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## Pseudodelirium: Psychiatric conditions to consider on the differential for delirium

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### Abstract

**Objective:** The phenotypes of several psychiatric conditions can very closely resemble delirium: we describe such presentations as pseudodelirium. However, because the clinical management of these conditions differs markedly from that of delirium, prompt differentiation is essential. Our objective is to provide an educational review to assist clinicians in identifying and managing psychiatric conditions that may be especially challenging to differentiate from delirium.

**Method:** Based on clinical experience, we identified four psychiatric conditions as being among the most difficult to differentiate from delirium—disorganized psychosis, Ganser syndrome, delirious mania, and catatonia. We provide an overview of each condition, describe its clinical features, differentiate its phenotype from delirium, and review clinical management.

**Results:** The thought and behavioral disorganization in disorganized psychosis can be mistaken for the clouded sensorium and behavioral dysregulation encountered in delirium. The fluctuating alertness and apparent confusion in Ganser syndrome resemble delirium's altered arousal and cognitive features. As its name suggests, delirious mania presents as a mixture of hyperactive delirium and mania; additional features may include psychosis, autonomic activation, and catatonia. Both delirium and catatonia have hypokinetic and hyperkinetic variants, and the two syndromes can also co-occur.

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**Conclusions:** The clinical presentations of several psychiatric conditions can blend with the phenotype of delirium, at times even co-occurring with it. Detailed evaluation is often required to differentiate such instances of pseudodelirium from delirium proper.

### Keywords

delirium; altered mental status; catatonia; delirious mania; Ganser syndrome; disorganized psychosis

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### Case study

A 52-year-old woman with unknown medical history was brought to the ED for “acting bizarrely.” A neighbor had called 911 after finding her wandering in their apartment complex agitated, picking at invisible objects, disheveled, and confused. No prior records for the patient were available at the hospital. Vital signs on arrival were remarkable for tachycardia and hypertension. Initial work-up in the ED—including complete blood count, comprehensive metabolic panel, liver function tests, urine toxicology screen, thyroid stimulating hormone, vitamin B12, chest X-ray and head CT—was remarkable only for prerenal azotemia. Creatine phosphokinase was 2,152 units/L. Urinalysis was equivocal and revealed many squamous cells. She received 1 mg IV haloperidol twice in the ED without appreciable effect. She was admitted to the general medical service for “altered mental status.”

Confusion Assessment Method (CAM) by nursing on initial assessment was positive as the patient was grossly altered, unable to attend to conversation, and hyperactive. Shortly after admission, collateral revealed that her medication regimen included divalproex sodium DR 500 mg qAM and 750 mg qhs, zolpidem 5 mg qhs, and hydrochlorothiazide 25 mg daily. Valproic acid level was found to be undetectable; liver function tests and ammonia were unremarkable. Outpatient medications were held out of concern that they might have contributed to delirium. CAMs continued to be positive. Despite rehydration and normalization of renal status, the patient continued to exhibit confusion, spoke in a shrill, staccato voice, and was occasionally found to be shirtless. Further 1 mg doses of IV haloperidol were ineffective.

Psychiatry was consulted to assist with delirium management. On psychiatric evaluation, the patient was unable to engage in cognitive testing or provide a meaningful narrative. The psychiatrist noted the shrill voice as manneristic speech and identified verbigeration when the patient repeated the phrase “Is it 10 o’clock?” several times, prompting consideration of catatonia (1). Bush-Francis Catatonia Rating Scale score was 13 for excitement, stereotypy, mannerism, verbigeration, rigidity, and autonomic abnormality. Lorazepam 2 mg was given IV, and assessment 30 minutes later revealed moderate improvement in speech fluency, reduction in mannerisms and verbigeration, and improvement in abnormal tone. The patient was able to explain that she has bipolar disorder and had not taken valproic acid for the past week due to an upset stomach, diarrhea, and feeling “under the weather.” Lorazepam 2 mg three times a day was recommended to treat catatonia secondary to Bipolar Disorder, type I, until valproic acid was again therapeutic.

## Introduction

Delirium presents as an acute change in mental status characterized by a disturbance in attention, awareness, cognition and arousal (2), and its clinical phenotype is often readily identifiable on bedside tests, including ultra-brief screening instruments (3). As opposed to most primary psychiatric conditions, in which only a subset of neuropsychiatric domains is affected (*e.g.*, mood or discrete psychotic symptoms), delirium represents a global disturbance in mentation, cognitive clarity and psychomotor activity. Differentiating between primary psychiatric conditions and delirium—which requires the presence of an underlying encephalopathy (4, 5)—is important for several reasons. Diagnostically, the DSM-5 disallows the diagnosis of primary psychiatric disorders during delirium, but, most importantly, differentiation is essential for timely and appropriate clinical management.

Whereas the phenotypic differences between primary psychiatric conditions and delirium are generally unambiguous on clinical evaluation, this is not always the case. In fact, occasionally the clinical phenotypes of certain psychiatric conditions are practically indistinguishable from delirium even to seasoned clinicians. Some psychiatric conditions can resemble the clinical phenotype of delirium so closely that they screen positive on common delirium instruments (*e.g.*, Confusion Assessment Method (6)), as in the opening Case Study. It is also noteworthy that no delirium instrument has been formally validated in cohorts of patients with serious mental illness.

The term pseudodelirium was first coined by Goldney and Lander to describe “acute functional psychoses” mimics of delirium (7). In this review we have extended their use of pseudodelirium as linguistic shorthand to describe the phenomenon of a psychiatric condition that presents with a clinical phenotype that very closely resembles delirium, especially where mistaken for delirium. Prompt differentiation between pseudodelirium and delirium is essential to guide clinical management. Whereas clinicians are often encouraged not to miss underlying medical conditions that might account for psychiatric symptoms, they receive far less guidance on the potential risks of managing primary psychiatric conditions *as* delirium. Rather, clinicians should bear in mind the risks of erring on either side—that is, the type I and type II errors of inaccurately ruling delirium in or out (Table 1).

There are many reviews that parse out the “three D’s” of geriatric psychiatry (delirium, dementia, and depression (8)); however, we are unaware of similar reviews that explore the phenotypes of other psychiatric conditions relative to delirium. This article describes psychiatric conditions that may be especially challenging to differentiate from delirium. Our goal is to bring awareness to these conditions and provide an educational resource for clinicians.

## Methods

Based on our pooled clinical experience, we identified the following four psychiatric conditions as being among the most difficult to differentiate from delirium: disorganized psychosis, Ganser syndrome, delirious mania, and catatonia. We conducted a clinically focused literature review for each condition to provide a conceptual overview, describe

its phenotype, differentiate its clinical presentation from delirium, and review its clinical management. This literature review was initially conducted in preparation for a workshop at a large psychiatric conference, and feedback received at the conference was incorporated into this manuscript.

## Results

### Disorganized psychosis

**Background**—Psychotic disorders can present with disorganized thoughts and behavior as well as the dissolution of reality-based thought content and sensory experiences. Several facets of psychotic disorders can make it difficult to differentiate acute episodes of psychotic decompensation from delirium, especially when patients present with prominent thought disorganization (9). In fact, the full spectrum of symptoms encountered in psychotic disorders can be found in delirium as well. Nevertheless, there is minimal overlap between the diagnostic criteria of psychotic disorders and delirium in DSM-5. Specifically, disorganized speech may lead clinicians to conclude that the patient has a disturbance in awareness (second half of criterion A for delirium), and hallucinations (*i.e.*, altered perceptions) would satisfy criterion C (9).

Psychotic disorders are often described as “formal thought disorders.” This term refers to the disordered nature of “thought form” (as opposed to thought content) and to various types of thought disorganization, especially those presenting with disruption of coherent narrative capacity. By way of parallel, some diagnostic systems for delirium, including DSM-III-R, ICD-10, and many well-validated delirium screening tools (e.g., the family of Confusion Assessment Method instruments) incorporate disorganized thinking/thought process among their assessment criteria (6, 10–12). Additionally, the comment section in ICD-10 indicates that “disturbances of perception (illusions or hallucinations, often visual) and transient delusions are typical but are not specific indications for the diagnosis” (12).

**Clinical features**—Patients with thought or behavior disorganization tend to think and act in an aimless, nonconstructive manner. As the severity of thought disorder increases, patients tend to become increasingly psychotic as the reality-basis of thoughts fades. Often a patient may be disheveled, use poor judgment, lack impulse control, and provide inappropriate responses (13). When thoughts are disorganized, a patient will have difficulty formulating ideas and language, which hinders effective communication. Patients may also exhibit loosening of associations, incoherence, thought blocking, flight of ideas, perseveration, reduced concentration, circumstantiality, tangentiality, poverty of thought content, concreteness, neologisms, echolalia, verbigeration, world salad, and mutism (13).

**Differentiation from delirium**—Detailed clinical evaluation for evidence of systemic illness, polypharmacy, and illicit drug use is indicated. The acuity of onset and course of psychotic symptoms, the patient’s age, and the patient’s medical and psychiatric history (*e.g.*, where a series of similar presentations might suggest recurrence of a primary psychotic illness) often guide diagnostic impressions (14). Electroencephalography (EEG) can help differentiate between primary psychotic illness and delirium: delirium classically presents with diffuse slowing and increased theta and delta activity whereas these findings would be

rare in primary psychotic disorders (15, 16) (Table 2). Despite its potential usefulness in disentangling delirium from a primary psychiatric disorder, the debate about the utility of EEG in detecting and diagnosing delirium persists: some have argued that the characteristic background slowing of an EEG in delirium is nonspecific and therefore a unnecessary clinical study, whereas others have reported findings suggesting that generalized slowing on EEG strongly correlates with delirium and may be a marker of delirium severity (16).

Careful characterization of the clinical phenotype can also provide diagnostic clues. Non-auditory hallucinations are uncommon in primary psychotic disorders. Additionally, when visual hallucinations occur in primary psychotic illness, these tend to be vague or of shadows; in delirium, visual hallucinations may be of any character: vivid, colorful, fragmentary, vague, or even multi-modal (*e.g.*, audiovisual). Patients with primary psychotic illness are typically alert with stability of symptoms over the course of the day, whereas delirium commonly presents with altered arousal and circadian fluctuation of symptoms. Clinicians should also be aware of the possibility of apparent disorientation due to “double bookkeeping” in some psychotic conditions, as when a patient has a factual understanding of their autobiographical information but maintains on direct questioning that they live somewhere else (*e.g.*, a person who believes they are the president saying their home address is the White House).

**Management**—The mainstay of treatment for disorganized psychosis includes antipsychotics, mood stabilizers for comorbid mania, benzodiazepines for behavioral activation, and occasionally electroconvulsive therapy (ECT) for severe symptoms. Although antipsychotics are still widely used to manage psychotic symptoms or agitation associated with delirium, their efficacy in preventing and treating delirium is unproven (17, 18). Delirium management, on the other hand, involves treating its precipitant(s), addressing underlying neurophysiological disruption where known (*e.g.*, hyper-adrenergic state in alcohol withdrawal delirium), reversing elements of cognitive vulnerability (*e.g.*, malnutrition, inanition), and managing dangerous or distressing symptoms of the delirium phenotype (*e.g.*, agitation, paranoid delusions).

### Ganser syndrome

**Background**—The German psychiatrist Dr. Sigbert Ganser first described this condition in 1897 among prisoners awaiting trial as a “peculiar hysterical twilight state,” but Ganser syndrome has garnered several terms since, including prison psychosis, the foolish or buffoonery syndrome (Ger. *faxensyndrom*), pseudo-dementia, and—especially relevant here—psychogenic delirium (7, 19, 20). Uncertainty over how best to formulate this condition is reflected in its historical traipse through the DSM: it was an adjustment disorder in DSM-II, factitious disorder in DSM-III, and a dissociative disorder from DSM-III-R to the present. The modern prevailing view is that it represents a psychological need to escape from an intolerable situation or psychosocial reality. Perhaps the simplest way to describe it is that it evinces “what ordinary people... think... madness looks like or should look like” (21). Because of this, malingering should be on the differential when evaluating someone with symptoms of Ganser syndrome.

**Clinical features**—The central feature of Ganser syndrome is approximate answers (Ger. *vorbeigehen* “to pass over” or *vorbeireden* “to talk at cross-purposes”). When asked even simple questions, the patient with Ganser syndrome routinely provides answers that are obviously incorrect but also indicate that they grasp the nature of the question and the kind of response called for (19). In response to the question “What’s the largest number on the face of that clock?” the patient might say “Ten.” Other cardinal symptoms of this condition include clouding of consciousness, audiovisual hallucinations (either reported or inferred based on the patient’s responses to internal stimuli), and conversion symptoms.

Additional clinical features may include disorientation, loss of identity, a fugue state, and regression (*puerilism*) (21). Patients can experience rapid, astonishing recovery and report amnesia for the episode. Nearly half of patients have a prior psychiatric diagnosis; 10% have a history of dissociation, 10% have prior unexplained physical symptoms, and 10% have a criminal history (22). Although this condition is thought to be generated psychologically, a third of patients have a neurological condition such as previously unrecognized brain pathology discovered as part of the work-up; accordingly, some authors have suggested certain brain conditions may confer vulnerability to this syndrome (22, 23).

**Differentiation from delirium**—Approximate answers are specific for Ganser syndrome because a patient must have intact cognition and sufficient awareness of the questions to generate such responses consistently and, as in most cases of Ganser syndrome, fluently. Verbal responses tend to offer conceptual clarity even if they are bizarre. The patient in this state may also exhibit unusually effortful engagement. In addition, a psychosocial history typically reveals a situation from which the patient would reasonably want to escape (*e.g.*, emotional trauma due to a recent sexual assault, legal charges, etc.). Electroencephalogram is generally normal as opposed to the generalized slowing seen in delirium (24).

**Management**—Accurate diagnosis is key to preventing unnecessary work-up. Although the condition is rare enough that a consensus on management has yet to emerge, patient interactions should honor the principles of trauma-informed care and emphasize safety, trust, and clarity of communication because dissociation is a response to perceived threat (25). In addition, person-focused psychological first aid that restores a sense of normalcy and establishes a daily routine should be implemented (26). Other considerations for treatment derive from approaches to conversion disorder and include acknowledgement of the symptoms as “real,” reassurance that the condition is not dangerous, life-threatening, or progressive, an affirmation of clinical expertise for this condition, and the suggestion that full recovery is anticipated.

## Delirious mania

**Background**—First described by Calmeil (1832) (27) and Bell (1849) (28), this potentially fatal syndrome is characterized by psychomotor agitation, emotional lability, acute psychosis (delusions and hallucinations) and disorientation. Max Fink later described delirious mania as, “a syndrome of the acute onset of the excitement, grandiosity, emotional lability, delusions, and insomnia characteristic of mania, and the disorientation and altered consciousness [characteristic of delirium]....not associated with prior mental or

systemic disorder” (29). In Fink’s description, catatonia was a consistent finding (29). The phenomenology of delirious mania remains unclear and has evolved over the decades, in large part owing to the lack of diagnostic criteria and, as a result, sporadic and discrepant reports.

**Clinical features**—In one review, 15 to 36 % of psychiatrically hospitalized patients with mania had co-occurring delirium (30). The typical course of delirious mania may vary, but patients often exhibit a prodrome of worsening symptoms of mania over days to weeks, followed by frank psychosis. This typically devolves further into an overt delirium-like phenotype including inattention, disorientation, altered and fluctuating arousal, psychomotor abnormalities, poor recall of events, perceptual abnormalities, and distorted thought process. At times, the patient enters an excited or stuporous catatonia. Symptoms may also fluctuate in severity much like the “waxing and waning” of delirium. The condition can resolve spontaneously or require intensive treatment to remit. In many cases, patients who experience delirious mania either have a personal history of or a first degree relative with bipolar disorder.

**Differentiation from delirium**—The inclusion of the term “delirious” in “delirious mania” chiefly denotes the mental status phenotype; however, delirious mania may at times meet DSM-5 criteria for delirium. The extreme psychomotor dysfunction in this condition often involves muscle rigidity and dehydration, accompanied by lab abnormalities (e.g., elevated creatine phosphokinase, leukocytosis, and creatine) reflecting end-organ dysfunction (acute renal injury and/or rhabdomyolysis). Additionally, delirious mania is often complicated by autonomic dysfunction (e.g., tachycardia, hypertension, tachypnea, fever), especially in patients with the *malignant* form (*n.b.*, the analogous historical descriptors *lethal* or *pernicious* are now generally discouraged). Further highlighting the ambiguity between mania and delirium, a chart review of 199 patients showed a 14.9% prevalence of delirium in bipolar disorder (30). In short, patients experiencing an episode of delirious mania may be simultaneously be manic, psychotic, delirious and catatonic. Unless conclusive empirical evidence were to suggest otherwise, the assignment of one diagnostic label (e.g., mania, psychosis or catatonia) should not exclude recognition of another (e.g., delirium).

**Management**—The management of delirious mania depends on the clinical presentation. Aside from identifying and treating co-occurring conditions and associated morbidities (e.g., dehydration, rhabdomyolysis, venous thromboembolism, autonomic abnormalities), one of the first steps should be to perform a complete diagnostic interview to elucidate whether there is a contributing bipolar diathesis. If so, that may support the use of mood stabilizing or antiepileptic medication. Next, a thorough physical exam should be performed with particular attention to the evaluation of catatonic features (e.g., rigidity, mutism, catalepsy, autonomic abnormalities) and if present should be treated promptly, generally with a trial of a benzodiazepine (typically lorazepam, which can be administered either orally, intravenously or intramuscularly). Depending on the severity of catatonic signs present, patients may require transfer to a medical floor and in rare circumstances an intensive care unit. ECT is typically reserved for those whose catatonic signs fail to respond

to benzodiazepines, or those with prominent mania symptoms not responding to mood stabilization efforts. If catatonic symptoms are present, antipsychotics are generally withheld until malignant features of catatonia have resolved. If antipsychotics are indicated, generally due to prominent positive psychosis symptoms (e.g., hallucinations or delusions), atypical antipsychotics are generally preferred.

## Catatonia

**Background**—Catatonia was first described in 1874 by German psychiatrist Karl Ludwig Kahlbaum (31) as a clinical syndrome of motor, vocal, and behavioral abnormalities. Emil Kraepelin proposed that catatonia was as a motoric presentation of dementia praecox, which was echoed by Eugen Bleuler's conceptualization of schizophrenia but debated by others (32, 33). Throughout the greater part of the 20<sup>th</sup> century, catatonia was classified as a subtype of schizophrenia, despite growing evidence that most patients with catatonia have a mood disorder—most commonly bipolar disorder—psychotic disorder, or a neurological or medical illness (34, 35). The DSM-5 classifies catatonia within the schizophrenia spectrum and other psychotic disorders chapter but no longer as a subtype of schizophrenia. DSM-5 diagnoses include: catatonia associated with another mental disorder, catatonic disorder due to another medical illness, or unspecified catatonia (2). The prevailing pathophysiologic hypothesis is that catatonia is caused by dysregulation in GABA-A and glutamate circuitry between the prefrontal cortex, parietal cortex, and basal ganglia (36, 37). Still, non-consensus about its nosology and pathophysiology persists.

**Clinical features**—The cardinal feature of catatonia is a psychomotor disturbance in which a person's volition to move or to act is disrupted. The three motoric subtypes of catatonia include hypokinetic, parakinetic, and hyperkinetic—of these, the hypokinetic type is most common (38). Common symptoms of catatonia include staring, immobility, mutism, withdrawal (not eating, drinking, or making eye contact), posturing, catalepsy, and negativism. The Bush-Francis Catatonia Rating Scale is the most widely used of many published catatonia instruments (39). After catatonia resolves, many describe that they had experienced intense anxiety, fear, or the belief that they were dead or dying (40). A catatonia diagnosis is often confirmed by response to intravenously-administered benzodiazepines, with response ranging from partial to full resolution of catatonic symptoms within minutes. However, some patients with catatonia, especially those with complex medical disease, neurologic injury, or chronic catatonia due to primary psychotic illness, may experience only partial or no response to benzodiazepines.

**Differentiation from delirium**—Both catatonia and delirium have hypoactive and hyperactive variants (41). Perseverative thought process, which may be scored as inattention on the CAM as it represents an inability to shift attention, is also common in catatonia. However, several other features of catatonia are not routinely seen in delirium, including abnormalities in tone (rigidity or waxy flexibility), speech (mutism, manneristic speech, or verbigeration), behavior (posturing, catalepsy, stereotypies, or mannerisms), echophenomena (echolalia or echopraxia), negativism, and severe withdrawal with refusal to eat or drink. Furthermore, the EEG is typically normal in primary catatonia (42), unlike in delirium (43).



Recent studies (44, 45) have revealed that delirium and catatonia frequently co-occur in the context of critical illness, so differentiation may not always be feasible.

Treatment response to benzodiazepines may prove decisive in differentiating catatonia from delirium. Most presentations of primary catatonia partially or fully respond to lorazepam. Even catatonic features in delirium may show some improvement in response to low-dose benzodiazepines; however, such patients are not expected to show improved cognition with benzodiazepines, especially when the dose is increased. Specifically, lorazepam dose is an independent risk factor for transitioning to delirium in intensive care unit patients (46), so clinicians should use benzodiazepines very cautiously in patients with or at risk for delirium.

**Management**—Benzodiazepines are the primary treatment of catatonia, beginning with an intravenous dose if possible and, if effective, followed by scheduled around-the-clock dosing (40, 43). Benzodiazepines are hypothesized to restore GABA-A signaling in the prefrontal cortex and hypothalamus. ECT is a highly effective treatment for catatonia, including in patients with inadequate response to benzodiazepines; ECT is first-line treatment for malignant catatonia because of its risk of fatality without assertive treatment (47). Supportive treatments including venous thromboembolism prophylaxis, repositioning, pressure-reducing devices, and physical therapy are pertinent for preventing complications of catatonia such as pulmonary embolism, pressure ulcers, dehydration, malnutrition, and contractures. If catatonia is misdiagnosed as delirium, treatment with benzodiazepines may be withheld due to concerns that they may worsen delirium. Delayed treatment of catatonia is associated with poorer treatment response and prognosis (48), thus highlighting the importance of prompt catatonia diagnosis and treatment.

## Discussion

Although the core neurocognitive features of delirium typically allow for clinical differentiation from primary psychiatric conditions, the clinical phenotype of delirium is not always unambiguous. Each of its core features may be encountered in primary psychiatric conditions. We consider each of its diagnostic features in turn (Table 3).

Disturbance in attention (Criterion A, part 1) involves a reduced ability to focus, sustain, or shift attention. These are assessed by a patient's ability to engage meaningfully in conversation, to perform a task of concentration (*e.g.*, vigilance A, serial 7's, or months backward), or to change topics appropriately (*e.g.*, perseveration is evidence of impaired ability to shift attention), respectively. Several acute psychiatric syndromes leave patients unable to demonstrate that attention is intact. For instance, patients with mutism in catatonia are unable to engage in conversation, and those with delirious mania may have flight of ideas and distractibility, preventing them from concentrating on a cognitive test.

Disturbance in awareness (Criterion A, part 2) describes disorientation to one's environment and may be thought of as the answer to the question, "Does the patient understand what's going on around them?" Its assessment typically involves narrative content; however, many acute psychiatric conditions present with disturbances in communication (*e.g.*, catatonia) or thought form (*e.g.*, psychotic syndromes), thus making it exceptionally difficult, if not

impossible at times, for a clinician to assess or even intuit a patient's degree of situational or environmental awareness.

Many primary psychiatric syndromes such as mania or acute psychosis satisfy Criterion B of delirium as they present over the course of days; however, most primary psychiatric conditions are unlikely to exhibit substantial fluctuation over the course of the day.

One notable exception to this is where acute response to specific medications (*e.g.*, an antipsychotic in disorganized psychosis or a benzodiazepine in catatonia) may, at times, be interpreted as evidence of a waxing and waning clinical course.

Criterion C for delirium diagnosis, which requires another cognitive disturbance (*i.e.*, in addition to a disturbance in attention and awareness), identifies several domains: memory, orientation, language, visuospatial ability, or perception. Patients with acute psychosis (especially catatonia, paranoia or irritable mania) often do not participate in formal cognitive testing, making it very difficult to ascertain cognitive status or evaluate for these findings. Beyond mutism, catatonia can present with a variety of abnormal speech patterns (49). Dissociation not infrequently presents with hallucinations or other perceptual changes, such as time or visual distortions.

Finally, it is important to reflect on the fact that many psychiatric constructs (*e.g.*, delirium, bipolar disorder, etc.) as currently defined by the DSM and ICD do not allow for a trans-diagnostic relationship between psychiatric entities (*e.g.*, mania, psychosis, catatonia). It is possible that the presence of mania or catatonia, like psychosis, can be driven by or embedded in another psychiatric condition, as in Major Depressive Disorder, Severe with Psychotic Features. Presentations such as Delirium "with Catatonic Features," "with Psychotic Features," etc. may also be thought of as the "behavioral and psychological symptoms of delirium," akin to the "behavioral and psychological symptoms of dementia." Further evaluation of the relationship(s) between such entities may prove useful to clinicians and researchers alike.

## Conclusions

Several psychiatric conditions can present with a clinical picture that closely resembles delirium or its any of its core diagnostic features, a clinical scenario we describe here as pseudodelirium. Specifically, we have reviewed disorganized psychosis, Ganser syndrome, delirious mania and catatonia as especially challenging to differentiate from delirium given syndromal overlap. At times, psychiatric syndromes can even co-occur with delirium (*e.g.*, delirious mania or catatonia), introducing further clinical complexity. The risk of false negative and false positive diagnoses of delirium deserve consideration in clinical care. Although difficult at times, differentiation of delirium from pseudodelirium is essential to ensure appropriate clinical care in a timely fashion.

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## References

1. Oldham MA, Wortzel JR, Francis A. The Bush-Francis Catatonia Rating Scale: Training Manual and Coding Guide 2020 [02/24/2021]; Available from: [bfcrs.urmc.edu](http://bfcrs.urmc.edu).
2. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders Washington, D.C.: American Psychiatric Association; 2013.
3. Motyl CM, Ngo L, Zhou W, Jung Y, Leslie D, Boltz M, et al. Comparative Accuracy and Efficiency of Four Delirium Screening Protocols. *J Am Geriatr Soc* 2020;68(11):2572–8. [PubMed: 32930409]
4. Slooter AJC, Otte WM, Devlin JW, Arora RC, Bleck TP, Claassen J, et al. Updated nomenclature of delirium and acute encephalopathy: statement of ten Societies. *Intensive care medicine* 2020;46(5):1020–2. [PubMed: 32055887]
5. Oldham MA, Holloway RG. Delirium disorder: Integrating delirium and acute encephalopathy. *Neurology* 2020;In press.
6. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 1990;113(12):941–8. [PubMed: 2240918]
7. Goldney R, Lander H. Pseudodelirium. *Med J Aust* 1979;1(13):630.
8. Downing LJ, Caprio TV, Lyness JM. Geriatric psychiatry review: differential diagnosis and treatment of the 3 D's - delirium, dementia, and depression. *Curr Psychiatry Rep* 2013;15(6):365. [PubMed: 23636988]
9. Association AP. Diagnostic and statistical manual of mental disorders (DSM-5®): American Psychiatric Pub; 2013.
10. Association AP. The Diagnostic and Statistical Manual of Mental Disorders, 3rd edition revised (DSM-III-R)1987.
11. Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA : the journal of the American Medical Association* 2001;286(21):2703–10. [PubMed: 11730446]
12. Organization WH. The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines Geneva: World Health Organization (WHO); 1992.
13. Sadock BJ, Sadock VA. Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry: Lippincott Williams & Wilkins; 2011.
14. Griswold KS, Del Regno PA, Berger RC. Recognition and Differential Diagnosis of Psychosis in Primary Care. *Am Fam Physician* 2015;91(12):856–63. [PubMed: 26131945]
15. Jacobson SA, Leuchter AF, Walter DO. Conventional and quantitative EEG in the diagnosis of delirium among the elderly. *J Neurol Neurosurg Psychiatry* 1993;56(2):153–8. [PubMed: 8437004]
16. Kimchi EY, Neelagiri A, Whitt W, Sagi AR, Ryan SL, Gadbois G, et al. Clinical EEG slowing correlates with delirium severity and predicts poor clinical outcomes. *Neurology* 2019;93(13):e1260–e71. [PubMed: 31467255]
17. Nikoie R, Neufeld KJ, Oh ES, Wilson LM, Zhang A, Robinson KA, et al. Antipsychotics for Treating Delirium in Hospitalized Adults: A Systematic Review. *Ann Intern Med* 2019;171(7):485–95. [PubMed: 31476770]
18. Oh ES, Needham DM, Nikoie R, Wilson LM, Zhang A, Robinson KA, et al. Antipsychotics for Preventing Delirium in Hospitalized Adults: A Systematic Review. *Ann Intern Med* 2019;171(7):474–84. [PubMed: 31476766]
19. Schorer CEt, Ganser SJM, Scott PD. The Ganser syndrome. *The British Journal of Criminology* 1965;5(2):120–6.
20. Refaat R, Firth DA, Robertson MM. Uncomplicated Gilles de la Tourette syndrome and probable Ganser syndrome. A case report and review of the literature. *Eur Child Adolesc Psychiatry* 2002;11(5):234–9. [PubMed: 12469241]

21. Dieguez S. Ganser Syndrome. In: Bogousslavsky J, editor. *Neurologic-Psychiatric Syndromes in Focus Part II - From Psychiatry to Neurology* Basel: Karger; 2018. p. 1–22.
22. Mendis S, Hodgson RE. Ganser syndrome: examining the aetiological debate through a systematic case report review. *Eur J Psychiat* 2012;26(2):96–106.
23. Lee HB, Koenig T. A case of Ganser syndrome: organic or hysterical? *Gen Hosp Psychiatry* 2001;23(4):230–1. [PubMed: 11569472]
24. Cocores JA, Santa WG, Patel MD. The Ganser syndrome: evidence suggesting its classification as a dissociative disorder. *Int J Psychiatry Med* 1984;14(1):47–56. [PubMed: 6735595]
25. Raja S, Hasnain M, Hoersch M, Gove-Yin S, Rajagopalan C. Trauma informed care in medicine: current knowledge and future research directions. *Fam Community Health* 2015;38(3):216–26. [PubMed: 26017000]
26. Jacobs GA, Gray BL, Erickson SE, Gonzalez ED, Quevillon RP. Disaster Mental Health and Community-Based Psychological First Aid: Concepts and Education/Training. *J Clin Psychol* 2016;72(12):1307–17. [PubMed: 27175614]
27. Calmeil L *Dictionnaire de médecine; ou repertoire general des sciences medicales considerees sous le rapport theorique et pratique* 2nd ed. Paris: Bechet; 1832.
28. Bell L On a form of disease resembling some advanced stage of mania and fever. *Am J of Insanity* 1849;6:97–127.
29. Fink M Delirious mania. *Bipolar Disord* 1999;1(1):54–60. [PubMed: 11256658]
30. Ritchie J, Steiner W, Abrahamowicz M. Incidence of and risk factors for delirium among psychiatric inpatients. *Psychiatr Serv* 1996;47(7):727–30. [PubMed: 8807686]
31. Kahlbaum K *Die Katatonie oder das Spannungsirresein. Eine klinische form psychischer Krankheit* Berlin 1874.
32. Kirby G The catatonic syndrome and its relation to manic-depressive insanity. *J Nerv Ment Dis* 1913;40:694–704.
33. Hoch A *Benign Stupor* New York, NY: Macmillan Co.; 1921.
34. Taylor MA, Fink M. Catatonia in psychiatric classification: a home of its own. *Am J Psychiatry* 2003;160(7):1233–41. [PubMed: 12832234]
35. Abrams R, Taylor MA. Catatonia. A prospective clinical study. *Arch Gen Psychiatry* 1976;33(5):579–81. [PubMed: 1267574]
36. Dhossche DM, Stoppelbein L, Rout UK. Etiopathogenesis of catatonia: generalizations and working hypotheses. *J ECT* 2010;26(4):253–8. [PubMed: 21076339]
37. Northoff G What catatonia can tell us about “top-down modulation”: a neuropsychiatric hypothesis. *Behav Brain Sci* 2002;25(5):555–77; discussion 78–604. [PubMed: 12958742]
38. Wilson JE, Niu K, Nicolson SE, Levine SZ, Heckers S. The diagnostic criteria and structure of catatonia. *Schizophr Res* 2015;164(1–3):256–62. [PubMed: 25595653]
39. Bush G, Fink M, Petrides G, Dowling F, Francis A. Catatonia. I. Rating scale and standardized examination. *Acta Psychiatr Scand* 1996;93(2):129–36. [PubMed: 8686483]
40. Rosebush PI, Mazurek MF. Catatonia and its treatment. *Schizophr Bull* 2010;36(2):239–42. [PubMed: 19969591]
41. Oldham MA, Lee HB. Catatonia vis-a-vis delirium: the significance of recognizing catatonia in altered mental status. *Gen Hosp Psychiatry* 2015;37(6):554–9. [PubMed: 26162545]
42. Carroll BT, Boutros NN. Clinical electroencephalograms in patients with catatonic disorders. *Clin Electroencephalogr* 1995;26(1):60–4. [PubMed: 7882543]
43. Rasmussen SA, Mazurek MF, Rosebush PI. Catatonia: Our current understanding of its diagnosis, treatment and pathophysiology. *World J Psychiatry* 2016;6(4):391–8. [PubMed: 28078203]
44. Grover S, Ghosh A, Ghormode D. Do patients of delirium have catatonic features? An exploratory study. *Psychiatry and clinical neurosciences* 2014;68(8):644–51. [PubMed: 24521083]
45. Wilson JE, Carlson R, Duggan MC, Pandharipande P, Girard TD, Wang L, et al. Delirium and Catatonia in Critically Ill Patients: The Delirium and Catatonia Prospective Cohort Investigation. *Crit Care Med* 2017;45(11):1837–44. [PubMed: 28841632]

46. Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology* 2006;104(1):21–6. [PubMed: 16394685]
47. Mann SC, Caroff SN, Bleier HR, Antelo RE, Un H. Electroconvulsive Therapy of the Lethal Catatonia Syndrome. *Convuls Ther* 1990;6(3):239–47. [PubMed: 11941074]
48. Sienaert P, Dhossche DM, Vancampfort D, De Hert M, Gazdag G. A clinical review of the treatment of catatonia. *Front Psychiatry* 2014;5:181. [PubMed: 25538636]
49. Ali S, Bayona E, Quinn D, Escalona R. “Narration,” an Atypical Catatonic Speech Symptom: A Case Report. *Psychosomatics* 2020;61(4):385–9. [PubMed: 31837828]
50. Cardinal RN, Bullmore ET. *The Diagnosis of Psychosis*: Cambridge University Press; 2011.

**Table 1.** Risks of incorrectly diagnosing primary psychiatric illness and delirium as the other

Risks of diagnosing primary psychiatric illness as delirium		Risks of diagnosing delirium as primary psychiatric illness	
Risks	Examples	Risks	Examples
Psychiatric treatments withheld	<ul style="list-style-type: none"> <li>- Benzodiazepines or ECT for catatonia</li> <li>- Mood stabilizers (e.g., lithium) for mania</li> <li>- Delayed pursuit of a “medication over objection” hearing for psychotic decompensation</li> <li>- Antidepressants for depression</li> </ul>	Reversible conditions overlooked	The list of medical causes of psychiatric symptoms is extremely long (50)
Inappropriate medications given	Antipsychotics are effective for psychosis in a formal thought disorder and for psychosis and mania in delirious mania. However, their use in catatonia requires careful consideration. Neuroleptic-induced extrapyramidal symptoms may be difficult to differentiate from features of catatonia, and patients with catatonia may be at higher risk of developing neuroleptic malignant syndrome, especially from high-potency agents.	Inappropriate psychiatric admission	Psychiatric settings are not equipped to manage acute medical conditions. For instance, IV antibiotics could not be given for infection (i.e., lines represent a safety risk) and supplemental oxygen is often unavailable.
Unnecessary workup completed	Expanded workup for delirium is costly, time-consuming (e.g., prolonged length of stay), and potentially invasive (e.g., lumbar puncture)	Inappropriate medications given	Benzodiazepines given to a delirious patient may worsen their cognition and delay recovery; use of antipsychotic medication may cause extrapyramidal side effects
Psychosocial and family history overlooked	<ul style="list-style-type: none"> <li>- Legal situation not obtained (e.g., pending charges re Ganser syndrome)</li> <li>- History of similar presentations for schizophrenia or bipolar disorder, including common delusional themes</li> </ul>	Medical deterioration	Delayed treatment of autoimmune encephalopathy is associated with cognitive and functional sequelae

**Table 2:**

Differentiating features of delirium from “pseudodelirium”

	<b>DELIRIUM</b>	<b>DISORGANIZED PSYCHOSIS</b>	<b>GANSER SYNDROME</b>	<b>DELIRIOUS MANIA</b>	<b>PRIMARY CATATONIA</b>
<b>EEG</b>	Diffuse slowing	No specific pattern	Typically normal	Unknown	Typically normal
<b>Clinical status</b>	Sick, often frail	Medically stable	Medically stable	Variable; often with autonomic activation	Medically stable
<b>Arousal</b>	Rarely appropriately alert	Alert	Fluctuates; may be alert for extended periods	Can alternate between hyperkinetic and stuporous	Usually stuporous, occasionally hyperkinetic
<b>Interpersonal</b>	Inattentive	Variable; often difficult to rule out inattention	Often engaged	Fluctuates; often inattentive	Disengaged, negativistic; occasionally automatically obedient
<b>Verbal responses</b>	Muddled thinking	Speech disorganized	Approximate answers common	Initially hyperverbal, may devolve to mutism	Mute, whispered, verbigeration, or echolalia
<b>Sensorium</b>	Clouded	Usually clear	Verbal content suggests clouding	Clouded in mid-to-late stages	Often clear but difficult to assess
<b>Emotional state</b>	Consistent with motor subtype	Often paranoid	Effortful engagement	Manic, may devolve to blunted state	Fearful, occasionally manic
<b>Psychosocial</b>	Reduced engagement	Difficult to engage	Bizarre; psychosocial stressor present	May be initially intrusive, then disengaged	Variable, related to underlying condition

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**Table 3:**

Diagnostic criteria of delirium reflected in primary psychiatric conditions

Diagnostic criterion*	Examples in primary psychiatric conditions**
Criterion A, part 1: "Disturbance in attention"	Catatonia: mutism and negativism can prevent a patient from demonstrating attention Mania (especially delirious mania): flight of ideas and distractibility prevent a patient from engaging consistently on evaluation Attention-deficit/hyperactivity disorder: inattention and reduced concentration are included as diagnostic features
Criterion A, part 2: "Disturbance... in awareness"	Catatonia: mutism and negativism can prevent a patient from demonstrating awareness Disorganized psychosis: although patients with psychotic illness are typically oriented, acute psychotic decompensation can present with word salad or grossly disrupted thought process Dissociative disorders (including Ganser syndrome): dissociation is a disruption in the normal integration of consciousness, experience, and actions, often leading to lack of situational awareness
Criterion B: "Develops over a short period...and tends to fluctuate"	Mania: typically develops over days Acute psychosis: typically develops over days Dissociative disorders: often occur over hours to days; Ganser syndrome can exhibit fluctuation over the course of the day
Criterion C: "An additional disturbance in cognition" including "memory, orientation, language, visuospatial ability, or perception"	Catatonia: mutism and negativism can prevent a patient from engaging in cognitive evaluation Acute psychosis: delusional recall may confound assessment; paranoia may prevent a patient from engaging in assessment Mania: profound irritability often prevents a patient from engaging in formal cognitive assessment Dissociative disorders: perceptual disturbances may be experienced
Specifier: Hyperactive, hypoactive, mixed level of activity	Catatonia: exhibits hypokinetic, hyperkinetic, and parakinetic subtypes Mania (especially severe or delirious mania): presents with marked psychomotor activation

\* Abbreviated criteria

\*\* Effects of psychotropics deserve consideration as well.

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