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Research Article

Prevalence and Clinical Implications of the Mirror and TV Signs in Advanced Alzheimer's Disease and Dementia with Lewy Bodies

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Keywords

Delusional misidentification syndrome · Sense of self · Lewy body dementia · Alzheimer's disease · Misidentification of television · Misidentification of the mirror image

Abstract

Objective: To explore the prevalence and clinical implications of the mirror and TV signs in the moderate to advanced stages of Alzheimer's disease (AD) and dementia with Lewy bodies (DLB). *Methods:* We retrospectively examined the prevalence of clinical and psychiatric symptoms including the mirror and TV signs in 200 subjects with AD and 200 with DLB and evaluated the relationships among the symptoms. **Results:** The mirror sign was found in 3.0% of AD and 4.5% of DLB subjects. The TV sign was found in 1.5% of AD and 4.0% of DLB subjects. The prevalence of the mirror and TV signs was not significantly different between the AD and DLB groups. Visual hallucination, visual illusion, misidentification of person, and sleep talking were significantly more frequent in DLB than in AD subjects. The mirror sign was significantly associated with lower Mini-Mental State Examination scores, whereas the TV sign was significantly associated with the misidentification of person. Conclusions: Both the mirror and TV signs were rare even in the moderate to advanced stages of AD and DLB. The mirror sign may be independent from other delusional misidentification syndromes (DMSs). Being associated mainly with global cognitive decline, the mirror sign is unlikely attributed to any specific cognitive impairment or the dysfunction of localized brain areas. In contrast, the TV sign was significantly more often coexistent with the misidentification of person, suggesting that the TV sign may partly share common neuropsychological mechanisms with DMSs.

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Introduction

Psychotic symptoms are common in patients with dementia. Behavioral and psychological symptoms of dementia (BPSDs) are associated with increased rates of admission to nursing homes as well as longer hospital stay and are a major contributor to caregiver stress. Delusional misidentification, which is a false belief about the identity of a person, place, or object, is one major category among BPSDs [1]. A representative symptom is Capgras syndrome, in which a patient believes that a familiar person, such as the spouse, has been replaced by an imposter [2, 3]. There is considerable variability in the classification of actual symptoms into the subcategories of delusional misidentification syndromes (DMSs) in previous publications [1, 4–7]. Notwithstanding, the DMSs and the other misidentification symptoms are considered to occur in Alzheimer's disease (AD), and more frequently in dementia with Lewy bodies (DLB), with a prevalence of up to 56% [5, 8, 9]. Previous studies using factor analysis [5, 10] demonstrated that the DMSs in DLB consisted of simple misidentification of person, misidentification of place, Capgras syndrome, phantom boarder, reduplication of people, and reduplication of place.

The mirror sign, or mirrored-self misidentification, is a misidentification phenomenon in which the patient cannot recognize their reflection in a mirror. There is disagreement on whether or not the mirror sign is one type of the DMSs; some authors describe the mirror sign as the "Capgras syndrome for the mirror image" [11], whereas others exclude it from the DMSs [12]. Previous studies argued that the mirror sign is mainly seen in patients with AD, and the mirror sign in patients with DLB has been considered quite a rare phenomenon. A PubMed search detected only one case of DLB with the mirror sign [13]. In our previous studies underlining psychiatric aspects in mild to moderate DLB, we did not find any single patient with the mirror sign [5, 10]. We may infer from these facts that the mirror sign may have a distinctive pathophysiology from other much more common DMSs in DLB, such as Capgras syndrome and simple misidentification of person.

The TV sign, in which patients recognize TV characters and events as a reality, is another infrequent misidentification seen in dementia. The frequency of the TV sign is also very low in both AD and DLB compared to other DMSs [7, 14]. In contrast to the almost nonexistent mirror sign, the TV sign was observed, admittedly rarely, in 3–4% of the population with early to moderate stage of DLB [5, 15]. This finding may indicate that the mirror sign and the TV sign have separate backgrounds, although these signs have similar features, such as the misidentification of two-dimensional images.

We conducted this study on the basis that there has been no systematic research investigating whether the mirror sign is truly rare even in moderate to advanced stages of AD and DLB. For this purpose, we compared the frequency of the mirror and TV signs in the moderate to advanced dementia stage of AD and DLB. By investigating the prevalence and contents of other psychoses such as hallucinations and the DMSs in these subjects, we further sought the possible relationship between the mirror and TV signs and other psychiatric symptoms.

Subjects and Methods

Subjects

We selected subjects from the AD and DLB patients admitted to Kawasaki Memorial Hospital for treatment of their BPSDs. The inclusion criteria for DLB was as follows: (1) patients fulfilled the fourth consensus diagnostic criteria for probable DLB [8], (2) with no or mild ischemic changes on head CT or MRI, and (3) their Mini-Mental State Examination (MMSE) score lay between 0 and 19. The inclusion criteria of AD was as follows: (1) patients fulfilled





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the clinical diagnostic criteria for probable AD dementia according to the NIA-AA recommendation [16], (2) with no or mild ischemic changes on head CT or MRI, (3) their MMSE score lay between 0 and 19, and (4) without recurrent visual hallucinations. According to these criteria, we selected 200 probable AD dementia and 200 probable DLB subjects from the consecutive patients who were admitted between June 2015 and October 2018. Pharmacological and nonpharmacological interventions against the BPSDs were allowed. Patients with a history of stroke, significant head trauma, alcohol abuse, major psychiatric illnesses, or evidence of other neurological disorders were excluded. All subjects underwent general physical, neurological, and neuropsychological examinations including MMSE, structural neuroimaging, and routine laboratory investigations including vitamin B1, vitamin B12, and thyroid functions.

Psychotic and mood symptoms were searched in the medical records from the first consultation to the day 3 months after admission. All symptoms noticed by family members, doctors, nurses, care staff, and social workers were documented. The symptoms during apparent delirium were excluded from the data. The target symptoms included visual hallucinations, visual illusions, auditory hallucinations, misidentification of person (including simple misidentification of person, Capgras syndrome, phantom boarder, reduplicative paramnesia for person), persecutory delusions (including delusion of theft, jealousy), depression, TV sign, and mirror sign. Previous studies using factor analysis showed that each symptom included in the misidentification of person loaded on the same factor [5, 10], suggesting that these symptoms corresponded to the DMSs in DLB. Recurrent sleep talking, which was suggestive of REM sleep behavior disorder, and parkinsonism were also examined. We determined parkinsonism as positive if one or more of the parkinsonian symptoms of tremor, akinesia, or rigidity were apparent.

Statistical Analyses

Statistical analyses were performed using the EZR software, which is based on R and R commander [17]. Differences between the AD and DLB groups in age and MMSE scores were analyzed using univariate analysis of variance. The difference in the frequency distribution of sex and parkinsonism was examined using Fisher's exact test. The statistical threshold was set at p < 0.05.

The differences in the frequency distribution of visual hallucinations, visual illusions, auditory hallucinations, misidentification of person, persecutory delusions, depression, TV sign, mirror sign, and sleep talking were also examined using Fisher's exact test and corrected for multiple comparisons by Bonferroni's correction. Thus, the statistical threshold for these symptoms was set at p < 0.0056 (= 0.05/9).

To examine the functional relationship between the mirror or TV sign and the other symptoms or demographic parameters, we performed multiple logistic regression analyses, with the mirror or TV sign as an dependent variable, and seven symptoms (visual hallucinations, visual illusions, auditory hallucinations, misidentification of person, persecutory delusions, depression, sleep talking) and four demographic parameters (age, sex, diagnosis, MMSE score) as independent variables. Parkinsonism was removed from the analysis because of the collinearity with visual hallucinations (r = 0.65). Predictable variables included in the model were selected by a stepwise forward/backward procedure using Akaike's information criterion.

Results

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The demographic data and frequency of observed symptoms in AD and DLB subjects are presented in Table 1. Age, sex distribution, and MMSE scores were similar in the AD and DLB subjects. Parkinsonism was significantly more frequent in DLB than in AD. Visual halluci-

	AD (<i>n</i> = 200)	DLB (<i>n</i> = 200)	Statistics
Age, years	82.7±7.5	81.9±6.4	F = 1.06, p = 0.30
Sex, f/m	122/78	118/82	$\chi^2 = 0.09, p = 0.76$
MMSE score	10.2±5.2	10.1±5.8	F = 0.04, p = 0.83
Parkinsonism	8 (4%)	164 (82%)**	$\chi^2 = 245.1, p < 0.001$
Visual hallucinations	0 (0%)	173 (86.5%)*	$\chi^2 = 301.3, p < 0.001$
Visual illusions	1 (0.5%)	33 (16.5%)*	$\chi^2 = 30.9, p < 0.001$
Auditory hallucinations	16 (8%)	35 (17.5%)	$\chi^2 = 7.28, p = 0.007$
Misidentification of person	23 (11.5%)	50 (25%)*	$\chi^2 = 11.3, p < 0.001$
Persecutory delusions	110 (55%)	131 (65.5%)	$\chi^2 = 4.18, p = 0.041$
Sleep talking	2 (1%)	53 (26.5%)*	$\chi^2 = 52.7, p < 0.001$
Depression	29 (14.5%)	38 (19%)	$\chi^2 = 1.15, p = 0.28$
TV sign	3 (1.5%)	8 (4%)	$\chi^2 = 1.50, p = 0.22$
Mirror sign	6 (3%)	9 (4.5%)	$\chi^2 = 0.28, p = 0.60$

Table 1. Demographics and clinical symptoms in patients with AD and DLB

Age and MMSE score are shown as mean \pm standard deviations. AD, Alzheimer's disease; DLB, dementia with Lewy bodies; MMSE, Mini-Mental State Examination. Significant statistical difference between AD and DLB: * p < 0.0056, ** p < 0.05.

nation, visual illusion, misidentification of person, and sleep talking were significantly more frequent in DLB than in AD subjects. Auditory hallucination was also found more often in DLB than AD, but the difference did not reach statistical significance. The mirror sign was found in 3.0% of AD and 4.5% of DLB subjects. The TV sign was found in 1.5% of AD and 4.0% of DLB subjects. The prevalence of the mirror sign, the TV sign, persecutory delusion, and depression was not significantly different between the AD and DLB groups. The prevalence of the mirror and TV signs was not correlated (Spearman's rank correlation rho = 0.05, p = 0.35).

Multiple logistic regression analyses revealed that the mirror sign was significantly associated with lower MMSE scores (odds ratio 0.89, p = 0.016, 95% confidence interval 0.80– 0.98). Actually, subjects with mirror sign performed significantly worse in the MMSE than those without (6.3 ± 4.1 vs. 10.3 ± 5.5 , F = 7.81, p = 0.0055). The TV sign was significantly associated with the prevalence of misidentification of person (odds ratio 3.93, p = 0.027, 95% confidence interval 1.17–13.3). About a half (45.5%) of the patients with TV sign had misidentification of person as well, whereas only 17.5% of those without TV sign had misidentification of person ($\chi^2 = 3.89$, p = 0.033).

Discussion

Previous studies suggested that the mirror sign was quite rare at the early and moderate stages of DLB [5, 10, 13]. The present study showed that the mirror sign was present but also rare at the moderate and advanced stages of DLB. DLB features wider varieties of psychotic symptoms when compared to AD. Consistent with previous studies [8, 9], visual hallucinations, visual illusions, and misidentification of person were more frequent in DLB than in AD even at the advanced stage. Some researchers claimed that the mirror sign belongs to the DMSs, representing "Capgras misidentification for the mirror image" [11]. If true, we could expect that the mirror sign will be found more often in DLB than in AD, i.e., as frequently as other DMSs. However, the result of the present study suggested that the mirror sign had a similar occurrence in DLB and AD and that it was not significantly related to the misidentifi-

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cation of person. Thus, this study supports the claim that the mirror sign is an independent misidentification phenomenon that should be considered separate from other DMSs [18].

Regardless of the causative diseases, the mirror sign is related to the severity of global cognitive decline. We could not analyze which aspects of cognitive impairments were associated with the mirror sign because the dementia levels in most patients were too severe for detailed cognitive evaluations. A recent comprehensive review of cases with the mirror sign [18] suggested the following: (1) The mirror sign is exceedingly rare compared to the other DMSs. (2) It is uniformly associated with neurological illness, most commonly with neurode-generative dementia. (3) While right hemisphere dysfunction appears to be required for this syndrome, patients with this condition do not have consistent neuropsychological or neuro-imaging findings for a localization of lesions. The authors concluded that these findings are consistent with the assumption that not one specific area of the brain is responsible for the functions that support self-cognition and self-awareness (i.e., sense of self). The result of the present study may corroborate their conclusions and suggest that the diffuse brain dysfunction is the prerequisite for the impairment of sense of self.

The second unrecognized issue that this study clarified is that the TV sign is also a rare symptom even in the advanced stage of both AD and DLB, and that it is pathophysiologically separate from the mirror sign. Furthermore, the TV sign is more closely associated with the misidentification of person. The TV and mirror signs share a common attribute of misidentification of two-dimensional images, but essentially differ in terms of whether the target is self or others. The present study suggested that the TV sign may somehow share common neuropsychological mechanisms with misidentification of person, whereas the mirror sign does not. Actually, our previous study demonstrated that in the very early stages of AD and DLB (MMSE score \geq 21), the TV sign was more frequently found in DLB than in AD (4 vs. 0%), $\chi^2 = 8.1, p < 0.05$) along with misidentification of person (10 vs. 0.5%, $\chi^2 = 15.5, p < 0.05$) [15]. Hashimoto et al. [19] reported that no significant difference was found in the severity of hallucinations and delusions (including misidentifications) across dementia stages in the DLB group, whereas such BPSDs significantly increased in parallel with advancing dementia stages in the AD group. This may be partly a reason why there was no significant difference in the prevalence of the TV sign between DLB and AD in our cohort because the increment speed of the TV sign and other BPSDs in advanced AD may have "caught up with" that in DLB.

Several limitations should be addressed. First, all dementia subjects were diagnosed clinically and were not proven pathologically. Second, the results may be affected by a sample selection bias because AD patients with visual hallucinations were excluded from the AD group. Some pathological research demonstrated that clinically diagnosed AD with visual hallucinations frequently shared Lewy body pathology [20–22]. Therefore, we expected that exclusion of these subjects reduced contamination of the AD group with clinically undiagnosed DLB subjects. Third, the frequency of symptoms may be underestimated because all symptoms were retrospectively extracted from medical records. More accurate data may be obtained by a prospective study design.

In summary, the present study showed that both the mirror and TV signs are rare even in the moderate to advanced stages of DLB and AD and that the prevalence of these symptoms is not significantly different between the diseases. The mirror sign may be a misidentification phenomenon that should be considered separate from other DMSs. Association of the mirror sign with global cognitive decline suggests that loss of the ability to recognize oneself in the mirror may not be simply related to specific cognitive impairment or the dysfunction of specific brain areas. In contrast, the TV sign was closely associated with misidentification of person, suggesting that it is more likely to share common neuropsychological mechanisms with the DMSs.





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Statement of Ethics

This study was approved by the ethics committee of Kawasaki Memorial Hospital (approval number 1-1-04).

Disclosure Statement

The authors have no conflicts of interest to declare.

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None.

Author Contributions

Y. Nagahama, T. Fukui, and H. Fujishiro designed the study. All authors examined the patients and collected data. Y. Nagahama and T. Fukui analyzed and interpreted the data and wrote the paper.

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