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Catatonia in clinical practice: from pathophysiology to treatment strategies

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Abstract

Catatonia is a complex neuropsychiatric syndrome involving motor, emotional, and behavioral symptoms. Once linked mainly to schizophrenia, it is now seen across various psychiatric, neurological, and medical conditions. Despite its prevalence, it remains underdiagnosed and undertreated, leading to serious health consequences. This review highlights the need for early recognition and intervention, discussing key diagnostic tools and treatments such as benzodiazepines and electroconvulsive therapy. It advocates for recognizing catatonia as a distinct clinical entity to improve clinical approach.

Keywords: *Catatonia. Benzodiazepines. Electroconvulsive therapy (ECT). Psychomotor syndrome. Diagnosis.*

Catatonía en la práctica clínica: de la fisiopatología a las estrategias de tratamiento

Resumen

La catatonia es un síndrome neuropsiquiátrico complejo con síntomas motores, afectivos y conductuales. Aunque antes se asociaba principalmente con la esquizofrenia, hoy se reconoce en múltiples trastornos psiquiátricos, neurológicos y médicos. A pesar de su frecuencia, sigue siendo poco diagnosticada y tratada, lo que conlleva graves consecuencias. Esta revisión destaca la importancia del diagnóstico y tratamiento temprano, abordando herramientas terapéuticas clave. Es importante reconocer la catatonia como una entidad clínica independiente para mejorar el abordaje clínico.

Palabras clave: *Catatonia. Benzodiacepinas. Terapia electroconvulsiva (TEC). Síndrome psicomotor. Diagnóstico.*

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Introduction

Catatonia a complex neuropsychiatric syndrome characterized by alterations in the motor, affective, and cognitive-behavioral areas. This syndrome is widely known in the psychiatric field, however, in the last years its conceptualization, diagnosis and treatment have been updated. Although often linked to schizophrenia, recent studies show that catatonia can also occur in various psychiatric and medical conditions, including mood disorders, neurological and autoimmune diseases, infections, and drug-related causes. This new conceptualization has led to updated diagnostic and therapeutic approaches, recognizing catatonia as a complex, multidisciplinary syndrome. However, detection remains clinically challenging, especially in non-psychiatric settings where symptoms may be mistaken for other conditions. This paradigm shift has important clinical implications, as misdiagnosis or delayed recognition can result in inadequate treatment, increasing morbidity and mortality.

The term *catatonia* was introduced in 1874 by German psychiatrist Karl Ludwig Kahlbaum (1828-1899), derived from the Greek *kata* ("down") and *tonos* ("tension"). He described 21 patients with unusual signs such as abnormal posturing, mutism, negativism, and catalepsy. Kahlbaum emphasized the affective component, noting that intense emotions often preceded catatonic episodes[1]. Emil Kraepelin (1856-1926) and Eugen Bleuler (1857-1939) advocated for including catatonia within dementia praecox (later termed schizophrenia) in psychiatric classifications. Kraepelin, particularly interested in its classification, defined catatonia as a subtype of dementia praecox in the sixth edition of his *Treatise on Psychiatry*. His work shaped the understanding of catatonia in the 19th and 20th centuries.

Following their contributions, catatonia was classified as a schizophrenia subtype marked by "prominent motor features" in systems such as the ICD and DSM[2]. In the past 20-30 years, interest in its features and underlying mechanisms has resurged[3]. The complexity of this syndrome, with its diverse forms of clinical presentation, makes it more likely to be identified not only in psychiatric units but also in general hospital settings, where it is more likely to be confused with other medical or neurological conditions. This underscores the importance of a comprehensive diagnostic and therapeutic approach.

Kahlbaum's original concept of catatonia as a complex syndrome involving affective, motor, and cognitive-behavioral dimensions, has been simplified by many clinicians, who focus mainly on motor/affective symptoms. Most clinical rating scales emphasize motor signs while neglecting affective and cognitive-behavioral aspects. Tools like the Bush-Francis Catatonia Rating Scale (BFCRS) prioritize features such as waxy flexibility and posture, leading to underrecognition of other critical symptoms. This narrow focus hinders early detection and treatment.

This conceptualization, focusing on motor or affective aspects of catatonia, is the one found in most of the current literature, which makes it difficult to provide adequate clinical care. The emphasis on motor signs tends to neglect affective and cognitive-behavioral symptoms, resulting in failure to detect catatonia, especially when motor features are not prominent. Consequently, this misperception can delay treatment initiation and may have negative consequences for patients.

Catatonia in the pediatric population is linked to significant morbidity and mortality. It is a distinct comorbidity seen in patients with genetic conditions, autism spectrum disorder (ASD), and other neurodevelopmental disorders. Fortunately, many cases respond well to timely treatment and interventions. However, diagnosing catatonia in this population presents challenges. Symptoms such as urinary incontinence, acrocyanosis, and schizophasia are frequently observed, but their presence can delay an accurate diagnosis. In addition, externalizing symptoms such as aggression and self-harm are more common in neurodiverse individuals with catatonia, further complicating clinical evaluation[4].

This review provides a comprehensive analysis of catatonia, reviewing its historical evolution, clinical presentation describing some particularities, pathophysiology, and current treatment strategies. By addressing current gaps in knowledge and emphasizing its broader clinical context, this article seeks to raise awareness and promote a reconceptualized approach to the recognition and treatment of catatonia in specialist and non-specialist physicians in the area.

Clinical manifestations

Since the presentation of catatonia may vary and present with different combinations of signs and symptoms, categorization must be individualized. Primarily, the evaluation focuses on a detailed observation of motor behaviors and the interaction of the patient with the evaluator and the environment. Within the examination, the evaluator must participate actively assessing the mobility, muscle tone, response to stimuli, and the ability to maintain or change postures. Furthermore, it is important to pay attention to the presence of automatic

behaviors (echolalia and echopraxia) or resistance to movement.

Signs of catatonia can be classified into three categories based on psychomotor behavior: increased, abnormal, and decreased, assessed by observation, interview, and physical examination (Table 1)[5]. Psychomotor behavior is considered abnormal when there is excessive reduction (akinesia), excessive increase (hyperkinesia), or when the motor act is presented abnormally (parakinesia)[6].

Many catatonic signs are triggered in response to the examiner and may depend on physical presence of the examiner. For example, the patient's mutism or hypokinesia may become more prominent in the presence of the evaluator but are typically transient, diminishing when the examiner leaves. An important feature of catatonia is the presence of autonomic abnormalities such as tachycardia, hypertension or fever but these are not present in all patients and particular attention should be paid to them due to their prognostic factor.

Pediatric considerations

With the pediatric population, it's important to keep in mind neurodevelopmental disorders, especially ASD. In these cases, the symptoms may overlap with catatonic syndrome, making clinical differentiation difficult. Careful assessment is required to determine whether episodes of aggression or regression represent a deviation from the patient's usual presentation or are simply part of their baseline symptomatology. Furthermore, autistic children with catatonia often exhibit increased impulsivity and aggression, adding another layer of complexity to diagnosis[7].

Clinically, catatonia in ASD manifests as a marked behavioral change, which helps distinguish it from baseline symptoms. However, overlapping features such as mutism, negativism, abnormal speech, rigid postures, and stereotypes can make differentiation challenging. A key diagnostic clue is that, in catatonia, these symptoms tend to appear suddenly or show significant deterioration compared to the patient's previous state. We summarize key points to take in mind for clinical evaluation in pediatric patients (Table 2)[4,8].

Treatment resistance is common in ASD-associated catatonia. Lorazepam response is often suboptimal. If antipsychotics are used, efficacy varies, and adverse effects must be carefully monitored[9].

This diagnostic approach not only helps to identify the clinical signs of catatonia but also distinguishes it from other neurological or psychiatric disorders with similar symptoms. Below are the main tests included in the directed examination for catatonia, which provide valuable information for the diagnosis and management of patient[9].

Catatonia can be classified into three different forms: akinetic catatonia, excitatory catatonia, and malignant catatonia, which depend on the intensity of the clinical manifestations and autonomic dysfunction. The most common form is akinetic catatonia, where patients show reduced motor activity, often staring and appearing unresponsive. Despite diminished reactions to verbal or painful stimuli, they remain conscious and aware. Contrary to common belief, many patients later recall these episodes, often describing them as distressing.

The second type is excitatory catatonia, which is characterized by an increase in the intensity of some signs, commonly observed when the patient presents apparently impulsive and aimless movements. Patients may show agitation, aggression, or even delirium. Excessive and intense motor activity can represent a danger to the patient as well as to others.

The third form characterized by being the most severe, malignant catatonia, is mainly characterized by autonomic instability, is often seen in the context of neuroleptic malignant syndrome (NMS) and may indicate an underlying medical condition that has a high mortality rate. Given its rapid progression, often in a matter of days, early recognition and immediate intervention are crucial to address the cause that generates it[10].

Another subtype described in the literature is periodic catatonia, marked by episodic fluctuations of motor symptoms such as rigidity, abnormal posture, and mutism lasting 4-10 days, followed by full remission. Its diagnosis is challenging due to the fluctuated nature. Dysfunction in the gamma-aminobutyric acid (GABA) system believed to underlie the condition, supported by positive responses to benzodiazepines. In some cases, atypical antipsychotics have also shown effectiveness[10].

A study in Mexico examined the coexistence of catatonia and delirium, conditions considered mutually exclusive in the DSM-5. Among 264 patients with delirium, 61 (23%) also met criteria for catatonia. Findings showed distinct associations: non-catatonic delirium was linked to brain tumors, subarachnoid hemorrhage, acute hydrocephalus, and ischemic stroke, while catatonic delirium was strongly associated with viral and anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis, epilepsy, and cerebral tuberculosis. An operational definition of catatonic delirium was proposed, requiring at least four specific signs on the BFCRS.

Table 1. This table outlines the 23 items of the Bush-Francis catatonia rating scale, along with the 12 DSM-5-TR items, marked with ✔. Additionally, it classifies the intensity of psychomotor activity and describes how each item can be assessed

Evaluation	Psychomotor activity	Concept	Definition	DSM-5 TR
Observation	Increased	Agitation, excitement	Extreme hyperactivity with unintentional movements and extreme, uncontrollable emotional reactions.	✔
		Impulsivity	The patient suddenly engages in inappropriate behaviors without provocation; afterward, they cannot provide an explanation or only offer a superficial one.	X
		Combativeness	Aggression toward others, with or without the potential to cause injury.	X
	Abnormal	Grimacing	Strange and inappropriate facial expressions, not in line with the context.	✔
		Mannerism	Exaggerated, rigid, or caricatured motor behavior that mimics normal actions in a strange or inappropriate manner.	✔
		Posturing	Spontaneous and active maintenance of a posture against gravity.	✔
		Sterotype	Repetitive and abnormally frequent movements that are not goal-directed.	✔
		Perseveration	Repetition, complete or partial, of actions or verbal content that is not goal-directed.	X
	Decreased	Stupor	No or markedly reduced psychomotor activity; no activity in relation to the environment.	✔
		Ambitendency	Appearance of being caught in indecisive or hesitant movements.	X
		Staring	Fixed gaze, reduced blinking, and wide-open eyes, or increased blinking.	X
Interview	Abnormal	Echolalia	Imitating another person's speech.	✔
		Echopraxia	Imitating another person's movements.	✔
		Automatic obedience	Mechanical and reproducible compliance with the examiner's requests, even if they are dangerous.	X
		Verbigeration	Continuous and undirected repetition of words, phrases, or sentences.	X
	Decreased	Withdrawal	No eye contact, refusal to take food or drink when offered, or both; turning away from the examiner or social isolation.	X
		Negativism	Opposition or lack of response to instructions or external stimuli.	✔
		Mutism	No or very little verbal response (exclude if aphasia is known).	✔
Physical examination	Abnormal	Mitgehen	Exaggerated movements in response to light pressure.	X
		Gegenhalten	Resistance to positioning by the examiner that increases proportionally to the force applied.	X
		Grasp reflex	Strong pressure of any object near the hand or touch.	X
		Rigidity	Resistance due to increased muscle tone.	X
		Catalepsy	Passive induction of a posture maintained against gravity.	✔
		Waxy flexibility	Mild and uniform resistance to positioning by the examiner.	✔
Autonomic abnormality			Diaphoresis, palpitations, abnormal temperature, blood pressure, pulse, respiratory rate.	X

Table 2. This table provides a quick and practical evaluation of the 14 key signs of catatonia and pediatric clinic considerations, aligned with the Bush-Francis catatonia rating scale. Ideal for initial screening in clinical or emergency settings

Initiating conversation	The examiner attempts to engage the patient in dialogue to assess for mutism, echolalia (involuntary repetition of another person's spoken words) or verbigeration (repetitive, meaningless utterance of stereotyped words or phrases).	Mutism may be confused with extreme anxiety or selective mutism. Echolalia may be an early sign of catatonia or a feature of autism spectrum disorder.
Exaggerated head scratching	The examiner scratches their head in an exaggerated manner, observing if the patient exhibits echopraxia (involuntary imitation of another person's movements or gestures).	Echopraxia may present as automatic repetition of movements from others or from media characters. It can be mistaken for playful imitation.
Muscle tone and posture tests	The patient is asked to relax their arm while the examiner observes for waxy flexibility (tendency to maintain limbs in positions in which they are placed, as if molded like wax), catalepsy (a state of muscular rigidity and fixed posture, with diminished response to stimuli), or gegenhalten (resistance to passive movement that increases proportionally to the force applied). The examiner may also attempt to change the patient's posture to assess rigidity or resistance.	Catalepsy may appear as unusual rigidity in forced positions, which could be misinterpreted as disinterest or extreme fatigue.
Arm extension test	The patient is instructed to extend their arms and maintain the position. The examiner then attempts to lift the arms, observing for mitgehen (the patient's arms moving involuntarily with the examiner's motion).	Mitgehen may be subtle and confused with an exaggerated response to physical contact or lack of motor control.
Negativism test	The examiner gives a simple instruction (e.g., 'raise your arm') and observes whether the patient does the opposite or resists without clear reason, indicating negativism (resistance or opposition to instructions or external stimuli, either actively or passively).	Negativism may be misinterpreted as oppositional behavior or stubbornness, especially in the context of neurodevelopmental disorders.
Response to painful stimuli	A mild painful stimulus (e.g., nail pressure) is applied to assess response; absence of reaction may indicate stupor (a state of unresponsiveness with immobility and mutism) or rigidity (sustained muscle tension with resistance to passive movement).	Lack of response to painful stimuli should be differentiated from pain desensitization seen in certain neurodevelopmental disorders.
Review of clinical records	Clinical records are reviewed for autonomic signs (e.g., fever, blood pressure changes) and reduced intake (e.g., food or fluids), which may indicate a catatonic state.	Dehydration and rapid weight loss may be key early signs, as catatonia can interfere with eating and hydration.

These results support the concept of catatonic delirium and challenge the DSM-5 classification of catatonia as a psychotic disorder. Given its strong association with autoimmune encephalitis and potential adverse reactions to antipsychotics, further studies are needed to reconsider DSM-5 criteria for catatonia due to another medical condition[11].

Recognizing the various forms of catatonia is key to accurate diagnosis and management especially in malignant catatonia, where early signs like autonomic instability are critical to prognosis. Symptom fluctuation in periodic catatonia adds diagnostic complexity, requiring close attention to the clinical course, even during apparent remission. Physicians must be aware that catatonia can present subtly or be masked by other psychiatric or medical conditions. A high index of suspicion and familiarity with the catatonic spectrum enable timely diagnosis and treatment, reducing the risk of life-threatening complications.

Epidemiology

The lack of a standardized definition and the diverse, overlapping symptoms of catatonia with other disorders make it difficult to assess its true incidence. Still, it is estimated to affect 5-18% of psychiatric inpatients and 3.3% of patients in tertiary neurology or neuropsychiatry units, with prevalence varying by underlying or comorbid conditions[12].

About 20% of reported cases of catatonia are a consequence of various general medical conditions. Infectious and autoimmune conditions (AIC) account for about 29% of cases related to medical causes. Among these, meningitis, encephalitis, and systemic bacterial, viral, or fungal infections are among the major contributors. AIC such as anti-NMDAR encephalitis and systemic lupus erythematosus show a strong association with catatonia. Notably, anti-NMDAR encephalitis accounts for 72% of autoimmune catatonia cases[13].

Given these statistics and the context, it would be prudent to initially consider catatonia in high-risk populations and use standardized tools for screening, particularly in non-psychiatric settings where it may be missed.

In recent years, there has been an increase in the reported incidence, which could be attributed to a higher prevalence of the disease, the increase in substance use, and the use of new psychotropic drugs and largely to changes in diagnostic criteria. Diagnostic heterogeneity, comorbidity with other disorders, and lack of case reporting are the main challenges in epidemiological research on catatonia[14].

Catatonia is rarely identified in pediatric patients (< 18 years) in general hospitals, often overshadowed by other serious medical and psychiatric conditions. A 2019 study in the USA reviewed 900 pediatric hospitalizations with a discharge diagnosis of catatonia (291 primary and 609 secondary). The mean age was 15.6 ± 2.6 years, with 9.9% under 13 years. The most common psychiatric diagnoses were psychotic disorders (18.3%), major depressive disorder (7.7%), bipolar disorder (4.3%), and substance-related disorders (2.2%) which make us consider psychotic disorders as the first suspicion in this population, unlike the adult population where affective disorders are the main cause[15].

Around 10% of people with ASD develop catatonia. This condition affects males much more frequently, making up between 70% and 100% of cases. It usually begins in late adolescence, most commonly between the ages of 15 and 19[7].

Catatonia in ASD frequently coexists with intellectual disability, with reported rates varying from 5.7% to 81%. In addition, obsessive-compulsive symptoms may precede catatonia, often accompanied by decreased speech, agitation, and self-injurious behavior[7].

In the older population, the prevalence of catatonia varies based on the setting and diagnostic criteria used. In liaison psychiatry services using the BFCRS, the prevalence was 5.5% and 8.9%. A study in an acute inpatient general psychiatry ward reported a prevalence of 11.2% with the BFCRS and 6.1% with DSM-5 criteria. The prevalence was higher in acute psychogeriatric units in the UK (27%) and Spain (24.3%), with the BFCRS and DSM-5 showing 39.6% and 20.8%, respectively[16].

Despite the diagnostic challenges, it is crucial to emphasize the significant clinical context across all age groups and the impact on morbidity and mortality.

Pathophysiology

It's important to understand the term "psychomotor," defined as the interaction between psychological processes and motor functions. In catatonia, this link is evident when psychological states, such as intense anxiety, manifest as motor disturbances such as paralysis, mutism, stupor, or catalepsy. This highlights how affective or cognitive changes can rapidly induce behavioral and motor disturbances.

The psychomotor nature of catatonia parallels neurodegenerative disorders such as Parkinson's and Huntington's disease, where non-motor symptoms (mood or cognitive disturbances) often precede and influence motor manifestations. Although modern brain models distinguish motor, affective, and cognitive networks, the complexity of catatonia suggests that these domains are interconnected, with frequent overlap[16].

The overlap of motor, affective, and cognitive symptoms in catatonia underscores the need for a broader neuropsychiatric perspective. Rather than viewing it solely as a movement disorder, its psychomotor features suggest dysfunction in brain circuits integrating emotion, cognition, and movement. This approach could improve diagnosis and treatment, highlighting the value of early detection and multimodal interventions.

Some theories propose that catatonia is a primitive defense mechanism – akin to tonic immobility in animals – triggered inappropriately by modern stressors. Its association with anxiety, depression, and responsiveness to benzodiazepines supports this view. Catatonia may represent a universal reaction to extreme threat, offering insights into broader psychiatric conditions[17]. Upcoming sections will explore the biochemical and neural mechanisms underlying its complex pathogenesis and treatment.

GABAergic dysregulation in catatonia

The potential mechanism that generates catatonia has been documented to be a dysregulation in the GABAergic system, particularly through the GABA-A and GABA-B receptors. A decrease in GABA-mediated inhibition can generate neuronal hyperexcitability, which

manifests with psychomotor symptoms and affective alterations. This substrate is consistent with the therapeutic quality of positive allosteric modulators of the GABA-A receptor[18,19].

Neuroanatomical pathways

Three key motor pathways are generally described in the pathophysiology of catatonia. The first pathway connects the primary motor cortex (M1) to the putamen, medial and lateral pallidum, and thalamus, and back to M1. This circuit is responsible for regulating the inhibition and intensity of movements. The second pathway connects M1, thalamus, cerebellum, and pontine nucleus, controlling the dynamics and timing of movements. The third pathway involves M1, the supplementary motor area (SMA), the posterior parietal cortex, and the medial prefrontal cortex, responsible for the organization and speed of movements. Dysfunction in any of these circuits may underlie the motor abnormalities observed in catatonia[20].

Dysregulation of the interaction between the SMA and the basal ganglia has been described in both schizophrenia and catatonia. In schizophrenia, reduced SMA activity is associated with motor deficits, whereas in catatonia, SMA hyperactivity has been detected, probably as a compensatory response to basal ganglia dysfunction. This hypothesis is supported by the efficacy of drugs such as lorazepam, which modulate basal ganglia activity and influence SMA function, resulting in improvement of motor symptoms[21].

Furthermore, in catatonia, reduced GABA activity, particularly at GABA-A receptors in the right lateral orbitofrontal cortex and right posterior parietal cortex, is thought to play an important role. This alteration in inhibitory signaling may explain both the motor and emotional symptoms characteristic of the syndrome. It also provides a rationale for the marked efficacy of benzodiazepines, which enhance GABAergic signaling and remain the cornerstone of catatonia treatment[21].

Catatonia results from both neuroanatomical and molecular dysfunctions. Hyperactivity in the SMA may compensate for basal ganglia deficits, while reduced GABA-A receptor activity disrupts inhibitory signaling in cortical regions. This dual disruption explains catatonia's varied symptoms and the effectiveness of benzodiazepines, which enhance GABAergic transmission and stabilize cortico-subcortical circuits[16]. These insights offer a unified framework linking molecular and anatomical factors in catatonia's pathogenesis and treatment.

Diagnosis

Catatonia is primarily diagnosed using the DSM-5-TR and ICD-11, though their criteria differ slightly. Clinimetric tools like the BFCRS are commonly used due to their accessibility and ease of use. In addition, therapeutic tests such as the lorazepam challenge are employed, with further details provided in the treatment section.

The DSM-5-TR classifies catatonia into three types: associated with another mental disorder, due to a medical condition, and unspecified catatonia. Diagnosis requires at least 3 of 12 defined symptoms. Rather than a standalone disorder, catatonia is recognized as a syndrome linked to various psychiatric and medical conditions[22].

ICD-11 classifies catatonia as an independent syndrome that can co-occur with various conditions, including psychiatric, medical, or substance-related disorders. Diagnosis requires at least three symptoms from categories of decreased, increased or abnormal psychomotor activity. It includes four subtypes: associated with mental disorders, substance/medication-induced, secondary catatonic syndrome, and unspecified catatonia[23].

Both classifications emphasize identifying catatonic signs and their link to medical or psychiatric conditions. The key difference is that DSM-5-TR links catatonia to underlying disorders, while ICD-11 treats it as an independent syndrome, allowing diagnosis without a clear cause. This reflects differing approaches: DSM-5-TR prioritizes etiology, whereas ICD-11 focuses on clinical presentation. Both systems are complementary, and their use depends on clinical context and professional needs.

A key innovation in ICD-11 is the inclusion of autonomic abnormalities, enabling the specification of malignant catatonia. ICD-11 also recognizes catatonia's temporal variability, which may present acutely, chronically, or fluctuate within a single episode. Unlike earlier versions, it allows a catatonia diagnosis even in the presence of delirium, if symptoms are not fully explained by it or another condition. These updates aim to enhance diagnostic sensitivity and promote earlier recognition across diverse clinical settings[24].

A summary table will be added below comparing the diagnostic criteria for catatonia according to DSM-5-TR and ICD-11, highlighting the main differences and similarities between both systems (Table 3)[22,23].

A systematic review identified seven rating scales for assessing catatonia in clinical settings: the Modified Rogers Catatonia Scale, the Rogers Catatonia Scale, the Northoff Catatonia Rating Scale (NCRS), the Braunig Catatonia Rating Scale (BCRS), the Kanner Scale, and the BFCRS[25].

Table 3. Provides a clear and concise comparison of the diagnostic approaches to catatonia in the ICD-11 and DSM-5-TR, highlighting their similarities and differences

Aspect	ICD-11	DSM-5-TR
Classification	Independent syndrome or associated with other disorders	Specifier for other mental or medical conditions
Symptom criteria	3 or more symptoms for at least 24 h	3 or more symptoms, no minimum duration specified
Etiology	Allows catatonia without a specific cause	Always requires an underlying cause
Focus	More flexible and descriptive	More tied to specific disorders
Subtypes	Catatonia associated with mental disorders, drug-induced, secondary, and unspecified	Catatonia associated with mental disorders, due to another medical condition, and unspecified
Autonomic symptoms/ Clinical course	Includes autonomic dysfunction and allows diagnosis even with delirium if catatonia is distinct	Doesn't emphasize autonomic symptoms; catatonia is excluded if better explained by delirium

Among these, the BFCRS, NCRS, and BCRS demonstrated the highest reliability across diverse populations. Another study evaluated three diagnostic tools the Bush-Francis screening instrument (BFCSI), the BFCRS, and the DSM-5 highlighting the superior sensitivity of the BFCSI in detecting catatonia cases. Notably, the DSM-5 criteria failed to identify nearly 64% of cases, underscoring the need for more precise diagnostic approaches in clinical practice[26,27].

BFCRS is a widely used tool for identifying and assessing the severity of catatonia. Comprising 23 items 14 of which form the screening instrument (BFCSI), it is valued for its ease of use, strong interrater reliability, and clinical validity. Its strong sensitivity and specificity make it effective in minimizing false positives, making it essential in psychiatric and neurology settings for early detection[28].

BFCRS is administered through direct observation of behaviors during clinical assessment and neurological examination. While it is typically scored over a minimum period of 5 min, it also allows for the incorporation of data on autonomic disturbances and withdrawal documented in nursing records from the previous 24 h[25].

Complementary studies

At present, there are no imaging studies or biomarkers sensitive enough to diagnose catatonia. Small clinical studies have investigated associations with inflammatory and acute-phase markers in catatonia but their role remains inconsistent.

A large-scale retrospective study found that patients with catatonia had lower serum iron levels compared to other psychiatric inpatients (11.6 vs. 14.2 μmol/L) and significantly elevated creatine kinase levels (2545 vs. 459 IU/L), suggesting potential muscle damage, secondary to motor symptoms. Notably, no significant differences were observed in C-reactive protein (CRP) or white cell count, indicating that systemic inflammation may not be a primary feature of catatonia[14].

Studies have found moderately elevated CRP and D-dimer levels in catatonic patients, suggesting inflammation and a potential risk of venous thromboembolism. Increased creatine kinase may result from muscle rigidity or immobility, raising the need to distinguish catatonia from NMS. Low serum iron, linked to dopamine synthesis, is also associated with higher NMS risk. While these biomarkers lack diagnostic specificity, they may aid in understanding mechanisms or assessing risk when interpreted carefully[13,29].

Although not routinely used, electroencephalography (EEG) has been employed to assess catatonia. A meta-analysis of 355 studies (707 patients) evaluated its role in distinguishing medical from psychiatric causes. In larger studies ($n \geq 5$), EEG showed 82% sensitivity and 66% specificity for medical causes (AUC = 0.83); smaller studies ($n < 5$) showed 76% sensitivity and 67% specificity (AUC = 0.71). Findings such as limbic abnormalities, epileptiform discharges, and non-convulsive status epilepticus were highly specific for medical catatonia. Encephalopathic slowing, seen in 23% of psychiatric cases, had moderate specificity. While EEG alone is insufficient for diagnosis, it can aid in uncertain cases when combined with clinical and complementary evaluations, helping differentiate organic from psychiatric origins[30].

Medical and psychiatric workup for pediatric catatonia

A thorough clinical evaluation is essential and should include multiple diagnostic studies. Brain magnetic resonance imaging (MRI) with and without contrast, pelvic or scrotal ultrasound, EEG, lumbar puncture, and comprehensive serum laboratory tests should take in mind. Other

assess antinuclear antibodies, antithyroid peroxidase antibodies (anti-TPO), antithyroglobulin antibodies, complete blood count, complete metabolic panel, myelin oligodendrocyte glycoprotein antibodies, NMDAR antibodies, and erythrocyte sedimentation rate could be helpful.

Given the high prevalence of genetic comorbidities in pediatric catatonia, genetic consultation is recommended whenever available. Post-operative catatonia has been reported in some cases and should be considered as part of the differential diagnosis.

Drug withdrawal or exposure can also trigger catatonia. Cases have been reported in infants following vaccine administration. In children, implicated drugs include haloperidol, ondansetron, and cyclosporine. Meanwhile, in adolescents, catatonia has been associated with chlorpromazine, benztropine, and olanzapine[31].

Autoimmune encephalitis is a closely related comorbidity that should always be considered in the evaluation of catatonia. While some treatment approaches overlap, key distinguishing factors include the use of immunomodulators, seizure occurrence, and the presence of an extreme brush-delta pattern on EEG[32].

Treatment

Catatonia treatment focuses on three main areas: managing the syndrome itself primarily with benzodiazepines or electroconvulsive therapy (ECT) addressing underlying medical or psychiatric conditions and preventing complications from immobility or psychomotor agitation. Lorazepam is a key treatment regardless of cause. Early intervention is crucial, as prolonged illness may reduce responsiveness, making prompt treatment essential[33,34].

Benzodiazepines

As previously noted, catatonia involves GABAergic system dysregulation, making benzodiazepines the gold standard treatment. These drugs modulate GABA receptors, with lorazepam being the most commonly used, typically in doses ranging from 6 to 24 mg[35]. Diagnostic tests, such as the lorazepam test, can help clarify the diagnosis. Lorazepam, a nonselective positive allosteric modulator of GABA-A receptors, is an effective and widely available diagnostic tool. It may be administered intravenously (1-2 mg), intramuscularly (1-2 mg), or orally (2 mg), although oral administration is slower and may be less practical for hyperkinetic or hypokinetic patients[33,35]. A positive response to the lorazepam challenge test, typically defined as a 50% reduction in catatonic signs on a standardized scale, supports the diagnosis of catatonia but is not completely specific. A strong response on the 1st day often predicts overall success of lorazepam treatment (Table 4)[33,36,37].

Table 4. Lorazepam challenge

Step	Action	Details
Baseline assessment	Assess catatonic features	Use a standardized instrument
Lorazepam administration	Administer lorazepam	1-2 mg IV 1-2 mg IM 2 mg orally
Reassessment	Reassess catatonic features	At 5 min (IV) At 15 min (IM) At 30 min (oral)
Response evaluation	Determine positive response	50% reduction in standardized catatonia score
Follow-up	If no positive response	Consider another lorazepam challenge (preferably parenteral) and reassess

In children, the lorazepam challenge has been described, and it should be initiated when the pediatric catatonia rating scale or the BFCRS indicate four or more positive items with a score above zero. If autonomic instability is present, malignant catatonia must be suspected. This severe condition carries a mortality rate of 10-20% if untreated. In such cases, intensive care management and urgent consideration of ECT are necessary[38]. In the largest study of lorazepam testing for pediatric catatonia, Luccarelli et al. evaluated 54 pediatric patients[39]. A significant response was observed, with mean BFCRS scores decreasing from 16.6 ± 6.1 to 9.5 ± 5.3 following lorazepam administration (Hedges' g = 1.20; 95% confidence interval: 0.85-1.55). Dosages ranged from 0.5 to 2 mg, with a mean of 0.029 mg/kg. Higher doses required close monitoring for potential side effects such as excessive sedation, paradoxical disinhibition, or glycol toxicity. A refractory or partial response to benzodiazepines is more common in patients with comorbid neurodevelopmental disorders or chronic catatonia[39].

The British Association for Psychopharmacology (BAP) recommends benzodiazepines as first-line treatment for catatonia, with several routes of administration available, including oral, sublingual, intramuscular, and intravenous. The choice of route should be individualized to the patient's clinical context and drug

availability. Lorazepam is generally the benzodiazepine of choice for treating catatonia. In some cases, high doses exceeding the usual prescribed range may be necessary to achieve optimal symptom relief. A trial of treatment is considered appropriate when catatonia has significantly improved, dose titration has been stopped due to side effects, or a daily dose of at least 16 mg has been reached.

Benzodiazepines should be tapered gradually to avoid withdrawal and minimize long-term risks. The tapering pace should balance therapeutic benefit with the risk of rapid reduction. If catatonic symptoms return, underlying conditions must be reassessed and treated. Zolpidem is also effective, particularly in lorazepam- or ECT-resistant cases, with a typical dose of 10 mg (or 5 mg for older adults) and effects lasting 3-6 h[33,40].

ECT

ECT has been used since the middle of the last century and is effective in cases with poor response to pharmacological treatments, with response rates of 80-100%, although efficacy is lower in cases where treatment is delayed. For patients with catatonia who see little or no benefit from benzodiazepine treatment, ECT remains the gold standard[41]. ECT might be considered earlier in the treatment algorithm if the situation is emergent, such as malignant catatonia. Response rates generally range from 80% to 100%.

Its high response rates warrant strong consideration in psychiatric and medical units where it is available. While benzodiazepines are first-line, delays in recognizing catatonia or initiating treatment may worsen outcomes, emphasizing the need for early intervention. In settings with access to ECT, its integration into treatment protocols (especially in cases of malignant or benzodiazepine-resistant catatonia) may improve outcomes.

Better outcomes are associated with younger age, autonomic dysfunction, and greater initial severity, while prolonged illness and neurological conditions may reduce responsiveness. If ECT fails, an underlying neurological disorder should be considered. Catatonia linked to mood disorders generally responds better to ECT than schizophrenia-related cases, though combining ECT with clozapine may improve outcomes. Variability in treatment response highlights the need for individualized care. The rapid response to ECT and benzodiazepines suggests catatonia may reflect a shared neurological endpoint involving maladaptive hyperexcitability, with ECT modulating cortical excitability and disrupting pathological synaptic activity[42].

There is no standardized ECT protocol for catatonia. Most evidence supports a robust approach with bitemporal, short pulse width, and high intensity stimulus ECT. Alternative locations, such as right unilateral stimulation or ultra-brief pulsatile stimulation, have been used, but their efficacy compared to bitemporal ECT remains unclear. Cognitive side effects are not usually a priority in cases of life-threatening catatonia. ECT is typically administered 3 times/week, with increased frequency in malignant catatonia. Adjustments to stimulus intensity are made if the duration of the seizure response is < 25 s.

ECT is effective in children, adolescents, and older adults, with response rates of approximately 75% in younger populations. While its use in pediatric populations requires careful consideration, available evidence supports its safety and efficacy in severe cases of catatonia[43].

Pediatric ECT is indicated for malignant or treatment-resistant catatonia. Bitemporal electrode placement is recommended, with sessions typically conducted 2-3 times/week. However, higher frequency may be required in some cases[38].

Other treatments

When first-line treatments for catatonia are unavailable or ineffective, the BAP guidelines recommend alternatives such as NMDAR antagonists (amantadine or memantine). Other options include levodopa, dopamine agonists, mood stabilizers (e.g., carbamazepine, valproate, and topiramate), or second-generation antipsychotics (SGAs). Antipsychotics should be avoided unless treating an underlying psychotic disorder, and used cautiously due to the risk of NMS. SGAs, especially clozapine, are preferred if antipsychotics are necessary. Caution is advised in patients with low serum iron or NMS history, particularly in pediatric cases, where gradual introduction and concurrent benzodiazepine use are recommended[44,45].

Future research directions

Future research on catatonia should focus on the following areas: (1) genetic and epigenetic studies, including genome-wide association analyses, to identify susceptibility loci and molecular mechanisms underpinning catatonic syndromes across populations. (2) Development of rapid diagnostic and screening tools validated for both pediatric and adult

populations, such as the Catatonia Quick Screen, to enable earlier detection in diverse clinical settings. (3) Multimodal neurobiological research, combining functional imaging (fMRI, PET) with biomarker analysis and genetic data, to map the neural circuits and biochemical pathways involved. (4) Rigorous evaluation of treatment strategies, including randomized trials of benzodiazepines, NMDA antagonists, Z-drugs, antipsychotics, and non-pharmacological interventions (e.g., TMS), with attention to safety and efficacy in children and adults. (5) Strengthened interdisciplinary collaboration – involving psychiatrists, neurologists, pediatricians, psychologists, and allied health professionals – to develop comprehensive care models, improve training, and promote timely recognition across all clinical settings.

Conclusion

This review highlights the heterogeneous presentation of catatonia, emphasizing the importance of recognizing clinical signs for optimal treatment. Early intervention with benzodiazepines or ECT is critical to improving outcomes. Clinicians, in general, must be sensitized to its varied manifestations to reduce diagnostic delays and prevent complications.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

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