文 献

- Alzheimer A: Über eignartige Krankheitfalle des spateren Alters. Z Gesamte Neurol Psychiatr 4: 356-385, 1911
- Baron-Cohen S, Lesliie AM, Frith U: Does the autistic child hare a "theory of mind"? Cognition 21: 37-46, 1985
- Bozeat S, Gregory CA, Ralph MA, Hodges JR: Which neuropsychiatric and behavioral features distinguish frontal and temporal variants of frontotemporal dementia from Alzheimer's disease? J Neurol Neurosurg Psychiatry 69: 178-186, 2000
- 4) 福原竜治, 池田 学, 田邉敬貴: MRI. 日本臨牀 61: 436-441, 2003
- 5) 古川良子, 井関栄三, 小田原俊成・他: 初老期・老年 期発症の精神疾患として経過した後に前頭葉変性型の 前頭側頭型痴呆が疑われた 2 症例. 精神医学 45:943-950, 2003
- 6) Gregory C, Lough S, Stone V, et al: Theory of mind in patients with frontal variant frontotemporal dementia and Alzheimer's disease: theoretical and practical implications. Brain 125: 752-764, 2002
- Gustafson L: Frontal-lobe degeneration of non-Alzheimer type. Clinical picture of and differential diagnosis. Arch Gerontol Geriatr 6: 209-223, 1987
- 8) Hodges JR, Patterson K, Oxbury S, et al: Semantic dementia. Progressive fluent aphasia with temporal lobe atrophy. Brain 115: 1783-1806, 1992
- 9) Hodges JR, Patterson K, Ward R, Garrard P, et al: The differentiation of semantic dementia and frontal lobe dementia (temporal and frontal variants of frontotemporal dementia) from early Alzheimer's disease: a comparative neuropsychological study. Neuropsychology 13: 31– 40, 1999
- 10) 鉾石和彦, 池田 学, 繁信和恵・他:「場合わせ, 取り 繕い反応」により介護保険モデル事業において実際に 必要な介護度よりも低く評価されたアルツハイマー病 の1例. 精神科治療学14:1241-1244, 1999
- 11) 鉾石和彦, 池田 学, 牧 徳彦・他: 顕著な葉性萎縮 を伴わない前頭側頭葉型痴呆の2例. 脳神経51:641-645, 1999
- 12) Hokoishi K, Ikeda M, Maki N, et al: Frontotemporal lobar degeneration: a study in Japan. Dement Geriatr Cogn Disord 12: 393-399, 2001
- 13) Hutton M, Lendon CL, Rizzu P, et al: Association of missense and 5'-splice-site mutation in tau with the inherited dementia FTDP-17. Nature 399: 702-705, 1009
- 14) 池 田 研 二:前 頭 側 頭 型 痴 呆 (Fronto-temporal Dementia) の位置づけ、精神経誌 102:529-542, 2000
- 15) 池田 学, 森 悦朗: ピック病における人格変化と行 動異常. 老精医誌 7: 255-261, 1996
- 16) Ikeda M, Hokoishi K, Maki N, et al: Increased prevalence of vascular dementia in Japan: a community-based epidemiological study. Neurology 11:839-844,

2001

- 17) Ikeda M, Brown J, Holland AJ, et al: Changes in appetite, food preference, and eating habits in frontotemporal dementia and Alzheimer's disease. J Neurol Neurosurg Psychiatry 73: 371-376, 2002
- 18) Ikeda M, Ishikawa T, Tanabe H: Epidemiology of frontotemporal lobar degeneration. Dement Geriatr Cogn Disord 17: 265-268, 2004
- 19) 梶谷康介,中川康司,尾籠晃司・他:九州大学医学部 附属病院もの忘れ外来(脳の健康クリニック)の現況: 創立1年のまとめ。老精医誌13:1063-1069,2002
- Kitagaki H, Mori E, Hirono N, et al: Alteration of white matter MR signal intensity in frontotemporal dementia. AINR Am I Neuroradiol 18: 367-378, 1997
- 21) 木谷友一, 小林克治, 林 眞弘・他: Frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17) の兄弟例. 精神医学 45:31-35, 2003
- 22) McKhann GM, Albert MS, Grossman M, et al: Clinical and pathological diagnosis of frontotemporal dementia: Report of the work group on frontotemporal dementia and Pick's disease. Arch Neurol 58: 1803-1809, 2001
- 23) Mendez MF, Selwood A, Mastri AR, et al: Pick's disease versus Alzheimer's disease; A comparison of clinical characteristics. Neurology 43: 289-292, 1993
- 24) Mituyama Y, Tamiya S: Presenile dementia with motor neuron disease in Japan. A new entity? Arch Neurol 36: 592-593, 1979
- 25) 森 悦朗:前頭前野病変による行為障害・行動障害、神経心理 12:106-113、1996
- 26) 中野今治: 運動ニューロン疾患を伴う痴呆症/歴史・ 疾患概念・分類, Clin Neurosci 23: 305-308, 2005
- 27) 成本 迅,北林百合之介,福永敏行・他:Knife-blade 様の葉性萎縮を欠いた前頭側頭型痴呆の1症例ーピッ ク型との行動障害パターンの違いについて一. 臨床精 神医学30:179-183,2001
- 28) Neary D, Snowden JS, Northen B, et al: Dementia of frontal lobe type. J Neurol Neurosurg Psychiatry 51: 353-361, 1988
- 29) Neary D, Snowden JS, Northen B, et al: Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. Neurology 51: 1546-1554, 1998
- 30) Neary D: Overview of frontotemporal dementia and the consensus applied. Dement Geriat Cogn Disord 10: 6-9, 1999
- 31) Onari K, Spatz H: Anatomische Beitrage zur Leben von der Pickschen umschriebe Grosshirnrinden-Atrophie (Picksche Krankheit). Z Ges Neurol Psychiat 101: 470-511, 1926
- 32) Pick A: Über einen weiteren Symptomenkomplex im Rahmen der Dementia senilis, bedingt durch umschriebene stär Kere Hirna trophie (gemische Apraxie). Mschr Psychiat Neurol 19: 97-108, 1906
- Ratnavalli E, Brayne C, Dawson K, et al: The prevalence of frontotemporal dementia. Neurology 58: 1615–1621, 2002
- 34) Rossor MN, Reresz T, Lantos PL, et al: Semantic

- dementia with ubiquitin-positive tau-negative inclusion bodies. Brain 123: 267-276, 2000
- 35) 斉藤 治:心の理論と前頭葉. Brain Medical 13:55-62, 2001
- 36) Spatz H: Über die Bedeutung der basalen Rinde. Auf Grund von Beobacatungen bei Picksher Krankheit und bei gedecken Hirnverletzungen. Z Neur 158: 208-232, 1937
- 37) Shigenobu K, Ikeda M, Fukuhara R, et al: The Stereotypy Rating Inventory for frontotemporal lobar degeneration. Psychiatry Research 110: 175-187, 2002
- 38) 品川俊一郎, 池田 学:前頭側頭型痴呆の前駆症状と 初発症状, 老精医誌 16:302-304, 2005
- 39) Shinagawa S, Ikeda M, Fukuhara R, et al: Initial symptoms in frontotemporal dementia and semantic dementia compared to Altzheimer's disease. (in submission)
- 40) ShimomuraT, Mori E: Obstinate imitation behaviour in differentiation of frontotemporal dementia from Alzheimer's disease. Lancet 352: 623-624, 1998
- 41) Snowden JS, Gouldding PJ, Neary D: Semantic Dementia: a form of circumscribed atrophy. Behav Neurol 2: 167-182, 1989
- 42) Snowden JS, Neary D, Mann DMA: Fronto-Temporal Lobar Degeneration: Fronto-Temporal Dementia,

- Progressive Aphasia, Semantic Dementia. Churchill Livingstone, New York, 1996
- 43) 高橋克朗: 痴呆と常同強迫行動(Pick 病など). 神経心 理 7: 19-26, 1991
- 44) 田邉敬貴, 池田 学, 中川賀嗣・他:語義失語と意味 記憶障害. 失語症研究 12:153-167, 1992
- 45) 田邉敬貴: 語義失語・その人となり一器質性病変と性格の変容一. 神経心理8:34-42,1992
- 46) 田邉敬貴:前頭葉型痴呆. KEY WORD 1997-98, 松下 正明・倉知正佳・樋口輝彦・編, 先端医学社, 東京, 1997, pp142-143
- 47) Tanabe H, Komori K, Ikeda M: Behavioral symptomatology and care of patients with frontotemporal lobe degeneration-based on the aspects of phylogenetic and ontogenetic processes. Dement Geriat Cogn Disord 10: 50-54, 1999
- 48) 田邉敬貴:痴呆の症候学、神経心理学コレクション, 医学書院,東京,2000
- 49) The Lund and Manchester Groups: Clinical and neuropathological criteria for frontotemporal dementia. J Neurol Neurosurg Psychiatry 57: 416-418, 1994
- 50) 山崎達二: Pick 病の臨床病理学的研究; とくに人格変 化を中心として. 精神経誌 68: 891-908, 1966

Abstract

Clinical pictures of dementia of frontal lobe type

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The term "dementia of frontal lobe type (DFT)" was first proposed by the Manchester group (U. K.) in 1988. Later DFT was replaced by "fronto-temporal dementia (FTD)". FTD correspond to the so-called frontal lobe dominant Pick disease. FTD is the most common cause of cortical dementia, following Alzheimer's disease and Dementia with Lewy bodies. FTD patients have a variety of behavioral and psychological symptoms, which may make it difficult to establish the initial diagnosis.

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A longitudinal study regarding conversion from mild memory impairment to dementia in a Japanese community

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SUMMARY

Objective To estimate the rate that subjects with Mild Memory Impairment /Not Dementia (MMI/ND) shifted to dementia in a population-based cohort and to establish simple diagnostic methods for identification of high-risk persons for dementia. Methods Subjects in a community-based elderly cohort of MMI/ND were followed longitudinally. Subjects were selected from the participants in the first Nakayama study. MMI/ND was defined as memory deficit with objective memory assessment, without dementia, impairment of general cognitive function, or disability in activities of daily living. The conversion rate was calculated using the person-year method.

Results At baseline, the sample consisted of 104 subjects (59 female; 45 male) selected from 1162 community dwellers aged over 65 year. During the five-year follow-up, 14 subjects died, 13 moved to other communities, and six refused to participate further. Eleven (10.6%) subjects were diagnosed with Alzheimer's disease (AD), five (4.8%) were diagnosed with vascular dementia (VaD), and six (5.8%) were diagnosed with dementia of other etiology. The annual conversion rate that MMI/ND shifted to AD is calculated on 8.5% per 100 person-year, and shifted to dementia on 16.1% per 100 person-year in this survey.

Conclusions The rate at which subjects with MMI/ND whose conditions shifted to dementia was the same as the rate that subjects with mild cognitive impairment (MCI) shifted to dementia in a previous report. It would be useful to identify groups of high-risk individuals for dementia by simple diagnostic methods. Copyright © 2006 John Wiley & Sons, Ltd.

KEY WORDS - Mild Cognitive Impairment; Alzheimer's disease; MMSE; conversion rate; dementia; Nakayama study

INTRODUCTION

For a boundary or transitional state between aging and dementia, Kral proposed the conception benign senescent forgetfulness (Kral, 1962). Afterwards, cognitive impairment, no dementia (CIND) was advocated as a state characterized by lower cognitive performance than would be expected given the age and educational attainment of the person (Graham *et al.*, 1997). Recently, the term 'mild cognitive impairment (MCI)' was proposed to describe the transitional state

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between normal cognition and Alzheimer's disease (AD) (Flicker et al., 1991; Petersen et al., 1997). MCI is increasingly recognized as an important public health problem because it is common and is associated with significant morbidity, especially the development of clinically diagnosed AD (Petersen et al., 1999; Bozoki et al., 2001; Morris et al., 2001). Interest in MCI has been stimulated by the hope that pharmacologic intervention, such as cholinesterase inhibitors at this stage may delay or prevent progression to AD (Sherwin, 2000; Petersen et al., 2005). Identification of subjects with MCI is gaining importance in the field of early preventive measures and community-based interventions for the emerge of dementia in public health (Dresser, 2000; Janus et al., 2000; Meyer et al., 2002a; Meyer et al., 2002b). MCI subjects could be, as high-risk

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individuals for dementia, a particularly suitable population for preventive approaches. Longitudinal studies of case series have revealed an increased risk of AD in MCI subjects, with a conversion rate ranging from 7 to 20% per year (Johnson *et al.*, 1998; Wolf *et al.*, 1998; Pertersen *et al.*, 2005).

Most studies investigating the natural history of MCI have been conducted on samples of subjects recruited in specialized outpatient clinics such as memory clinics for AD. Such samples are highly selected, and it would be essential to identify highrisk subjects of dementia from community-based surveys to carry out early intervention. To our knowledge, one community-based prospective cohort study reported that an annual conversion rate was 8.3% for 5 years (Larrieu *et al.*, 2002). The incidence and outcome of MCI in the general population are still largely unknown.

Standardized memory examinations such as the Wechsler memory scale revised (WMS-R) can be used to identify subjects satisfying a strict definition of MCI (Flicker *et al.*, 1991; Petersen *et al.*, 1997). However, it may be very difficult to carry out such time-consuming examinations in community-based epidemiological surveys.

We extracted a group of mild memory impairment/ no dementia (MMI/ND) with Mini-Mental State Examination (MMSE) (Folstein *et al.*, 1975; Mori *et al.*, 1985), based on the results of a populationbased dementia study in Nakayama. The aim here is to report on a diagnostic system for MCI-like highrisk community dwellers by simple methods, which could be employed for community-based interventions and public health activities.

SUBJECTS

In the current study, we selected subjects who were participants in the first Nakayama study, and who satisfied the following criteria: (1) normal general cognitive function, with MMSE ≥ 24; (2) objective memory impairment, assessed by three-words recall in MMSE (delayed recall 0/3 or 1/3); (3) neuropsychiatric examination: absence of dementia or depression, diagnosed by geriatric neuropsychiatrists according to the *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edn, revised (DSM-III R) (American Psychiatric Association, 1987) criteria; (4) no ADL impairment. Subjects above mentioned could be defined as MMI/ND.

For comparison, 74 subjects who did not receive a diagnosis of dementia or MMI/ND at baseline were investigated with the same protocol in a 5-year

follow-up. All subjects were hung in one randomly selected village (one of 43) in Nakayama town.

METHODS

Baseline assessment (The first Nakayama study)

Nakayama is a Japanese rural community adjacent to Matsuyama City, a metropolis on Shikokou Island. We selected this town because of its population size (5038 total residents, of whom 1438 were over 65 years of age), population stability (only 3.1% of people more than 65 years of age had moved elsewhere, including institutions, in the 3 years preceding the first survey), and active collaboration offered by family doctors.

The first Nakayama study included all residents over 65 years at home in the rural community of Nakayama town in Japan between January 1997 and March 1998 by means of a door-to-door survey with a three-phase design. Of 1438 inhabitants, 1162 (81.0%) completed the protocol. A more detailed description of the methods has been reported previously (Ikeda *et al.*, 2001; Ikeda *et al.*, 2004).

The screening interview (Phase 1) consisted of a semistructured questionnaire (questions on education, occupation, daily life activities, alcohol consumption, exposure and risk factor profile, previous disease, medication, sleep, and appetite), followed by the MMSE for participants and the short memory questionnaire (SMQ) (Koss *et al.*, 1993) for a family member of each participant. All subjects were examined by neuropsychiatrists. Participants were submitted to clinical evaluation according to the cut point of these tests for the presence of a cognitive disorder, based on previous studies (MMSE \leq 23 and/or SMQ \leq 39).

The clinical evaluation (Phase 2) included a semistructured interview of the participant's medical history; standard physical and neurological examination; severity evaluation using the clinical dementia rating scale (CDR) (Hughes *et al.*, 1982), and psychiatric evaluation using the neuropsychiatric inventory (NPI) (Cummings *et al.*, 1994). Based upon the results of these evaluation, participants were selected for diagnostic procedures (Phase 3).

Participants were asked to undergo cranial computed tomography (CT) and routine blood tests including serum vitamin B 12 and thyroid function tests. A final diagnosis was made based on combined information, using three diagnostic steps. The diagnosis of dementia was established using the DSM-III R criteria. MMI/ND subjects were selected from Phase 1.

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Follow-up assessment and diagnosis

Five-year follow-up was conducted on all these individuals between April and December in 2003. A senior neuropsychiatrist administered MMSE to subjects, while a public health nurse interviewed Physical Self-Maintenance Scale (PSMS) and Instrumental Activities of Daily Living Scale (IADL) (Lawton and Brody, 1969) to a family member of each subject. Subjects hospitalized or entered institutions were included. Cranial CT was conducted on all subjects whose MMSE score had declined by more than 2 points since baseline (Mohs *et al.*, 2001).

The diagnosis of dementia was established according to the DSM-III R criteria. Finally, demented subjects were classified into subgroups by the cause of dementia. AD was defined according to the NINCDS-ADRDA criteria for probable AD (McKhann *et al.*, 1984), VaD was defined according to the NINDS-AIREN criteria (Roman *et al.*, 1993).

This survey was conducted after obtaining informed consent from all subjects or their relatives.

Statistics

The conversion rate was calculated using the personyear method (Beth and Robert, 2001).

RESULTS

The sample consisted of 104 subjects at baseline; 59 were women and 45 were men. The mean age was 75.5 ± 6.7 years (range, 65.1 to 90.2 years) for women and 73.6 ± 6.8 years (range, 65.1 to 101.4 years) for men.

Five years after the first Nakayama study, 14 subjects were dead, 13 had moved to other communities (mainly due to institutionalization), and six refused to participate in the follow-up investigation. Eleven (10.6%) subjects were diagnosed with AD (five men, six women), five (4.8%) were diagnosed with VaD (three men, two women), and six (5.8%) were diagnosed with dementia of other etiology. There were nine (8.7%) subjects who remained in MMI/ND. Furthermore, 40 (38.5%) subjects showed restored MMSE score (Table 1, Figure 1). In our survey, the conversion rate from MMI/ND to AD was 8.5% per 100 person-year and to dementia was 16.1% per 100 person-year for 5 years.

The comparison group consisted of 74 participants at baseline; 41 were women and 33 were men. The mean age was 75.4 ± 7.2 years (range, 65.1-89.2 years) for women and 73.2 ± 6.7 years (range, 65.1-92.4 years) for men. There were no significant differ-

Table 1. As a result of 104 MMI/ND subjects and 74 control subjects in 5 years follow-up

	MMI/ND subjects	Free of dementia and MMI/ND subjects
	No. of samples	No. of samples
Died	14	9
Moved to other community	13	2
refused	6	0
AD	11	0
VaD	5	2
other type of dementia	6	1
MMI/ND	9	1
Free of dementia and MMI	'ND 40	59

ences in age or in gender ratio between the MMI/ND group and the comparison group. Of the 74 participants without dementia or MMI/ND at baseline, nine subjects had died, two moved to other communities, two subjects were diagnosed with VaD (one woman, one man), one was diagnosed with dementia of other etiology, one with MMI/ND, and none who developed AD (Table 1).

The Odds ratio for dementia was 5.2.

DISCUSSION

This is the first report of the five-year outcomes of MCI in a population-based study of dementia in Asia. Our survey differs from previous investigations in the following aspects. First, even in the screening interview, subjects were examined directly by a neuropsychiatrist, and, cranial CT was conducted on all subjects with any signs of dementia. Secondly, we have continued follow-up over five years in the Nakayama community after the first Nakayama investigation with a definite examination at 5 years.

The MCI group only has real value if the majority of people who develop dementia pass through this stage. Several studies have been undertaken to determine the natural course of MCI in attempts to estimate the 'conversion' rate to AD in this group (Petersen et al., 2001). As expected from its concept, most longitudinal studies of case series revealed a much increased risk of AD in MCI subjects (Flicker et al., 1991; Meyer et al., 2002a; Meyer et al., 2002b). MCI subjects may constitute a particularly suitable population for preventive approaches.

In previous clinic-based reports, MCI progresses to AD at a rate of 7 to 20% per year (Flicker *et al.*, 1991; Meyer *et al.*, 2002b; Tierney *et al.*, 1996). Standardized episodic memory examinations

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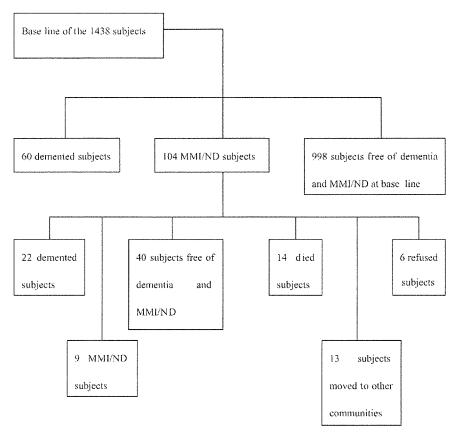


Figure 1. General design of the MMI/ND follow up study in Nakayama

(e.g. WMS-R) with comprehensive neuropsychological tests have been suggested to select a subject satisfying one strict definition of MCI. Therefore, measured cognitive function with MMSE, WMS-R, Wechsler Adult Intelligence Scale Revised (WAIS-R), Auditory Verbal Learning Test were adopted in those studies. The differences in these rates are probably related to the different instruments and cut-off limits chosen to define MCI across studies.

To our knowledge, there are a few community-based prospective cohort studies, following a community-dwelling MCI elderly people for several years (Larrieu et al., 2002; Tuokko et al., 2003; Gangluli et al., 2004). In one of these studies (Larrieu et al., 2002), comprehensive test batteries for an evaluation of global mental status (MMSE), visual memory (Benton's Visual Retention Test), verbal fluency (Isaacs Set Test), visuospatial attention (Zazzo's Cancellation Test), and simple logical reasoning and attention (Wechsler's Digit Symbol Test) were adopted. The conversion rate from MCI to AD was

8.3% per 100 person-year for 5 years (Larrieu *et al.*, 2002). This conversion rate is compatible with our result.

It may be difficult to administer comprehensive tasks in ordinal epidemiological surveys. It takes not only money and time (more than 1 h) but is also a large burden for any substantial size participants, particularly the very old. Therefore, it is an unsuitable method for extracting a high-risk group to AD in public health. There is an increasing need for brief but efficient cognitive screening instruments suitable for detecting MCI from normal aging individuals (Loewenstein et al., 2000). Such screening tests would lighten the burden on patients and physicians, economize medical resources, and provide opportunities for dementia prevention and treatment when there is evidence that effective interventions exist (Bland and Newman, 2001). In the current study, we used MMSE to select subjects who present MMI/ND. We measured general cognitive performances with total score of MMSE and evaluated

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memory impairment with three-words recall in MMSE. The MMSE total score was used to screen subjects and select them for neuropsychiatric evaluation/diagnosis, and then a subset of the MMSE (three-word recall) was used to further classify them as MMI/ND. Neuropsychiatric examinations were independent of the MMSE results. MMSE is a widely used and well validated instrument for assessing global cognitive function (Xu *et al.*, 2002), and used as screening instrument for cognitive decline or cognitive impairment in population-based studies as well as in clinical practice. MMSE is easily administered with a short operation time, thus it is suitable for use in the community.

We do not use standardized memory tests except for MMSE three-word recall to detect prodromal dementia cases. Therefore, subjects are not strictly defined as MCI, although they show apparent deficits in memory without dementia. Some previous reports have stated that MCI could not be distinguished from normal aging by simple examination (O'Connor et al., 1991; Devanand et al., 1997). However, the conversion rate of MMI/ND in this study was almost the same as a previous community-based MCI study with strict memory examinations (Larrieu et al., 2002). In this study, we do not check for subjective memory complaints preferably corroborated by informants, which are considered characteristic of MCI based on strict criteria (Petersen et al., 1997). The observations by knowledgeable informants regarding an individual's cognitive abilities in everyday functioning have been shown to be sensitive and reliable for MCI detection (Carr et al., 2000; Morris et al., 2001). However, it is difficult to carry out informant-based scales as screening tools, because considerable dwellers live alone in modern Japanese society and in many Western societies.

Although the population examined here is reasonably stable, over 10% had moved to other communities during the first year period including those who needed institutional care. In Japan a new system of long term care insurance (i.e. kaigo hoken) was implemented in 2000 which may have been an influence in this movement and could be a limitation.

As a consequence of global aging of the human population, the occurrence of cognitive impairment and dementia is rapidly becoming a significant burden for medical care and public health systems. Primary and secondary prevention of dementia through population-level interventions could reduce age associated risk. Reliable identification of high-risk individuals for dementia is vitally important to test effects of early therapeutic interventions. If community interac-

tions are to be developed at the individual level, practical and simple methods will be needed for identification of those at risk of 'conversion' at low cost. MMI/ND selected by our method might be a possible candidate for trials of preventive intervention on public health. MMI/ND might be a promising therapeutic target and an important target for screening and possible early intervention.

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REFERENCES

American Psychiatric Association. 1987. *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edn, rev. American Psychiatric Association: Washington, DC.

Beth D, Robert GT. 2001. Basic and Clinical Biostatistics (Lange Medical Books), 3rd edn. McGraw-Hill: New York.

Bozoki A, Giordani B, Heidebrink JL, Berent S, Foster NL. 2001. Mild cognitive impairments predict dementia in nondemented elderly patients with memory loss. Arch Neurol 58: 411–416.

Bland RC, Newman SC. 2001. Mild dementia or cognitive impairment: the Modified Mini-Mental State Examination (3MS) as a screen for dementia. *Can J Psychiatry* **46**: 506–510.

Carr DB, Gray S, Baty J, Morris JC. 2000. The value of informant vs. individual's complaints of memory impairment in early dementia. *Neurology* 55: 1724–1726.

Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. 1994. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology* 44: 2308–2314.

Devanand DP, Folz M, Gorlyn M, Moeller JR, Stern Y. 1997. Questionable dementia: clinical course and predictors of outcome. *J Am Geriatr Soc* 45: 321–328.

Dresser R. 2000. Weighing the benefits of new Alzheimer's treatments. *Science* **289**: 869.

Flicker C, Ferris SH, Reisberg B. 1991. Mild cognitive impairment in the elderly: predictors of dementia. *Neurology* 41: 1006–1009.

Folstein MF, Folstein SE, McHugh PR. 1975. 'Mini-Mental State'. A practical method for grading the cognitive state of patients for clinician. J Psychiat Res 12: 189–198.

Ganguli M, Dodge HH, Changyu S, DeKosky ST. 2004. Mild cognitive impairment, amnestic type: an epidemiologic study. *Neurology* **63**: 115–121.

Graham JE, Rockwood K, Beattie BL, *et al.* 1997. Prevalence and severity of cognitive impairment with and without dementia in an elderly population. *Lancet* **349**: 1793–1796.

Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. 1982. A new clinical scale for the staging of dementia. Br J Psychiatry 140: 566–572.

Ikeda M, Fukuhara R, Shigenobu K, et al. 2004. Dementia associated mental and behavioural deisturbances in elderly people

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- in the community: findings from the first Nakayama study. *J Neurol Neurosurg Psychiatry* **75**: 146–148.
- Ikeda M, Hokoishi K, Maki N, et al. 2001. Increased prevalence of vascular dementia in Japan: a community-based epidemiological study. Neurology 57: 839–844.
- Janus C, Pearson J, McLaurin J, et al. 2000. A beta peptide immunization reduces behavioral impairment and plaques in a model of Alzheimer's disease. Nature 408: 979–982.
- Johnson KA, Jones K, Holman BL, et al. 1998. Preclinical prediction of Alzheimer's disease using SPECT. Neurology 50: 1563–1571.
- Koss E, Patterson MB, Ownby R, Stuckey JC, Whitehouse PJ. 1993. Memory evaluation in Alzheimer's disease: caregiver's appraisals and objective testing. Arch Neurol 50: 92–97.
- Kral VA. 1962. Senescent forgetfulness; Benign and malignant. J Can Med Assoc 86: 257–260.
- Larrieu S, Letenneur L, Orgogozo JM, et al. 2002. Incidence and outcome of mild cognitive impairment in a population-based prospective cohort. Neurology 59: 1594–1599.
- Lawton MP, Brody EM. 1969. Assessment of older people: self maintaining and instrumental activities of daily living. Gerontologist 9: 179–186.
- Loewenstein DA, Barker WW, Harwood DG, et al. 2000. Utility of a modified Mini-Mental State Examination with extended delayed recall in screening for mild cognitive impairment and dementia among community dwelling elders. Int J Geriatr Psychiatry 15: 434–504.
- Mckhann G, Drachman D, Fostein F, Katzman R, Price D, Stadlan EM. 1984. 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 of Alzheimer's disease. *Neurology* 34: 939–944.
- Meyer JS, Xu G, Thornby J, Chowdhury M, Quach M. 2002a. Is mild cognitive impairment prodromal for vascular dementia like Alzheimer's disease? *Stroke* 33: 1981–1985.
- Meyer JS, Xu G, Thornby J, Chowdhury M, Quach M. 2002b. Longitudinal analysis of abnormal domains comprising mild cognitive impairment (MCI) during aging. J Neuro Sci 201: 19–25.
- Mohs RC, Doody RS, Morris JC, et al. and the 312 Study Group. 2001. A 1-year, placebo-controlled preservation of function survival study of donepezil in AD patients. Neurology 57: 481–488.

- Mori E, Mitani Y, Yamadori A. 1985. Useffulness of a Japanese version of the Mini-Mental State Test in neurological patients [in Japanese]. *Jap J Neuropsychol* 1: 82–90.
- Morris JC, Storandt M, Miller JP, et al. 2001. Mild cognitive impairment represents early-stage Alzheimer disease. Arch Neurol 58: 397–405.
- O'Connor DW, Pollitt PA, Hyde JB, Miller ND, Fellowes JL. 1991. Clinical issues relating to the diagnosis of mild dementia in a British community survey. *Arch Neurol* 48: 530–534.
- Petersen RC, Smith GE, Waring SC, Ivnik RJ, Kokmen E, Tangelos EG. 1997. Aging, memory, and mild cognitive impairment. *Int Psychogeriatr* **9**: 65–69.
- Petersen RC, Smith GE, Waring SC, Ivnik RJ, Targalos EG, Kokmen E. 1999. Mild cognitive impairment-clinical characterization and outcome. Arch Neurol 56: 303–308.
- Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. 2001. Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 8: 1133–1142.
- Petersen RC, Thomas RG, Grundman M, et al. 2005. Vitamin E and Donepezil for the Treatment of Mild Cognitive Impairment. N Engl J Med 352: 2439–2441.
- Roman GC, Tatemichi TK, Erkinjuntti T, et al. 1993. Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. Neurology 43: 250– 260.
- Sherwin BB. 2000. Mild cognitive impairment: potential pharmacological treatment options. J Am Geriatr Soc 48: 431–441.
- Tierney MC, Szalai JP, Snow WG, et al. 1996. Prediction of probable Alzheimer's desease in memory-impaired patients: a prospective longitudinal study. Neurology 46: 661–665.
- Tuokko H, Frerichs R, Graham J, et al. 2003. Five-year follow-up of cognitive impairment with no dementia. Arch Neurol 60: 577–582.
- Wolf H, Grunwald M, Ecke GM, et al. 1998. The prognosis of mild cognitive impairment in the elderly. J Neural Transm 54: 31–50.
- Xu G, Meyer JS, Thornby J, Chowdhury M, Quach M. 2002. Screening for mild cognitive impairment (MCI) utilizing combined mini-mental-cognitive capacity examinations for identifying. Int J Geriatr Psychiatry 17: 1027–1033.

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Initial Symptoms in Frontotemporal Dementia and Semantic Dementia Compared with Alzheimer's Disease

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Key Words

Frontotemporal dementia · Semantic dementia · Alzheimer's disease

Abstract

Background: Despite many reports about cognitive decline and behavioral changes in patients with frontotemporal lobar degeneration (FTLD), there have been very few systematic studies of initial symptoms of frontotemporal dementia (FTD) and semantic dementia (SD). Objective: It was the aim of this study to investigate FTD and SD and to establish whether they are characterized by different initial symptoms. Methods: Three groups of patients were studied: FTD (n = 36), SD (n = 17) and agematched Alzheimer's disease (AD) patients (n = 52). Information on initial symptoms was obtained from caregivers. Symptoms were classified into 22 distinct categories from the following domains, based on previous studies of symptoms of FTLD: (1) change in social behavior, affection, and daily activities, (2) cognitive decline, (3) language impairments, and (4) other abnormal symptoms. Results: Change in social behavior, affection, and daily activities was significantly more common in patients with FTD; on the other hand, language impairments were significantly more common in patients with SD as initial symptoms. Apathy and stereotypic behaviors were the most common initial symptoms among patients with FTD, while anomia, paraphasia, and impairment in word comprehension were the most common initial symptoms among patients with SD. Memory disturbance was the most common initial symptom among patients with AD. *Conclusions:* Behavioral and psychiatric symptoms are predominant initial symptoms in FTD, while language symptoms are predominant initial symptoms in SD. In addition to the assessment of current symptoms, the assessment of initial symptoms is useful for differential diagnosis in patients with FTD, SD and AD.

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Introduction

Currently, frontotemporal lobar degeneration (FTLD) is the preferred term used to describe primary cerebral degeneration involving the frontal and/or temporal lobes associated with non-Alzheimer's pathology [1, 2]. It is the second most common form of primary dementia in the presenium and associated with a high degree of caregiver

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burden as it produces changes in personality, behavior, and communication abilities [3]. FTLD gives rise to three different clinical syndromes determined by the distribution of atrophy within the frontal and temporal lobes, i.e. frontotemporal dementia (FTD), semantic dementia (SD), and progressive non-fluent aphasia (PNFA).

Patients with FTD may experience disorders predominantly related to behavior, including loss of insight, disinhibition, apathy, mood changes, mental rigidity, stereotypic behavior, and eating behaviors [4–7]. SD, by contrast, is a form of dementia in which progressive loss of conceptual knowledge about words and objects are the main symptoms [8–10]. Although the semantic deficit is the main clinical feature, changes in behavior and personality are also present [5, 6, 11, 12]. When the concept of FTLD was proposed, it was suggested that some overlap in symptomatology between SD and FTD would be anticipated with disease progression [1]. Recent reports, however, have highlighted that some symptoms commonly occur in these subtypes at an early stage of the disease [5, 7].

Despite many reports about behavioral changes and cognitive decline in patients with FTLD, there have been very few systematic studies of the initial symptoms of FTLD. From a clinical point of view, it is important to investigate the initial symptoms of FTLD for the following reasons. First, there is a possibility to gather knowledge about the prodromal state of FTLD, just like the mild cognitive impairment state in Alzheimer's disease (AD). Second, behavioral features in the presenium are often misdiagnosed as psychiatric disorders such as schizophrenia or mood disorder. This misdiagnosis has led to the under-recognition of FTD, and hence, to underestimation of its prevalence [1]. Third, cognitive decline in the presenium is frequently misdiagnosed as AD. Although the concept of SD has recently become more widely appreciated, loss of semantic memory for words or objects in SD is still difficult to understand for many physicians and caregivers [1]. Cases of SD with semantic memory impairment are erroneously diagnosed as AD because the unique symptoms are considered to be ordinary forgetfulness. Fourth, because both patients with FTD and SD present behavioral changes at an early stage of the disease, it might be generally difficult to distinguish these subtypes according to their behavioral symptoms.

From a therapeutic point of view, it is important to distinguish AD from FTLD at an early stage of the disease, particularly with the advent of cholinesterase inhibitors for the treatment of AD [13]. There is also the possibility that serotonin selective reuptake inhibitors

may be beneficial in reducing behavioral symptoms in FTLD [14]. This new therapeutic strategy could reduce the burden of care for patients with FTLD.

The main aims of this study were twofold: (1) to investigate initial symptoms of FTD and SD, and (2) to establish the nature by which the initial symptoms of FTD and SD differ among each other and from AD.

Methods

After a complete description of the study to all patients or their caregivers, written informed consent was obtained.

Patients

Patients were recruited from the Higher Brain Function Clinic of the Department of Neuropsychiatry, Ehime University Hospital, between June 1999 and August 2004, and were seen by a senior neuropsychiatrist. All patients underwent both physical and neurological examinations. Patients underwent magnetic resonance imaging (MRI) and HMPAO-SPECT, together with the usual battery of screening blood tests including vitamin B₁₂ and thyroid function. We also used a standard psychiatric evaluation to exclude major functional psychiatric disorders such as schizophrenia and mood disorder. Patients with a history of significant head trauma and alcoholism were excluded. Patients were assessed with a comprehensive battery of neuropsychological and neuropsychiatric tests, including the mini-mental state examination (MMSE) [15], digit span test, verbal fluency test, Raven's Coloured Progressive Matrices [16], clinical dementia rating (CDR) [17], and neuropsychiatric inventory (NPI) [18, 19] at the first visit. Patients were rated on the NPI for assessment of behavioral features. Caregivers were asked if the behavior had been present during the previous month. In aphasic patients, the language function was evaluated by the Japanese Standard Language Test of Aphasia [20] within 2 months from the first visit. Two patients could not complete MMSE because of their behavioral symptoms, and 1 patient could not complete NPI at the first visit.

Three groups of patients were involved in this study: FTD (n =36), SD (n = 17) and AD patients (n = 52). All patients in the FTD and SD groups fulfilled the recent consensus criteria for FTLD, which recognizes the subtypes of FTD, SD, and PNFA [2]. Patients with PNFA were excluded because they were too few (n = 4) to enable meaningful comparisons with the other groups. There was no family history in all subtypes of FTLD patients, as in most Japanese cases of FTLD [3]. All patients with FTD showed either frontal atrophy on MRI and/or frontal lobe hypoperfusion on HMPAO-SPECT [21]. All brain MRI images of SD patients showed focal atrophy involving the polar and inferolateral regions of the temporal lobe [22, 23]. Fifty-two patients with AD, matched for age and MMSE score at first consultation and education, were also selected. Patients with AD satisfied probable AD criteria according to the criteria developed by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association [24]. Brain MRI showed either a mild degree of medial temporal lobes or diffuse atrophy.

Table 1. Demographic variables of the three patient groups

	FTD (n = 36)	SD (n = 17)	AD (n = 52)
Sex, male/female	17/19	6/11	15/37
Age at consultation, years	$68.8 \pm 9.1 (49 - 85)$	$64.9 \pm 7.8 (52 - 81)$	$66.1 \pm 7.3 (56 - 85)$
Duration from initial symptom			
appearance to consultation, months	$36.0 \pm 24.0 (3-117)$	$39.6 \pm 16.8 (12-78)$	$37 \pm 34.3 (1-162)$
CDR grade, 0.5/1/2/3	13/8/13/2	8/4/5/0	13/21/13/5
MMSE score	19.0 ± 9.0	17.5 ± 10.0	18.7 ± 6.1
NPI score	21.6 ± 14.1	19.5 ± 16.4	16.2 ± 13.7

Data are given as number of patients or means ± SD; figures in parentheses indicate range.

Assessment of Initial Symptoms

We routinely and systematically gathered information about initial symptoms from caregivers. Caregivers were asked to recall the onset of the illness to permit demarcation of the period of illness. It was emphasized that the 'initial symptom' was the first change the caregiver noticed and should reflect a substantive change from the patient's premorbid state, rather than a longstanding character trait. After having recorded the content as described by caregivers, all symptoms were categorized into the following domains, which relate to components from the FTLD diagnostic criteria [2, 25], NPI [18, 19], and previous studies regarding the symptoms of FTLD [5–7, 12]:

- (1) Change in social behavior, affection, and daily activities: loss of social awareness (lack of social tact, misdemeanors), loss of personal awareness (neglect of personal hygiene and grooming), disinhibition (unrestrained sexuality, violent behavior), apathy or social withdrawal or aspontaneity, stereotypic behavior (stereotypic movement, stereotypic speaking, stereotypic daily routines, obsessive-compulsive behavior), mental rigidity and inflexibility, depression or anxiety, irritability or aggression, delusion or hallucination, abnormal eating and oral behaviors (overeating, altered food preference, food fads, mouthing of inedible objects), and decline in daily activities not caused by a specific symptom.
- (2) Cognitive decline except language impairments: memory disturbance, deficits in visuospatial function, disorientation (time or date), disturbance of attention or distractibility, and prosopagnosia
- (3) Language impairments: reduction of speech, paraphasia, anomia or impairment in word naming, and impairment in word comprehension.
- (4) Other abnormal symptoms: physical symptoms, not otherwise classified.

The examining clinician confirmed the context in which each symptom occurred, together with the caregiver, to avoid misclassification. For example, if a caregiver mentioned that the patient had begun to speak the same phrases repeatedly, further clarification was sought to ascertain whether this represented repetitive questioning in the context of a memory disorder versus stereotypic catch-phrase usage. Likewise, if a caregiver reported that the patient's language had become rough and/or blunt, the caregiver was asked to elaborate so that the clinician could decide whether this

referred to crude speech due to lack of social awareness versus the usage of generic terms due to aphasia. When the caregiver reported multiple symptoms as first changes, all symptoms were classified as initial symptoms (maximum three symptoms).

Data Analysis

Data analyses were carried out using the SPSS-PC software package. Statistical differences between the three groups were assessed by the Kruskal-Wallis test for non-parametric variables, as well as the χ^2 test with post hoc Fisher's exact test for nominal variables.

Results

The demographic characteristics of the three groups including sex, age at consultation, duration from initial symptom appearance until consultation, CDR grade, MMSE score, and NPI score are summarized in table 1. There were no significant differences between the three groups in sex, education, age at consultation, and duration from initial symptom appearance until consultation. There were also no significant differences in the severity of dementia according to CDR and the total score of MMSE, as well as the total severity of psychiatric symptoms according to the total score of NPI at the first visit.

The initial symptoms of the three groups are summarized in table 2. Thirty-six patients with FTD showed a total of 64 initial symptoms, with an average of 1.8 initial symptoms per patient. 'Change in social behavior, affection, and daily activities' occurred as initial symptoms in 62.5% of all patients with FTD, 'cognitive decline' involving distractibility in 18.8%, and 'language impairments' in 14.1% of FTD patients. Seventeen patients with SD showed a total of 24 initial symptoms, with an aver-

Table 2. Frequency of initial symptoms (%) in FTD, SD and AD

	FTD	SD	AD	p value	
Number of initial symptoms per 1 patient	1.8	1.4	1.4	NS	
Change in social behavior, affection, and daily activities	62.5	20.8	19.2	0.000	FTD>SD FTD>AD
Loss of social awareness	7.8	0.0	0.0	0.022	FTD>AD
Loss of personal awareness	3.1	4.2	0.0	NS	
Disinhibition	6.3	0.0	1.4	NS	
Apathy or social withdrawal of aspontaneity	14.1	4.2	2.7	0.0043	FTD>AD
Stereotypic behavior	12.5	4.2	0.0	0.002	FTD>AD
Mental rigidity and inflexibility	3.1	0.0	0.0	NS	
Depression or anxiety	1.6	0.0	2.7	NS	
Irritability or aggression	3.1	4.2	4.1	NS	
Delusion or hallucination	0.0	0.0	5.5	NS	
Abnormal eating and oral behaviors	3.1	0.0	0.0	NS	
Decline in daily activities not reduced to a specific symptom	7.8	4.2	2.7	NS	
Cognitive decline	18.8	16.7	74.0	0.000	AD>FTD AD>SD
Memory disturbance	9.4	8.3	61.6	0.000	AD>FTD AD>SD
Deficits in visuospatial function	0.0	4.2	6.8	NS	
Disorientation (time/date)	0.0	0.0	4.1	NS	
Disturbance of attention or distractibility	7.8	0.0	1.4	NS	
Prosopagnosia	1.6	4.2	0.0	NS	
Language impairments	14.1	62.5	2.7	0.000	SD>FTD SD>AD FTD>AD
Reduction in speech	3.1	4.2	0.0	NS	
Anomia or impairment in word naming	7.8	25.0	2.7	0.004	SD>AD
Paraphasia	1.6	16.7	0.0	0.001	SD>FTD SD>AD
Impairment in word comprehension	1.6	16.7	0.0	0.001	SD>FTD SD>AD
Other abnormal symptoms	4.7	0.0	4.1	NS	
Physical symptoms	3.1	0.0	2.7	NS	
Not otherwise classified	1.6	0.0	1.4	NS	

age of 1.4 initial symptoms per patient. 'Language impairments' occurred as initial symptom in 62.5% of all SD patients, 'change in social behavior, affection, and daily activities' in 20.8%, and 'cognitive decline' in 16.7% of SD patients. Fifty-two patients with AD showed a total of 73 initial symptoms, with an average number of 1.4 initial symptoms per patient. 'Cognitive decline' occurred as initial symptom in 74.0% of AD patients, 'change in social behavior, affection, and daily activities' in 19.2%, and 'language impairments' in 2.7% of AD patients.

The domain of 'change in social behavior, affection, and daily activities' was significantly more common in patients with FTD than in patients with SD and AD (p < 0.01), and 'language impairments' was significantly more common in patients with SD than in patients with FTD and AD (p < 0.01). Apathy and stereotypic behaviors were the most common initial symptoms in patients with

FTD, while anomia, paraphasia, and impairment in word comprehension were the most common initial symptoms in patients with SD. In patients with AD, memory disturbance was the most common initial symptom.

There was no significant difference between FTLD and AD groups in the frequency of other items, such as disinhibition, depression or anxiety, irritability or aggression, delusion or hallucination, disorientation, disturbance of attention or distractibility, or reduction in speech.

Discussion

Clear and significant differences existed in initial symptoms between FTD and SD compared with AD. The most common initial features of FTD patients were 'change in social behavior, affection, and daily activities',

while the most common initial feature of SD patients was 'language impairments'. The most common initial feature of AD patients was 'cognitive decline', with 61% of all initial symptoms begin memory disturbance. By contrast, the frequency of cognitive deficits in patients with FTD and SD was low and we found no significant differences between these two groups. This result is consistent with many other studies that have found memory disturbance in AD usually precedes other cognitive deficits [26–28]. Lindau et al. [29] reported that memory disturbance was the first symptom of 76% of AD patients, whereas only 2% of FTD patients presented with memory disturbance.

There are 8 patients with FTLD whose caregivers reported memory disturbances as their initial symptom; nevertheless, 4 of them scored more than 2 points on the 'recall of three words' item at the MMSE when performed at the first visit. In contrast, AD patients who typically present with memory disturbance do not score well on this item [30, 31]. Therefore, it is unclear whether these FTLD patients who scored more than 2 points on the 'recall of three words' item at the MMSE genuinely had memory disturbance at their onset. Caregivers may have mistaken apathy or aphasia in FTLD for memory disturbance. These might be factors of misdiagnosis for FTLD patients at the examination.

Apathy and stereotypic behavior were remarkably more common initial symptoms in FTD compared with AD; on the other hand, anomia, paraphasia, and impairment in word comprehension were remarkably more common initial symptoms in SD compared with AD. Some recent reports mentioned that changes in behavior commonly occur in both FTD and SD at an early stage of the disease [6, 7]. Indeed, in our study, there was no significant difference in the severity of psychiatric symptoms according to the total NPI score between patients with FTD and SD at the time of the first visit, which in both groups was on average 3 years after initial symptom appearance. However, there was a significant difference in the quality of initial symptoms between these groups. This result suggests that in SD, isolated language impairment is the initial feature and that, subsequently, there is a gradual development of behavioral changes. This result may also suggest that anatomical heterogeneity between FTD and SD led to distinctive initial symptoms.

There were 6 patients with FTLD (5 patients with FTD and 1 patient with SD) whose initial symptoms were classified as 'decline in daily activities not caused by a specific symptom'. For example, those whose cooking ability deteriorated without any specific reason were cat-

egorized in this group. Such declines in daily activities may be due to a variety of symptoms which are connected with one another, for instance, mental rigidity and inflexibility, apathy, disturbance of attention, or distractibility. The number of initial symptoms per patient was higher in patients with FTD than in other groups, although this was not statistically significant. The possible reasons for these various symptoms in patients with FTD are the following. First, several different neural circuits of the frontal lobe may be impaired at the same time even at a very early stage [32]. Second, all symptoms which seemed to be different may be manifestations of one common factor.

We could find no significant differences between the three groups in the frequency of disinhibition, irritability or aggression, abnormal eating behavior, disturbance of attention, or distractibility. Although these symptoms are very common in patients with FTD [1, 2, 7] and included in clinical diagnostic criteria of FTD [2, 25] as the core or supportive symptoms, these symptoms might not occur frequently in the very early stage. We could not find a significant difference between the three groups in the frequency of visuospatial dysfunction and disorientation either, although these are very common symptoms in AD.

We also investigated the sensitivity and specificity for each symptom of the three patient groups. Memory disturbance achieved 87% sensitivity and 85% specificity for the classification of AD and FTLD groups. Memory disturbance might be an overwhelming initial symptom in AD and useful for differential diagnosis. On the other hand, anomia achieved 35% sensitivity and 92% specificity for the differentiation between the SD group and the other two patient groups, although it was a most popular initial symptom in the SD group. This may be because SD patients present various language impairments as initial symptoms, such as anomia, paraphasia, and impairment in word comprehension. The whole language impairments achieved 71% sensitivity and 89% specificity for the differentiation between the SD group and the other two patient groups. Apathy achieved 25% sensitivity and 92% specificity for the differentiation between the FTD group and the other two patient groups, although it was a most frequent initial symptom in the FTD group. This may be because FTD patients develop plural behavioral symptoms as initial symptoms, as described previously. This variety of symptoms is a characteristic of FTD patients, as is also described in diagnostic criteria. It is plausible that they present low sensitivity for only one symptom, even if it is a most frequent symptom.

In this study, we clinically diagnosed FTD and SD groups according to the consensus criteria for FTLD [2]. We did not perform lumbar puncture and could not discuss abnormal tau deposits. Recent researches have revealed that FTD patients consist of pathological heterogeneous groups including Pick's disease with or without Pick bodies, FTD and parkinsonism linked to chromosome 17, dementia lacking distinctive histology, corticobasal degeneration, and motor neuron disease [33, 34]. They have also demonstrated that clinical assessments fail to discriminate between either types of pathology. We need a longitudinal follow-up to observe a symptomatic change with progression. Further studies of clinicopathological correlation are required.

There are a few methodological issues that should be taken into consideration to fully appreciate our results. First, as this study is based on a retrospective recall of caregivers, it can be claimed that the informants' memories may have been inaccurate [35]. However, it seems implausible that the ability of caregivers of FTLD patients to remember initial symptoms would be different from that of caregivers of AD patients. Furthermore, using a clinical interview to obtain a medical history is the usual way of diagnosing dementia, so any possible bias introduced by the current methods are likely to be similar in routine clinical practice. Second, there is a possibility that the initial symptoms for which there was an overlap between FTD, SD and AD (for example, irritability or aggression) may be qualitatively different. Snowden et al. [6] have described possible differences in the quality of symptoms found in FTD and SD, although their study did not concern initial symptoms. Therefore, we cannot exclude the possibility that our study categorized different qualities of symptoms as same symptoms. Furthermore, it is difficult to standardize the severity of dementia between subgroups of FTLD and AD. Although we used CDR for determination of dementia severity, it is not specifically designed for FTLD. Third, as the investigation items of initial symptoms are related to items of clinical diagnostic criteria, it can be claimed that initial symptoms and diagnostic criteria seem circular. However, psychiatric symptoms and behavioral features were assessed during the month prior to the first visit using NPI [18, 19] for diagnosis. Likewise, language symptoms of aphasic patients were assessed within 2 months from the first visit, using the Standard Language Test of Aphasia [20]. Therefore, we believe that clinical diagnosis at the examination and information about initial symptoms may be basically independent.

Many studies have attempted to address the issue of differential diagnosis of early-stage FTLD and AD, including brain imaging and neuropsychological testing [27, 36–38]. However, there are many inconsistencies and it often remains difficult to make a clear diagnosis in the early stage of the disease. We think that initial symptoms should be taken into account in the assessment of patients with dementia as their evaluation may helpfully contribute to the differential diagnosis of FTD, SD and AD.

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References

- Snowden JS, Neary D, Mann DMA: Fronto-Temporal Lobar Degeneration: Fronto-Temporal Dementia, Progressive Aphasia, Semantic Dementia. New York, Churchill Livingstone, 1996.
- 2 Neary D, Snowden JS, Gustafson L, Passant U, Stuss D, Black S, Freedman M, Kertesz A, Robert PH, Albert M, Boone K, Miller BL, Cummings J, Benson DF: Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. Neurology 1998; 51:1546–1554.
- 3 Ikeda M, Ishikawa T, Tanabe H: Epidemiology of frontotemporal lobar degeneration. Dement Geriatr Cogn Disord 2004;17:265–268.
- 4 Gregory CA, Hodges JR: Frontotemporal dementia: use of consensus criteria and prevalence of psychiatric features. Neuropsychiatry Neuropsychol Behav Neurol 1996;9:145–153.
- 5 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 Psychiatry 2000; 69:178–186.
- 6 Snowden JS, Bathgate D, Varma A, Blackshaw A, Gibbons ZC, Neary D: Distinct behavioural profiles in frontotemporal dementia and semantic dementia. J Neurol Neurosurg Psychiatry 2001;70:323–332.
- 7 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 Psychiatry 2002;73:371–376.
- 8 Snowden JS, Goulding PJ, Neary D: Semantic dementia: a form of circumscribed cerebral atrophy. Behav Neurol 1989;2:167–182.
- 9 Hodges JR, Patterson K, Oxbury S, Funnell E: Semantic dementia. Progressive fluent aphasia with temporal lobe atrophy. Brain 1992;115: 1783–1806.
- 10 Snowden JS: Semantic dysfunction in frontotemporal lobar degeneration. Dement Geriatr Cogn Disord 1999;10(suppl 1):33–36.

- 11 Edwards-Lee T, Miller BL, Benson DF, Cummings JL, Russell GL, Boone K, Mena I: The temporal lobe variant of frontotemporal dementia. Neurology 1996;46:2023.
- 12 Shigenobu K, Ikeda M, Fukuhara R, Maki N, Hokoishi K, Nebu A, Yasuoka T, Komori K, Tanabe H: The Stereotypy Rating Inventory for frontotemporal lobar degeneration. Psychiatry Res 2002;110:175–187.
- 13 Cummings JL: Cholinesterase inhibitors: a new class of psychotropic compounds. Am J Psychiatry 2000;157:4–15.
- 14 Ikeda M, Tanabe H: Reducing the burden of care in dementia through the amelioration of BPSD by drug therapy. Expert Rev Neurother 2004;4:921–922.
- 15 Folstein MF, Folstein SE, McHugh PR: Minimental state: a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–198.
- 16 Raven JC, Court JH, Raven J: Manual for Raven's Coloured Progressive Matrices. Oxford, Oxfords Psychologists Press, 1990.
- 17 Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL: A new clinical scale for the staging of dementia. Br J Psychiatry 1982;140:566– 572.
- 18 Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J: The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. Neurology 1994;44:2308–2314.
- 19 Hirono N, Mori E, Ikejiri Y, Imamura T, Shimomura T, Hashimoto M, Yamashita H, Ikeda M: Japanese version of the Neuropsychiatric Inventory A scoring system for neuropsychiatric disturbance in dementia patients. No To Shinkei 1997;49:266–271.
- 20 SLTA Committe: Standard Language Test of Aphasia Manual. Tokyo, Shinkou Igaku Shuppan-sha, 1997.
- 21 Miller BL, Gearhart R: Neuroimaging in the diagnosis of frontotemporal dementia. Dement Geriatr Cogn Disord 1999;10(suppl 1):71-74.

- 22 Chan D, Fox NC, Scahill RI, Crum WR, Whitwell JL, Leschziner G, Rossor AM, Stevens JM, Cipolotti L, Rossor MN: Patterns of temporal lobe atrophy in semantic dementia and Alzheimer's disease. Ann Neurol 2001;49: 433–442.
- 23 Galton CJ, Patterson K, Graham K, Lambon-Ralph MA, Williams G, Antoun N, Sahakian BJ, Hodges JR: Differing patterns of temporal atrophy in Alzheimer's disease and semantic dementia. Neurology 2001;57:216–225.
- 24 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.
- 25 The Lund and Manchester Groups: Clinical and neuropathological criteria for frontotemporal dementia. J Neurol Neurosurg Psychiatry 1994;57:416–418.
- 26 Cummings JL, Benson DF: Dementia of the Alzheimer type. An inventory of diagnostic clinical features. J Am Geriatr Soc 1986;34: 12–19.
- 27 Welsh KA, Butters N, Hughes JP, Mohs RC, Heyman A: Detection and staging of dementia in Alzheimer's disease. Use of the neuropsychological measures developed for the Consortium to Establish a Registry for Alzheimer's Disease. Arch Neurol 1992;49:448–452.
- 28 Gregory CA, Orrell M, Sahakian B, Hodges JR: Can frontotemporal dementia and Alzheimer's disease be differentiated using a brief battery of tests? Int J Geriatr Psychiatry 1997;12:375– 383.
- 29 Lindau M, Almkvist O, Kushi J, Boone K, Johansson SE, Wahlund LO, Cummings JL, Miller BL: First symptoms Frontotemporal dementia versus Alzheimer's disease. Dement Geriatr Cogn Disord 2000;11:286–293.

- 30 Galasko D, Klauber MR, Hofstetter CR, Salmon DP, Lasker B, Thal LJ: The Mini-Mental State Examination in the early diagnosis of Alzheimer's disease. Arch Neurol 1990;47:49–52
- 31 Loewenstein DA, Barker WW, Harwood DG, Luis C, Acevedo A, Rodriguez I, Duara R: Utility of a modified Mini-Mental State Examination with extended delayed recall in screening for mild cognitive impairment and dementia among community dwelling elders. Int J Geriatr Psychiatry 2000;15:434–440.
- 32 Cummings JL: Frontal-subcortical circuits and human behavior. Arch Neurol 1993;50:873– 880.
- 33 Hodges JR, Davies RR, Xuereb JH, Casey B, Broe M, Bak TH, Kril JJ, Halliday GM: Clinicopathological correlates in frontotemporal dementia. Ann Neurol 2004;56:399–406.
- 34 McKhann GM, Albert MS, Grossman M, Miller B, Dickson D, Trojanowski JQ: Clinical and pathological diagnosis of frontotemporal dementia: report of the Work Group on Frontotemporal Dementia and Pick's Disease. Arch Neurol 2001;58:1803–1809.
- 35 Oppenheim G: The earliest signs of Alzheimer's disease. J Geriatr Psychiatry Neurol 1994;7:116–120.
- 36 Gregory CA, Serra-Mestres J, Hodges JR: Early diagnosis of the frontal variant of frontotemporal dementia: how sensitive are standard neuroimaging and neuropsychologic tests? Neuropsychiatry Neuropsychol Behav Neurol 1999;12:128–135.
- 37 Mathuranath PS, Nestor PJ, Berrios GE, Rakowicz W, Hodges JR: A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. Neurology 2000;55:1613–1620.
- 38 Kertesz A, Nadkarni N, Davidson W, Thomas AW: The Frontal Behavioral Inventory in the differential diagnosis of frontotemporal dementia. J Int Neuropsychol Soc 2000;6:460– 468.

神経心理学

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abstract

アルツハイマー病では主に脳の後方領域が障害され、記憶障害の他、失語や失行がみられる。近年、画像診断技術が進歩し、また、MMSEをはじめ痴呆の神経心理検査バッテリーの開発、普及もめざましい。しかし、神経心理学的所見とは、単に認知機能検査の結果をさすものではなく、神経心理症状ないし精神神経症候の的確な把握、記載が望まれる。

把握, 記載が望まれる.

はじめに

近年の画像診断技術の進歩により、 痴呆を含む脳 損傷者ならびに健常人を対象とした脳の研究が発展 し、また数々の痴呆の神経心理検査バッテリーの開 発, 普及もめざましいが, 神経心理学的症状の把握 はテストを施行すれば可能であるというものではな いことに留意する必要がある. アルツハイマー病 (AD) では変性過程が進行すると、さまざまな道具 障害, すなわち一般知性の底にあって道具となりう る言語,認知,記憶といった作能の障害である,失 語,失行,失認,健忘などの巣症状が出現し,同時 に一般知性障害や全般性注意障害が加わる.このた め個々の道具障害を純粋に抽出することが困難とな る. したがって、長谷川式簡易知能評価スケール (HDS-R)¹⁾ やMini-Mental State Examination (MMSE)^{2). 3)} の下位項目の粗点の低下は、単にあ る一つの道具障害によるものではなく、さまざまな 要因が関与してくるようになる。したがって、そこ では神経心理症状ないし精神神経症候の的確な把握 が求められる40.50. ここではADにみられる代表的

な神経心理学的所見と,実際の神経心理学的検査に ついて解説する.

記憶障害

ADの初期症状として注目される健忘あるいは物忘れは記銘力障害であり、エピソード記憶の障害である。臨床的には即時記憶は比較的保たれており、その場その場での会話は成立するものの、著明な近時記憶の障害を呈し、数分前のことも忘れてしまう^{6),7)}。例えば、診察時に3つの物品を引き出しに隠し、なにがあったか答えさせると、直後には正答するが、数分後にもう一度尋ねると正しく答えられなかったり、隠したこと自体も忘れていたりする。

通常は語が思い出せないという語想起障害(喚語 困難)に始まり、さらに了解障害が加わり、まれに は非流暢性失語像を呈することもあるが、通常は流 暢性の失語像を呈する、進行した例ではウェルニッ

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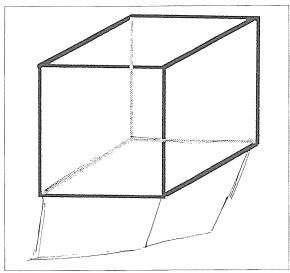


図1 アルツハイマー病患者にみられたなぞり描き(closing in)

ケ失語のように錯語やジャルゴンを呈する場合もあるが、本質的には復唱は保たれ呼称や理解に障害を認め、超皮質性失語の範疇でとらえられる場合が多い。復唱障害とされている場合でも実際には復唱の指示が十分入っていなかったり、取り繕い反応のため、なにを検査したのか判然としない場合もあり、注意を要する.

$\mathbb{I} \mathbb{V}$

植成障害

問題行動として徘徊はよく挙げられるが、空間的見当能力の障害が強くなると、よく知っている場所でも迷うようになり、家の中でも迷ってしまうことがある50.60.ゴルフのパターがうまく打てない、自動車を車庫にうまく入れられない、バスなどのパスカードをうまく差し込めないがといった客体を空間的に正しく定位できない症状から、さらにはベッドに斜めに寝る、電車の中で他人の膝の上に座るといった自己身体さえも空間的に正しく定位できない症状もみられる100.検査では立方体の模写ができなかったり、clock drawing test (CDT)で正しく時計の絵を描くことができなかったりする。模写の課題では重症の場合にはなぞり描きがみられることもある(図1).CDTはごく短時間で実施でき、視空間構成能力をはじめ、抽象概念や数の概念などの言語

理解能力,言語的記憶などさまざまな認知機能を評価でき,ADのスクリーニングや重症度評価の補助手段としても有用である^{11)、12)}.

\mathbb{V}

神経心理学的検査施行にあたっての一般的な注意事項

難聴や視力障害、言語障害などが存在する場合、 検査の成績が低下するのは当然であり、これらの障 害の有無や程度を考慮する必要がある。また、身体 症状(体調)や精神状態は特に注意集中に影響する。 施行当日の体調不良や拒否が強いなどの不安定な精 神状態では、実際の能力よりも低く評価されるか、 施行できない場合もある。また高齢の患者の場合は 注意集中を維持することが困難な場合もあり、患者 の様子を見ながら1回の検査時間を短くしたり、途 中に休憩を挟んだりする必要がある。また検査の項 目で施行の順番が厳密に決まっていないものであれ ば患者の様子を見ながら順番を入れ替えるか、中断 可能なものであれば何度かに分けて施行するといっ た工夫も必要である^{13)、14)}.

評価にあたっては対象者の教育歴(教育年数)も確認することが必要である¹⁵⁾. 対象者が高い教育歴を有する場合,簡易知能検査であればたやすく回答してしまったり,WAIS-R成人知能検査法(WAIS-R)においても正常範囲内,ないし軽度の低下にとどまったりする場合がある. 高い教育歴の患者では,より多様性のある認知機能障害を示すという報告もある¹⁶⁾. また,検査の得点や時間だけでなく,施行時の患者の様子などを文章で記載しておくことも重要である. 非協力的な患者の0点も協力的な患者の0点も、数字上は同一であるが,症候学的には意味が異なるためである.

\mathbb{M}

実際の検査

1) 一般的認知機能検査15)

認知機能検査には対象者本人に対して行う質問式 (直接式)と対象者の状態をよく知る家族などの主 たる介護者から情報を得る観察式(間接式)がある.

SMQ	評価	年	月	B	氏名	(回答者)	できない		時にはできる		大体はできる		いつもできる
1. 昨日	看ていた	服装を知	覚えてい	います	か?				1	٠	2	•	3	•	4
2. 0	つも利用す	るバス/	電車の位	停留所	を覚えて	いますか?			1	•	2	•	3	•	4
3. 自分	か家の電	話番号	を言えま	きすか	?				1	•	2	•	3	•	4
4. 雑貨	貨店で,メ [.]	モを持た	たずに5	つの品	占物を忘れ	ぃずに買うこ。	とができま	すか?	1	•	2	٠	3	٠	4
5. いつ	つでも自分の	の眼鏡	をどこに	こ置い	たか覚え゛	ていますか?			1	٠	2	٠	3	•	4
6. いっ	つでも自分の	の鍵を	どこに置	置いた	か覚えて	いますか?			1	•	2	•	3	•	4
7. 家族	笑の誕生日:	を覚え	ています	トか?					4	•	3	٠	2	•	1
8. 誰か	νに訊ねら:	れると,	自分の)家へ(の道筋を	教えることが	できますた	? י	1	•	2		3		4
9. 外出	出したとき	に,家(の戸締ま	ミりを	したか覚	えていますか	· ?		1	•	2	٠	3	٠	4
10. スー	-パーを出	るときに	にお釣り	丿をい	くらもら	ったかを覚え	ていますた	p ?	1	•	2	•	3	•	4
11. 先退	圆の日曜日	の午後	に,なに	こをし	たかを話	すことができ	ますか?		1	•	2	•	3	٠	4
12. 家の)人や他の.	人が頼ん	んだ用事	事を , 5	覚えてお	くことができ	ますか?		1	٠	2	•	3	•	4
13. 言志	3うとして!	いる言語	葉がすく	でに出て	てきます	か?			4	٠	3	•	2	•	1
14. 自分	でお金の	管理が	できます	ナか?	(支払い	銀行口座,	預貯金など	<u>:</u>)	1	•	2	•	3	•	4
	[3	主意:7	····································	番の得	点は合計	†から減じる.			待	点	ī		/4	16,	点

表 I 日本語版short memory questionnaire(SMQ)

〔文献20)より引用〕

それぞれに長所短所があり、両者を組み合わせることにより、より正確な認知機能を測定することが可能である。また、ピック病にみられるような考え無精50.60や、せん妄のような注意障害がある場合には教示そのものが正しく保持されないため、認知機能を正しく評価することはできない。したがって検査施行にあたっては、最初からWAIS-Rやウエスクラー記憶検査法(WMS-R)、前頭葉機能検査などを施行するのではなく、まずMMSEのような簡易な検査を施行したうえで、より複雑な課題ないし特殊な課題を施行することが望ましい。

①MMSE

Folsteinら²⁾ によって考案され、わが国では森ら³⁾ によって邦訳、標準化された.見当識、記銘力、注意と計算、言語、構成の課題からなり、30点満点である.通常15分程度で施行可能であり、痴呆による認知機能の低下を検出するための、簡便で信頼度の高い検査である.邦訳版では23/24点をカットオフ値とすると、痴呆の検出率は83%、健常者を痴呆なしと判別できる特異性は93%を示す.老年期の典型的なADでは、記銘力(3単語の遅延再生)、時の見当識、計算、構成、場所の見当識、言語の順に障害される.若年性のADなどでは構成の著しい障害がみられることもある.また、会話の印象や通常の行動からかけ離れて成績が悪く、3段階命令や、書字

命名、計算課題などの障害が目立つ場合には、失語があるか、せん妄などなんらかの原因で注意力低下をきたしている可能性がある。本検査は簡便で、かつ認知機能を多角的にとらえられるためスクリーニングに適していると思われる。わが国でよく使用されているHDS-RはMMSEと比較して記憶に重点が置かれ、近時記憶障害の検出に優れている。また、語産生課題により前頭葉機能低下や喚語困難を検出できる項目が含まれていることも特徴である。しかし、記憶障害の著しい症例では意欲低下や拒否をきたしやすく、施行時に配慮が必要であると思われる14.

②リバーミード行動記憶検査

イギリスのリバーミードリハビリテーションセンターで日常記憶の障害を発見し、治療による変化を観察するために開発されたテストバッテリーである¹⁷⁾. 日常記憶とは実際の日常生活場面で必要とされる記憶のことである. この検査では、名前の記憶や会話内容の記憶、展望記憶(約束)、絵の記憶、行為(用件を含む)の記憶、見当識など日常生活に直接影響を与えるような記憶障害を検出できるのが特徴である. これまでの記憶の検査では評価されることのなかった展望記憶(近い将来の約束や実行の記憶)が評価できる唯一の記憶検査である. また、リハビリテーションの効果判定という繰り返しの評価を前提に作成されており、同等の難易度の4つの平行検

評価 年 月 日 氏名

御料のはい士

A.	電話の使い方	
	1. 自由に電話をかけることができる	1
	2. いくつかのよく知っている番号であればかけることができる	1
	3. 電話で対応できるが電話をかけることはできない	1
	4. 全く電話を使うことができない	0
В.	買い物	
	1. 1人で買い物ができる	1
	2. 少額の買い物であれば1人でできる	0
	3. だれかが付き添っていれば買い物ができる	0
	4. 全く買い物ができない	0
C.	食事の支度	
	1. 人数にあった支度をして必要十分な用意ができる	1
	2. 材料が用意してあれば食事の支度ができる	0
	3. 食事をつくることはできるが、人数にあった用意ができない	0
	4. 他人に支度をしてもらう	0
D.	家事	
	1. 力仕事など以外は1人で家事をすることができる	1
	2. 食事のあとの食器を洗ったり布団を敷くなどの簡単なことはできる	1
	3. 簡単な家事はできるが、きちんとあるいは清潔に維持できない	1
	4. 他人の助けがなければ家事をすることができない	1
	5. 全く家事をすることができない	0
E.	洗濯	
	1, 1人で洗濯できる	1
	2. 靴下などの小さなものは洗濯できる	1
	3. 他人に洗濯してもらう	0
F.	移動・外出	
	1. 自動車を運転したり、電車やバスを利用して出かけることができる	1
	2. タクシーを自分で頼んで出かけられるが、電車やバスは利用できない	1
	3. 付き添いがあれば電車やバスを利用することができる	1
	4. 付き添われてタクシーや自動車で出かけることができる	1
	5. 全く出かけることができない	0
G.	服薬の管理	
	1. きちんとできる	1
	2. 前もって飲む薬が用意されていれば自分で服薬できる	0
	3. 自分では全く服薬できない	0
Н.	金銭の管理	
	1. 自分でできる (家計費, 家賃, 請求書の支払い, 銀行での用事など)	1
	2. 日常の買い物はできるが、大きな買い物や銀行へは付き添いが必要	
	A AD de 177 % on 1 commission de	^

得点 男性 /5, 女性 /8

表2 日本語版instrumental activities of daily living scale (IADL) 得点は、男性では0~5点、女性では0~8点

査が用意され、繰り返しによる練習効果の影響を排除できる。わが国では2002年に邦訳版が標準化され¹⁸⁾、さらに軽症AD患者における有用性が報告された。本検査は初期AD患者の検出や、治療効果の判定のみならず、AD患者の日常生活上の問題を予測し家族や介護者に対する介入法の指導に役立つものと期待される。

(3) short memory questionnaire (SMQ)

3. 金銭を扱うことができない

AD患者の記憶障害に対する自覚は、比較的早期 に失われる。また医療機関を家族などに連れられて 受診している状況では、診察、検査を含めて本人の 協力が得られない場合もある。したがって記憶障害の程度については家族などの主たる介護者から聴取することが多い。SMQはKossら¹⁹⁾ によってADの早期発見を目的として開発された観察式の評価尺度で,筆者ら²⁰⁾ により邦訳,標準化された。**表1**に日本語版SMQを示す。SMQはRiegeらが高齢者の記憶の自己評価用として作成した30項目の質問内容²¹⁾ から健常高齢者と軽度AD患者の鑑別に有用であった14の項目をKossらが抜粋したもので,それぞれ1から4までの4段階で評価する。7番と13番の2項目の点数を他の12項目の合計点から減じたものが得点と

(文献25)より引用]

評価 年 月 日 氏名

計価 年 月 口 氏名		
A. 排 泄		
1. 排泄は全く介助を要しない	1	
2. 誘導あるいは後始末に介助が必要,時に(多くても週に1度)失り	坎 0	
がある		
3. 週に1度以上,寝ている間に失禁がある	0	
4. 週に1度以上,日中に失禁がある	0	
5. 常に失禁がある	0	
B. 食 事		
1. 介助なしで食事ができる	1	
2. 食事のときに多少の介助が必要,特別な調理法が必要あるいは食	0	
事のときに汚したものを片づけてもらう		
3. 食事に介助が必要であり、食べるときにも散らかってしまう	0	
4. 常に介助が必要	0	
5. 自力では全く摂取できない	0	
C. 着替え		
1. タンスから適切な服を選んで自分で着替えられる	1	
2. 多少の介助で脱ぎ着できる	0	
3. 服を選んだり、脱ぎ着に手助けが必要	0	
4. 着替えに介助を要するが,本人も協力する	0	
5. 常に介助が必要であり、着替えに拒否的	0	
D. 身繕い(身だしなみ,髪や爪の手入れ,洗面など)		
1. いつも身だしなみがきちんとしている	1	
2. 1人で身繕いができるが髭などは剃ってもらう	0	
3. いつも多少は手伝ってもらう	0	
4. 常に介助を要するが,そのあとはきちんとしていられる	0	
5. 介助に抵抗する	0	
E. 移動能力		
1. 1人で出かけることができる	1	
2. 家の中か家の周囲まで出かけることができる	0	
3. 杖 (),歩行器 (),車椅子 ()の助けが必要	0	
4. 椅子や車椅子に座っていられるが、自分では動かせない	0	
5. 終日の半分以上は寝たきり	0	
F. 入 浴		
1. 介助なしで入浴できる	1	
2. 浴槽の出入りには介助が必要	0	
3. 手や顔は洗えるが他の部分を洗えない	0	
4. 自分では洗えないが協力的	0	表3
5. 介助に抵抗する	0	日本語版physical (PSMS)
得点	/6	得点は0~6点
可加	,0	〔文献26)より引用〕

なる. 日本語版SMQは日本語版MMSEと高い相関を示し、39/40をカットオフ値とした場合、ADの検出率は100%、特異度は94%であり、スクリーニング検査として優れている.

2) ADLの評価方法

痴呆が,脳の器質性の要因により,いったん獲得,

成立した知的機能に欠損が生じ、それまで可能であった日常生活や社会生活に支障をきたした状態をさす以上、痴呆患者の総合的機能評価に際しては認知能力の障害と並んで日常生活活動能力(ADL)の障害の評価が不可欠である。ADLには、更衣、排泄などの基本的な生活機能であるbasic ADLと買い