



## Clinical Review Article

# Catatonia in Dementia: A Systematic Review of Case Reports and Case Series

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## ABSTRACT

**Background:** Catatonia is a neuropsychiatric syndrome characterized by motor, behavioral, and autonomic abnormalities. It is often underdiagnosed in geriatric patients with dementia despite established diagnostic criteria and treatment options. **Objective:** This systematic review investigates catatonia in the elderly, particularly those with dementia, to examine their clinical presentation, treatment response, and prognosis compared to elderly patients without dementia. **Methods:** We comprehensively searched MEDLINE and EMBASE, including case reports and series on catatonia in elderly patients. Reviewers independently performed data extraction and quality assessments. Statistical significance was set at a  $p$  value  $\leq 0.05$ , and a multivariate logistic regression model was used to analyze differences between patients with and without dementia. **Results:** Our review included 182 articles with 225 cases. We found no significant differences in the clinical presentation of catatonia between patients with and without dementia, with both groups commonly exhibiting the hypokinetic variant. However, patients with dementia were more frequently treated with NMDA receptor antagonists (OR: 3.27; CI: 1.05–10.11;  $p = 0.040$ ) and had a lower complete response rate to treatment (OR: 0.37; CI:

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0.19–0.75;  $p = 0.006$ ). Patients with dementia also exhibited fewer acute medical conditions (OR: 0.17; CI: 0.05–0.65;  $p = 0.009$ ). **Conclusions:** Catatonia in dementia does not have a different syndromic presentation. However, the diagnosis of dementia leads to varying preferences regarding the choice of symptomatic therapy and seems to be a predictor of a poorer therapeutic response. Actively treating catatonia, particularly in patients with dementia, addressing the characteristics of these patients is of paramount importance. (Am J Geriatr Psychiatry 2024; 32:1297–1308)

### Highlights

- **What is the primary question addressed by this study?**  
What are the clinical features of catatonia in patients with dementia?
- **What is the main finding of this study?**  
Catatonia in dementia does not have a different syndromic presentation. However, the diagnosis of dementia leads to varying preferences regarding the choice of symptomatic therapy and seems to be a predictor of a poorer therapeutic response.
- **What is the meaning of the finding?**  
Actively treating catatonia, particularly in patients with dementia, addressing the characteristics of these patients is of paramount importance and may contribute to a better overall prognosis.
- **Twitter**  
This systematic review investigates catatonia in the elderly. Dementia influences treatment choices for catatonia and seems to be a predictor of a poorer therapeutic response.

## INTRODUCTION

Catatonia is a complex neuropsychiatric syndrome first described by Karl Kahlbaum in 1874.<sup>1,2</sup> It encompasses motor, behavioral, and autonomic abnormalities in general medical, neurological, and psychiatric conditions or because of medications and substance use.<sup>3,4</sup> This syndrome manifests through a diverse array of clinical features, with common signs including immobility, staring, rigidity, mutism, negativism, and refusal to eat or drink. Less frequently observed symptoms can also be found, including stereotypy, impulsivity, excitement, waxy flexibility, echolalia, and echopraxia.<sup>4</sup>

Two primary catatonia variants are distinguished based on predominant psychomotor abnormalities: the hypokinetic or retarded-stuporous variant and the hyperkinetic or excited variant.<sup>4</sup> The former is characterized by reduced movement, mutism, and withdrawal, commonly associated with depressive disorders and general medical conditions. In contrast,

the latter involves increased, aimless motor activity, confusion, and frequent autonomic dysfunction, often observed during manic episodes.

The contemporary concept of catatonia has evolved significantly.<sup>5,6</sup> In Diagnostic and Statistical Manual—Fifth Edition (DSM-5),<sup>7</sup> catatonia is diagnosed in association with another mental disorder, secondary to a general medical condition, and catatonia not otherwise specified. The International Classification of Diseases—11th Edition (ICD-11) classifies catatonia as a new independent diagnostic group.<sup>8</sup> Diagnosing and treating catatonia in geriatric patients poses unique challenges.<sup>9</sup> Confounding factors such as somatic and cognitive comorbidities, *delirium*, and the concurrent use of multiple medications are frequent in this population.<sup>10</sup> Timely recognition and appropriate treatment, particularly in the elderly, are crucial, as failure to diagnose catatonia may adversely affect somatic outcomes and lead to fatal consequences.<sup>11</sup> Disappointingly, the available literature on catatonia in elderly patients is surprisingly scarce, as only mainly case reports and small case series deal with catatonia in geriatric patients. This information

was compiled in a significant systematic review on catatonia in the geriatric population, published in 2022.<sup>10</sup> Given that dementia is arguably the most pertinent geriatric syndrome and can coexist with the diagnosis of catatonia,<sup>12,13</sup> it is intriguing that the literature on this topic is similarly scarce and once again based on clinical cases and case series.<sup>14,15</sup> This issue is particularly pertinent because dementia and catatonia are frequently considered differential diagnoses rather than co-diagnoses,<sup>16,17</sup> particularly in the latter stages,<sup>17</sup> which naturally has implications for treatment and prognosis. Therefore, it seems especially relevant to understand how catatonia can be clinically defined in patients with dementia, which therapeutic approaches for catatonia treatment are being used, and what prognosis is associated with catatonia in dementia. To study these inherently more clinical and detailed aspects, we deemed it necessary to conduct a systematic review of clinical cases and case series in the geriatric population, with a cross-sectional design, where we could compare clinically, therapeutically, and diagnostically, elderly patients with catatonia with and without dementia. (Fig. 1)

## METHODS

### Protocol and Registration

A systematic search of MEDLINE and EMBASE was conducted, adhering to the recommendations outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) protocol and is registered in the PROSPERO online database (PROSPERO Identifier: CRD4202124779118).<sup>18</sup>

### Review Questions

The primary review questions were:

1. Does catatonia in patients with dementia has a different syndromic presentation compared to catatonia in other conditions?
2. Does catatonia in patients with dementia has a different treatment approach when compared to catatonia in other conditions?
3. Does catatonia in patients with dementia has a different treatment response when compared to catatonia in other conditions?

The secondary review questions were:

1. Does catatonia in patients with dementia occur more frequently associated with previous psychiatric history when compared to catatonia in other conditions?
2. Does catatonia in patients with dementia occur more frequently associated with antipsychotic exposure when compared to catatonia in other conditions?
3. Does catatonia in patients with dementia occur more frequently associated with acute or chronic medical conditions when compared to catatonia in other conditions?

### Search Strategy and Information Sources

The scope of our search was restricted to peer-reviewed case reports and case series on human subjects in English, Portuguese, Italian, and Spanish published between January 1994 and March 2021. Editorials, letters to the editor, literature reviews, systematic literature reviews, systematic reviews, and meta-analyses were excluded (Supplement 1).

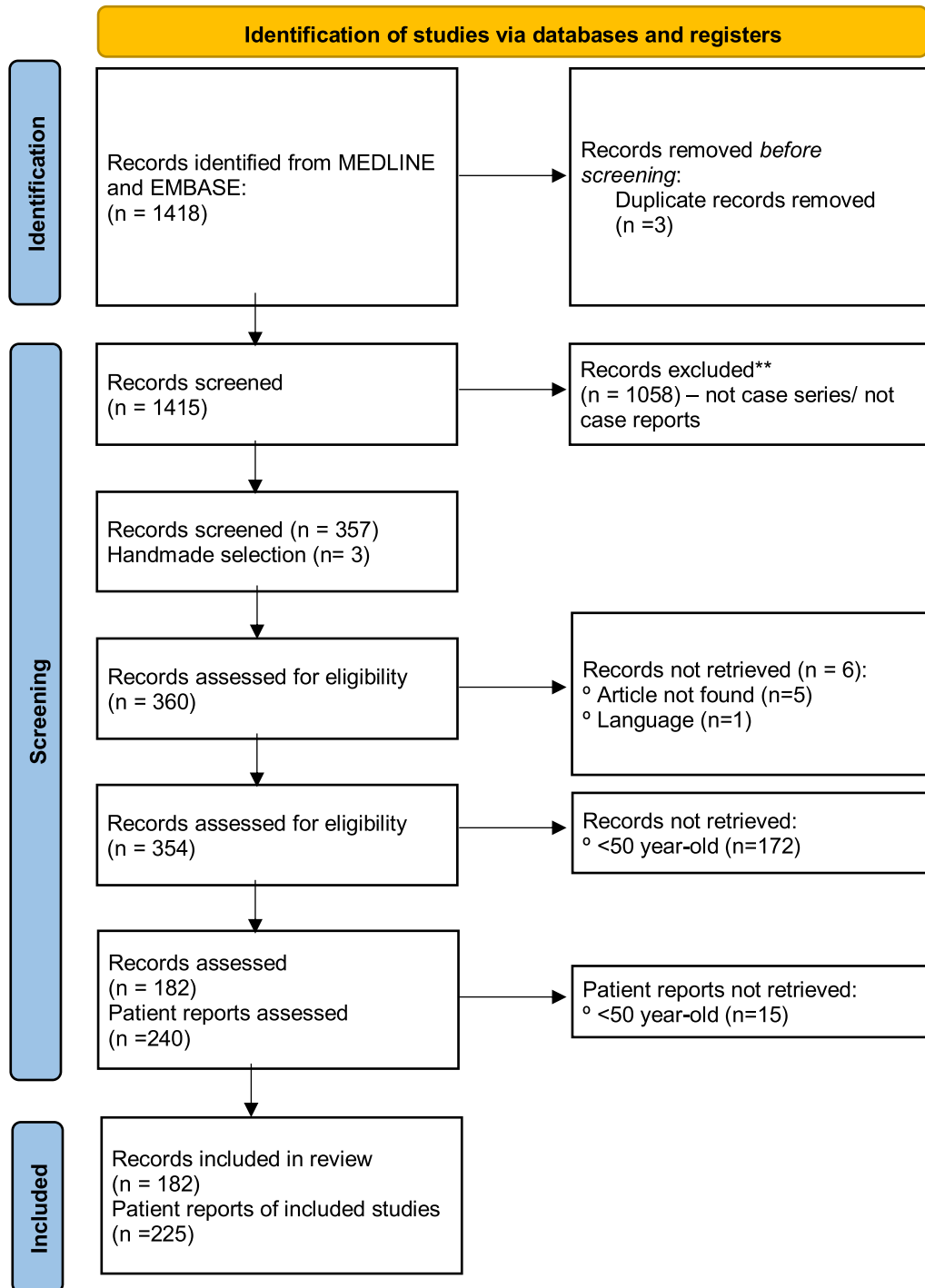
### Eligibility Criteria

We included case reports and case series that met the following inclusion criteria: 1) adult patients (50 ≥ years) and 2) catatonia based on clinical diagnosis or diagnosis using specific criteria, including the Fink and Taylor criteria,<sup>6</sup> Bush–Francis Catatonia Rating Scale,<sup>19</sup> Diagnostic and Statistical Manual - Fourth Edition (DSM-IV),<sup>20</sup> Diagnostic and Statistical Manual—Fourth Edition, text revision (DSM-IV-TR),<sup>21</sup> International Classification of Diseases—10th Edition (ICD-10),<sup>22</sup> and DSM-5. Malignant/Lethal Catatonia, Neuroleptic Malignant Syndrome, Periodic Catatonia, and Delirious Mania were considered special forms of catatonia and were, therefore, included in the review.

Patients were included in the dementia group if, additionally, they have been diagnosed with dementia or major neurocognitive disorders based on clinical diagnosis or using the DSM-IV, DSM-IV-TR, ICD-10, or DSM-5 criteria.

We use 50 years old or older as a cut-off since the frequency of dementia is very low before 50, and the incidence of catatonia due to other causes (especially schizophrenia) is relatively high.<sup>23</sup>

FIGURE 1. PRISMA flow diagram showing the process of identification of included studies.



### Study Selection

Two reviewers (BCR, PCP) conducted the initial screening search, identifying, screening, and selecting abstracts using the Rayyan software.<sup>24</sup> After duplicate removal, 360 catatonia case reports were identified and evenly distributed among six independent reviewers (BCR, CC, IS, FN, MJE, PCP) for full-text appraisal. To mitigate bias, each case underwent review by two independent reviewers, and consensus within the team resolved discrepancies.

Among the screened reports, 225 cases focused on patients over 50 years of age with catatonia, meeting additional inclusion criteria such as demographic details, clinical symptoms, treatment measures, treatment response, and, when present, a clearly defined dementia subtype—additionally, articles needed to report effect sizes (ES) or provide enough numerical information for computation.

### Data Extraction

Data extraction used a standard extraction table covering author names, country, journal and publication year, method of obtaining catatonia data, subject's age and gender, prior dementia diagnosis, previous psychiatric or neurological disorders, acute or chronic medical conditions, and past exposure to antipsychotic drugs. Information on the method of diagnosing catatonia, its age of onset, duration, clinical symptoms and subtype, blood test results, neuroimaging findings, treatment methods, and the subject's treatment response were recorded. Catatonic symptoms were characterized using the Bush–Francis Catatonia Rating Scale (BFCRS) terminology, and clinical symptoms were coded using the Medical Dictionary for Regulatory Activities (MedRA) Preferred Terms (PTs).

### Quality of Studies

Two reviewers (MJE, PCP) employed a modified version of the Methodological Quality and Synthesis of Case Series and Case Reports Protocol, proposed by Murad et al., to assess the methodological quality of each article.<sup>25</sup> The Protocol questions unrelated to our review's scope, specifically "Was there a challenge/rechallenge phenomenon?" and "Was there a dose-response effect?" were omitted. Articles were

systematically classified based on a scoring system ranging from 0 to 6, with <3, 3–4, and >4 scores denoted poor, moderate, or good quality, respectively (Supplement 2). All articles meeting the predefined criteria for minimum patient information requirements were considered for further analysis.

### Data Analysis

The collected data were entered into a Microsoft Excel spreadsheet (version 2021; Microsoft Corporation, Redmond, WA) and analyzed using Stata software (version 14.2; StataCorp, Texas, USA). Values were generally expressed as a percentage and as the number of patients. Using all variables of interest as predictors, Fisher's exact test was used to determine the variables that showed statistically significant differences between patients with and without dementia. Using stepwise selection, a multivariate logistic regression model was then created with the variables that showed association. A  $p$  value  $\leq 0.05$  was considered statistically significant.

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## RESULTS

The systematic review included 182 articles, encompassing data on 225 patients. Using the Murad tool for quality assessment,<sup>25</sup> 48% of the articles were classified as good quality, 44% as moderate, and 7% as poor.

Demographic details of the population are outlined in Table 1, revealing a mean age of 62 years (range 50–92), with 122 patients (54%) identified as female. Twenty-four patients, constituting approximately 11% of the total study population, had a concurrent dementia diagnosis. Among the dementia subtypes, frontotemporal dementia (FTD) (29%) and Lewy body dementia (LBD) (17%) were the most frequently associated with catatonia.

After performing Fisher's exact test, four variables were identified as statistically significant (Treatment with Anti-NMDA, Complete Treatment Response, Psychiatric Comorbidity, and Acute Medical Conditions). They were thus incorporated into the multivariate logistic regression model. In this initial analysis, the variable Psychiatric Comorbidity demonstrated no statistical significance (OR: 0.59; CI: 0.21–1.67;  $p = 0.316$ ) and was subsequently removed from the

**TABLE 1. Demographic Features**

	<b>Dementia Group (N = 24)</b>	<b>Nondementia Group (N = 201)</b>
<b>Age</b>		
Mean	67	62
Minimum	51	50
Maximum	88	92
<b>Gender</b>		
Female	12 (50%)	110 (55%)
Male	12 (50%)	91 (45%)
<b>Dementia subtype</b>		
Alzheimer's dementia	2 (8%)	
Vascular dementia	2 (8%)	
Mixed dementia	1 (4%)	
Lewy body dementia	4 (17%)	
Frontotemporal dementia	7 (29%)	
Unknown	8 (33%)	

model. In the final analysis, the remaining three variables retained their statistical significance (Table 3).

### Clinical Features of Catatonia

Regarding the clinical manifestations of catatonia (Table 2), no statistically significant differences were found between patients with and without dementia, as outlined in Table 3. Across both groups, the hypokinetic variant emerges as the predominant subtype, accounting for 58% of dementia patients and 70% of those without dementia, with an overall occurrence of 68%. The most reported catatonic symptoms in patients with dementia were mutism (83%), rigidity (58%), and immobility (54%). In patients without dementia, the most frequent symptoms were mutism (74%), immobility (67%), and negativism (43%). Additionally, 17% of patients with dementia and 20% of patients without dementia presented with special forms of catatonia. Neuroleptic Malignant Syndrome was identified as the most common special form in both groups.

### Treatment Regimens

When comparing catatonia treatment regimens between patients with and without dementia, benzodiazepines were the most frequently chosen therapeutic strategy in both groups, encompassing 69% of all patients (75% in the dementia group and 68% in the nondementia group), followed by Electroconvulsive

Therapy (ECT) encompassing 34% of all the patients (33% in dementia patients, and 34% in nondementia patients). Finally, NMDA receptor antagonists (memantine or amantadine) were used in 11% of all catatonia cases in this review. However, significantly more patients with dementia received NMDA receptor antagonists (33%) compared with patients without dementia (8%) (OR: 3.27; CI: 1.05–10.11; p = 0.040).

### Catatonia Prognosis

Most patients (74%) exhibited a complete resolution of catatonic symptoms with the treatment. However, patients with dementia had a significantly lower rate of complete response (46%) when compared to patients without dementia (77%) (OR: 0.37; CI: 0.19–0.75; p = 0.006). Detailed findings for the used treatments and prognosis are provided in Table 2.

### Psychiatric Comorbidity

More than two-thirds of the studied population, comprising 157 patients, had an identified psychiatric comorbidity, as detailed in Table 2. Affective disorders were present in 42% of the patients, followed by psychotic disorders. However, these differences were not significant.

### Exposure to Antipsychotics

More than half of the population had a history of prior exposure to antipsychotics, with no significant differences between patients with and without dementia.

### Associated Acute and Chronic Medical Conditions

Nearly half of both groups presented chronic medical conditions. However, patients with dementia exhibited a significantly lower rate of acute medical conditions (13%) than patients without dementia (51%) (OR: 0.17; CI: 0.05–0.65; p = 0.009). Delirium accounted for 11% of the recorded acute medical conditions in the group of patients without dementia and was not identified in the dementia group.

TABLE 2. Catatonia Clinical Features

	Dementia Group (N = 24)	Nondementia Group (N = 201)
<b>Catatonia subtype</b>		
Hyperkinetic variant	5 (21%)	18 (9%)
Hypokinetic variant	14 (58%)	140 (70%)
Mixed variant	5 (21%)	43 (21%)
<b>Special forms of catatonia</b>		
Malignant catatonia	1 (4%)	14 (7%)
Neuroleptic malignant syndrome	3 (13%)	21 (10%)
Periodic catatonia	0	5 (2%)
Delirious mania	0	4 (2%)
<b>Symptoms of catatonia (BFCRS)</b>		
Immobility / stupor	13 (54%)	134 (67%)
Mutism	20 (83%)	149 (74%)
Staring	7 (29%)	64 (32%)
Posturing/catalepsy	11 (46%)	80 (40%)
Grimacing	5 (21%)	27 (13%)
Echopraxia / echolalia	5 (21%)	36 (18%)
Stereotypy	7 (29%)	34 (17%)
Mannerisms	4 (17%)	14 (7%)
Stereotyped & meaningless repetition of words & phrases	5 (21%)	33 (16%)
Rigidity	14 (58%)	84 (42%)
Negativism	6 (25%)	86 (43%)
Waxy flexibility	9 (38%)	57 (28%)
Withdrawal	12 (50%)	77 (38%)
Excitement	4 (17%)	49 (24%)
Impulsivity	3 (13%)	12 (6%)
Automatic obedience	4 (17%)	16 (8%)
Passive obedience	4 (17%)	11 (5%)
Muscle resistance	4 (17%)	24 (12%)
Motorically stuck	2 (8%)	6 (3%)
Grasp reflex	4 (17%)	11 (5%)
Perservation	4 (17%)	23 (11%)
Combativeness	2 (8%)	9 (4%)
Autonomic abnormality	3 (13%)	50 (25%)
<b>Treatment modality</b>		
Benzodiazepines	18 (75%)	137 (68%)
Electroconvulsive therapy	8 (33%)	68 (34%)
Anti-NMDA drugs	8 (33%)	17 (8%)
Other or unknown	14 (58%)	100 (50%)
<b>Prognosis</b>		
Complete response	11 (46%)	155 (77%)
Partial response	5 (21%)	24 (12%)
Absent response	5 (21%)	8 (4%)
Unknown	3 (13%)	14 (7%)
<b>Psychiatric comorbidity</b>		
Overall	12 (50%)	145 (72%)
Psychotic disorder	4 (17%)	48 (24%)
Affective disorder	8 (33%)	87 (43%)
Anxiety disorder	0	13 (6%)
Substance use disorder	1 (4%)	8 (4%)
Other	0	9 (4%)
<b>Exposure to antipsychotics</b>	11 (46%)	111 (55%)
<b>Acute medical conditions</b>	3 (13%)	102 (51%)
<b>Chronic medical conditions</b>	11 (46%)	92 (46%)

BFCRS: Bush–Francis Catatonia Rating Scale

## DISCUSSION

Our literature analysis suggested the absence of relevant differences in the clinical expression of catatonia between patients with and without dementia. Significantly more patients with dementia are treated with a drug interfering with NMDA receptors (memantine or amantadine). Patients with dementia have a significantly lower rate of complete response. Additionally, no significant differences between patients with and without dementia are documented in terms of antipsychotic exposure or psychiatric comorbidity. Patients with dementia exhibit a significantly lower rate of acute medical conditions.

### Clinical Features of Catatonia

The hypokinetic variant emerged as the predominant subtype of catatonia in both dementia and nondementia patients. Both subgroups consistently reported mutism and immobility as two of the most prevalent clinical features. Our findings are consistent with previous literature in the geriatric context. Specifically, Takács et al., reported analogous trends, highlighting the hypokinetic variant as the prevailing form of catatonia in elderly patients hospitalized in psychiatric settings.<sup>26,27</sup>

Regarding special catatonia forms, Neuroleptic Malignant Syndrome was found to be the most prevalent subtype among the general population included. This observation aligns with expectations, given that approximately more than half of the population had a history of prior exposure to antipsychotics.

### Therapeutic Regimens

Recommendations for treating catatonia primarily rely on case reports and observational studies.<sup>28</sup> Symptomatic treatment typically involves first-line administration of positive allosteric modulators (PAM) of GABA-A receptors, such as lorazepam and diazepam. If these medications prove ineffective, alternative options include ECT and NMDA receptor antagonists, mainly memantine and amantadine, as second-line and third-line options, respectively.<sup>28</sup>

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**TABLE 3. Comparison Between Patients With and Without Dementia Using a Fisher's Exact Test and Multivariate Logistic Regression Analysis**

Dementia versus Nondementia	Fisher's Exact Test p Value	1st Analysis p Value	Multivariate Logistic Regression Analysis						
			Final Analysis						
			p Value	Std. Err.	z	Odds Ratio	[95% Conf. Interval]		
Catatonia subtype	0.183								
Treatment with benzodiazepines	0.333								
Treatment with ECT	0.579								
Treatment with anti-NMDA	0.002 <sup>a</sup>	0.051	0.040	1.8839	2.06	3.2708	1.0578	10.1139	
Treatment with others	0.282								
Complete treatment response	0.006 <sup>a</sup>	0.012	0.006	0.1332	-2.76	0.3745	0.1866	0.7521	
Psychiatric comorbidity	0.026 <sup>a</sup>	0.316 <sup>b</sup>							
Exposure to antipsychotics	0.227								
Acute medical conditions	0.000 <sup>a</sup>	0.009	0.009	0.1162	-2.61	0.1731	0.0464	0.6455	
Chronic medical conditions	0.520								

X<sup>2</sup> of the first multivariate logistic regression model analysis = 25.12.  
X<sup>2</sup> of the final multivariate logistic regression model analysis = 24.14.  
<sup>a</sup> Statistical significance using the Fisher's exact test.  
<sup>b</sup> Removed variable after first analysis due to lack of statistical significance.

Consistent treatment patterns were observed across patients with and without dementia. Benzodiazepines were, by far, the most frequently prescribed symptomatic treatment, followed by ECT. When employed, ECT often followed unsuccessful benzodiazepine trials.

A distinction surfaces in the utilization of NMDA receptor antagonist drugs between subgroups with and without dementia, as individuals with dementia were administered more often NMDA receptor antagonist drugs in comparison to those without dementia.

Careful examination of the subgroup of patients with dementia who received NMDA receptor antagonist drugs reveals that this treatment was initiated or reinstated after a period without therapy to treat catatonia symptomatically rather than serve as primary antidementia therapy. In all cases, it was employed as a second or third-line treatment, predominantly following a partial or absent response to benzodiazepines.

When attempting to understand the rationale behind the more frequent use of these drugs as second- and third-line therapy in patients with dementia compared to those without dementia, NMDA receptor antagonists might be prescribed more often due to the belief that they could potentially exert a dual therapeutic effect targeting both dementia and catatonia. Alternatively, or in a complementary manner, when confronted with benzodiazepine-resistant catatonia,

clinicians may find it more prudent to contemplate the use of NMDA receptor antagonist drugs for patients with dementia rather than subjecting these patients to repeated benzodiazepine trials or ECT.

### Prognosis

Catatonia in elderly patients, akin to their younger counterparts, typically has an overall excellent prognosis when promptly diagnosed and appropriately treated,<sup>10</sup> resulting in complete resolution of catatonic symptoms in most patients. However, despite standard treatment, a significant proportion of dementia patients (42%) experienced only a partial response or no response at all, in contrast to nondementia elderly patients (16%). This significantly diminished response in the dementia subgroup may stem from inherent characteristics commonly observed in dementia patients, including a higher propensity for immobility and poorer treatment compliance.<sup>29</sup>

### Psychiatric Comorbidity

Despite the lack of significant differences in terms of psychiatric comorbidity rates in our multivariate logistic regression analysis, we cannot discount the possibility that the intricate symptomatology of dementia may obscure additional psychiatric

comorbidities. This could contribute to the underdiagnosis and a misperception of their frequency in older patients with dementia.

Affective disorders were the most associated conditions with catatonia, regardless of dementia status. This finding supports the hypothesis proposed by some authors that age may itself be a risk factor for the development of catatonia in patients with affective disorders.<sup>10</sup>

### Exposure to Antipsychotics

No discernible differences emerged between patients with and without dementia. Antipsychotic drug exposure was present in more than half of the cases in each group. This notable frequency of antipsychotic exposure among older patients was expected and is in line with the hypothesis that catatonia appears to stem from dysfunction in NMDA receptors, leading to disturbances in cortico-striated or cortico-cortical pathways due to a loss of GABA-A activity, dopamine activity, glutamate hyperactivity, or a combination of these phenomena.<sup>9</sup> Patients exposed to antipsychotic drugs, which antagonize dopamine activity by blocking D<sub>2</sub> dopamine receptors, could, therefore, be at risk of developing or exacerbating catatonia through the reinforcement of abnormal dopamine receptor activity.<sup>9</sup> However, there are alternative hypotheses for the genesis of catatonic symptoms, with some authors even seeking to establish an association between the catatonic symptom and a specific pathophysiological mechanism and suggesting that the predominant neurobiological alteration may vary from patient to patient.<sup>28</sup>

### Associated Acute and Chronic Medical Conditions

A contrast is observed regarding acute medical conditions, which were significantly less linked to the onset of catatonia in patients with dementia compared to their nondementia counterparts. While dementia does not appear to be a direct risk factor for catatonia,<sup>30</sup> we hypothesize that dementia processes may act as facilitators, altering brain regions structurally and biochemically involved in psychomotor activity. In contrast, patients without dementia may require more significant pathological triggers, such as acute medical conditions, to induce abnormal activity consistent with catatonia. Regarding delirium, whose association with

catatonia has been well-documented,<sup>10</sup> it was found to account for 11% of the acute medical conditions in patients without dementia. Despite the bidirectional relationship between delirium and dementia,<sup>15</sup> the low percentage of catatonic patients with dementia concomitantly with an acute medical condition may explain the absence of documented delirium. Additionally, we cannot rule out, particularly in patients with dementia, that the challenging differential diagnosis between catatonia and delirium, particularly its hypoactive form,<sup>12</sup> might contribute to its underestimation.

As expected, nearly half of the studied population, including patients both with and without dementia, presented with chronic medical conditions, reflecting the prevalent burden of chronic diseases in an aging demographic above 50 years of age.<sup>10</sup>

### Additional Findings

The identification of catatonia among patients with various forms of dementia was an expected outcome, aligning with existing literature on the subject.<sup>10</sup> However, despite Alzheimer's disease overwhelmingly being recognized as the most prevalent form of dementia within the corpus of published case reports and case series, FTD emerged as the predominant subtype in elderly individuals presenting catatonic symptoms. Some putative hypotheses have been proposed: a shared dysfunction in the frontal network in catatonia and FT.<sup>31</sup> Moreover, a reduction in serotonin 5-HT<sub>1A</sub> receptors is noted in FTD, raising the possibility that the remaining receptors may undergo upregulation, contributing to the manifestation of catatonic signs in FTD.<sup>32</sup> Despite our meticulous literature review, we cannot entirely discount the potential for misdiagnosis between catatonia and FTD. This is especially pertinent given the shared symptoms between these conditions,<sup>32</sup> reports of lingering cognitive deficits following catatonia remission,<sup>33</sup> and documented cases of frontal lobe atrophy in catatonic patients without FTD.<sup>34</sup>

The specific brain mechanisms that could be the source of the catatonic symptoms, particularly in patients with dementia and other forms of cognitive impairment are still poorly understood.<sup>35</sup> Although not targeted to directly answer this question, this review provided some insights that could be translated to different treatment approaches. The lower complete response rate and the fewer acute medical

comorbidities in patients with dementia found in this review raise the hypothesis that catatonia in these patients might have different biological mechanisms. Abnormalities of GABA neurotransmission in motor (and other) circuits have been reasonably documented in the biology of catatonia, along with normalization following exposure to lorazepam.<sup>36</sup> The structural damage of the basal ganglia, involving GABA neurotransmission, that occurs in Alzheimer's disease, Parkinson's disease, and other dementias could be responsible for a lower involvement in GABA deficits in the biology of catatonia in these disorders and explain a lower treatment response to the treatment with PAM. The involvement of glutamate is less clearer and more complex. Catatonia has been associated with both deficits<sup>37</sup> and excess<sup>38</sup> of glutamate or NMDA receptor activity. Although the mechanisms are complex, simplistically, it can be said that low NMDA transmission is a significant neurobiological finding in schizophrenia,<sup>39</sup> and the opposite is found in Alzheimer's disease and other dementias.<sup>40,41</sup> This higher glutamate neurotransmission and the higher use of NMDA antagonists found in this study could suggest that, in dementia, NMDA-mediated transmission is most probably involved. If this hypothesis is confirmed in subsequent studies, the use of NMDA antagonists in patients with dementia and catatonia could be considered more frequently in the treatment of these conditions.

### **Limitations**

While this systematic review offers valuable insights into the characteristics of catatonia among elderly patients, it is essential to acknowledge and address several limitations inherent in our methodology and data synthesis.

Firstly, our review was intentionally designed to include only single case reports and case series to ensure clinical precision. However, this approach limits our ability to make epidemiological assertions regarding the prevalence or incidence of catatonia in the studied population. Consequently, our findings can only be interpreted as frequency reports, and we advise caution against generalizing the results in clinical practice. A subsequent systematic review including diverse article modalities could offer a more comprehensive understanding of the prevalence of catatonia, its symptoms, comorbidities, and treatment response in elderly patients with and without dementia.

Furthermore, the heterogeneity in catatonia symptom descriptions across included reports underscores another limitation. While we applied the BFCRS uniformly to all case reports to mitigate interpretation errors, variations in assessment methodologies remain a potential source of bias.

Publication bias is another consideration, as cases with unfavorable outcomes are less likely to be published, potentially inflating the perceived positive outcomes in elderly catatonia patients. While we aimed to include as many reports as possible to provide a diverse outlook, prospective studies on elderly patients are necessary to mitigate this bias.

Notably, the limited number of articles reporting on catatonia patients with concomitant dementia presents a significant sample size disparity compared to those without dementia. Consequently, conclusions drawn from our results must account for this underrepresentation. Despite this limitation, our use of statistical methodologies, which enable comparison across samples of varying sizes, still allows for a nuanced insight into catatonia in dementia patients.

Lastly, the risk of including articles with insufficient methodological quality is inherent in our approach to inclusivity. To address this, two independent reviewers utilized a modified Murad tool for methodological quality assessment, ensuring a rigorous evaluation of included records and the reliability of our findings.

### **Conclusion**

Catatonia in dementia does not have a different syndromic presentation compared with elderly patients without dementia. However, the diagnosis of dementia leads to varying preferences regarding the choice of symptomatic therapy and seems to be a predictor of a poorer therapeutic response. Actively treating catatonia, particularly in patients with dementia, addressing the characteristics of these patients, such as increased immobility and lower therapeutic compliance, is of paramount importance.

Prospective studies focusing on patients with dementia and concomitant catatonia are warranted to deepen our understanding of this intricate relationship. Additionally, further research into the underlying mechanisms of catatonia is imperative to develop more precise and effective treatment approaches. By addressing these gaps in knowledge, we can optimize

the management of catatonia in elderly patients, particularly in those with a concurrent dementia diagnosis, ultimately improving clinical outcomes and quality of life.

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## AUTHOR'S CONTRIBUTIONS

PCP: study conception and design; data extraction; analysis and interpretation of data;

MJE: analysis and interpretation of data; draft manuscript preparation;

BCR: initial data screening; data extraction; data analysis;

CC: data extraction; data analysis;

IS: data extraction; data analysis;

GD: study conception and design; data collection;

FSC: study conception and design; supervision; manuscript critical revision;

FN: study conception and design; supervision; manuscript critical revision;

All authors revised and approved the final manuscript.

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## DATA STATEMENT

The data has not been previously presented orally or by poster at a scientific meeting.

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## DISCLOSURES

The authors report no conflicts with any product mentioned or concept discussed in this article.

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## SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.jagp.2024.07.012>.

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