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Analysis of clinical characteristics of mirror and TV signs in Alzheimer's disease and dementia with Lewy bodies

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Abstract

Objective: This study explored the clinical features of dementia with Lewy bodies (DLB) and Alzheimer's disease (AD) and analyzed the differences in neurologic syndromes, including mirror and TV signs, between different groups.

Methods: Patients with AD and DLB (325 and 115, respectively) hospitalized in our institution were enrolled. We compared psychiatric symptoms and neurologic syndromes between the DLB and AD groups and within each subgroup, including the mild-moderate and severe subgroups.

Results: The prevalence rates of visual hallucination, parkinsonism, rapid eye movement sleep behavior disorder, depression, delusion, and the Pisa sign were significantly higher in the DLB group than in the AD group. Furthermore, within the mild-moderate subgroup, the mirror sign and Pisa sign prevalence rates were significantly higher in the DLB group than in the AD group. In the severe subgroup, no significant difference was found in any neurologic sign between the DLB and AD groups.

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Conclusion: Mirror and TV signs are rare and often disregarded because they are not usually invoked during routine inpatient or outpatient interviews. According to our findings, the mirror sign is uncommon in early AD patients but common in early DLB patients and should receive increased attention.

Keywords
Dementia with Lewy bodies, Alzheimer's disease, mirror sign, TV sign, delusional misidentification syndrome, psychiatric symptom

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Introduction

Dementia with Lewy bodies (DLB) and Alzheimer's disease (AD) are cognitive disorders with the first and second highest prevalence rates worldwide, respectively.[1] Psychiatric symptoms are prevalent in these two diseases, which cause a great burden to caregivers and are the main reasons for patient visits and hospitalization.[2] Delusional misidentification syndromes (DMSs) are psychiatric symptoms of dementia in which the patient develops false beliefs about the identity of people, places, or objects because of a mental or neurological illness.[3,4] The mirror sign, or mirror delusional misidentification, is a type of DMS in which patients fail to identify their reflection in a mirror.[5,6] There is a debate over whether the mirror sign is a DMS, and some authors have described the mirror sign as "mirror Capgras syndrome".[7]

Previous research has revealed that the mirror sign is more common in AD patients, while mirror sign in DLB patients is considered a rare phenomenon.[8] Some studies have revealed that the mirror sign is lacking in patients with mild to moderate DLB.[9,10] Compared with other DMSs, the mirror sign might have distinct pathophysiological properties.[11] Further studies with ancillary examinations including biological markers and neuroimaging data may confirm this hypothesis. Another common misidentification in people with dementia is the TV sign, in which people and events on TV are referred to as reality by patients. Compared with other DMSs, the prevalence of TV sign in AD and DLB is quite low.[12] The TV sign is rare, representing 3% to 4% of individuals with severe DLB.[10] However, we found that the mirror and TV signs could be observed in patients with mild-moderate DLB. We evaluated the frequency of the mirror and TV sign in patients with mild-severe DLB and AD, compared the similarities and differences, and analyzed the relevant variables by evaluating the prevalence and content of other mental symptoms. These results will improve the understanding of clinicians and provide references for managing clinical psychiatric symptoms in AD and DLB patients.

Methods

Study design and participants

This retrospective, observational, multicenter study involved data collected from four units in China between January 2017 and June 2021. The study was first approved by the lead institutional ethics committee of Tianjin Huanhu Hospital (approval No. 2019-39), followed by ethical approval from each of the participating hospitals. The reporting of this study conforms to

the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[13] All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). The patients provided written informed consent for publication of the data and participation in this study.

The subjects included those who were first examined in other departments, including psychiatric clinics, and then transferred to our cognitive impairment outpatient department. We diagnosed dementia according to the Diagnostic and Statistical Manual of Mental Disorders IV criteria.[14] The National Institute of Neurological and Communicative Disorders-AD and Related Disorders Association criteria were adopted to diagnose AD.[15] Probable DLB was diagnosed according to consensus criteria for DLB established by McKeith in 2017 with two or more core clinical features of DLB present, with or without the presence of indicative biomarkers.[14] Two experienced neurologists reviewed the patient's signs and symptoms and reached a consensus. The inclusion criteria included the following: age 40 to 90 years, clinical diagnosis of probable AD or DLB, cooperation, and ability to complete the assessment scales. The exclusion criteria included the following: (1) patients with consciousness disorders, severe aphasia, or hemiplegia and an inability to complete neuropsychological tests; (2) patients with malnutrition, malignant tumor, blood disease, or connective tissue disease; (3) patients with a history of mental disorders; and (4) rejection by patients or their guardians.

Measures

Clinical characteristics, dementia scales, and neurological characteristics were evaluated at the time of diagnosis. We also performed the Montreal Cognitive Assessment and Mini-Mental State Examination (MMSE).[16] The severity of dementia was rated using the Clinical Dementia Rating Scale.[14] All patients were evaluated clinically by two trained neurologists. We collected data regarding the following symptoms in our interviews with patients and caregivers:

- Mental symptoms, such as delusions, depression, visual and auditory hallucinations, anxiety, and apathy (mirror and TV signs were documented by interviewing subjects or their caregivers in face-to-face or telephone surveys to determine whether the TV sign occurred and the time of the first symptom);
- Symptoms of Parkinson's disease, such as resting tremor, muscle stiffness, bradykinesia, and postural instability;
- Memory loss, including forgetting old memories and inability to learn new memories;
- Sleep-related behavior disorders, including rapid eye movement sleep behavior disorder (RBD), complex motor behaviors during sleep, and/or repeated episodes of sleep-related vocalization;
- Autonomic symptoms, including gastrointestinal, urinary, and cardiovascular symptoms.

Statistical analyses

Normally distributed, continuous variables are provided as means and standard deviations and were compared using a *t*-test. The Mann–Whitney U test was used to analyze non-normally distributed variables. The chi-square test and Fisher's exact test were used to compare categorical variables, which are given as frequencies and percentages. Multiple binary logistic regression analysis was also performed to determine the factors most closely associated with the mirror and TV sign, with a significance level of $P < 0.05$. All statistical analyses were conducted using SPSS 22.0 software

(IBM Corp., Armonk, NY, USA). A *P*-value <0.05 was considered statistically significant.

Results

Demographics and prevalence of baseline data

We retrospectively surveyed 441 consecutive subjects, including 115 patients with probable DLB and 326 patients with probable AD. The clinical features of the DLB and AD patients are shown in Table 1.

In the DLB group, 44 patients (38.26%) were female, the mean age of onset was 71.47 ± 0.73 years, and the average MMSE score was 15.33 ± 0.65. The psychiatric symptoms, listed in descending order of prevalence, included the following: parkinsonism (61.7%), visual hallucination symptoms (54.8%), RBD (54.3%), depression (36.5%), and delusion (34.8%). The neurologic syndromes, listed in descending order of prevalence, included the following: Pisa sign (13.91%), Tourette-like syndrome (TS) (12.17%), mirror sign (11.3%), and TV sign (6.09%).

In the AD group, 152 patients (46.63%) were female, the mean age of onset was 71.16 ± 0.48 years, and the average MMSE score was 14.49 ± 0.39. The psychiatric symptoms, listed in descending order of prevalence, included the following: delusions (5.82%), visual hallucination symptoms (4.29%), depression (3.38%), RBD (2.15%), and parkinsonism (1.54%). The neurologic syndromes, listed in descending order of prevalence, included the following: mirror sign (7.98%), TS (7.36%), Pisa sign (4.6%), and TV sign (3.99%).

Compared with the AD group, the DLB group had higher prevalence rates of parkinsonism, visual hallucinations, RBD, depression, and delusion. The prevalence of Pisa sign in the DLB group was significantly higher than that in the AD group ($P < 0.001$). Nevertheless, there was no significant difference between the two groups for the mirror sign, TV sign, and TS.

Differences in neurological signs between the mild-moderate DLB and AD subgroups

Compared with the AD subgroup, the prevalence of the mirror sign ($P = 0.007$) and Pisa sign ($P < 0.001$) was significantly higher in the DLB subgroup. Although there was

Table 1. The clinical features and findings of DLB and AD patients.

	DLB (n = 115, %)	AD (n = 326, %)	*P*-value
Age/years	71.47 ± 0.73	71.16 ± 0.48	0.17
Sex, F/M	44/71	152/176	0.12
MMSE score	15.33 ± 0.65	14.49 ± 0.39	0.26
Visual hallucinations	66 (54.8)	14 (4.29)	**<0.001***
Parkinsonism	71 (61.7)	5 (1.54)	**<0.001***
RBD	63 (54.3)	7 (2.15)	**<0.001***
Depression	42 (36.5)	11 (3.38)	**<0.001***
Delusion	40 (34.8)	19 (5.82)	**<0.001***
Mirror sign	13 (11.3)	26 (7.98)	0.28
TV sign	7 (6.09)	13 (3.99)	0.35
Pisa sign	16 (13.91)	15 (4.6)	**<0.001***
Tourette-like syndrome	14 (12.17)	24 (7.36)	0.35

DLB, dementia with Lewy bodies; AD, Alzheimer's disease; MMSE, Mini-Mental State Examination; RBD, rapid eye movement sleep behavior disorder, F, female; M, male.

a trend toward a higher prevalence rate of the TV sign in the mild-moderate DLB subgroup than in the AD subgroup, the analysis did not show a significant difference (Table 2).

Differences in neurological signs between the severe DLB and AD subgroups

There was a clear trend toward a lower prevalence rate of the mirror sign in the severe DLB subgroup than in the AD subgroup, but the analysis did not indicate a significant difference. No significant difference was found between the severe DLB and AD subgroups in the prevalence rate of the TV sign (Table 2).

Determination of independent factors for the mirror and TV signs using multivariate logistic regression analysis

Multiple logistic regression analyses revealed that the mirror and TV sign were significantly associated with lower MMSE scores (odds ratio (OR) 0.77, 95% confidence interval 0.56–2.11, $P = 0.01$; OR 3.61, 95% confidence interval 3.98–8.49, $P = 0.02$). The mirror sign also was significantly associated with the prevalence of visual hallucinations (OR 2.31, 95% confidence interval 2.98–632, $P = 0.02$). In contrast, the TV sign was significantly associated with the prevalence of delusion (OR 5.23, 95% confidence interval 2.66–9.74, $P = 0.001$) (Table 3).

Table 2. Comparison of pathological signs in mild-moderate and severe DLB and AD patients.

	DLB (n = 115, %)	AD (n = 326, %)	*P*-value
Mirror sign	13 (11.3)	26 (7.98)	0.28
mild-moderate	10 (9.83)	9 (3.13)	**0.007***
severe	3 (23.08)	17 (44.74)	0.16
TV sign	7 (6.09)	13 (3.99)	0.35
mild-moderate	4 (3.92)	4 (1.39)	0.12
severe	3 (23.08)	9 (23.68)	0.96

DLB, dementia with Lewy bodies; AD, Alzheimer's disease.

Discussion

DMSs were originally reported to be related only to psychiatric disorders. However, in recent years, DMSs have also been described as being related to neurological disorders, especially neurodegenerative diseases such as DLB and AD.[17] The misidentification of mirror and TV signs was listed as a clinical manifestation of DMSs in recent studies.[18] However, such misidentified recognitions are rare forms of DMSs in patients with dementia.

Previous studies indicated that the mirror sign mainly occurs in AD and rarely in DLB patients.[14] However, another report recently demonstrated that the mirror sign is not rare in DLB patients, particularly in those with moderate and severe DLB.[14] A recent report analyzed the clinical features of mirror and TV signs in Japanese patients with advanced dementia caused by AD and DLB.[11] In contrast to former studies, we divided the patients into mild, moderate, and severe subgroups for further comparison and analysis. Because rare neurological signs may be ignored in routine diagnosis and treatment procedures, to ensure accuracy of the data, we further conducted face-to-face or telephone interviews.

To our knowledge, our present work was the first study to investigate the epidemiological distribution of mirror and TV signs in AD and DLB populations in China. Our results showed that the mirror and TV sign can also appear in the mild-moderate AD and DLB populations. Another comparative study of DMSs in patients with DLB and AD indicated that the frequency of DMSs in DLB patients (40%) was significantly higher than that in AD patients (10%).[16] Our study showed that the prevalence of auditory and visual hallucinations was much greater in DLB patients than in

Table 3. Associated factors analyzed using the multivariate binary logistic regression model.

	Mirror sign		TV sign	
Profile	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	0.98 (0.79–1.45)	0.78	0.32 (0.08–1.36)	0.16
Sex	1.89 (0.23–5.89)	0.34	0.99 (0.98–0.99)	0.99
Visual hallucinations	2.31 (2.98–632)	0.02*	0.13 (0.01–1.78)	0.13
RBD	3.25 (0.76–5.85)	0.76	0.36 (0.08–1.54)	0.75
Delusion	0.67 (0.92–1.23)	0.24	5.23 (2.66–9.74)	0.001*
Depression	0.11 (0.00–3.78)	0.72	1.59 (2.21–2.08)	0.46
MMSE score	0.77 (0.56–2.11)	0.01*	3.61 (3.98–8.49)	0.02*
CDR	1.48 (0.48–2.31)	0.67	1.24 (1.29–3.27)	0.52
CDT	2.14 (1.23–2.51)	0.77	2.31 (1.26–2.61)	0.35
MoCA	0.06 (0.00–1.68)	0.29	1.25 (2.42–3.21)	0.28
ADL	1.09 (0.97–1.27)	0.46	0.67 (0.76–1.28)	0.31
HAMD	0.96 (0.78–2.12)	0.29	1.58 (1.78–2.98)	0.27

OR, odds ratio; CI, confidence interval; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; CDT, Clock drawing test; CDR, Clinical Dementia Rating; HAMD, Hamilton Depression Scale; ADL, Activities of daily living; RBD, rapid eye movement sleep behavior disorder.

AD patients, especially in the early phases of the disease. In addition, in the mild-moderate subgroup, the prevalence of the mirror sign was significantly higher in DLB patients than that in AD patients.

In this study, there was a clear trend toward a higher mirror sign prevalence in the severe AD subgroup compared with that in the DLB subgroup, but the difference was not statistically significant. In contrast, the prevalence increased significantly with dementia progression in the AD group, but the prevalence of the mirror sign in the mild-moderate subgroups was greater in the DLB group than that in the AD group. As a result, we discovered that the prevalence of the mirror sign was associated with visual hallucinations and a decline in the overall cognitive level.

The TV sign is a very rare symptom. Instead of treating it as a separate symptom, previous studies have attributed it to a manifestation of DMS, and thus it has received little attention.[19,20] Only two studies have been published to date. Nagahama found that the prevalence rates of the TV sign in AD and DLB patients were 1.5% and 4.0%, respectively.[11] Guido Dorman reported seven patients with cognitive impairment who presented the TV sign during the COVID-19 pandemic.[21,22] The diagnoses of these patients included AD, vascular dementia, and DLB. The authors found that the prevalence rate of the TV sign was approximately 3% in patients with dementia. In this study, the TV sign was found in 6.09% of DLB patients and 3.99% of AD patients. The prevalence rate in the DLB group was slightly higher than that in the AD group, but no significant difference was identified between the two groups. We found that the prevalence of the TV sign may be related to delusions. The TV sign was rarely reported in previous studies, and thus it may have been overlooked. Therefore, it is necessary to carry out further multi-center, prospective, and observational studies.

This study has several limitations. First, because the present study was cross-sectional, we could not determine a causal relationship between the mirror and TV

signs, as well as between other possible causative factors. Furthermore, the results were only based on psychiatric symptoms and neurologic syndromes, without the support of biological markers, such as Aβ42 or the Aβ42:Aβ40 ratio, or neuroimaging data, such as 18-F fluorodeoxyglucose positron emission tomography.

Conclusion

We analyzed the clinical characteristics and neurologic syndromes of different subgroups of DLB and AD patients admitted to our hospital. There were no significant differences in the overall prevalence of the mirror sign and TV sign in the AD and DLB groups, but we found that the mirror sign and TV sign were present in the mild-moderate AD and DLB populations. With disease progression, the mirror and TV sign prevalence gradually increased and was associated with hallucinations and overall cognitive decline. The prevalence of the mirror sign could be associated with hallucinations, delusions, and a reduced overall cognitive level. According to our findings, the mirror sign was common in patients with early DLB and should receive increased attention.

Author contributions

Each author significantly contributed to the manuscript by participating in the project proposal, data collection, data analysis, writing, and editing. All authors made substantial contributions to the concept and design as well as data acquisition. Gang Chen, Shuai Liu, Hao Wu, Jinghuan Gan, and Xiaodan Wang made further substantial contributions to the analysis and interpretation of the data. Yong Ji and Gang Chen drafted the article. All authors participated in revising the manuscript. All authors gave their final approval for the version to be submitted.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

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