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RESEARCH LETTER

Factors related to institutionalization among disabled older people; a two-year longitudinal study

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INTRODUCTION

Nursing home placement among disabled older people means discontinuing home care provision by family caregivers. Care recipient factors related to their institutionalization, such as activities of daily living (ADL), instrumental activities of daily living (IADL) and some medical conditions have been well examined in previous studies (e.g. Andel *et al.*, 2007). By contrast, caregiver factors (e.g. caregiver burden, care recipient-caregiver kinship) with respect to institutionalization have not been well examined. However, such caregiver factors need the same level of investigation as has been given to care recipient factors (e.g. Oura *et al.*, 2006).

In addition, concern about potentially harmful behaviors (PHB) by family caregivers that affect disabled older people (Williamson *et al.*, 2001; Beach *et al.*, 2005) or mistreatment of disabled older people has been increasing. Such a caregiver factor needs to be included in order to help identify those factors related to institutionalization among disabled older people.

The authors recently reported factors related to PHB towards disabled older people in a cross-sectional study (Sasaki *et al.*, 2007). The present study is a two-year follow-up study. This longitudinal study aimed to identify factors related to institutionalization among community-dwelling disabled older people.

METHODS

Four hundred and twelve pairs of community-dwelling disabled older adults who used visiting nursing services under the public Long-Term Care insurance system in Japan and their co-residing family caregivers participated in the study. The present study was approved by the Ethical Committee of the National Institute for Longevity Sciences.

At Time 1, the family caregivers were asked to provide the following information: PHB towards their older family adults; family caregiver burden; care recipient-caregiver kinship; age and sex; behavioral disturbances and cognitive impairment of their older adults. In addition, visiting nurses obtained the following information regarding the older adults: severity of dementia; severity of physical impairment; vision problems; hearing problems; age and sex. The details of the survey and the characteristics of the subjects have been described elsewhere (Sasaki *et al.*, 2007).

At Time 2 (two years later), care recipients' subsequent institutionalization was identified from nursing documentation.

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Data from the 398 pairs of disabled older adults and their caregivers were subjected to analyses. The factors at Time 1 related to institutionalization at Time 2 among disabled older people were examined by χ^2 tests. Subsequently, the relative risk (RR) and its 95% confidential interval (95%CI) were calculated.

RESULTS

At Time 2, 6.8% ($n=27$) of the older people were institutionalized and 52.5% ($n=209$) remained in their own home (with or without their caregiver). Table 1 compares the following two groups regarding the variables concerned; those who had remained in their own home and those who had been institutionalized after the survey at Time 1. Among the variables concerned, PHB by family caregiver at Time 1 was the only factor that was related to institutionalization of the disabled older adult at Time 2 ($\chi^2=4.31$, RR = 2.43, 95%CI = 1.02–5.78). The other variables at Time 1 had no correlations with institutionalization among disabled older people.

DISCUSSION

In the present study, PHB towards disabled older people by family caregivers at the previous time point was the only factor associated with institutionalization among disabled older people at the follow-up. It was suggested that detection of PHB by family caregivers is a warning sign for future nursing home placement for disabled older people. In order to assist disabled older people to remain in their own homes, it is necessary to provide interventions that will help prevent family caregivers from engaging in PHB.

In our previous study (Sasaki *et al.*, 2007), behavioral disturbances of older people and an adult child as the caregiver have been found to be associated with PHB towards disabled older people. Thus, these two factors should be taken into account in order to prevent PHB from family caregivers; thereby delaying institutionalization among community-residing disabled older people.

CONFLICT OF INTEREST

None.

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Table 1. Comparisons between institutionalized disabled older people and those remaining in their own home

	Remaining in home		Institutionalized		χ^2	p
Care recipients						
Sex (Female vs Male)	130 *vs* 79	$n=209$	16 *vs* 11	$n=27$	0.088	0.834
Age (Years) (−80 *vs* 81+)	108 *vs* 101	$n=209$	11 *vs* 16	$n=27$	1.144	0.312
Behavioral disturbance (TBS) (0 *vs* 1+)	89 *vs* 41	$n=130$	9 *vs* 8	$n=17$	1.630	0.273
Severity of dementia (no problem,I, II vs III, IV, M)	141 *vs* 63	$n=204$	18 *vs* 9	$n=27$	0.067	0.826
Severity of physical impairment (no problem, J, A *vs* B, C)	88 v *vs* 116	$n=204$	13 *vs* 14	$n=27$	0.243	0.682
Cognitive impairment (SMQ) (−39 *vs* 40+)	120 *vs* 16	$n=136$	18 *vs* 3	$n=21$	0.109	1.000
Hearing problems (0 *vs* 1)	143 *vs* 52	$n=195$	18 *vs* 8	$n=26$	0.195	0.815
Vision problems (0 *vs* 1)	149 *vs* 43	$n=192$	19 *vs* 7	$n=26$	0.266	0.622
Caregivers						
Sex (Female vs Male)	165 *vs* 44	$n=209$	21 *vs* 6	$n=27$	0.020	1.000
Age (Years) (−62 *vs* 63+)	106 *vs* 102	$n=208$	9 *vs* 18	$n=27$	2.972	0.103
Hours of caregiving/day (−5.9 *vs* 6+)	75 *vs* 98	$n=173$	10 *vs* 10	$n=20$	0.321	0.638
Duration of caregiving (year) (−3.9 *vs* 4+)	91 *vs* 109	$n=200$	15 *vs* 11	$n=26$	1.373	0.298
Hours caregivers can be relieved/day (−1.9 *vs* 2+)	74 *vs* 118	$n=192$	11 *vs* 14	$n=25$	0.277	0.665
Spouse as caregiver (no *vs* yes)	120 *vs* 89	$n=209$	15 *vs* 12	$n=27$	0.034	1.000
Adult child as caregiver (no *vs* yes)	136 *vs* 73	$n=209$	19 *vs* 8	$n=27$	0.298	0.671
Daughter-in-law as caregiver (no *vs* yes)	168 *vs* 41	$n=209$	21 *vs* 6	$n=27$	0.102	0.798
Caregiver burden (J-ZBI) (−27 *vs* 28+)	79 *vs* 93	$n=172$	8 *vs* 13	$n=21$	0.464	0.643
Potentially harmful behaviors (0 *vs* 1+)	123 *vs* 63	$n=186$	8 *vs* 11	$n=19$	4.313	0.046

The details of the dichotomization for the above variables have been described elsewhere (Sasaki *et al.*, 2007).

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Original Research Article

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Cognitive Function and Psychiatric Symptoms in Early- and Late-Onset Frontotemporal Dementia

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Key Words
Cognitive function/psychiatric symptoms, frontotemporal dementia · Early-onset frontotemporal dementia · Late-onset frontotemporal dementia

Abstract
Background/Aim: Some recent studies mentioned that late-onset frontotemporal dementia (FTD) is more common than previously assumed. Although much research has been done in the field, there are no systematic studies which have compared clinical characteristics of early- and late-onset FTD. The aim of this study was to compare cognitive function and psychiatric symptoms in patients with early- and late-onset FTD. ***Methods:*** Study participants were consecutive outpatients. There were 35 FTD patients; their mean age at onset was 63.0 years. We studied sex, education, duration from onset to consultation, Clinical Dementia Rating (CDR) scores, Mini-Mental State Examination (MMSE) scores, Raven's Coloured Progressive Matrices (RCPM) scores, and Neuropsychiatric Inventory (NPI) scores at first consultation of early- and late-onset FTD patients. ***Results:*** There were no significant differences in sex ratio, education, CDR scores, and duration from onset to consultation. There were significant differences in the total MMSE scores, 'three-word recall task', 'construction task', and RCPM scores; late-onset groups scored significantly lower than early-onset groups. There were significant differences in the apathy domain of NPI and total NPI scores; late-onset groups scored significantly higher than early-onset groups. ***Conclusion:*** Late-onset FTD patients may have memory and visuospatial deficits in addition to their behavioural changes, even if they are clinically diagnosed according to consensus diagnostic criteria. They also present more apathy, and they may have a different histolopathological background.

Introduction

Frontotemporal lobar degeneration (FTLD) is the term for primary cerebral degeneration involving the frontal and/or anterior temporal lobes associated with a spectrum of non-Alzheimer-type cortical pathology [1, 2]. Because it gives rise to three different clinical syndromes determined by the distribution of atrophy, FTLD is comprised of three subgroups called frontotemporal dementia (FTD), semantic dementia, and progressive non-fluent aphasia [2]. FTD is the most common clinical phenotype of FTLD, accounting for approximately half of all

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Table 1. Demographic variables of the patient groups (mean ± SD)

	Early-onset FTD	Late-onset FTD	p
Number of patients	21	14	
Age at onset, years	58.0 ± 5.6	70.7 ± 5.0	0.000
Male/female ratio	11/10	7/7	1.000
CDR score (0.5/1/2/3)	8/6/5/2	1/5/6/2	0.211
Education, years	11.0 ± 3.7	10.2 ± 3.2	0.536
Duration from onset to consultation, years	4.5 ± 2.9	3.7 ± 2.1	0.394

FTLD cases [3, 4]. As patients with FTD may present characteristic behavioural changes, including loss of insight, disinhibition, apathy, mood changes, stereotypic behaviour, and abnormal eating behaviour, it is associated with a high degree of caregiver burden [1, 5–8].

It was generally reported that FTD occurs mainly among individuals aged 50–65 years, and FTD is the common cause of primary dementia in the presenium, accounting for up to 20% of all presenile dementia cases [9–11]. However, some recent hospital-based studies reported that late-onset FTD patients were more common than previously assumed [4, 12]. As far as we know, there are only few studies about late-onset FTD [13], and there are no systematic studies comparing clinical characteristics of early- and late-onset FTD.

The aim of this study was to compare cognitive function and psychiatric symptoms in consecutive patients with early- and late-onset FTD attending a memory clinic in Japan.

Patients and Methods

Study participants were 35 consecutive outpatients of the Higher Brain Function Clinic of the Department of Neuropsychiatry, Ehime University Hospital, with a diagnosis of FTD between January 1997 and September 2005. All the patients were evaluated by senior neuropsychiatrists, underwent both physical and neurological examinations, as well as standard psychiatric evaluation to exclude major functional psychiatric disorders such as schizophrenia or mood disorders. We also used the usual battery of screening blood tests including vitamin B_{12} and thyroid function assessment to exclude treatable causes of dementia. FTLD patients, including FTD, semantic dementia, and progressive non-fluent aphasia, were diagnosed according to the international consensus criteria [2].

All patients with FTD underwent MRI or CT, and almost all patients underwent HMPAO-SPECT. All patients with FTD showed either frontal atrophy on structured imaging and/or frontal lobe hypoperfusion on HMPAO-SPECT [14, 15]. Patients were assessed by means of a comprehensive neuropsychological test battery, including the Mini-Mental State Examination (MMSE) [16], Clinical Dementia Rating (CDR) [17], Raven's Coloured Progressive Matrices (RCPM) [18], digit span tasks, word fluency tasks, clock drawing test, and ADAS-Jcog (Alzheimer's Disease Assessment Scale – cognitive component; Japanese version). The presence of psychiatric symptoms was assessed during a structured caregiver interview using the Neuropsychiatric Inventory (NPI) [19]. The NPI evaluates ten neuropsychiatric disturbances common in dementia: delusion, hallucination, agitation, dysphoria, anxiety, apathy, irritability, euphoria, disinhibition, and aberrant motor behaviour. The validity and reliability of the NPI have been proven both in Western countries and Japan [20].

We routinely and systematically gathered information to determine the onset of the illness according to caregivers with a standard interview; the 'onset' was the time when the caregiver initially noticed any changes in the patient which reflected a substantial change from the patient's premorbid state, rather than a long-standing character trait.

Early-onset dementia was defined as dementia with age at onset <65 years, and late-onset dementia was defined as dementia with age at onset ≥65 years. We examined differences in sex, education, duration from onset to consultation, and CDR, MMSE, RCPM, and NPI scores at first consultation between early- and late-onset FTD groups.

All examinations were conducted after obtaining informed consent from all subjects or their caregivers.

Statistical Analysis

Data analyses were carried out using SPSS. Statistical differences between the two groups were assessed by the t test for age, education, and duration from onset to consultation. The Mann-Whitney U test was conducted for the comparison of MMSE total score, MMSE recall domain, RCPM score, NPI total score, and NPI subscores. The χ^2 test with post hoc Fisher's exact test was conducted for comparison of CDR grade and MMSE construction domain.

Results

There were a total of 35 FTD patients, the mean age at onset was 63.0 ± 8.3 years, and 40% of them were over 65 years old at onset. Demographic variables of the two patient groups are summarized in table 1. There were no significant differences between the two groups with re-

gard to sex, education, CDR, and duration from disease onset to consultation. As an initial symptom, 19 out of 21 early-onset and 11 out of 14 late-onset patients showed behavioural changes.

Table 2 shows the cognitive function between the two patient groups. There were significant differences in the total MMSE score, 'recall of three words' domain, 'construction' domain, and RCPM scores between the two groups; patients in the late-onset FTD group scored significantly lower than those in the early-onset FTD group. We did not compare other neuropsychological results because some FTD patients did not manage to complete these tasks because of their behavioural symptoms (7 out of the 21 early-onset patients and 4 out of the 14 late-onset patients).

Table 3 shows the comparison of psychiatric symptoms between the two groups according to NPI score. There were significant differences in the apathy domain of the NPI and in the total NPI score between the two groups; late-onset FTD patients scored significantly higher than early-onset FTD patients.

Table 2. Comparison of cognitive function between the two groups (mean ± SD)

	Early-onset FTD	Late-onset FTD	p
MMSE total score	21.3 ± 7.6	14.1 ± 9.9	0.023
MMSE recall domain	1.6 ± 1.2	0.8 ± 1.1	0.048
MMSE construction domain (0/1)	4/17	10/4	0.002
RCPM score	23.1 ± 5.4	14.3 ± 9.5	0.006

Table 3. Comparison of psychiatric symptoms (total NPI score) between the two groups (mean ± SD)

	Early-onset FTD	Late-onset FTD	p
Delusion	0.6 ± 1.3	1.3 ± 3.5	0.778
Hallucination	0.2 ± 0.9	1.1 ± 3.3	0.630
Agitation	1.9 ± 2.6	3.9 ± 3.7	0.103
Dysphoria	0.8 ± 1.5	0.8 ± 1.8	0.881
Anxiety	1.6 ± 3.1	1.2 ± 1.9	0.934
Euphoria	0.8 ± 1.9	1.6 ± 2.6	0.377
Apathy	4.5 ± 3.8	7.1 ± 3.0	0.040
Disinhibition	2.6 ± 3.8	4.5 ± 4.3	0.278
Irritability	0.9 ± 1.6	3.0 ± 4.1	0.342
Aberrant motor behaviour	5.6 ± 5.1	7.3 ± 4.1	0.293
Total NPI score	19.5 ± 11.1	31.9 ± 17.3	0.012

Discussion

This study is the first to compare the cognitive function and psychiatric symptoms in patients with early- and late-onset FTD using standardized test batteries. It was generally reported that FTD occurs mainly among individuals aged 50–65 years; the average onset age was reported to be around 57 years in European and North American patients [21]. However, the mean onset age of our series of FTD patients was 63.0 ± 8.3 years, which is older than that reported in European and North American studies [1, 9, 10, 22]. Forty-percent of all FTD patients were in the late-onset group, i.e., age at onset ≥65 years.

The reason for this difference may be based on the role of heredity; namely, most Japanese cases of FTLD are sporadic [23], while the FTLD cases in European and North American countries were accompanied by an extensive family history. In a community-based study in the UK [9], almost one third of the cases (29%) with FTLD had a positive family history. In a nationwide survey in The Netherlands, 38% of the FTD patients had 1 or more first-degree relatives with dementia before the age of 80 years [24]. Among our 35 patients, there were none with a family history of FTLD, and only 5 patients with a family history of any kind of dementia. Onset age of sporadic FTD patients may be later than that of familial FTD patients, although a study done in the UK [25] reported that there were no significant differences in onset age between those with tau mutation-positive, familial tau mutation-negative, and sporadic patients. We need further studies on the relationship between onset age and genetics.

In our research, late-onset FTD patients showed significantly lower values than early-onset FTD patients in the total score of MMSE, 'recall of three words' domain and 'construction' domain of MMSE, and in the RCPM score, although the severity of dementia according to the CDR score did not differ between the two groups. This result suggests that late-onset FTD patients might present different cognitive impairment compared to early-onset FTD patients. FTD patients were known to have better memory abilities and visuospatial abilities than Alzheimer's disease (AD) patients [2, 26, 27]. The 'recall of three words' domain of the MMSE reflects memory function of the subject, and those who have memory disturbance such as AD patients did not score well in this domain [28, 29]. The RCPM score reflects visuoconstructive or visuo-

spatial functions of a subject, and those who have visuospatial dysfunction such as AD or Lewy body dementia did not score well on this item [30]. Late-onset FTD patients tend to have some memory and visuospatial deficits at least on neuropsychological test batteries. In fact, 4 out of the 14 caregivers of late-onset FTD patients noticed forgetfulness, while 2 out of 21 caregivers of early-onset FTD patients noticed it during the course of the disease. They may have cortical pathology of temporal/parietal lobes or vascular disease behind the primal atrophy in frontal lobes [31]. For this reason, we compared the differences on MRI scans between early- and late-onset FTD patients with three senior neuropsychiatrists separately and blinded to the patients and found no difference in the presence of parietal atrophy or ischemic changes between the two groups. However, as we did not conduct volumetry or other statistical analysis of MRI, there is a possibility of effects from other pathologies.

Apathy was one of the most predominant psychiatric symptoms following aberrant motor behaviour in both early- and late-onset FTD patients. Late-onset FTD patients presented more apathy compared to early-onset FTD patients according to NPI scores, although the severity of dementia according to CDR scores did not differ between the two groups. Apathy is known to be a very common change that occurs in FTD patients [7, 32], and is aggravated with the progression of dementia. Apathetic FTD patients have atrophy extending into the dorsolateral frontal cortex or into the anterior cingulate cortex [7, 33]. Previous studies demonstrated an association between anterior cingulate hypoperfusion and the severity of apathy in AD patients [34, 35]. These results suggest that apathy of late-onset FTD patients may be associated with the pathology of the frontal cingulate or dorsolateral frontal area. Late-onset FTD patients may have different pathological and genetic backgrounds compared to early-onset FTD patients, even though we still need to accumulate data.

Turning to the comparison of early-onset AD and late-onset AD, early-onset AD patients were reported to have rapid deterioration, as well as language problems and visuospatial dysfunction [36–38]. Our previous research comparing behavioural and cognitive functions in early-onset AD and late-onset AD using the same methodology [39] showed that in both groups there was no difference in the prevalence of apathy and cognitive functions. The results of our FTD patients differed from these findings in AD patients. Late-onset FTD patients had deficits in memory and visuospatial function and tended to be more apathetic. Characteristics of early-onset AD patients may not be generally applicable to all early-onset neurodegenerative diseases.

There are a few methodological issues that should be taken into consideration to appreciate our results fully. Firstly, to determine the age at onset of degenerative dementia is difficult, especially in FTD. In this study, the onset of dementia was defined as the time when the caregiver initially noticed the patient's changes; however, there is a possibility that the estimated time of onset is a subjective estimate given by the caregivers. Initial symptoms of FTD patients are variable as we reported previously [40], which may make it difficult for caregivers to estimate the time of onset.

Secondly, as this study is based on hospital-based data of the neuropsychiatry department rather than community-based data, it can be claimed that selection bias affects our results. General physicians may refer patients without behavioural symptoms or patients with distinct neurological signs to other departments. Nevertheless, epidemiologic data of non-AD dementias are insufficient because pure cross-sectional or population studies are impractical for diseases with a low prevalence. Furthermore, epidemiologic studies of dementia typically survey people aged 65 years and older, so they may exclude a considerable number of cases of FTD. Therefore, data from hospital-based studies are more realistic.

Thirdly, in this study, we clinically diagnosed FTD patients according to consensus criteria for FTLD [2]. We did not perform lumbar puncture or pathological examination and we could not discuss abnormal tau deposits or pathological background in this study. Recent research revealed that FTD patients consist of pathological heterogeneous groups, including Pick's disease with or without Pick bodies, FTDP-17 (FTD with parkinsonism linked to chromosome 17), dementia lacking distinctive histology, corticobasal degeneration, and motor neuron disease [31, 41, 42]. There is a possibility that early- and late-onset FTD patients had different pathological backgrounds as we described above, although antemortem consensus diagnosis of FTLD was moderately sensitive and very specific [43].

Fourthly, although there was no significant difference between the two groups in the severity of dementia according to the CDR score, the CDR was designed to assess the severity of dementia mainly in AD patients and was not specifically designed to assess the severity of FTD accurately. The severity of dementia in FTD patients could not be assessed with complete accuracy in this study; however, so far this is the only standardized assessment scale of FTD severity available. This is the common lim-

itation of clinical research of FTD as in other previous clinical studies. Although we found no difference between the two groups regarding the duration from onset to consultation, there is also a possibility that in both groups disease proceeds at a different speed.

In conclusion, FTD is a common cause of early-onset dementia; as previously reported, late-onset FTD patients should not be overlooked especially in spontaneous cases. Late-onset FTD patients may have memory and visuospatial impairments to some extent and tend to be more apathetic than early-onset FTD patients, in addition to other symptoms which are the same as in early-onset FTD. Further clinicopathological studies are required.

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