

2C-B's hallucinogenic activity is reported to be similar to LSD, mescaline, and psilocybin



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Clinical Point

The literature is scant on the acute effects of 2C intoxication or long-term sequelae of 2C ingestion

Table 2

Medical workup of first-episode psychosis

Common initial workup	Additional tests based on clinical picture
Broad screening and medical baseline	Brain MRI (preferred over CT)
Chemistry panel	EEG
Complete blood count	Hormone levels
Liver function tests	Heavy metal screen
Pregnancy test	Hepatitis C
Urinalysis	Karyotype
Urine drug screen	Lumbar puncture
Specific treatable disorders	Rheumatologic workup, including lupus and paraneoplastic disorders
Ceruloplasmin level	
HIV	
Syphilis (VDRL/RPR)	
Thyroid-stimulating hormone	
Vitamin B ₁₂	

RPR: rapid plasma regain; VDRL: Venereal Disease Research Laboratory test
Source: Reference 7

a complete blood count, comprehensive metabolic panel, urinalysis, and thyroid-stimulating hormone are normal. Blood alcohol level is <10 mg/dL. Acetaminophen and salicylate levels are normal (<5 mg/dL). Records from his recent hospitalization reveal normal head CT, chest radiography, EEG, and urinalysis, and a negative urine drug screen.

What is the next step in managing Mr. D's catatonic symptoms?

- IV normal saline
- IV lorazepam
- emergent electroconvulsive therapy (ECT)
- IM haloperidol
- IM olanzapine

TREATMENT Saline and psychotropics

While in the emergency room, Mr. D receives 2 L of IV saline. His CK level falls to 137 U/L. A challenge with IV lorazepam, 2 mg, also is performed. Mr. D becomes talkative and follows commands with fluid movements, but his disorganized, delusional thoughts persist. BFCRS score has improved to 9 (*Table 1, page 59*). He is admitted to the psychiatric unit and started on

oral lorazepam, 2 mg, 3 times daily, for catatonia, and olanzapine, 10 mg/d, for psychosis.

The differential diagnosis for Mr. D's psychosis includes substance-induced psychotic disorder, schizophrenia, bipolar disorder, and psychosis with another organic cause (*Table 2*).⁷ Further medical workup is completed, including a urine drug screen, testing for HIV, hepatitis B, syphilis, lead and heavy metals, ceruloplasmin, vitamin B₁₂, folate, antinuclear antibody, sedimentation rate, and brain MRI. Cannabinoids are detected in his urine drug screen. Another urine sample is sent to an outside lab to test for several synthetic drugs, including MDMA, 3,4-methylenedioxy-N-ethyl-amphetamine, 2C-B, 2C-C, 2C-I, and 2C-P, results of which also are negative.

By the second day of hospitalization, Mr. D appears less disorganized but continues to complain of "scrambled thoughts" and appears guarded. Despite initial response to IV lorazepam and its continuation in oral form, over the next day Mr. D appears more psychomotor-slowed, with motor stiffness. His score on the BFCRS increases, with significant posturing; vital signs remain stable, however.

Table 3

Common causes of catatonia

Psychiatric	Bipolar disorder Major depressive disorder Schizophrenia
CNS injury or disorder	Anoxia Neoplasm Seizure disorder Stroke, especially when the anterior cerebral circulation is involved Trauma
Substance use and medication	Antipsychotic medications Corticosteroids Disulfiram Substances of abuse, especially MDMA and PCP Withdrawal, especially sedative-hypnotics
Endocrine	Addison's disease Cushing's disease Hyperthyroidism
Infectious	Bacterial sepsis Encephalitis (acute or post-infectious) HIV encephalopathy Malaria Neurosyphilis Viral hepatitis
Other	Systemic lupus erythematosus Uremia Vitamin deficiency

MDMA: 3,4-methylenedioxy-methamphetamine; PCP: phencyclidine

Source: Reference 8

Clinical Point

It is thought that catatonia is associated with decreased GABA and dopamine D2 receptor activity, and increased NMDA receptor activity

What is your next step in managing his catatonic symptoms?

- increase olanzapine
- decrease olanzapine
- decrease lorazepam
- emergent ECT
- switch to haloperidol

The authors' observations

Although catatonia can be associated with a mood or psychotic disorder, it also can be induced by a medication or general medical condition (Table 3).⁸ It is thought that catatonia is associated with decreased γ -aminobutyric acid (GABA) and dopamine D2 receptor activity, and increased *N*-methyl-D-aspartate (NMDA) receptor activity.⁹ Antipsychotics could worsen catatonia through D2 blockade. Benzodiazepines, however, improve cata-

tonia by increasing GABA and decreasing NMDA receptor activity. In this case, Mr. D was naïve to antipsychotics and seemed to be sensitive to them, as evidenced by his worsening symptoms.

Which condition should be considered in the differential diagnosis?

- parkinsonian-hyperpyrexia syndrome
- neuroleptic malignant syndrome (NMS)
- stiff person syndrome
- serotonin syndrome
- CNS infection

The authors' observations

NMS, catatonia, and parkinsonian-hyperpyrexia syndrome are all related to diminished action of dopamine at the D2 receptor. Although the mechanism of catatonia is not completely understood, NMS

Clinical Point

Because of the similarity in symptoms and proposed mechanisms, some hypothesize that NMS is a drug-induced malignant catatonia

is thought to be caused by blockade at the D2 receptors by antipsychotics, whereas parkinsonian-hyperpyrexia syndrome is related to withdrawal of dopamine agonists. Because of the similarity in symptoms and proposed mechanisms, some experts hypothesize that NMS is a drug-induced malignant catatonia.^{10,11} Interestingly, NMS and catatonia respond to withdrawal of antipsychotics, and addition of benzodiazepines and ECT.

Mr. D showed posturing and other behavioral abnormalities, which are less common in NMS. Furthermore, although he had episodes of mild tachycardia, autonomic dysregulation—a hallmark of NMS—was not found. Given the common shared deficiency of activity at the D2 receptor in both NMS and catatonia, antipsychotics could cause or worsen either condition.

TREATMENT ECT

Mr. D's olanzapine dosage is decreased to 2.5 mg/d. His catatonic symptoms improve with each dosage of oral lorazepam; however, effects seem to lessen and last for shorter periods over the following day. Additionally, Mr. D again becomes more disorganized, stiff, and unable to feed or bathe himself, and develops episodes of mild tachycardia.

Given Mr. D's partial and poorly sustained response to lorazepam, a trial of ECT is pursued. On the third day of hospitalization, he receives ECT with bi-frontal lead placement at 25% energy. Concurrently, olanzapine is discontinued because of worsening muscle stiffness and concern about neuroleptic sensitivity. His BFCRS score after ECT is 2, and he is noted to be more interactive on the inpatient unit. He continues to receive ECT 3 times a week, with notable improvement, but ongoing psychotic symptoms and catatonic symptoms partially reemerge between ECT treatments. Lead placement is changed to bi-temporal by the third treatment, and the energy setting is increased from 25% to 50%, and to 75% by the sixth treatment. An additional nighttime dose

of oral lorazepam, 2 mg, is added after the sixth treatment, in an attempt to reduce "wearing off" by morning.

After the seventh treatment, Mr. D is able to maintain logical conversation without re-emergence of catatonic symptoms over 2 days, signifying a turning point in the treatment course. The ECT energy setting is decreased to 50% to minimize potential memory deficits. His insight into his illness and treatment dramatically improve over the next few days. ECT is discontinued after the tenth treatment and Mr. D is discharged home to the care of his family.

The authors' observations

Randomized clinical trials studying the effectiveness of ECT for catatonia are limited. Much of what we know about ECT comes from case reports that describe excellent outcomes for a variety of treatment-resistant illnesses, including catatonia in mood disorders, schizophrenia, autism, and other organic brain disease.¹²

Although benzodiazepines often are the first-line treatment for catatonia caused by any underlying illness, one study showed only 1 of 41 patients achieved remission with benzodiazepines, compared with 100% of those treated with ECT¹³; another study supported these results with 8 of 9 lorazepam non-responders responding to ECT.¹⁴ There are few case reports of substance-induced catatonia in the absence of other chronic mental illness, although none report use of ECT. However, a study showed no significant difference in the effectiveness of ECT for catatonia caused by an affective disorder or schizophrenia.¹⁵

Mr. D's case exemplifies complete remission of catatonia induced by a psychoactive substance.

OUTCOME Steady improvement

Mr. D is followed in the outpatient clinic for 1 month after discharge; lorazepam is tapered successfully. During this time frame, psychotic

and catatonic symptoms do not re-emerge. He reports some initial working memory deficits that improve steadily. There is no evidence of any significant psychiatric signs or symptoms, including neurovegetative symptoms of depression, mania or hypomania, perceptual disturbances, or disorganized thoughts or behaviors. He remains abstinent from alcohol, tobacco, and all psychoactive substances.

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Related Resources

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Drug Brand Names

Haloperidol • Haldol	Olanzapine • Zyprexa
Lorazepam • Ativan	

Clinical Point

A study showed no significant difference in the effectiveness of ECT for catatonia that is caused by an affective disorder or schizophrenia

Bottom Line

Persistent psychosis and catatonia after the use of newer designer drugs such as 2C-B are rare, but these drugs carry serious potential complications that clinicians should be aware of. Benzodiazepines and electroconvulsive therapy have been proved effective for catatonia that is related to a number of psychiatric illnesses, often resulting in good outcomes. However, current evidence on their use is limited, particularly regarding treatment of substance-induced psychosis and catatonia.