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Tanaka H., Hashimoto M., Fukuhara R., Ishikawa T., Yatabe Y., Kaneda K., Yuuki S., Honda K., Matsuzaki S., Tsuyuguchi A., Hatada Y, Ikeda M.	Relationship between dementia severity and behavioral and psychological symptoms in early-onset Alzheimer's disease.	Psychogeriatrics	15(4)	242-247	2015
Kai K., Hashimoto M., Amano K., Tanaka H., Fukuhara R., Ikeda M	Relationship between eating disturbance and dementai severity in patients with Alzheimer's disease.	PLoS One	10(8)	e0133666	2015
田中　譽、福原竜治、池田　学	前頭側頭型認知症（DSM-5）	精神科治療学	30	311-316	2015
田中　譽、橋本衛、池田　学	アルツハイマー病のBPSDとその対応	老年精神医学雑誌	26（11）	1222-1228	2015
Tatsuru Kitamura, Shinnichi Tochimoto, Maki Kitamura, Shuhei Madachi, Shoryoku Hino	Outcomes of Impatient Treatment for Behavioral and Psychological Symptoms of Dementia in Altzheimer's Disease Versus Dementia With Lewy Bodies	Prim Care Companion CNS Disord	17(5)		2015
Shinnichi TOCHIMOTO, Maki KITAMURA, Shoryoku HINO, Taturu KITAMURA	Predictors of home discharge among patients hospitaiized for behaviourai and psychoiogicai symptoms of dementia	Psychogeriatrics	15	248-254	2015
北村　立，塩田繁人	精神科リハビリテーションの実際	Journal of Clinical Rehabilitation	24(6)	602-606	2015
北村　立	目指せ！日本のアドミラルナース－石川県立高松病院・認知症訪問看護チームの紹介－	全国自治体病院協議会雑誌	54(6)	139-142	2015
塩田繁人，杉本優輝，　稲口葉子，北村　立，村井千賀	精神科病院における認知症高齢者に対する作業療法	作業療法ジャーナル	49(7)	685-691	2015
村井千賀，北村立	社会参加の再開により娘に対する被害妄想が消失した一例	老年精神医学雑誌	26(1)	84-88	2015
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平野佳奈子，上城憲司，田平隆行，村田　伸，太田保之	寝たきり高齢者に対する声かけの反応と家族の言動変容の分析 -近赤外分光法（NIRS）を用いた検討	作業療法ジャーナル	49（9）	963-968	2015
田平隆行	総説：認知症高齢者に対するリハビリテーション介入のレビュー　-地域での介入研究を中心に	作業療法ジャーナル	50（2）	117-121	2016
堀田　牧，村田美希，吉浦和宏，福原竜治，池田　学	前頭側頭型認知症（FTD）の症候学と非薬物療法	作業療法ジャーナル	49(7)	603-609	2015

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Regular Article

Classifying eating-related problems among institutionalized people with dementia

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Aims: Various eating-related problems are commonly observed among people with dementia, and these problems place a huge burden on the caregivers. An appropriate classification of these problems is important in order to understand their underlying mechanisms and to develop a therapeutic approach for managing them. The aim of this study was to develop a possible classification of eating-related problems and to reveal the background factors affecting each of these problems across various conditions causing dementia.

Methods: The participants were 208 institutionalized patients with a diagnosis of dementia. Care staff were asked to report all kinds of eating-related problems that they observed. After the nurses' responses were analyzed, 24 items relating to eating-related problems were extracted. A factor analysis of these 24 items was conducted, followed by a logistic regression analysis to investigate the independent variables that most affected each of the eating-related factors.

Results: Four factors were obtained. Factor 1 was overeating, factor 2 was swallowing problems, factor 3 was decrease in appetite, and factor 4 was obsession with food. Each factor was associated with different background variables, including Mini-Mental State Examination scores, Clinical Dementia Ratings, and neuropsychiatric symptoms.

Conclusions: This study suggests that eating-related problems are common across conditions causing dementia and should be separately considered in order to understand their underlying mechanisms.

Key words: appetite, dementia, obsession with food, overeating, swallowing.

IT IS WELL known that individuals with dementia experience various eating-related problems in association with cognitive dysfunction, psychiatric problems, and a decline in daily activity.[1,2] As these eating problems have to be managed on a daily basis, they become a huge burden on the patients' caregivers, which could lead to a diminished quality of life for the patient.[3] These eating problems sometimes disrupt home caring, become a trigger for institutionalization, and can even become a major issue within a nursing care facility. However, until recently, research assessing eating problems in dementia has mainly focused on dietary consequences, nutritional deficiency, and weight loss.[4,5] There are relatively few systematic studies on other eating-related problems, such as 'overfilling the mouth,' 'deteriorating table manners,' and 'eating non-edible foodstuffs.'[6,7] There are several studies on the abnormal eating behaviors of patients with frontotemporal dementia (FTD) as these eating behaviors are common and predominant features among such patients;[8–10] however, only a few studies have been conducted on the eating-related problems of patients with Alzheimer's disease (AD)[6,7] and other types of dementia, such as dementia with Lewy bodies (DLB).[11] There is still a lack of

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clarity regarding the kinds of eating-related problems that are common across individuals with various conditions causing dementia, and the underlying mechanisms of these problems. In addition, there have been no studies wherein the researchers have adopted an empirical approach to separate the eating-related problems of patients with dementia into symptom groups.

The appropriate classification of these eating-related problems is important for understanding their underlying mechanisms and for developing a therapeutic approach to managing them. The aims of this study were: (i) to reveal the types and frequencies of eating-related problems that are common across patients with various conditions causing dementia; (ii) to develop a possible classification of eating-related problems; and (iii) to reveal the relation between eating-related problems and the background factors they are associated with.

METHODS

Participants

All of the patients were recruited from among the inpatients of two psychiatric hospitals, one rehabilitation hospital, and two nursing homes. Patients with a diagnosis of dementia according to DSM-IV-TR criteria during the research period (i.e. October 2011 to March 2012) were included in this research.[12] A total of 208 people with dementia were included in the study, and were classified into diagnostic groups according to the established international consensus clinical criteria. The diagnosis of AD was based on the probable AD criteria of the National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer's Disease and Related Disorders Association.[13] The diagnosis of vascular dementia (VaD) was based on the probable VaD criteria of the National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche´ et l'Enseignement en Neurosciences or the Alzheimer's Disease Diagnostic and Treatment Centers.[14,15] The diagnosis of DLB was based on recent clinical diagnostic criteria,[16] and the diagnosis of FTD was based on international diagnostic criteria.[17] For other types of dementia, the diagnosis was based on the consensus criteria.

To rule out the presence of major functional psychiatric disorders, such as schizophrenia and mood disorders, all the participants were evaluated by senior neuropsychiatrists and underwent both physical and neurological examinations as well as a standard psychiatric evaluation. In addition, each patient underwent a brain magnetic resonance imaging or computed tomography scan. The patients were assessed using a battery of neuropsychological and neuropsychiatric tests, including the Mini-Mental State Examination (MMSE), Clinical Dementia Rating (CDR), and the Neuropsychiatric Inventory (NPI).[18–20]

After a complete description of the study was provided to all the patients or their proxy, informed consent was obtained. The present study was approved by the Ethics Committee of the Jikei University School of Medicine.

Assessment of eating-related problems

Information about eating-related problems was gathered by expert nurses who cared directly for the patients at their facilities. Geriatric psychiatrists carried out semi-structured systematic interviews with nurses that were based on the Eating and Swallowing questionnaire.[8,9,11] This questionnaire is designed to assess eating problems in patients with FTD, AD and DLB. The mean conducting time is about 30 min. Details of this questionnaire are described elsewhere.[8] In addition, in order to reveal every eating-related symptom, nurses were asked to report any kinds of eating-related problems that they felt caused difficulty in their daily caring and management of the patients. Nurses were asked to report participants' usual eating-related problems in order to avoid eating-related problems that may have been caused by acute medical conditions, such as pneumonia. After the nurses' responses were analyzed, the participants' eating-related problems were summarized into 24 items, as some of the items on the questionnaire were excluded as they were very rare. For all 208 cases, the nurses were asked to rate the frequency of each of the 24 items (0, never; 1, occasionally, less than once per week; 2, often, about once per week; 3, frequently, several times per week but less than every day; 4, very frequently, once or more per day or continuously).

Statistical analyses

Data analyses were carried out using SPSS (SPSS, Chicago, IL, USA).

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ORIGINAL ARTICLE

Comparing the driving behaviours of individuals with frontotemporal lobar degeneration and those with Alzheimer's disease

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Declaration of interest: The authors have no conflicts of interest to declare.

Abstract

Background: Assessing driving aptitude in dementia patients is critically important for both patient and public safety. However, there have been only a few reports on the driving behaviours and accident risk of patients with dementia, especially frontotemporal lobar degeneration (FTLD). Therefore, we compared the characteristics of driving behaviours in patients with FTLD and those with Alzheimer's disease (AD).

Methods: The subjects were 28 FTLD and 67 AD patients who visited the Department of Psychiatry, Kochi Medical School Hospital. We conducted semi-structured interviews with their families and caregivers about traffic accident history and changes in patient driving behaviours after dementia onset and then compared the findings between the two groups.

Results: Overall changes in driving behaviours were reported in 89% (25/28) and 76% (51/67) of the FTLD and AD patients, respectively ($P = 0.17$). In the FTLD group, difficulty in judging inter-vehicle distances, ignoring road signs and traffic signals, and distraction were reported in 50% (14/28), 61% (17/28), and 50% (14/28) of patients, respectively, and 75% (21/28) patients had caused a traffic accident after dementia onset. The risk of causing an accident was higher in the FTLD group than in the AD group (odds ratio = 10.4, 95% confidence interval = 3.7–29.1). In addition, the mean duration between dementia onset and a traffic accident was 1.35 years in the FTLD group compared with 3.0 years in the AD group ($P < 0.01$).

Conclusions: Patients with FTLD were more likely to show dangerous driving behaviours than those with AD, and the risk of causing a traffic accident may be higher in patients with FTLD from an early disease stage.

Key words: *dementia, driving behaviour, frontotemporal lobar degeneration, traffic accidents.*

INTRODUCTION

With the increased interest in dementia patients, there has also been an increased interest in their driving skills. Dementia patients at the wheel is an issue directly related to public safety, but there is no established medical gold standard for evaluating their driving aptitude.[1,2] There are various causes for dementia, with markedly varying clinical symptoms and behaviours, but driving behaviour assessment according to disease entities seems to be scarce. Most previous studies concerning dementia and driving have reported an association with cognitive functions, such as visual function, visual attention, and executive function,[3–8] and have focused on patients with Alzheimer's disease (AD), whereas only few systematic studies for driving behaviours of patients with frontotemporal lobar degeneration (FTLD) have been conducted.

FTLD is the umbrella term for degenerative dementia with predominant symptoms involving personality/behaviour changes and language impairment with lesions in the frontal and/or temporal lobes.[9] Clinically, FTLD is divided into frontotemporal dementia (FTD or behavioural variant FTD), semantic dementia, and progressive non-fluent aphasia. Ikeda *et al.* and Ratnavalli *et al.* reported that FTLD was the second

most common cause of primary dementia among the presenile dementias,[10,11] and FTLD has become an increasingly recognized cause of dementia. Characteristic clinical symptoms of FTLD include disinhibition, stereotypic behaviour, eating disorders, and semantic memory loss; these are markedly different from the symptoms of AD.[12–17] In FTLD, the posterior regions of the brain remain intact, unlike in AD, and the memory and visuospatial skills are relatively preserved in the initial stages. Therefore, it is reasonable to assume that the driving behaviours of patients with FTLD and AD will be completely different from one another.

To the best of our knowledge, there have been few reports regarding driving behaviour in patients with FTLD and its relation to traffic accidents. A review article by Turk and Dugan on FTD and driving identified only four reports from several electronic databases.[18] Although specific driving issues have been related to antisocial behaviours in FTD, the risk of such patients causing traffic accidents has not been studied yet.

The aim of this study was to compare the characteristics of driving behaviours and traffic accident history between patients with FTLD and AD. We hypothesized that patients with FTLD would show characteristic driving behaviours that differ from those shown by patients with AD, and they would be at a higher risk of causing traffic accidents than patients with AD.

METHODS

Subjects

This study was conducted after approval by the Ethics Committee of Kochi Medical School. We explained the aim of this study to the subjects or their legally authorized representatives, and obtained written consent.

We enrolled consecutive patients who had visited the Department of Psychiatry of Kochi Medical School Hospital between September 1995 and December 2012. Subjects who fulfilled the clinical diagnostic criteria of FTLD and met the definition of one of its types as established by Neary *et al.* were enrolled.[9] The FTLD group included 28 patients (18 men and 10 women; mean age ± SD: 67.9 ± 9.2 years) who had retained their driving licence and drove a car at the time of the first examination. The clinical subtype was FTD in 13 patients, semantic dementia in 13, and progressive non-fluent aphasia in 2. Patients with AD who met the diagnostic criteria established by the National Institute of Neurological and Communicative Disease and Stroke and Alzheimer's Disease and Related Disorders Association for probable AD were selected.[19] The AD group included 67 patients (42 men and 25 women; mean age ± SD: 69.8 ± 10.2 years) who had retained their driving licence and drove a car at the time of the first examination.

No patient had any physical problem, marked visual disturbance, or motor impairment that interfered with driving. Patients who had been followed for less than 1 year after clinical diagnosis were excluded from this study.

Clinical assessment

The age at first examination, sex, age at onset, and disease duration were evaluated at first examination along with the scores for the Mini-Mental State Examination (MMSE),[20] instrumental activities of daily living (IADL) scale,[21] and Clinical Dementia Rating (CDR).[22] Based on interviews with the main caregiver or a family member at the first visit, we estimated the onset of dementia and disease duration. For the IADL scale, men and women were evaluated on 5-point and 8-point scales, respectively, and the score was presented as a percentage.

Driving interviews

Semi-structured interviews for evaluating driving behaviours were conducted by senior neuropsychiatrists or clinical psychologists familiar with geriatric psychiatry. The main caregiver or a family member living with the patient was interviewed about the patient's driving behaviours after dementia onset. The questionnaire included items about whether the patient did the following: (i) forgot the destination; (ii) failed to get the car in/out of the garage; (iii) had difficulty judging inter-vehicle distances; (iv) ignored road signs and traffic signals; (v) was distracted (e.g. took their eyes off the road); and (vi) showed overall changes in driving behaviour. We also identified patients' history of traffic accidents, characteristics, and time to first accident from dementia onset. Only traffic accidents caused by a patient were considered. Accidents processed through legal administrative procedures by the police and self-inflicted accidents recognized by family members were included.

Table 1 Characteristics of subjects

	FTLD (n = 28)	AD (n = 67)	P-value
Sex, men (n)	18 (64%)	42 (63%)	0.88
Age, mean ± SD (years)	67.9 ± 9.2	69.8 ± 10.2	0.15
MMSE, mean ± SD	19.6 ± 7.6	19.5 ± 5.8	0.54
CDR (n)			0.06
0.5	16 (57.1%)	21 (31.3%)	
1	9 (32.1%)	32 (47.8%)	
2	3 (10.7%)	14 (20.9%)	
IADL, mean ± SD (%)†	67.4 ± 35.2	64.1 ± 23.4	0.65
Disease duration, mean ± SD (years)	2.0 ± 1.9	1.7 ± 1.5	0.37

†For the IADL scale, men were evaluated on a 5-point scale and women on an 8-point scale. AD, Alzheimer's disease; CDR, Clinical Dementia Rating; FTLD, frontotemporal lobar degeneration; IADL, instrumental activities of daily living; MMSE, Mini-Mental State Examination.

Statistical analysis

Continuous variables were expressed as mean ± SD. Categorical variables were expressed as numbers and percentages. For analyzing continuous variables, t-test or Mann–Whitney U-test was used. For analyzing categorical variables, χ^2 test was used, and Fisher's exact test was selected when expected frequencies were less than five. The time to first accident from dementia onset was compared between the FTLD and AD groups with the Mann–Whitney U-test. Two-sided P-values <0.05 were considered significant. All analyses were carried out using SPSS version 21.0 (IBM, Armonk, NY, USA).

RESULTS

Table 1 shows the characteristics of the subjects. There were no significant differences in sex ratio, age, MMSE score, CDR score, IADL score, or disease duration between the two groups.

Figure 1 shows the driving behaviours and traffic accident history after dementia onset based on the driving-related interviews with caregivers and family members. An overall change in driving behaviours was reported at a high frequency in both the groups with no significant difference (P = 0.17). Among the characteristics of driving behaviour, the frequency of difficulty in judging inter-vehicle distances, ignoring traffic signals, and distraction were significantly higher in the FTLD group than in the AD group (P < 0.001 for all). No significant difference was observed in the frequencies of failure to get the car in/out of the garage between the two groups (P = 0.17), and the frequency of forgetting the destination was higher in the AD group than in the FTLD group (P < 0.001). The risk of causing an accident was higher in the FTLD group than in the AD group (odds ratio = 10.4, 95% confidence interval = 3.7–29.1).

With regard to the characteristics of traffic accidents in the FTLD group, rear-end collision was the most frequent type of accident; among the subjects involved rear-end collisions were one in a hit-and-run accident and one involving injury. In contrast, in the AD group, minor accidents due to a failure to get the car in/out of the garage were frequent, but there were no serious accidents resulting in injury or death. Thirteen patients (FTLD: 12, AD: 1) showed difficulties in both judging inter-vehicle distances and distraction, and all had caused a traffic accident.

Table 2 shows the difference between individuals in the FTLD group who had caused accidents and those who had not. No significant differences were observed in sex, age, MMSE score, CDR score, or IADL score between these groups within the FTLD group. Among the characteristics of driving behaviour, only distraction was significantly more frequent in the patients who had caused accidents.

Table 3 shows the difference between individuals in the AD group who had caused accidents and those who had not. No significant differences were observed in sex, age, MMSE score, CDR score, or IADL score between these groups within the AD group. Among the characteristics of driving behaviour, failure to get the car in/and out of the garage and difficulty in judging inter-vehicle distances were significantly more frequent in the patients who had caused accidents.

The mean time between dementia onset and the first traffic accident was 1.35 ± 0.83 years in the FTLD group and 3.0 ± 1.36 years in the AD group (P < 0.01).

DISCUSSION

Our results indicated that driving behaviours were remarkably different between the two groups, and the risk of causing a traffic accident was much higher in the FTLD group than in the AD group. Difficulty in judging inter-vehicle distances, ignoring traffic signals, and distraction were significantly more frequent in the FTLD group. These driving behaviours may be related to neuropsychiatric manifestations and behavioural changes, such as aggression, impulsivity, restlessness, disinhibition, and environmental dependency syndrome, which can be characteristics

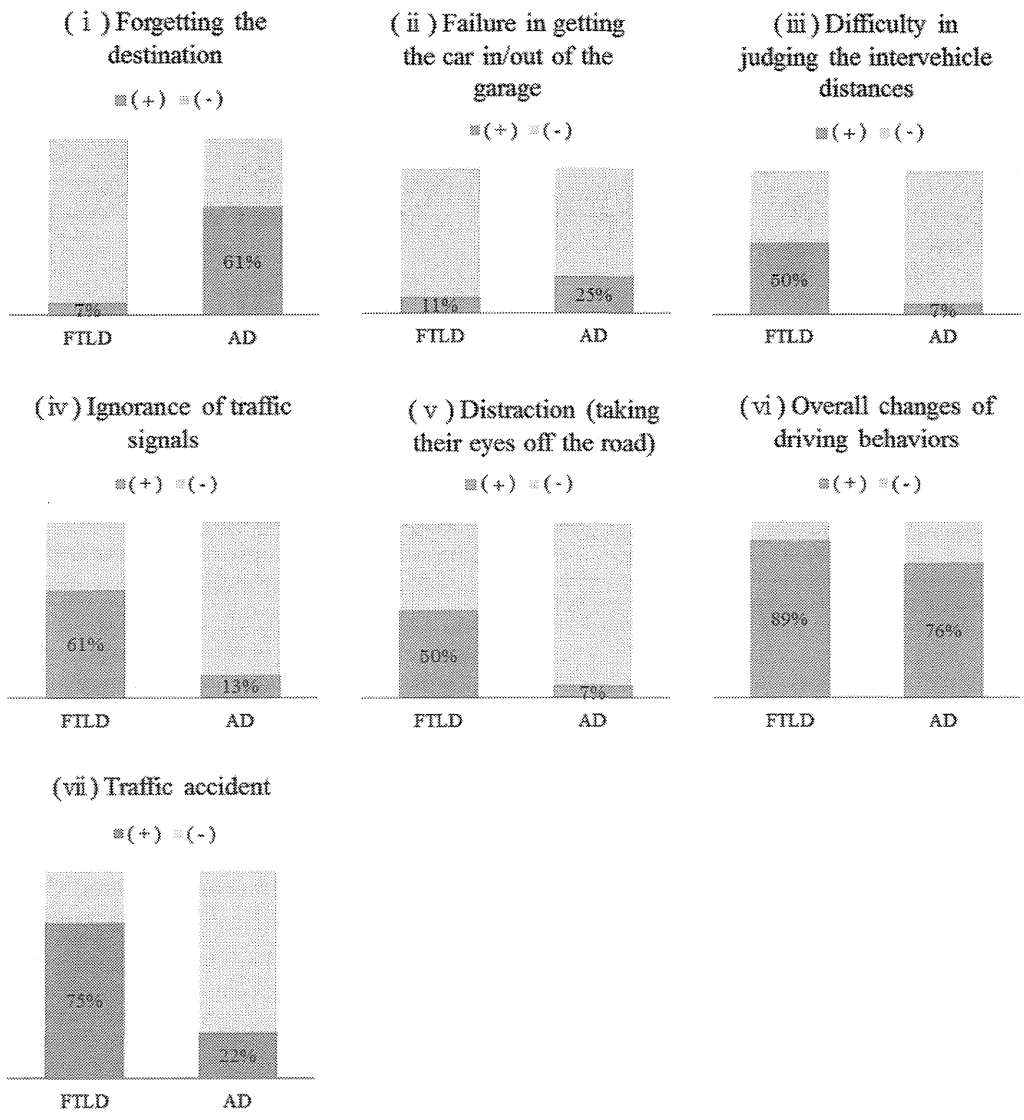

Figure 1 Data concerning the driving behaviours and traffic accident history after dementia onset are shown. Overall changes in driving behaviours were reported at a high frequency in both the FTLD and AD groups. Driving behaviours, difficulty judging inter-vehicle distances, ignoring traffic signals, and taking eyes off the road were significantly more frequent in the FTLD group than in the AD group. No significant difference between the two groups was observed with regard to getting the car in/out of the garage, but forgetting the destination was more frequent in the AD group than in the FTLD group. The frequency of traffic accidents was significantly higher in the FTLD group than in the AD group. AD, Alzheimer's disease; FTLD, frontotemporal lobar degeneration.

of FTLD. Only distraction was shown to have statistically significant difference for increasing the risk of traffic accidents in FTLD. Other driving behaviours did not show statistically significant differences for increasing the risk of traffic accidents in the FTLD group, probably because of the relatively small sample size. Difficulty in judging inter-vehicle distances and ignoring traffic signals were shown to have a tendency to increase the risk of traffic accidents. The frequency of forgetting the destination was lower in the FTLD group, which may have been due to a lower incidence of memory deficit and visuospatial impairment. All patients who had difficulty with both judging inter-vehicle distances and distraction had caused traffic accidents. Therefore, this result suggests that physicians may be able to identify patients with a higher risk of causing traffic accidents by confirming these two items in any type of dementia.

Table 2 Differences between individuals in the FTLD group who had caused accidents and those who had not

Accident	(+)	(–)	*P*-value
	n = 21	*n* = 7	
Sex, men (*n*)	15 (71%)	3 (75%)	0.17
Age, mean ± SD (years)	67.1 ± 9.4	68.1 ± 9.3	0.80
MMSE, mean ± SD	19.9 ± 7.6	18.6 ± 8.2	0.69
CDR (*n*)			0.19
0.5	10	6	
1	8	1	
2	3	0	
IADL, mean ± SD (%)	64.5 ± 38.7	75.1 ± 21.7	0.83
Forgetting the destination (*n*)	1 (4.7%)	1 (14.3%)	0.44
Failure to get the car in/out of the garage (*n*)	2 (9.5%)	1 (14.3%)	1.0
Difficulty judging inter-vehicle distances (*n*)	13 (61.9%)	1 (14.3%)	0.07
Ignoring traffic signals (*n*)	15 (71.4%)	2 (28.6%)	0.07
Distraction (*n*)	14 (66.7%)	0 (0%)	0.006
Overall changes in driving behaviours (*n*)	20 (95.2%)	5 (71.4%)	0.14

CDR, Clinical Dementia Rating; FTLD, frontotemporal lobar degeneration; IADL, instrumental activities of daily living; MMSE, Mini-Mental State Examination.

Table 3 Differences between individuals in the AD group who had caused accidents and those who had not

Accident	(+)	(–)	*P*-value
	n = 15	*n* = 52	
Sex, men (*n*)	11 (73%)	31 (60%)	0.33
Age, mean ± SD (years)	69.9 ± 12.1	69.8 ± 9.8	0.96
MMSE, mean ± SD	18.5 ± 6.3	19.8 ± 5.6	0.46
CDR (*n*)			0.05
0.5	1	20	
1	9	23	
2	5	9	
IADL, mean ± SD (%)	62.1 ± 21.2	64.6 ± 24.1	0.71
Forgetting the destination (*n*)	9 (60%)	32 (61.5%)	0.91
Failure to get the car in/out of the garage (*n*)	8 (53.3%)	9 (17.3%)	0.01
Difficulty judging inter-vehicle distances (*n*)	4 (26.6%)	1 (1.9%)	0.008
Ignoring traffic signals (*n*)	4 (26.6%)	5 (9.6%)	0.10
Distraction (*n*)	3 (20.0%)	2 (3.9%)	0.07
Overall changes in driving behaviours (*n*)	13 (86.7%)	38 (73.1%)	0.49

AD, Alzheimer's disease; CDR, Clinical Dementia Rating; IADL, instrumental activities of daily living; MMSE, Mini-Mental State Examination.

The clinical characteristics of FTD include disinhibition, stereotypic behaviour, loss of social awareness and insight, aggression, impulsivity, restlessness, aspontaneity, environmental dependency syndrome, and distractibility.[12,17,23] Although semantic memory impairment, such as loss of word meaning and impaired object recognition, is a striking facet of semantic dementia, patients with semantic dementia also showed behavioural changes.[24] All these neuropsychiatric and neuropsychological symptoms influence compliance with traffic rules and understanding of road signs, and the may interfere with the driving ability of patients with FTLD. Lack of insight into one's own impairment may also lead to dangerous driving.[9] In a previous study, an association between a reduced ability to drive and lack of insight had been reported in patients with AD.[25]

A previous study reported a strong correlation between MMSE scores and driving behaviours in elderly drivers.[26] However, it is generally difficult to evaluate driving ability in dementia patients based on neuropsychological test batteries alone.[27–30] de Simone *et al*. reported that there was no correlation between a general measure of cognitive functioning and driving performance in patients with FTD.[31] We also observed no correlation between MMSE scores and the occurrence of traffic accidents in either group, suggesting that MMSE alone may not be useful in predicting traffic accidents caused by patients with dementia.

CDR is a generally used tool to assess dementia severity that can clinically be very useful. However, no correlation was observed between CDR scores and traffic accidents in the current study. CDR mainly evaluates disturbances of memory, orientation, and judgement. Thus, CDR alone may be inappropriate for evaluating the driving ability of patients with FTLD because they mainly develop changes in personality and behaviour in the early stage. In contrast, in the AD group, only one patient who had caused an accident had a CDR score of 0.5, and the other 14 patients who had caused an accident had a CDR score of ≥1. Our findings showed that some patients in the very early stage of AD could drive safely and that AD patients with a CDR score of ≥1 could pose a significant problem in safe driving, which is consistent with the results of previous studies.[32–35]

IADL is an appropriate instrument to assess independent living skills in the elderly, but no correlation with traffic accidents was observed in this study. Thus, the use of IADL as an index to predict traffic accidents caused by dementia patients may be limited.

In agreement with previous studies,[31,36,37] we believe that it is dangerous for patients with FTLD to

drive. However, to the best of our knowledge, this is the first report that compared the characteristics of driving behaviours and time until the first accident after disease onset between patients with FTLD and AD. The mean time to the first traffic accident after dementia onset in the FTLD group was 1.35 years, which was shorter than that in the AD group (3 years). Of particular note in this study is that the mean time between disease onset and first accident was shorter than the mean disease duration in patients with FTLD. Therefore, it may be necessary to pay careful attention to the driving behaviours of patients with FTLD and to instruct families to consider the accident risk from a very early stage.

In previous reports, driving was investigated mainly in association with AD. According to a meta-analysis reported by Reger *et al.*, visuospatial skills were the only neuropsychological tasks that correlated with driving ability.[38] This correlation probably explains why individuals who had caused an accident in the AD group were significantly more likely to have difficulty parking in a garage and judging inter-vehicle distances in the present study. However, patients with FTLD have little or no visuospatial dysfunction in the early stage. Impaired driving ability in FTLD appears more likely to relate to personality and behavioural changes, such as an increase in aggressiveness, impulsivity, and disinhibition. Thus, apart from dementia severity, physicians should be aware of marked variation in driving behaviours among different types of dementia.

Several limitations should be noted in this study. First, this study did not include assessments for the behavioural and psychological symptoms of dementia. Earlier studies have suggested that agitated and aggressive behaviours measured by the Neurobehavioural Rating Scale are related to speeding and collisions in patients with FTD.[33] Second, changes in driving behaviours were not based on an on-road assessment but on the evaluation of caregivers. However, the main caregiver or a family member living with the patient could closely observe changes in driving; thus, their impressions were considered to be suitable for assessing on-road driving behaviours. Third, factors such as psychosocial background, including place of residence, and medication use were not considered. These factors may affect the risk of traffic accidents, although all subjects were from the same catchment area near one university hospital. Fourth, we did not measure driving mileage. However, the subjects drove several times a week, and professional drivers were not included as subjects. Therefore, the driving mileage of the subjects can be regarded as the average of their Japanese contemporaries. Finally, there were a small number of patients with FTLD who were evaluated in this study; therefore, future studies will need to increase the number of subjects and evaluate driving behaviours according to the FTLD clinical subtypes.

The results of present study have clarified that patients with FTLD show characteristic driving behaviours that are clearly different from patients with AD, and the risk of causing a traffic accident is much higher among patients with FTLD. Moreover, this risk was high in patients with early-stage FTLD. Physicians need to recognize that the characteristics of driving behaviours of patients with FTLD differ from those with AD, and for both patient and public safety, these patients should cease driving as soon as possible after FTLD has been diagnosed.

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REFERENCES

1 Snyder CH. Dementia and driving: autonomy versus safety. *J Am Acad Nurse Pract* 2005; **17**: 393–402.
2 Carr DB, Ott BR. The older adult driver with cognitive impairment: 'It's a very frustrating life'. *JAMA* 2010; **303**: 1632–1641.
3 Duchek JM, Hunt L, Ball K, Buckles V, Morris JC. Attention and driving performance in Alzheimer's disease. *J Gerontol B Psychol Sci Soc Sci* 1998; **53**: 130–141.
4 Owsley C, Ball K, Sloane ME, Roenker DL, Bruni JR. Visual/cognitive correlates of vehicle accidents in older drivers. *Psychol Aging* 1991; **6**: 403–415.
5 Owsley C, Ball K, McGwin G Jr *et al.* Visual processing impairment and risk of motor vehicle crash among older adults. *JAMA* 1998; **279**: 1083–1088.
6 Rizzo M, Reinach S, McGehee D, Dawson J. Simulated car crashes and crash predictors in drivers with Alzheimer disease. *Arch Neurol* 1997; **54**: 545–551.
7 Silva MT, Laks J, Engelhardt E. Neuropsychological tests and driving in dementia: a review of the recent literature. *Rev Assoc Med Bras* 2009; **55**: 484–488.
8 Dawson JD, Anderson SW, Uc EY, Dastrup E, Rizzo M. Predictors of driving safety in early Alzheimer disease. *Neurology* 2009; **72**: 521–527.
9 Neary D, Snowden JS, Gustafson L *et al.* Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. *Neurology* 1998; **51**: 1546–1554.

10 Ikeda M, Ishikawa T, Tanabe H. Epidemiology of frontotemporal lobar degeneration. *Dement Geriatr Cogn Disord* 2004; **17**: 265–268.
11 Ratnavalli E, Brayne C, Dawson K, Hodges JR. The prevalence of frontotemporal dementia. *Neurology* 2002; **58**: 1615–1621.
12 Mendez MF, Perryman KM. Neuropsychiatric features of frontotemporal dementia: evaluation of consensus criteria and review. *J Neuropsychiatry Clin Neurosci* 2002; **14**: 424–429.
13 Boone KB, Miller BL, Swartz R, Lu P, Lee A. Relationship between positive and negative symptoms and neuropsychological scores in frontotemporal dementia and Alzheimer's disease. *J Int Neuropsychol Soc* 2003; **9**: 698–709.
14 Liu W, Miller BL, Kramer JH *et al*. Behavioral disorders in the frontal and temporal variants of frontotemporal dementia. *Neurology* 2004; **62**: 742–748.
15 Kertesz A, Davidson W, McCabe P, Munoz D. Behavioral quantitation is more sensitive than cognitive testing in frontotemporal dementia. *Alzheimer Dis Assoc Disord* 2003; **17**: 223–229.
16 Ikeda M, Brown J, Holland AJ, Fukuhara R, Hodges JR. Changes in appetite, food preference, and eating habits in frontotemporal dementia and Alzheimer's disease. *J Neurol Neurosurg Psychiatr* 2002; **73**: 371–376.
17 Bozeat S, Gregory CA, Ralph MA, Hodges JR. Which neuropsychiatric and behavioural features distinguish frontal and temporal variants of frontotemporal dementia from Alzheimer's disease? *J Neurol Neurosurg Psychiatr* 2000; **69**: 178–186.
18 Turk K, Dugan E. Research brief: a literature review of frontotemporal dementia and driving. *Am J Alzheimers Dis Other Demen* 2014; **29**: 404–408.
19 McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984; **34**: 939–944.
20 Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state': a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; **12**: 189–198.
21 Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969; **9**: 179–186.
22 Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. *Br J Psychiatr* 1982; **140**: 566–572.
23 Rascovsky K, Hodges JR, Knopman D *et al*. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain* 2011; **134**: 2456–2477.
24 Kashibayashi T, Ikeda M, Komori K *et al*. Transition of distinctive symptoms of semantic dementia during longitudinal clinical observation. *Dement Geriatr Cogn Disord* 2010; **29**: 224–232.
25 Wild K, Cotrell V. Identifying driving impairment in Alzheimer disease: a comparison of self and observer reports versus driving evaluation. *Alzheimer Dis Assoc Disord* 2003; **17**: 27–34.
26 Odenheimer GL, Beaudet M, Jette AM, Albert MS, Grande L, Minaker KL. Performance-based driving evaluation of the elderly driver: safety, reliability, and validity. *J Gerontol* 1994; **49**: M153–M159.
27 Cox DJ, Quillian WC, Thorndike FP, Kovatchev BP, Hanna G. Evaluating driving performance of outpatients with Alzheimer disease. *J Am Board Fam Pract* 1998; **11**: 264–271.
28 Barbas NR, Wilde EA. Competency issues in dementia: medical decision making, driving, and independent living. *J Geriatr Psychiatry Neurol* 2001; **14**: 199–212.
29 Lundberg C, Johansson K, Ball K *et al*. Dementia and driving: an attempt at consensus. *Alzheimer Dis Assoc Disord* 1997; **11**: 28–37.
30 Frittelli C, Borghetti D, Iudice G *et al*. Effects of Alzheimer's disease and mild cognitive impairment on driving ability: a controlled clinical study by simulated driving test. *Int J Geriatr Psychiatry* 2009; **24**: 232–238.
31 de Simone V, Kaplan L, Patronas N, Wassermann EM, Grafman J. Driving abilities in frontotemporal dementia patients. *Dement Geriatr Cogn Disord* 2007; **23**: 1–7.
32 Dubinsky RM, Stein AC, Lyons K. Practice parameter: risk of driving and Alzheimer's disease (an evidence-based review): report of the quality standards subcommittee of the American Academy of Neurology. *Neurology* 2000; **54**: 2205–2211.
33 Reuben DB, St George P. Driving and dementia California's approach to a medical and policy dilemma. *West J Med* 1996; **164**: 111–121.
34 Duchek JM, Carr DB, Hunt L *et al*. Longitudinal driving performance in early-stage dementia of the Alzheimer type. *J Am Geriatr Soc* 2003; **51**: 1342–1347.
35 Molnar FJ, Patel A, Marshall SC, Man-Son-Hing M, Wilson KG. Systematic review of the optimal frequency of follow-up in persons with mild dementia who continue to drive. *Alzheimer Dis Assoc Disord* 2006; **20**: 295–297.
36 Miller BL, Darby A, Benson DF, Cummings JL, Miller MH. Aggressive, socially disruptive and antisocial behaviour associated with fronto-temporal dementia. *Br J Psychiatr* 1997; **170**: 150–154.
37 Frisoni GB, Pizzolato G, Geroldi C, Rossato A, Bianchetti A, Trabucchi M. Dementia of the frontal type: neuropsychological and [99Tc]-HM-PAO SPET features. *J Geriatr Psychiatry Neurol* 1995; **8**: 42–48.
38 Reger MA, Welsh RK, Watson GS, Cholerton B, Baker LD, Craft S. The relationship between neuropsychological functioning and driving ability in dementia: a meta-analysis. *Neuropsychology* 2004; **18**: 85–93.

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Original Research Article

Adequacy of Using Consensus Guidelines for Diagnosis of Dementia with Lewy Bodies in Clinical Trials for Drug Development

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Key Words
Dementia · Lewy bodies · Clinical characteristics · Diagnosis · Randomised controlled trials · Psychiatry · Neurology

Abstract
Background/Aims: To evaluate the adequacy of using the consensus diagnostic criteria for dementia with Lewy bodies (DLB) to recruit patients with homogeneous characteristics in future clinical trials, where multiple departments of multinational centres are expected to participate with a long enrolment period, and additionally, to contribute to the possible future criteria revision. ***Methods:*** Using data from 2 trials of donepezil for DLB, conducted 3 years apart, characteristics in patients with probable DLB were analysed and compared between studies and between psychiatric and neurological centres. ***Results:*** In 273 patients (phase II: 135, phase III: 138; psychiatric: 73, neurological: 184), clinical characteristics overall were very similar between studies, and between specialty centres, excluding distinctive parkinsonism in the neurological versus psychiatric centres: incidence of parkinsonism (91.8 vs. 71.2%, $p < 0.001$), Hoehn and Yahr stage (III: 55.0 vs. 21.2%, $p < 0.001$), and concomitant anti-Parkinson medication (24.5 vs. 11.0%, $p = 0.017$). Rapid eye movement sleep behaviour disorder, depression, and delusion, suggestive or supportive features, were observed in 35–40%. Additionally, a high prevalence (55.3%) of anxiety was observed. ***Conclusion:*** Employing the consensus criteria is adequate to enrol homogeneous DLB patients into future clinical trials regardless of the specialty of centres and time. Further discussion could involve adding anxiety to future criteria.

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Introduction

Dementia with Lewy bodies (DLB) is a common type of dementia among the elderly and accounts for the second largest group of patients with dementia, following Alzheimer's disease (AD) [1]. DLB includes the core clinical features of neuropsychiatric symptoms and motor symptoms of parkinsonism as well as cognitive impairment characterised by deficits of attention, executive function, and visual perception.

The currently accepted diagnostic criteria for DLB were published in 1996 by the Consortium on DLB [2] and revised in 2005 [3]. All core features and some of the suggestive features defined in the revised criteria were adopted in the recently published diagnostic criteria for neurocognitive disorders with Lewy bodies in the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [4]. Several studies reported that these consensus criteria offer high specificity but relatively low sensitivity [5–7]. Therefore, further refinement of the criteria is indicated [8, 9]. Therapeutic research, including research on non-pharmacological approaches, as well as clinical research require both high specificity and sensitivity in diagnostic criteria, although disease-modifying drug trials and etiological research require as homogeneous a disease as possible.

The pharmacological management of DLB can be one of the most challenging issues that neurologists, psychiatrists, geriatricians, and primary care physicians face [10]. However, only a few randomised placebo-controlled trials (RCTs) targeting DLB have been conducted, and no drug has been approved in any country except Japan, where only donepezil is available for DLB. Moreover, it is difficult to enrol a large number of patients into clinical trials for DLB, especially RCTs, owing to its wide variety of treatment targets and high caregiver burden [11]. Therefore, future RCTs in DLB will inevitably recruit patients from various specialty departments (e.g. neurology, psychiatry, geriatrics) of a large number of multinational centres and have a long enrolment period. However, there is little information about whether DLB patients with homogeneous characteristics can be enrolled in such trials using the current consensus diagnostic criteria.

We have previously conducted 3 clinical trials [12–16] on donepezil for DLB including 2 RCTs [12, 14] that enrolled a total of 281 patients diagnosed with probable DLB according to the original consensus criteria [2]. These studies were conducted 3 years apart. In this paper, data on clinical characteristics of these patients were further analysed to examine the adequacy of using currently accepted diagnostic criteria in future studies. We also investigated the prevalence of suggestive and supportive features defined in the revised criteria [3] in these patients to contribute to the possible future revision of the diagnostic criteria.

Methods

Data Utilised for the Analysis

Data for the present analysis were collected from 1 phase II and 1 phase III study of donepezil in patients with DLB conducted in Japan. A 12-week, phase II, exploratory RCT was conducted to investigate the efficacy and safety of donepezil at 3, 5, and 10 mg/day from October 2007 (clinicaltrials.gov reference: NCT00543855). Subsequently, a confirmatory phase III trial including a 16-week RCT phase was conducted from February 2011 to confirm the superiority of donepezil at 5 and 10 mg/day for 12 weeks over placebo (clinicaltrials.gov reference: NCT01278407). Each study was conducted in accordance with the principles of the Declaration of Helsinki. The protocols were approved by the institutional review board at each participating centre. The results of the studies have previously been reported [12–16].

Patients

Patients were recruited according to nearly identical criteria in both studies. Patients diagnosed with probable DLB in accordance with the original consensus criteria [2] were recruited mainly from psychi-

atric or neurological specialty centres throughout Japan (48 and 72 centres in phase II and III, respectively).

Eligible patients were outpatients aged ≥50 years with mild to moderate-severe dementia [a score of 10–26 on the Mini-Mental State Examination (MMSE) and Clinical Dementia Rating (CDR) ≥0.5] and behavioural and psychiatric symptoms (BPSD) [Neuropsychiatric Inventory-plus (NPI-plus), 12 items: original 10 NPI items, sleep [17, 18], and cognitive fluctuation reported as Cognitive Fluctuation Inventory [19, 20] ≥8, and NPI-2 (hallucinations and cognitive fluctuation [12], only in phase III) ≥1]. The evidence or rationale for the presence of the core features, on which each diagnosis of DLB was based, was provided and examined by the review board (Mori, Ikeda, and Kosaka) to assure the validity of the diagnosis. In the board, the rating in Short Fluctuations Questionnaire, developed based on the Mayo Fluctuation Questionnaire [21, 22], and scores in each item of the NPI and Unified Parkinson's Disease Rating Scale (UPDRS) part III [23] were also referred.

Exclusion criteria were Parkinson's disease diagnosed at least 1 year prior to the onset of dementia; focal vascular lesions on magnetic resonance imaging or computed tomography scan that might cause cognitive impairment; other neurological or psychiatric diseases; complications or a history of severe gastrointestinal ulcer, severe asthma or obstructive pulmonary disease; systolic hypotension (<90 mm Hg); bradycardia (<50 bpm); sick sinus syndrome; atrial or atrioventricular conduction block; QT interval prolongation (≥450 ms); severe parkinsonism (Hoehn and Yahr stage ≥IV) [24], and treatment with the cholinesterase inhibitors (ChEIs) or any investigational drug within 3 months prior to screening. ChEIs, antipsychotics, and anti-Parkinson drugs other than levodopa or dopamine agonists were not allowed during the study. Written informed consent was obtained from the patient (if at all possible) and his/her primary family member before initiating the study procedures.

Measures for Clinical Characteristics

Severity of dementia was measured using the CDR [25]. Cognitive function was assessed with the MMSE [26]. Severity of extrapyramidal disorders was classified using the Hoehn and Yahr stage [24]. Additionally, motor functions were assessed with the UPDRS part III with a score range of 0 (no) to 108 (severe) [23]. Subscales were defined as the following four symptoms: tremor, akinesia, rigidity, and postural instability and gait difficulty with a score range of 0–36, 0–28, 0–20, and 0–16, respectively [27, 28].

BPSD were assessed using the NPI. The original NPI-10 includes 10 domains: delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, elation/euphoria, apathy/indifference, disinhibition, irritability/lability, and aberrant motor behaviour [17]. Each domain is scored based on frequency and severity with a score range of 0–12, with a maximum total score of 120. Cognitive fluctuation was assessed using the Cognitive Fluctuation Inventory, with the same format as the original NPI [19, 20], of which content validity and reliability has been previously assured [19] (online suppl. file 1; for all online suppl. material, see www.karger.com/doi/10.1159/000441443). The NPI-2 [12] was calculated as the sum of the scores for hallucinations and cognitive fluctuation [19, 20], corresponding to two of the three core features of DLB, with a score range of 0–24.

Statistical Analysis

This analysis included the full analysis set of each study, comprising all patients who received the study drug at least once and had valid efficacy assessment data at more than one point. The data of the two studies were pooled, and the data on demographics and clinical characteristics were analysed and summarised descriptively.

Subsequently, patient characteristics between the two studies were compared. The characteristics of the patients enrolled at psychiatry and neurology specialty centres, where most were enrolled, were also compared by types of centre. Fisher's exact or χ^2 test was performed for categorical variables and t test for continuous variables. Logistic regression analysis or analysis of variance was performed for interaction between the two studies and types of specialty centres.

All statistical analyses have been performed using SAS for Windows, version 9.3 (SAS Institute Inc., Cary, N.C., USA) with a two-tailed 0.05 significance level.