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## Research Article

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# Catatonia in Autism Spectrum Disorder from Preschool to Adolescence: A Retrospective Analysis of Clinical Profiles and Management Outcomes

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## Abstract

**Background:** Catatonia is increasingly recognized in autism spectrum disorder (ASD), yet it remains poorly characterized in children, particularly those of preschool age, hindering early recognition and treatment.

**Methods:** We conducted a retrospective cohort study of 40 children with ASD and catatonia (aged 47 months–18 years) to delineate the clinical profile, with particular attention to developmental-stage-specific manifestations, and to preliminarily evaluate outcomes of clinical management.

## Results:

The cohort was predominantly male (65%), and 30% were preschool-aged, demonstrating that catatonia occurs across the pediatric age range. Symptom profiles showed a distinct age-associated pattern: stereotypy, negativism, and agitation were common across ages, whereas mutism decreased significantly with age ( $FDR\text{-}p^* = .001$ ) and posturing increased among older children ( $FDR\text{-}p^* < .001$ ). Precipitating factors, predominantly psychosocial stressors, were identified in 85% of cases. Among patients receiving lorazepam combined with psycho-ecological therapy, 82.4% showed improvement, although individual responses varied.

**Conclusion:** Catatonia can occur in children with ASD as young as preschool age, with symptom profiles that differ across development. Early identification of psychosocial triggers is paramount. Our retrospective data suggest that an integrated management model—short-term lorazepam combined with long-term psycho-ecological therapy—is associated with clinical improvement and may benefit a substantial subset of patients. These findings provide a foundational clinical profile of catatonia in young children with ASD and underscore the importance of early intervention.

Keywords: autism; catatonia; children; symptom profiles; psychosocial triggers; treatment response

## Introduction

Catatonia, first described by Kahlbaum in 1874, is a complex psychomotor syndrome characterized by a range of atypical motor, vocal, and behavioral manifestations. It presents transdiagnostically across various medical and neuropsychiatric conditions and is associated with significant functional impairment

and long-term adverse consequences [1-3] .

There is growing recognition of catatonia as a significant comorbid syndrome in individuals with autism spectrum disorder (ASD) [3, 4–8]. In a subset of patients with ASD, a period of relative stability in childhood may be followed by marked functional regression during adolescence or early adulthood, with catatonia identified as a frequent cause of such deteriorative courses[9]. Reported prevalence rates of catatonia in ASD vary, with systematic reviews indicating figures between 12% and 20%, influenced by the assessment tools employed [4,5,7,10]. Notably, these estimates are considered conservative, likely reflecting under-recognition among clinicians managing ASD populations [11].

Although catatonic symptoms in ASD most commonly emerge in adolescence and early adulthood, onset can occur at other developmental stages, including earlier childhood [6]. Despite its clinical severity, catatonia remains underdiagnosed in pediatric ASD populations, partly due to its perceived rarity and overlapping symptomatology with core autistic features [12].

To date, systematic research on catatonia in children and adolescents with ASD remains sparse. Only one study has specifically focused on this pediatric population [13], while a few others have included younger participants within broader samples [7,10,14–18]. Among these, the largest reported cohort comprises 45 cases, with a minimum age of 6 years [7, 10,14–18]. Isolated case reports have also documented symptom onset as early as 6 years of age [19]. Consequently, there is a substantial evidence gap regarding developmental-stage-specific manifestations, underlying etiology, and effective treatment strategies for catatonia in pediatric ASD.

The Child Development and Behavior Center (CDBC) of the Third Affiliated Hospital of Sun Yat-Sen University was established in 1999 as the first center in China dedicated to clinical practice in developmental-behavioral pediatrics. It is currently one of the largest level 3 developmental-behavioral pediatric diagnostic and treatment centers in mainland China.

CDBC specializes in the assessment and intervention of neurodevelopmental disorders, with a core focus on the evaluation and support for autism spectrum disorder (ASD). With nearly 25 years of clinical experience, the center provides over ten thousand clinical consultations annually for children with neurodevelopmental disorders and their families from across the country. It has accumulated tens of thousands of cases nationwide, including many rare and complex conditions such as catatonia.

This study aims to bridge this gap by characterizing the demographic and clinical profiles of catatonia in children with ASD, identifying age-specific symptom patterns and precipitating factors, and evaluating acute treatment responses. The findings are expected to enhance clinical recognition and inform management approaches for this under-researched comorbidity in pediatric populations.

## **Methods**

### **Study Design and Setting**

This single-center retrospective cohort study was conducted at the Children's Development and Behavior Center of the Third Affiliated Hospital of Sun Yat-sen University. The study protocol was approved by the hospital's Medical Ethics Committee (#II2024-132-01), and the requirement for informed consent was waived due to the retrospective nature of the research.

### **Participants**

Participants included children and adolescents aged 3–18 years who were diagnosed with autism spectrum disorder (ASD) accompanied by symptoms of catatonia between January 1, 2017, and March 31, 2025. Cases were identified by querying the clinical medical record system of the hospital.

Inclusion criteria consisted of: 1) A documented diagnosis of ASD based on DSM-5 or ICD-10

criteria[20,21]; 2) Presence of at least three catatonic symptoms according to the DSM-5 diagnostic criteria for catatonia associated with another mental disorder[20].

Exclusion criteria included: presence of organic brain disorders, primary psychotic or mood disorders, other neurodevelopmental disorders not attributed to ASD, Substance-induced catatonia.

**Data Collection**

Demographic and clinical data were extracted from electronic medical records, including: Gender, age at visit, chief complaint, and previous diagnoses, identified onset triggers, clinical symptoms at presentation (core ASD symptoms, catatonic features, and developmental-behavioral manifestations), results of clinical assessments, family history, and family environmental conditions, laboratory test results, electroencephalogram (EEG), and brain imaging findings, details of interventional treatments and follow-up information. Follow-up data were collected from hospital records, outpatient notes, and telephone follow-up records until April 2025.

**Statistical Analysis**

Descriptive statistical analyses were performed using R Language, R version 4.4.1 (2024-06-14 ucrt). Categorical variables were summarized as frequencies and proportions. A series of Fisher’s exact tests was employed to compare the prevalence of each of the 12 catatonic symptoms across the three age groups (preschool, school-age, adolescent), given the small sample sizes in some subgroups. These tests were also applied to analyze primary treatment outcomes and to explore potential prognostic factors.

**Results**

**Demographic and Clinical Characteristic**

A total of 40 children and adolescents diagnosed with ASD and exhibiting symptoms of catatonia were included in this study. All patients sought medical attention for the current episode due to observed regression or significant abnormalities in language, social functioning, and/or behavior. Clinical suspicion of ASD with comorbid catatonia was initially raised in the outpatient department, following which comprehensive assessments and examinations were completed. ASD diagnosis was confirmed in all cases through evaluation with the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule-Second Edition (ADOS-2), supplemented by detailed history-taking and behavioral observations conducted by specialists in developmental and behavioral pediatrics. Accordingly, all patients met the DSM-5 diagnostic criteria for autism spectrum disorder. Furthermore, all patients in the cohort demonstrated documented symptoms meeting criteria for catatonia based on comprehensive medical histories and behavioral observations. Standardized assessment in 36 cases revealed substantial symptom severity: one patient scored 17 on the Bush-Francis Catatonia Rating Scale (BFCRS) [22], while the remaining 35 cases evaluated with the Pediatric Catatonia Rating Scale (PCRS) [23] showed scores ranging from 10 to 24 (mean: 15.1). Notably, only one case scored 10 on the PCRS, meeting the DSM-5 diagnostic threshold with three catatonic symptoms.

The sample was predominantly male, with a male-to-female ratio approaching 2:1. Participants ranged in age from 47 months (youngest) to 18 years, encompassing 12 preschool-aged children, 11 school-aged children, and 17 adolescents. Among school-aged and adolescent children, 20 (71%) were enrolled in general education schools. A family history of neurological or psychiatric disorders was reported in 14 cases. Detailed demographic and clinical characteristics of the cohort are summarized in Table 1.

**Table 1. Demographic and Clinical Characteristics of Children and Adolescents with ASD and**

**Catatonia (N=40)**

| <b>Characteristic</b>                                | <b>n (%)</b> |
|------------------------------------------------------|--------------|
| <b>Sex</b>                                           |              |
| Male                                                 | 26 (65.0)    |
| Female                                               | 14 (35.0)    |
| <b>Age Group</b>                                     |              |
| Preschool (< 6 years)                                | 12 (30.0)    |
| School-age (6–10 years)                              | 11 (27.5)    |
| Adolescence (10–20 years)                            | 17 (42.5)    |
| <b>School Attendance</b>                             |              |
| General School                                       | 20 (50.0)    |
| Special School                                       | 3 (7.5)      |
| Kindergarten                                         | 17 (42.5)    |
| <b>Family History</b>                                |              |
| Schizophrenia or Psychotic Disorder                  | 5 (12.5)     |
| Mood Disorder                                        | 3 (7.5)      |
| ASD                                                  | 3 (7.5)      |
| Intellectual Disability                              | 2 (5.0)      |
| Epilepsy                                             | 2 (5.0)      |
| Speech and Language Delay                            | 2 (5.0)      |
| <b>Onset Form</b>                                    |              |
| Acute (< 2 weeks)                                    | 3 (7.5)      |
| Subacute (2 weeks – 3 months)                        | 12 (30.0)    |
| Chronic ( $\geq$ 3 months)                           | 25 (62.5)    |
| <b>Previous Diagnosis</b>                            |              |
| ASD                                                  | 23 (57.5)    |
| Global Developmental Delay / Intellectual Disability | 6 (15.0)     |
| Other Neurodevelopmental Disorders*                  | 7 (17.5)     |
| Mental Disorder                                      | 3 (7.5)      |
| Autoimmune Encephalitis                              | 2 (5.0)      |
| Mood Disorder                                        | 1 (2.5)      |
| No Previous Diagnosis                                | 8 (20.0)     |
| <b>Current Principal Diagnosis</b>                   |              |
| ASD + Catatonia                                      | 32 (80.0)    |
| ASD + Suspected Catatonia                            | 6 (15.0)     |
| ASD Only                                             | 2 (5.0)      |
| <b>Comorbid Diagnoses</b>                            |              |
| Intellectual Disability                              | 7 (17.5)     |
| Mood Disorder                                        | 5 (12.5)     |
| Tic Disorder                                         | 6 (15.0)     |
| ADHD                                                 | 3 (7.5)      |
| Psychotic Disorder                                   | 2 (5.0)      |
| OCD                                                  | 1 (2.5)      |
| Anxiety Disorder                                     | 1 (2.5)      |

|              |         |
|--------------|---------|
| Epilepsy     | 1 (2.5) |
| Malnutrition | 3 (7.5) |

*Note: ADHD = Attention-Deficit/Hyperactivity Disorder; ASD = Autism Spectrum Disorder; OCD = Obsessive-Compulsive Disorder.*

*\*\*Other Neurodevelopmental Disorders included speech and language delay, pervasive developmental disorder, tic disorder, and ADHD.*

## 2. Age related clinical profile and Catatonic Symptoms

Figure 1 illustrates the prevalence of individual DSM-5 catatonia symptoms across the entire cohort (N=40). The most frequent symptoms, each present in more than half of the patients, were stereotypy (n=33, 82.5%), mutism (n=31, 77.5%), agitation (n=30, 75.0%), negativism (n=30, 75.0%), stupor (n=24, 60.0%), and posturing (n=20, 50.0%). Less common symptoms included echolalia (n=12, 30.0%), while grimacing and mannerisms (each n=5, 12.5%), catalepsy (n=4, 10.0%), waxy flexibility (n=2, 5.0%), and echopraxia (n=1, 2.5%) were relatively rare.

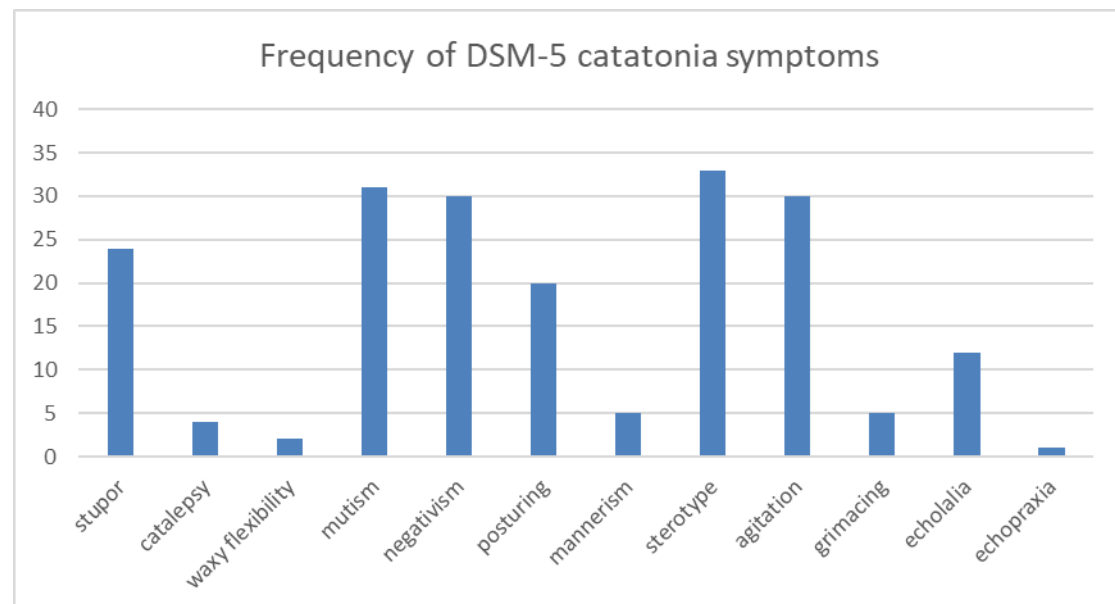


Fig. 1 Frequency of DSM-5 catatonia symptoms

Developmental variations in catatonic symptom profiles were observed across age groups (Figure 2). Stereotypy, negativism, and agitation were consistently present across all developmental stages. However, distinct patterns emerged: mutism was highly prevalent in preschool (100%) and school-aged children (100%) but less common in adolescents (47%), whereas posturing showed an opposite trend, being most frequent in adolescents (94%) but rare in younger children. Stupor became notably more prevalent from school age onward (73% in school-aged children, 65% in adolescents).

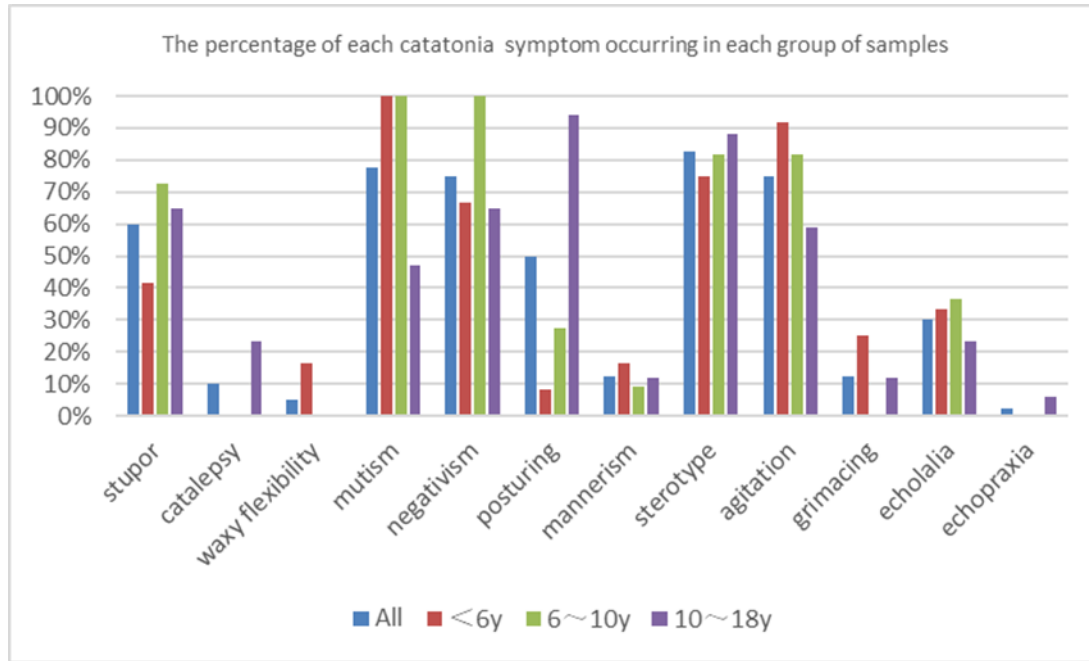


Fig. 2 The percentage of each catatonia symptom occurring in each group of samples

Statistical analyses using Fisher's exact tests with FDR correction revealed that only two of the twelve catatonic symptoms showed significant differences across age groups. A clear developmental divergence was observed: mutism decreased significantly with age (FDR- $p^* = .001$ ), whereas posturing increased markedly in older children (FDR- $p^* < .001$ ). These opposing trends reflect a distinct phenotypic shift from speech inhibition in young children to increased motor symptomatology in adolescents. The p-values from the Fisher's exact tests, both before and after FDR correction, are presented below (Table 2).

Table 2. Statistical Comparison of 12 Catatonic Symptoms Across Age Groups in Children with ASD

| Symptom          | Preschool<br>(<6y) | School<br>(6-10y) | Adolescent<br>(10–20y) | P-Value1<br>(Unadj.) | P-Value2<br>(FDR) | Sig.       |
|------------------|--------------------|-------------------|------------------------|----------------------|-------------------|------------|
| Stupor           | 5 (41.7%)          | 8 (72.7%)         | 11 (64.7%)             | 0.3019               | 0.45279           | ns         |
| Catalepsy        | 0 (0%)             | 0 (0%)            | 4 (23.5%)              | 0.0567               | 0.21594           | ns         |
| Waxy Flexibility | 2 (16.7%)          | 0 (0%)            | 0 (0%)                 | 0.1551               | 0.31026           | ns         |
| Mutism           | 12 (100%)          | 11 (100%)         | 8 (47.1%)              | <b>&lt;0.001</b>     | <b>0.00143</b>    | <b>**</b>  |
| Negativism       | 8 (66.7%)          | 11 (100%)         | 11 (64.7%)             | 0.0720               | 0.21594           | ns         |
| Posturing        | 1 (8.3%)           | 3 (27.3%)         | 16 (94.1%)             | <b>&lt;0.001</b>     | <b>&lt;0.001</b>  | <b>***</b> |
| Mannerism        | 2 (16.7%)          | 1 (9.1%)          | 2 (11.8%)              | 1.0000               | 1.00000           | ns         |
| Stereotype       | 9 (75%)            | 9 (81.8%)         | 15 (88.2%)             | 0.7749               | 0.92990           | ns         |
| Agitation        | 11 (91.7%)         | 9 (81.8%)         | 10 (58.8%)             | 0.1034               | 0.24823           | ns         |
| Grimacing        | 3 (25%)            | 0 (0%)            | 2 (11.8%)              | 0.2446               | 0.41935           | ns         |
| Echolalia        | 4 (33.3%)          | 4 (36.4%)         | 4 (23.5%)              | 0.7487               | 0.92990           | ns         |
| Echopraxia       | 0 (0%)             | 0 (0%)            | 1 (5.9%)               | 1.0000               | 1.0000            | ns         |

Figure 3 illustrates the distribution of catatonic symptoms per patient, with the number of symptoms ranging from three to eight across the cohort. The majority of patients exhibited five or six symptoms. Specifically, twelve patients (30.0%) presented with six symptoms, ten (25.0%) with five symptoms, eight (20.0%) with three symptoms, seven (17.5%) with four symptoms, two (5.0%) with eight symptoms, and one (2.5%) with seven symptoms.

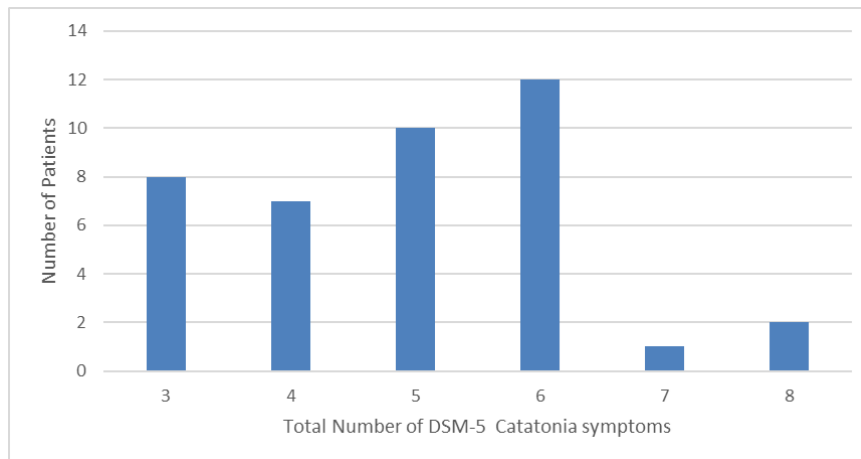


Fig. 3 Frequency of total number of DSM-5 catatonia symptoms

Beyond core catatonic criteria, a range of accompanying behavioral symptoms was observed (Figure 4). Social withdrawal was the most frequently identified feature. Other commonly documented manifestations included a marked increase in repetitive language, inappropriate or context-free laughter, a significant reduction in previous interests, motor stuckness, food refusal, sleep disturbances, diminished spontaneous activity, urinary incontinence, movement initiation difficulties, cognitive or memory regression, unexplained crying, and self-injurious behavior (SIB).

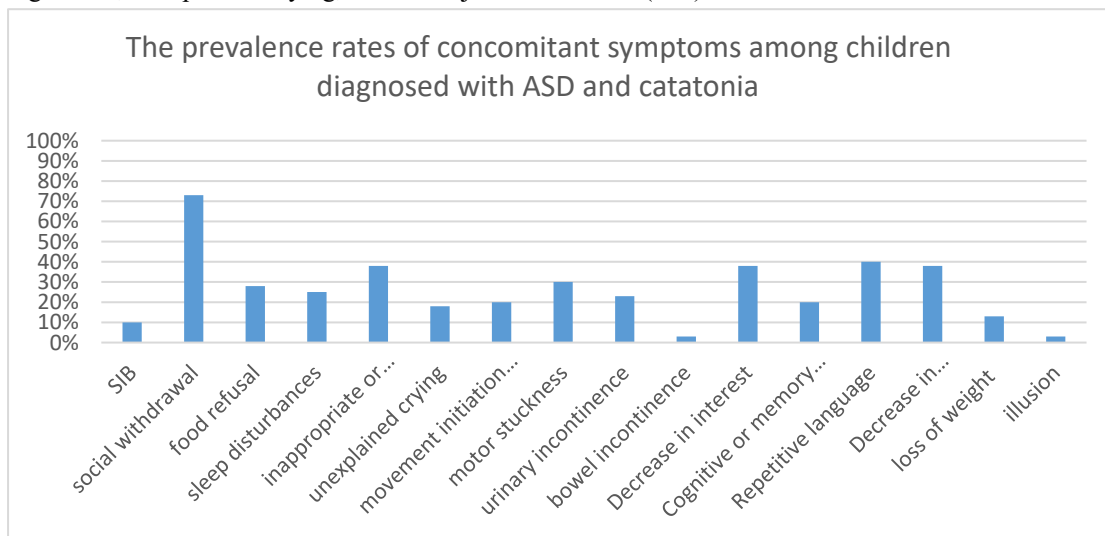


Fig. 4 The prevalence rates of concomitant symptoms among children diagnosed with ASD and catatonia

### 3. Precipitating Factors for Catatonia in Children with ASD

Identifiable precipitating factors for catatonic symptoms were documented in the majority of cases (Table 3). Psychosocial stressors constituted the most common category of triggers (90%). Psychosocial factors referred to identifiable external events or chronic situations that imposed demands misaligned with the patient's neurodevelopmental capacities, thereby inducing significant stress. These included interpersonal conflicts (e.g., bullying, parental criticism), academic/social pressures, disruptions to routine (e.g., school transitions, changes in caregivers), and significant adverse life events (e.g., bereavement). The specific coded factors in this sample primarily involving chronic stress situations such as parental criticism or punishment, peer bullying, academic or social pressures, bereavement, and anxiety triggered by negative information; changes in daily routine or living environment exemplified

by transitions such as starting or changing kindergarten, alterations in teaching or caregiving staff, separation from caregivers at bedtime, school closures, or hospitalization. Physiological factors (20%), including infection, general discomfort, physical trauma, and endocrine changes (e.g., menstruation), were also noted. A small subset of cases (10.0%) had no clearly identifiable trigger.

Table 3. Distribution of identified precipitating factors for catatonia in children with ASD (N=40)

| Precipitating Factor             | n (%) (double for some) |
|----------------------------------|-------------------------|
| Psychosocial factors             | 36 (90.0)               |
| Physiological factors            | 8 (20.0)                |
| No clearly identifiable triggers | 4 (10.0)                |

#### 4. Laboratory and Diagnostic Investigations

A comprehensive diagnostic workup was performed, including hematological tests (complete blood count, biochemistry, liver and renal function, ammonia, thyroid function, immunological and infection markers), urinalysis, cerebrospinal fluid (CSF) analysis, electroencephalography (EEG), magnetic resonance imaging (MRI), and genetic/chromosomal testing. The results of these investigations are summarized in Table 3.

Table 3. Laboratory and Diagnostic Findings in Children with ASD and Catatonia (N=40)

| Test Category                | Completed (n) | Normal (n) | Abnormal (n, %) | Key Findings                                                                                                                                                                                                                                                                        |
|------------------------------|---------------|------------|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Body Fluid Analyses *</b> | 35            | 35         | 0 (0.0)         | All parameters within normal limits; autoimmune encephalitis antibodies negative in all 7 suspected cases                                                                                                                                                                           |
| <b>EEG</b>                   | 31            | 19         | 12 (38.7)       | <ul style="list-style-type: none"> <li>Borderline findings: 5</li> <li>Mildly abnormal: 6 (19.4%) predominantly atypical sharp waves or diffuse slow-wave activity</li> <li>Significantly abnormal: 1 (3.2%) with epileptiform discharges (confirmed epilepsy diagnosis)</li> </ul> |
| <b>Brain MRI</b>             | 33            | 23         | 10 (30.3)       | <ul style="list-style-type: none"> <li>Arachnoid cysts: 4</li> <li>Enlarged cavum septum pellucidum: 2</li> <li>Minor gliotic foci: 5 †</li> <li>White matter hyperintensities: 1</li> <li>Suspected pituitary nodule: 1</li> </ul>                                                 |
| <b>Genetic Testing (WES)</b> | 8             | 5          | 3 (37.5)        | <ul style="list-style-type: none"> <li>VUS: SLC6A8 hemizygous</li> <li>Likely pathogenic: HERC2 heterozygous</li> <li>VUS: AARS2, CHD8</li> </ul>                                                                                                                                   |

**Abbreviations:** CSP = Cavum Septum Pellucidum; WM = White Matter; WES = Whole-Exome Sequencing; VUS = Variant of Uncertain Significance.

\*Body fluid analyses included: hematology, biochemistry, liver/kidney function, ammonia, metabolic panel, thyroid function, immunology, infection markers, urinalysis, and CSF analysis.

†Gliotic foci locations: Left frontal (2), Right parietal (1), Bilateral frontoparietal (1), Bilateral parieto-occipital (1).

‡Non-completion: Body fluids (n=5), EEG (n=9), MRI (n=7), Genetic (n=32).

*Note: All MRI abnormalities were considered incidental findings without apparent clinical correlation to catatonic symptoms.*

## 5. Clinical Management Strategies and Follow-up Outcomes

All patients received psycho-ecological therapy (PET), consisting of ASD-adapted interventions, environmental modifications, identification and removal of potential stressors, catatonia-specific support strategies, and parental psychoeducation [11,24,25]. Only one preschool-aged patient (4 years) demonstrated improvement with PET monotherapy, while the remaining 39 cases (97.5%) required adjunctive pharmacotherapy.

Treatment response was evaluated at 1-month post-intervention using standardized criteria: Complete remission denoted full functional recovery to premorbid levels; Marked improvement indicated significant progress in  $\geq 2$  behavioral domains; Some improvement represented amelioration of  $\geq 2$  regressive behaviors; Minimal improvement involved amelioration of  $\geq 1$  regressive behavior; and No change reflected no measurable behavioral improvement.

As summarized in Table 4, risperidone monotherapy (n=5) showed limited efficacy, while lorazepam-based regimens (n=34) demonstrated substantially better outcomes. Primary efficacy analysis using Fisher's exact test revealed a significantly higher response rate (defined as marked or some improvement) in children treated with the lorazepam-based regimen (82.35%) compared to those receiving risperidone monotherapy (20.0%) (\*p\*=0.011). Despite the imbalanced group sizes (5 vs. 34), the difference remained statistically significant.

Mann-Whitney U sensitivity analysis showed that the lorazepam-based regimen demonstrated significantly superior overall performance compared to risperidone monotherapy across ordinal efficacy categories (Wilcoxon W = 37.5, \*p\* = 0.032), further supporting its role as the preferred option for short-term treatment of ASD with catatonia. This conclusion carries both statistical and clinical significance.

**Table 4. Short-term Pharmacotherapy Response in ASD with Catatonia (N=40)**

| Treatment Regimen              | n  | Marked Improvement | Some Improvement | Minimal Improvement | No Change | Other Adjunctive Agents (n) |
|--------------------------------|----|--------------------|------------------|---------------------|-----------|-----------------------------|
| <b>Risperidone monotherapy</b> | 5  | 1 (20.0%)          | 0                | 2 (40.0%)           | 2 (40.0%) | None                        |
| <b>Lorazepam-based therapy</b> | 34 | 9 (26.5%)          | 19 (55.9%)       | 5 (14.7%)           | 1 (2.9%)  | 9 (26.5%)†                  |

*Treatment response criteria:*

*Marked improvement: Significant progress in  $\geq 2$  behavioral domains; Some improvement: Amelioration of  $\geq 2$  regressive behaviors; Minimal improvement: Amelioration of  $\geq 1$  regressive behavior; No change: No measurable behavioral improvement*

*† Other adjunctive agents (Polypharmacy) : Some improvement subgroup (n=6): Required adjunctive medications for comorbid conditions (oxcarbazepine:1, risperidone:4, valproate:4, aripiprazole:1, quetiapine:1); Minimal improvement subgroup (n=2): One switched to diazepam; one received add-on risperidone for tic disorder; No change case: Later responded to fluvoxamine and risperidone augmentation.*

The cohort exhibited varied follow-up periods: >3 years (n=7), 1-3 years (n=10), 6-12 months (n=6), and 1-3 months (n=4), with 13 patients (32.5%) lost to follow-up. Symptomatic recurrence of catatonia

occurred in 6 patients (15.0%), predominantly among adolescents (n=5, 83.3% of recurrences), including two with comorbid mood disorders and one with psychotic disorder. One school-aged child (age 9) also experienced recurrence.

Outcomes at the most recent follow-up assessment were defined as follows:

Good: Restoration of near-baseline premorbid functioning with minimal support required for daily living and academic activities.

Fair: Measurable socio-educational progress achieved under structured support, despite persistent significant abnormalities in emotional regulation or interpersonal functioning.

Poor: Developmental stagnation or regression with severe emotional-behavioral disturbances substantially compromising adaptive functioning.

The distribution of outcomes and associated factors are detailed in Table 5.

Table 5. Outcomes at Most Recent Follow-up and Associated Factors

| Outcomes          | n (%)    | Age at Onset Distribution (n) |            |            | Key Comorbidities (n) | Follow-up Duration (n) |         |          |         |
|-------------------|----------|-------------------------------|------------|------------|-----------------------|------------------------|---------|----------|---------|
|                   |          | Preschool                     | School-age | Adolescent |                       | >3 yrs                 | 1-3 yrs | 0.5-1 yr | <0.5 yr |
| Good              | 7(18.0)  | 4                             | 2          | 1          | 1†                    | 3                      | 3       | 1        | 0       |
| Fair              | 8(20.0)  | 4                             | 2          | 2          | 0                     | 1                      | 2       | 4        | 1       |
| Poor              | 12(30.0) | 1                             | 3          | 8          | 12‡                   | 3                      | 5       | 1        | 3       |
| Lost to follow-up | 13(32.5) | 3                             | 4          | 6          | 8 #                   |                        |         |          |         |

†Mood disorders (n=1); ‡Mood disorders (n=6), Psychotic disorders (n=5), Epilepsy+ADHD (n=1);

# Mood disorders (n=1); Psychotic disorders (n=1), ADHD (n=2), Intellectual disorders (n=4), Tic disorders (n=5).

Associations between selected factors and long-term functional outcomes (Good vs. Fair/Poor) were examined using a series of Fisher's exact tests. In this sample, no statistically significant associations were found between long-term outcomes and the following variables: recurrence of catatonia, lorazepam monotherapy, or polypharmacy.

Two factors showed trend-level associations: 1) Diagnostic complexity was associated with a lower likelihood of a "Good" outcome (OR = 0.11, 95% CI [0.00, 1.15]; \*p\* = 0.073), suggesting that comorbid psychiatric/neurological conditions may reduce the probability of favorable functional recovery; 2) Age ≤ 6 years at onset/intervention showed a trend toward a better prognosis (OR = 6.41, 95% CI [0.76, 88.52]; \*p\* = 0.069), indicating that preschool onset and early intervention may be linked to improved long-term outcomes. These results should be interpreted cautiously due to the limited sample size and wide confidence intervals, which highlight the need for replication in larger cohort.

## Discussion

This case series elucidates the complex clinical presentation and management challenges of catatonia in children with autism spectrum disorder (ASD), with particular implications for younger populations. The predominant manifestation of severe behavioral dysregulation and functional regression necessitating clinical intervention underscores the critical nature of this comorbidity. Our findings reveal substantial developmental heterogeneity in catatonic symptom expression and highlight the profound functional deterioration associated with this condition.

### **Epidemiology and Diagnostic Challenges**

Contrary to previous reports suggesting catatonia primarily emerges after age 10 in ASD [3-7], our data demonstrated that while peak incidence occurs during adolescence, catatonia can manifest across all developmental stages. The substantial proportion of preschool-aged children (30%) in our sample indicates that catatonia is not uncommon in early childhood. The male predominance (65%) aligns with both ASD epidemiology and prior catatonia literature (70–100%) [4,5,7,13,16,17,26], reflecting potential sex-specific vulnerabilities.

The diagnostic challenges observed in our cohort are particularly noteworthy. Most cases exhibited chronic or subacute onset, and while all presented with clear catatonic symptoms, prior diagnoses varied widely across neurodevelopmental, mood, and psychotic disorders, and autoimmune encephalitis—with only half having an established ASD diagnosis. The fact that only 80% received a definitive catatonia diagnosis during evaluation reveals significant under-recognition among clinicians. This diagnostic ambiguity likely stems from the insidious and complex manifestation of catatonia in ASD, which demonstrates substantial phenotypic overlap with other conditions, and the developmental variations in symptom expression. In our cohort, approximately 50% of the children attended mainstream schools, which typically suggests the absence of significant co-occurring intellectual disability. This finding contrasts with a recent report indicating that 91.1% of individuals with ASD and catatonia also have intellectual disability [18]. Furthermore, eight children in our sample developed catatonia following psychosocial stressors without any prior formal diagnosis. This pattern suggests that even individuals with normative intellectual ability and subtle autistic traits—due to their distinct cognitive and perceptual profile—may be particularly vulnerable to catatonic deterioration under adverse environmental circumstances.

### **Developmental Trajectory and Clinical Presentation**

Our findings reveal age-related symptom patterns of catatonia in ASD. While stereotypies, negativism, and agitation were common across all ages, mutism predominated in younger children whereas posturing and stupor became more prominent with increasing age. This pattern suggests that classic motor features of catatonia may be developmentally mediated, with younger children exhibiting more speech atypicality and fewer typical motor signs, whereas older children and adolescents demonstrate more pronounced motor symptoms, including stupor and posturing that are consistent with previous literature [4,8,13,14]. To better understand the natural progression of catatonia in ASD, future research should prioritize longitudinal studies that systematically track symptom evolution from childhood through adulthood.

The associated behavioral features observed—social withdrawal, echolalia, diminished interest, and others—largely align with existing literature [8], though repetitive self-injury was less prevalent in our younger cohort compared to reports involving older populations [12,17]. This difference may reflect developmental variations in symptom expression or sampling biases.

### **Etiological Considerations and Precipitating Factors**

The etiological understanding of catatonia in ASD remains limited. Our laboratory investigations yielded predominantly normal or non-specific findings, consistent with the previous few case reports [19,27]. The 35% rate of neuropsychiatric family history and emerging evidence of genetic overlap between ASD, catatonia, and major psychiatric disorders suggest shared susceptibility factors, though specific genetic mechanisms require further elucidation through genome-wide approaches.

Notably, identifiable precipitating factors were present in most cases, predominantly psychosocial stressors, followed by changes in routine or environment. This aligns with prior clinical observations

[4,28] and supports the hypothesis that sustained stress from adverse life events is a key trigger [29]. This observation supports the hypothesis that ASD individuals, due to their unique cognitive and perceptual characteristics, may experience ordinary environmental challenges as significant stressors, potentially overwhelming their regulatory capacities and precipitating catatonic states [24,27]. This underscores the critical importance of understanding ASD-specific cognitive profiles, identifying and mitigating environmental triggers (including sensory and social stressors), maintaining predictable routines, and providing supportive environments to prevent catatonia.

### **Treatment Considerations and Long-term Outcomes**

Benzodiazepines and electroconvulsive therapy (ECT) are first-line acute and maintenance treatments for catatonia [2,25,30]. In our data, short-term lorazepam-based treatment demonstrated significantly superior overall performance compared to risperidone monotherapy across ordinal efficacy categories, supporting its role as the preferred option for short-term treatment of ASD with catatonia. This treatment response supports the GABAergic dysfunction theory as a potential common biological mechanism underlying both catatonia and ASD [31]. Our findings somewhat contrast with literature suggesting less robust responses to benzodiazepines in ASD-related catatonia [16]. In our sample, younger age, presence of slow movement/stupor, acute onset, absence of comorbid psychiatric conditions, and higher lorazepam doses appeared associated with better response. Our results, like those in earlier literature, emphasizes the need for early, effective treatment [25,31,32].

Additionally, in this sample, some children improved with low-dose atypical antipsychotics (e.g., risperidone), and those with comorbid psychotic or mood disorders often required adjunctive antipsychotics for effective management (the single use of lorazepam often did not yield satisfactory results), consistent with previous reports [33,34]. Thus, the variable response to lorazepam may relate to age, symptom subtype, onset pattern, comorbidity, and dosing, necessitating larger prospective studies to evaluate efficacy across different subtypes and treatment regimens. The absence of ECT utilization in our cohort reflects ongoing ethical considerations in pediatric populations.

In the present study, all families received structured psychoeducation emphasizing the importance of long-term psycho-ecological therapy. During follow-up, symptomatic recurrence occurred in a subset of patients, with advancing age emerging as a potential risk factor. Developmental stage and psychiatric comorbidity may influence outcomes: preschool onset and early intervention generally demonstrated more favorable prognosis, whereas adolescents and those with co-occurring emotional or behavioral disorders experienced less favorable outcomes. Nevertheless, these results should be interpreted cautiously due to the limited sample size and wide confidence intervals, which highlight the need for replication in larger cohort. The bipolar distribution of longer follow-up duration—concentrated in either excellent or poor outcome cases—likely reflects both better adherence to psycho-ecological therapy in the former group and the need for repeated medical interventions in more severe, functionally impaired cases.

These findings collectively support a comprehensive management model for catatonia in ASD that integrates acute pharmacological approaches with sustained, individualized psycho-ecological support. The demonstrated association between earlier intervention and improved long-term outcomes underscores the critical importance of timely detection and treatment initiation to prevent chronicity and minimize functional deterioration.

### **Limitations and Future Directions**

This study has several limitations inherent to its retrospective design and single-center nature. The relatively small sample size, absence of a control group, and limited biological data constrain the generalizability of findings. The inability to assess intellectual functioning during acute catatonic episodes precluded analysis of its relationship with symptom severity. Future studies should employ prospective, longitudinal designs to systematically investigate the neurobiological mechanisms, susceptibility traits, and environmental factors contributing to catatonia in ASD. Such research would provide a stronger evidence base for developing targeted interventions and preventive strategies for this vulnerable population.

## **Conclusion**

In summary, our findings demonstrate that catatonia can occur in children with ASD at any age, including preschool years, and exhibits developmental variations in clinical presentation. Psychosocial factors represent crucial triggers, while integrated treatment approaches combining pharmacological and psycho-ecological interventions show promise. Early recognition and developmentally- sensitive intervention is essential for improving outcomes in this complex neuropsychiatric condition.

## **Declarations**

### **Ethics approval and consent to participate**

This study was reviewed by the medical ethics committee of the third affiliated hospital of Sun Yat-sen University (#II2024-132-01), with a waiver of informed consent from participants as data which was collected was based on retrospective routine clinical activities.

## **Author contributions**

LY designed the study, analyzed and interpreted data, and was a major contributor to writing the manuscript draft. XY contributed to data collection, organization, analysis and interpretation as well as writing the manuscript. LX participated in the work of data collection and organization. ZH contributed to data analysis, the writing and revision of the manuscript, and funding acquisition. DH contributed to the study design and funding acquisition. ZX contributed to the study design and conception, funding acquisition, draft reviewing, supervision of the overall research project, and final draft revision. All authors read and approved the final manuscript.

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## **Consent for publication**

Not applicable.

### **Competing interests**

The authors declare that they have no competing interests.

### **Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### **Clinical trial number**

Not applicable.

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