ハビリテーション料の算定については、調査時点で算定している施設と準備中の施設を含めても31%であった、69%のこれは、入院時の病棟が急性期治療病棟や精神一般病棟であると回答した病院も多いためではないかと考えられる。

＜退院先について＞

認知症治療病棟から退院する患者の退院先で最も多かったのは介護施設（約42%）、一般及び精神科の病院又は診療所への転院は25%であり、自宅へ退院した患者は19.7%であった。これは、認知症治療病棟からの退院後も自宅退院は難しく、介護や医療のために施設入所又は入院が必要であることが明らかになった。

＜地域連携について＞

地域連携会議などの開催については半数以上の患者について実施していると回答した施設が40.8%となっており、3年前の調査では76.6%の病院が2割以下の患者でしか実施していなかったことと比較すると退院支援、地域連携が図られてきていると考えられる。

＜認知症に関連するクリニカルパスの使用について＞

急性期認知症患者クリニカルパスについては、前回の調査との比較はできないが、多くの施設において使用されていないことが分かった。また、認知症版地域連携クリニカルパスの使用・経験については、3年前の尾嵜らの研究では12.0%であったが、本調査においても14.8%であり、これらの認知症に関連するクリニカルパスの使用・経験について、未だ普及していないのではないかと考えられる。

Ｅ．結論

今回、精神科病院における認知症患者の入院期間と退院を困難にしている要因や、認知症患者の退院支援に関してどのような支援が行われているかについて調査した。

入院期間については595.6日と600日近くあり、3年前に我々が行った調査からはやや短くなっている。しかし、2か月以内に退院する割合は約10%と厚生労働省の目標としている割合よりも低いことが分かった。退院を困難にしている要因などについては、BPSDが最も多く、ついで、施設入所待ちであり、ほぼ同様の結果であったことが分かった。地域ケア会議などの地域連携は行われつつあるが、認知症に関連するクリニカルパスの普及はまだ進んでいなかった。

これらの結果について、更に詳細な分析を行い、入院期間が短縮する要因、また、長期化する要因について検討する必要がある。

また今後は、入院患者一人一人についてどのような治療やケアが行われているかについて詳細な調査が必要と考える。

Ｆ．健康危険情報

なし

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H．知的財産権の出願・登録状況
（予定を含む）
１．特許取得
　なし
２．実用新案登録
　なし
３．その他
　なし

Ⅲ．研究成果の刊行に関する一覧表

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Ⅳ. 研究成果の刊行物・別刷

Geriatrics Gerontology — Medline Indexed

Geriatr Gerontol Int 2014; **14 (Suppl. 2):** *35–44*

ORIGINAL ARTICLE

Unclassified cases of behavioral variant of major frontotemporal neurocognitive disorder in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition

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Aim: In the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5), the behavioral variant of major frontotemporal neurocognitive disorder (bvFT-NCD) is subclassified into "probable bvFT-NCD" or "possible bvFT-NCD." When genetic evidence is unavailable, cases without clinical neuroimaging are subclassified into "possible bvFT-NCD," whereas cases whose clinical images show the typical characteristics are subclassified into "probable bvFT-NCD." Thus, the cases that meet the diagnostic criteria of bvFT-NCD based on their symptoms, but lack the neuroimaging characteristics, fall between the two categories of probable and possible bvFT-NCD. These cases herein are defined as "unclassified bvFT-NCD," and the present study aims at considering an appropriate diagnostic approach to such cases, that is, whether unclassified bvFT-NCD should be included in bvFT-NCD as a third subcategory, or whether it should be classified into diseases other than bvFT-NCD.

Methods: All patients who presented at the Department of Psychiatry of the National Center for Geriatrics and Gerontology with suspicion of the behavioral variant of frontotemporal dementia between 1 May 2011 and 30 April 2013 were retrospectively rediagnosed based on the DSM-5 criteria.

Results: A total of 16 cases met the criteria of bvFT-NCD, and among them, eight cases corresponded to unclassified bvFT-NCD. From a cross-sectional and clinical perspective, all eight cases of unclassified bvFT-NCD fulfilled the symptomatic criteria for bvFT-NCD, although the possibilities of Alzheimer's disease and other mental disorders could not be ruled out completely.

Conclusions: To establish clinical diagnostic criteria for unclassified bvFT-NCD, accumulation of cases and evidence will be required along with longitudinal observation using various diagnostic technologies and post-mortem examination. **Geriatr Gerontol Int 2014; 14 (Suppl. 2): 35–44.**

Keywords: behavioral variant frontotemporal dementia, *Diagnostic and Statistical Manual of Mental Disorders* 5th edition, major frontotemporal neurocognitive disorder, neuroimaging, unclassified case.

Introduction

The *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5)[1] was published in 2013, superseding the previous version of the DSM-IV-TR.[2] The DSM-5 includes changes to the diagnostic criteria of dementia, including a significant revision of the behavioral variant of frontotemporal dementia (bvFTD). In the previous version of the DSM-IV-TR, bvFTD was referred to as "dementia due to Pick's disease," and was classified into the dementia subtype of "dementia due to other general medical conditions." The essence of the diagnostic criteria of dementia due to Pick's disease was "to meet the diagnostic criteria of dementia caused by Pick's disease by exclusion of Alzheimer's disease (AD) and vascular disorders." Consequently, accurate knowledge about Pick's disease was a prerequisite for diagnosing Pick's disease. However, the DSM-IV-TR gives a brief account of Pick's disease, categorizing it into axis III, which contains general medical conditions of "physical diseases." In this sense, it could be said that the DSM-IV-TR set quite incomplete diagnostic criteria of Pick's disease as a "psychiatric disease."

In DSM-5, the condition previously designated as dementia due to Pick's disease in the DSM-IV-TR is classified as a subtype of major frontotemporal neurocognitive disorder (FT-NCD), called the behavioral variant of NCD (bvFT-NCD), whose diagnostic

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Table 1 *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition diagnostic criteria for major or mild frontotemporal neurocognitive disorder

A. The criteria are met for major or mild neurocognitive disorder.
B. The disturbance has insidious onset and gradual progression.
C. Either (1) or (2):
   1. Behavioral variant:
      a. Three or more of the following behavioral symptoms:
         i. Behavioral disinhibition.
         ii. Apathy or inertia.
         iii. Loss of sympathy or empathy.
         iv. Perseverative, stereotyped or compulsive/ritualistic behavior.
         v. Hyperorality and dietary changes.
      b. Prominent decline in social cognition and/or executive abilities.
   2. Language variant:
      a. Prominent decline in language ability, in the form of speech production, word finding, object naming, grammar or word comprehension.
D. Relative sparing of learning and memory and perceptual-motor function.
E. The disturbance is not better explained by cerebrovascular disease, another neurodegenerative disease, the effects of substance, or another mental, neurological or systemic disorder.

Probable frontotemporal neurocognitive disorder is diagnosed if either of the following is present; otherwise, possible frontotemporal neurocognitive disorder should be diagnosed:
1. Evidence of a causative frontotemporal neurocognitive disorder genetic mutation, from either family history or genetic testing.
2. Evidence of disproportionate frontal and/or temporal lobe involvement from neuroimaging.

Possible frontotemporal neurocognitive disorder is diagnosed if there is no evidence of a genetic mutation, and neuroimaging has not been performed.

Coding note: For probable major neurocognitive disorder due to frontotemporal lobar degeneration, with behavioral disturbance, code first 331.19 (G31.09) frontotemporal disease, followed by 294.11 (F02.81) probable major neurocognitive disorder due to frontotemporal lobar degeneration, with behavioral disturbance. For probable major neurocognitive disorder due to frontotemporal lobar degeneration, without behavioral disturbance, code first 331.19 (G31.09) frontotemporal disease, followed by 294.10 (F02.80) probable major neurocognitive disorder due to frontotemporal lobar degeneration, without behavioral disturbance.

For possible major neurocognitive disorder due to frontotemporal lobar degeneration, code 331.9 (G31.9) possible major neurocognitive disorder due to frontotemporal lobar degeneration. (Note: Do *not* use the additional code for frontotemporal disease. Behavioral disturbance cannot be coded but should still be indicated in writing.)

For mild neurocognitive disorder due to frontotemporal lobar degeneration, code 331.83 (G31.84). (Note: Do *not* use the additional code for frontotemporal disease. Behavioral disturbance cannot be coded but should still be indicated in writing.)

criteria are shown in Table 1. Regarding subclassification of bvFT-NCD, probable bvFT-NCD and possible bvFT-NCD are defined. Probable bvFT-NCD is diagnosed when there is "evidence of a causative frontotemporal neurocognitive disorder genetic mutation,"[1] or "evidence of disproportionate frontal and/or temporal lobe involvement from neuroimaging."[1] Possible bvFT-NCD is diagnosed when there is "no evidence of a genetic mutation and neuroimaging has not been performed."[1]

In daily practice, we examine the cases that meet the diagnostic criteria of bvFTD, but are devoid of the *clinical neuroimaging characteristics*. It remains ambiguous whether or not these cases should be diagnosed by clinical manifestations without referring to clinical images. According to the revised DSM, the DSM-5, such cases meet the criteria of neither "probable bvFT-NCD" nor "possible bvFT-NCD." In the present work, we define these cases, which meet the symptomatic criteria but lack imaging characteristics, as cases of "unclassified bvFT-NCD," when genetic evidence is unavailable, and we consider an appropriate diagnostic approach to these unclassified cases based on the DSM-5.

Methods

Participants were all patients who presented at the Department of Psychiatry of the National Center for Geriatrics and Gerontology (NCGG) with suspected bvFTD between 1 May 2011 and 20 April 2013. They were retrospectively rediagnosed based on the new bvFT-NCD criteria in the DSM-5. The following information was obtained for all participants: sex, age, marital status, age of onset, duration of illness (years), age of the first visit to our hospital, duration between appearance of symptoms and treatment (years), chief complaint at first visit, and comorbid diagnosis. For multidimensional evaluation of the patients, a comprehensive geriatric assessment (CGA) was carried out; the CGA consisted of neuropsychological tests, and assessments of the functions of activities of daily living (ADL), behavioral and psychological symptoms of dementia (BPSD), the patient's mood, and the caregiver burden. The neuropsychological tests included the Mini-Mental State Examination (MMSE), Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) and Frontal Assessment Battery (FAB). ADL was assessed using the Barthel Index (Barthel) and Lawton Instrumental Activities of Daily Living scale (Lawton), and BPSD was assessed by an informant-based questionnaire – the Dementia Behavior Disturbance Scale (DBD). The mood of patients was evaluated using a self-rated scale of the Geriatric Depression Scale (GDS), and caregiver burden was assessed by the Zarit Caregiver Burden Interview (ZBI). Neuroimaging data were also obtained using head computed tomography (CT), magnetic resonance imaging (MRI) and single-photon emission computed tomography (SPECT). In the Department of Psychiatry of NCGG, before the revision of the DSM in May 2013, bvFTD was diagnosed based on the international consensus criteria for the behavioral variant of FTD;[3,4] the diagnostic criteria of the DSM-5 are shown in Table 1, and the international consensus criteria for the behavioral variant of FTD are shown in Table 2.

Results

A total of 636 patients presented at the Department of Psychiatry of NCGG between 1 May 2011 and 30 April 2013, and 41 of these patients were suspected of having bvFTD. Among the 41 cases, 16 cases met the criteria of bvFT-NCD, whereas 25 did not meet the criteria. Table 3 shows the following information for these 16 cases: sex, age, marital status, age of onset, duration of illness (years), age of the first visit to our hospital, duration between appearance of symptoms and treatment (years), chief complaint at first visit, and comorbid diagnosis. As all 16 patients diagnosed with bvFT-NCD

Table 2 International consensus criteria for behavioral variant frontotemporal dementia

Neurodegenerative disease
Must be present for any FTD clinical syndrome
Shows progressive deterioration of behavior and/or cognition by observation or history
Possible bvFTD
Three of the features (A–F) must be present; symptoms should occur repeatedly, not just as a single instance:
A Early (3 years) behavioral disinhibition
B Early (3 years) apathy or inertia
C Early (3 years) loss of sympathy or empathy
D Early (3 years) perseverative, stereotyped or compulsive/ritualistic behaviour
E Hyperorality and dietary changes
F Neuropsychological profile: executive function deficits with relative sparing of memory and visuospatial functions
Probable bvFTD
All the following criteria must be present to meet diagnosis:
A Meets criteria for possible bvFTD
B Significant functional decline
C Imaging results consistent with bvFTD (frontal and/or anterior temporal atrophy on CT or MRI or frontal hypoperfusion or hypometabolism on SPECT or PET)
Definite bvFTD
Criteria A and either B or C must be present to meet diagnosis:
A Meets criteria for possible or probable bvFTD
B Histopathological evidence of FTLD on biopsy at post-mortem
C Presence of a known pathogenic mutation
Exclusion criteria for bvFTD
Criteria A and B must both be answered negatively; criterion C can be positive for possible bvFTD, but must be negative for probable bvFTD:
A Pattern of deficits is better accounted for by other non-degenerative nervous system or medical disorders
B Behavioural disturbance is better accounted for by a psychiatric diagnosis
C Biomarkers strongly indicative of Alzheimer's disease or other neurodegenerative process
Additional features
A Presence of motor neuron findings suggestive of motor neuron disease
B Motor symptoms and signs similar to corticobasal degeneration and progressive supranuclear palsy
C Impaired word and object knowledge
D Motor speech deficits
E Substantial grammatical deficits

bvFTD, behavioral variant of frontotemporal dementia; CT, computed tomography; FTD, frontotemporal dementia; MRI, magnetic resonance imaging; PET, positron emission tomography, SPECT, single-photon emission computed tomography.

Table 3 Profiles of the patients with the behavioral variant of major frontotemporal neurocognitive disorder

Diagnosis	Patient number	Sex (male/female)	Age (years)	Marital status	Onset (years)	Duration of illness (years)	Age of first visit to our hospital (years)	Duration between appearance of symptoms and treatment (years)	Chief complaint at first visit	Comorbid diagnosis
Probable FT-NCD	1	f	84	Widow	82	2	84	2	Violence, visual hallucination, persecutory delusion	Diabetes mellitus
Probable FT-NCD	2	f	82	Married	76	6	80	4	Anxiety, appetite loss, depressed mood	Hypertension, osteoporosis
Probable FT-NCD	3	f	81	Unmarried	72	9	80	8	Odd behavior	thyroid dysfunction
Probable FT-NCD	4	f	84	Widow	80	4	83	3	Irritability, personality change	Diabetes mellitus
Probable FT-NCD	5	m	77	Married	75	2	75	0	Hypochondria	Silicosis
Probable FT-NCD	6	m	70	Married	63	7	66	3	Panic attack, selfish behavior	Hyperlipidemia
Probable FT-NCD	7	m	74	Married	73	1	73	0	Palpitation, hyperventilation, anxiety	HCV, cerebellar tumor
Probable FT-NCD	8	m	81	Divorced	81	0	81	0	Odd behavior	Hypertension, hyperlipidemia
Unclassified FT-NCD	I	f	78	Married	66	12	76	10	Stealing	Hypertension
Unclassified FT-NCD	II	f	80	Divorced	67	13	77	10	Depressed mood	Myocardiac infarction
Unclassified FT-NCD	III	f	74	Widow	70	4	71	1	Hypochondria, insomnia, appetite loss	None
Unclassified FT-NCD	IV	f	73	Married	65	8	72	7	Odd behavior, personality change, persecutory delusion	Epilepsy
Unclassified FT-NCD	V	m	81	Married	71	10	73	2	cognitive impairment	None
Unclassified FT-NCD	VI	m	87	Married	79	8	83	4	Depressed mood, insomnia	Cerebral infarction, prostatic carcinoma
Unclassified FT-NCD	VII	m	66	Married	63	3	63	0	Depressed mood, insomnia	Chronic liver cirrhosis type C, hepatic carcinoma
Unclassified FT-NCD	VIII	m	67	No information	64	3	67	3	Stealing, confabulation, panic attack, odd behavior	None

Diagnosis	Diagnostic criteria of bvFT-NCD						CGA profile								Neuroimaging		
	C1 a-i	C1 a-ii	C1 a-iii	C1 a-iv	C1 a-v	C b	MMSE	ADAS	FAB	Barthel	Lawton	DBD	GDS	ZBI	CT	MRI	SPECT
Probable FT-NCD	○	○	○	×	○	○	23	×	×	×	×	×	15	×	×	FTD	FTD
Probable FT-NCD	○	○	○	×	○	○	15	×	×	25	0	25	4	30	×	FTD	×
Probable FT-NCD	○	○	○	○	×	○	25	12.4	×	×	×	×	×	×	FTD	×	×
Probable FT-NCD	○	○	○	×	×	○	23	16.4	8	95	6	39	6	45	×	×	FTD
Probable FT-NCD	○	○	○	×	×	○	26	×	×	100	3	12	11	12	×	FTD	×
Probable FT-NCD	○	○	○	○	×	○	22	14.4	10	×	×	×	×	×	×	FTD	FTD
Probable FT-NCD	×	○	○	○	×	○	20	20	11	100	4	10	8	0	×	FTD	nonFTD
Probable FT-NCD	○	○	○	×	×	○	16	×	×	90	6	29	1	44	×	FTD	×
Unclassified FT-NCD	○	○	○	×	×	○	×	10.7	13	×	×	×	13	×	×	nonFTD	×
Unclassified FT-NCD	○	○	○	×	×	○	29	×	×	100	8	11	9	33	×	nonFTD	×
Unclassified FT-NCD	×	○	○	×	○	○	28	8.3	×	×	×	×	×	×	×	nonFTD	nonFTD
Unclassified FT-NCD	×	○	○	○	×	○	17	13.6	5	85	3	31	1	19	×	nonFTD	nonFTD
Unclassified FT-NCD	×	○	○	○	×	○	20	11.7	×	100	2	30	×	18	×	nonFTD	nonFTD
Unclassified FT-NCD	○	○	○	×	×	○	12	×	×	×	×	×	×	×	nonFTD	×	×
Unclassified FT-NCD	○	○	×	×	○	○	24	×	×	95	2	14	2	19	×	nonFTD	nonFTD
Unclassified FT-NCD	○	○	○	×	×	○	23	×	×	100	5	5	2	4	×	nonFTD	×

The profile of each case is summarized in the table. The diagnostic criteria of the behavioral variant of major frontotemporal neurocognitive disorder (bvFT-NCD) are described in Table 1. The comprehensive Geriatric Assessment (CGA) consists of Mini-Mental State Examination (MMSE), Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog), Frontal Assessment Battery (FAB), Barthel Index (Barthel), Lawton Instrumental Activity of Daily Life (Lawton), Dementia Behavior Disturbance Scale (DBD), Geriatric Depression Scale (GDS) and Zarit Caregiver Burden Interview (ZBI). Neuroimaging data were obtained using head computed tomography (CT), magnetic resonance imaging (MRI) and single-photon emission computed tomography (SPECT). Imaging data were used to evaluate whether a case had characteristics of the behavioral of variant frontotemporal dementia (FTD) or not (nonFTD). HCV, hepatitis C virus infection.

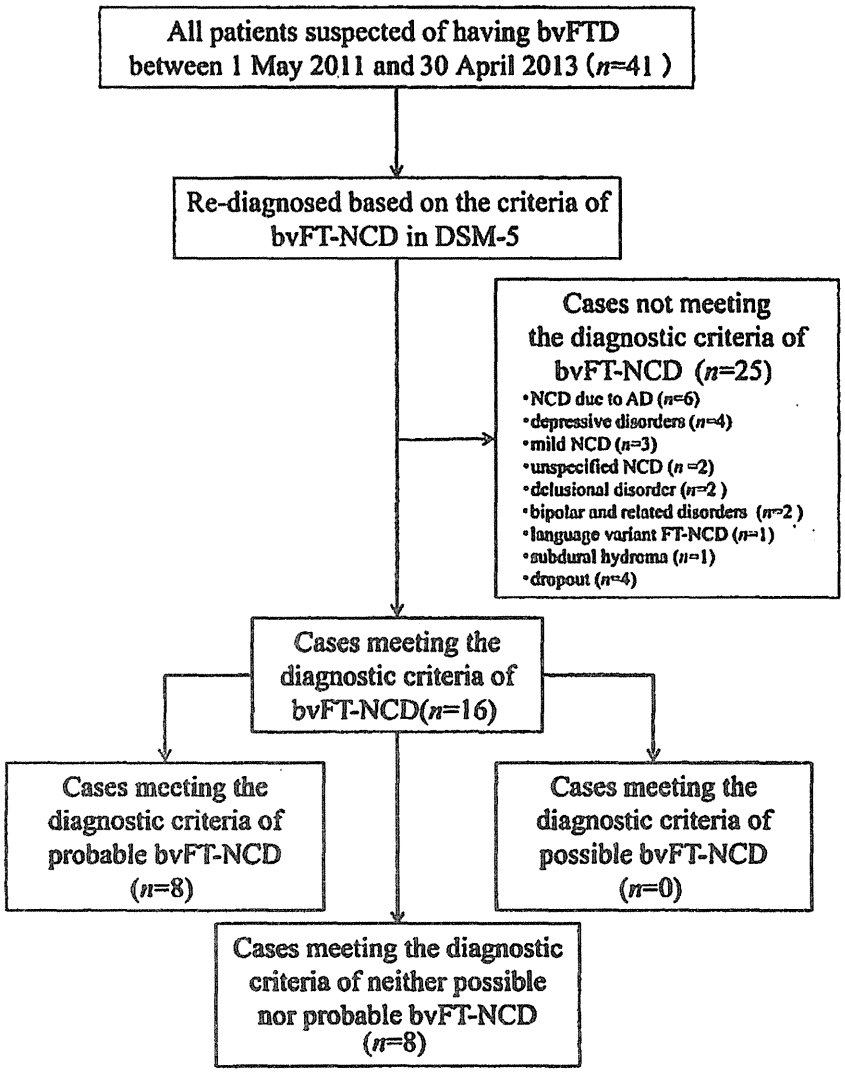

Figure 1 Selection of the study patients. bvFTD, behavioral variant of frontotemporal dementia; bvFT-NCD, behavioral variant of major frontotemporal neurocognitive disorder; DSM-5, *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition; FT-NCD, major frontotemporal neurocognitive disorder; NCD due to AD, major neurocognitive disorder due to Alzheimer's disease.

underwent neuroimaging tests, there were no cases who met the criteria of possible bvFT-NCD.

Among the 16 cases, eight patients had clinical neuroimaging characteristics of bvFT-NCD, and thus were diagnosed as having probable bvFT-NCD, whereas eight patients did not show the neuroimaging characteristics. Thus, the latter eight patients corresponded to our present definition of unclassified bvFT-NCD, as they met the criteria of neither probable bvFT-NCD nor possible bvFT-NCD (Fig. 1).

Among the eight patients diagnosed as having probable bvFT-NCD, three patients (patients 1, 6, 7; Table 3) underwent both an MRI brain scan and SPECT brain scan. Two of these patients (patients 1, 6) showed the characteristics of bvFT-NCD by both imaging modalities, whereas one patient (patient 7) showed the characteristics only by MRI morphological imaging, and not by SPECT functional imaging. Among the eight patients of unclassified bvFT-NCD, four patients underwent both an MRI brain scan and a SPECT brain scan (patients III, IV, V, VII; Table 3), and none of the four patients showed the characteristics of bvFT-NCD in MRI morphological imaging or in SPECT functional imaging. Representative MRI and SPECT brain images of probable bvFT-NCD are shown in Figure 2, and those of unclassified probable bvFT-NCD are shown in Figure 3.

All 16 cases diagnosed as having bvFT-NCD based on DSM-5 also met the international consensus criteria for the behavioral variant of FTD; thus, the same diagnosis was made using either set of criteria.

The comparison of patient data between the probable bvFT-NCD group and unclassified bvFT-NCD group was as follows: sex ratio, 1:1 in both groups; familial dementia, none in either group; age of onset, 68.1 ± 5.2 years in unclassified bvFT-NCD, 75.3 ± 6.2 in

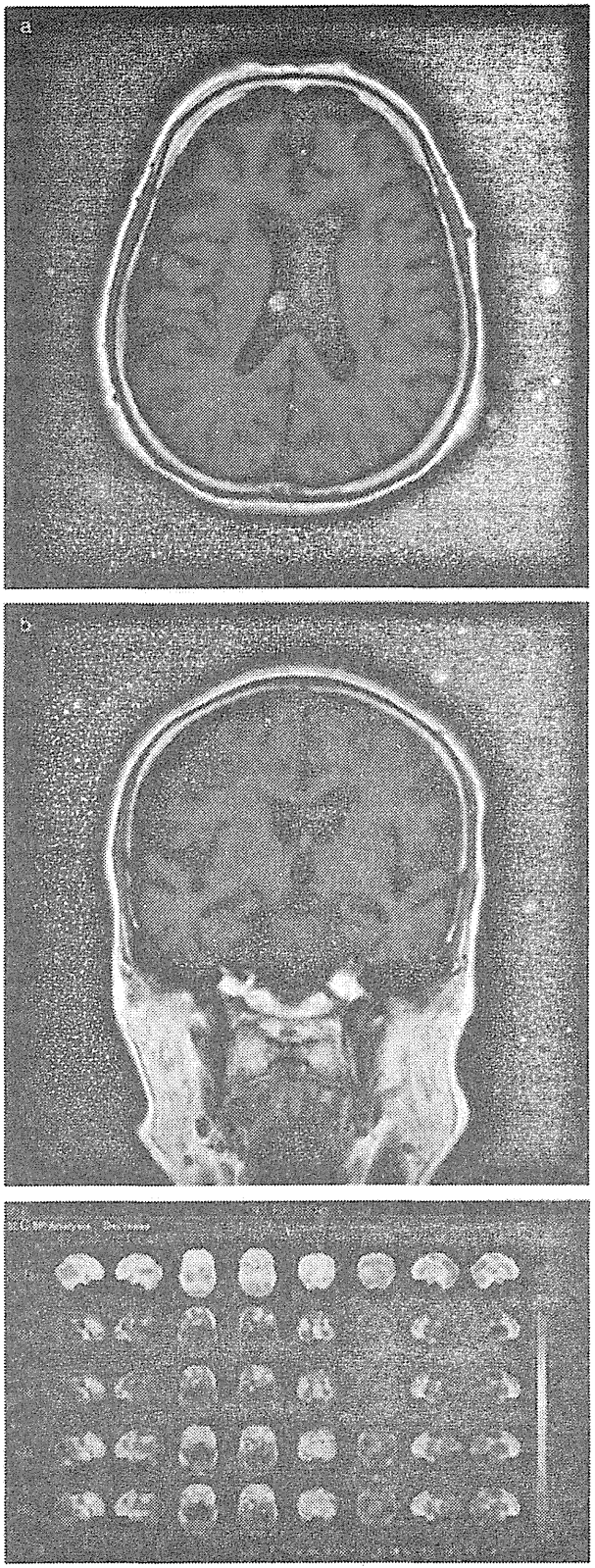

Figure 2 Representative neuroimaging of probable behavioral variant of major frontotemporal neurocognitive disorder (bvFT-NCD). (a) Coronal T1-weighted magnetic resonance imaging (MRI). (b) Axial T1-weighted MRI. MRI images are horizontally flipped; the observer's right is the left side of the patient's brain, and vice versa. (c) Single photon emission computed tomography imaging. Images are reconstructed using the three-dimensional stereotactic surface projection (3D-SSP) technique and superimposed on normalized images of standardized brain MRI. Color-coding represents the statistical significance (Z-score) of the decrease in regional cerebral blood flow (r-CBF) in the resting mode. Red represents more significant rCBF reduction. From left to right, eight directions of the brain surface images are shown: right lateral (RT.LAT), left lateral (LT.LAT), superior (SUP), inferior (INF), anterior (ANT), posterior (POST), right medial (RT.MED) and left medial (LT.MED). Vertically from the second to the fifth lines, Z-score maps are shown (high Z-score indicates decrease): the Z-score map was normalized to the cerebral global mean (GLB) in the second line, to the thalamus (TH) in the third line, to the cerebellum (CBL) in the fourth line and to the pons (PONS) in the fifth line. The distribution of rCBF is shown in the first line (red color-coding represents increment of rCBF). The cortical atrophy shown in MRI images and rCBF reduction patterns of the 3D-SSP images are typical for frontotemporal dementia.

probable bvFT-NCD, $P = 0.026$ (unpaired t-test, 95% confidence interval [CI] 0.98–13.26); age of first visit to our hospital, 72.8 ± 6.2 years and 77.8 ± 6.0 years, respectively, $P = 0.12$ (95% CI −1.5 to 11.5); duration of illness, 7.6 ± 4.0 years and 3.9 ± 3.2 years, respectively, $P = 0.057$, (95% CI −7.6 to 0.12); and duration between appearance of symptoms and treatment, 4.3 ± 3.9 years and 2.5 ± 2.7 years, respectively, $P = 0.23$ (95% CI −5.8 to 1.5). Age of onset was significantly lower in unclassified bvFT-NCD than in probable bvFT-NCD, and duration of illness was marginally longer in unclassified bvFT-NCD, although the difference did not reach statistical significance ($P = 0.057$, 95% CI −7.6 to 0.12). There were no significant differences between the two groups in either the age of first visit to our hospital or the duration between appearance of symptoms and treatment.

The results of the neurocognitive tests were as follows: MMSE score, 21.9 ± 2.3 ($n = 7$) in unclassified bvFT-NCD, 21.3 ± 1.4 ($n = 8$) in probable bvFT-NCD, $P = 0.82$ (unpaired t-test, 95% CI −6.24 to 5.03); ADAS score, 11.1 ± 2.2 ($n = 4$) and 15.8 ± 3.2 ($n = 4$), respectively, $P = 0.06$ (95% CI −0.25 to 9.65); and FAB, 9.0 ± 5.7 ($n = 2$) and 9.7 ± 1.5 ($n = 3$), respectively. There were no significant differences in the MMSE or ADAS scores between the two groups, and the FAB scores were not compared because of an insufficient number of patients who underwent the assessment.

All 16 cases of bvFT-NCD met the DSM-5 criterion (ii) of "Apathy or inertia,"[1] whereas 15 cases (all except

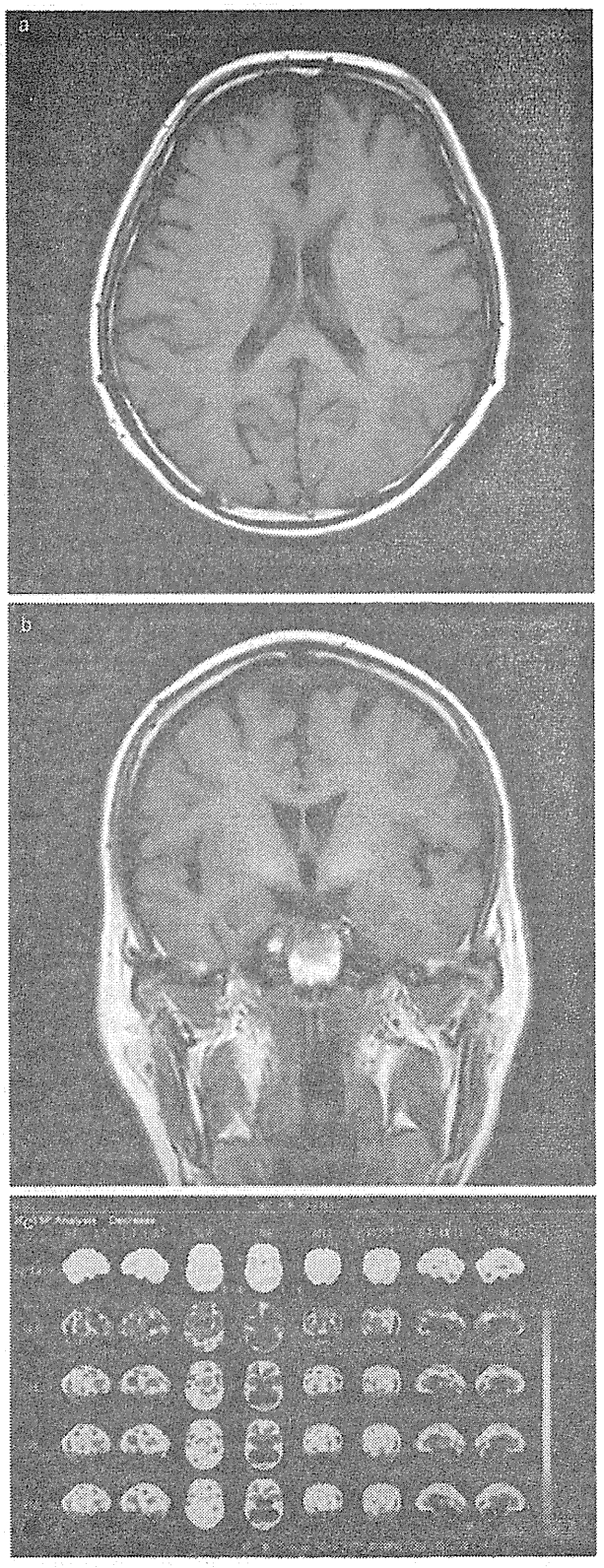

Figure 3 Representative neuroimaging of unclassified behavioral variant of major frontotemporal neurocognitive disorder (bvFT-NCD). (a) Coronal T1-weighted magnetic resonance imaging (MRI). (b) Axial T1-weighted MRI. (c) Single photon emission computed tomography imaging. Images are reconstructed using the three-dimensional stereotactic surface projection (3D-SSP) technique and superimposed on normalized images of standardized brain MRI. Color-coding represents the statistical significance (Z-score) of the decrease in regional cerebral blood flow (r-CBF) in the resting mode. Red represents more significant rCBF reduction. From left to right, eight directions of the brain surface images are shown: right lateral (RT.LAT), left lateral (LT.LAT), superior (SUP), inferior (INF), anterior (ANT), posterior (POST), right medial (RT.MED) and left medial (LT.MED). Vertically from the second to the fifth lines, Z-score maps are shown (high Z-score indicates decrease): the Z-score map was normalized to the cerebral global mean (GLB) in the second line, to the thalamus (TH) in the third line, to the cerebellum (CBL) in the fourth line and to the pons (PONS) in the fifth line. The distribution of rCBF is shown in the first line (red color-coding represents increment of rCBF). Neither the cortical atrophy shown in MRI images nor the rCBF reduction pattern of the three-dimensional stereotactic surface projection images is typical for frontotemporal dementia.

one case of unclassified bvFT-NCD) met the criterion (iii) of "Loss of sympathy or empathy."[1] Seven of eight cases of bvFT-NCD met the criterion (i) of "Behavioral disinhibition,"[1] whereas five of eight cases of unclassified bvFT-NCD met criterion (i).

Discussion

All 16 patients diagnosed as having bvFTD based on the diagnostic criteria of the international consensus criteria for the behavioral variant of FTD also met the diagnostic criteria of bvFT-NCD based on DSM-5, as the two systems have nearly identical symptomatic criteria. Regarding the subcategory of possible bvFTD/bvFT-NCD, one of the differences between the two sets of criteria involves diagnostic neuroimaging: the international consensus criteria for behavioral variant FTD do not refer to imaging for diagnosis of possible bvFTD, whereas the DSM-5 stipulates that possible bvFT-NCD should be diagnosed if neuroimaging has not been carried out. Probable bvFTD/bvFT-NCD is diagnosed if neuroimaging has been carried out and the characteristic neuroimaging representation is shown. Thus, the DSM-5 does not refer to cases in which neuroimaging has been carried out, but no clinical neuroimaging characteristics of FT-NCD are shown, whereas such cases are diagnosed as possible bvFTD in the international consensus criteria for the behavioral variant of FTD.

At NCGG, neuroimaging scans are carried out for almost all cases with suspected dementia, so that there

would be almost no cases that met the criteria of possible bvFT-NCD. In the present study, eight out of 16 cases met neither criteria of probable or possible bvFT-NCD.

Unclassified bvFT-NCD is diagnosed as possible bvFTD based on the international consensus criteria for the behavioral variant of FTD. However, the DSM-5 does not explicitly mention the diagnostic criteria for cases with symptoms of bvFT-NCD, but without the imaging characteristics. Thus, the diagnosis of these cases remains ambiguous, as aforementioned. It is likely that the revised DSM-5 intends to confine bvFT-NCD to the explicitly stated "possible" and "probable" categories, and thus if the DSM-5 is strictly interpreted, the cases without imaging characteristics will be excluded from bvFT-NCD. In contrast, those cases can be included into bvFT-NCD with emphasis on clinical manifestation, although they are classified into neither probable nor possible bvFT-NCD. The present article considers whether the unclassified bvFT-NCD should be included in bvFT-NCD as a third subcategory along with possible or probable bvFT-NCD, or whether it should be classified into diseases other than bvFT-NCD.

First, we will consider the diagnosis of unclassified bvFT-NCD from the perspective of the epidemiological characteristics of FT-NCD. In the DSM-5, the epidemiological characteristics are listed as follows:[1] (i) major and mild frontotemporal NCD is a common cause of early-onset NCD in individuals aged younger than 65 years; (ii) approximately 20–25% of cases of frontotemporal NCD occur in individuals aged older than 65 years, whereas the range of age onset varies widely from the 30s to the 90s; (iii) population prevalence estimates are in the range of 2–10 per 100 000; (iv) prevalence estimates of the behavioral variant are higher among males; and (v) approximately 40% of individuals with major or mild frontotemporal NCD have a family history of early-onset NCD. In the present study, the characteristics of the cases of unclassified bvFT-NCD were as follows: age of onset, 68.1 ± 5.2 years; age of first visit to our hospital, 72.8 ± 6.2 years; sex ratio, 1:1; and no familial dementia. The characteristics of the patients with probable bvFT-NCD were as follows: age of onset, 75.3 ± 6.2 years; age of first visit to our hospital, 77.8 ± 6.0 years; sex ratio, 1:1; and no familial dementia. Our data showed significantly lower age of onset in unclassified bvFT-NCD than in probable bvFT-NCD. However, neither unclassified nor probable bvFT-NCD met the epidemiological characteristics mentioned in the DSM-5. Consequently, from an epidemiological perspective, the characteristics cannot be rational reasons to exclude unclassified bvFT-NCD from bvFT-NCD. As to why the cases of unclassified bvFT-NCD had an earlier onset than cases of probable bvFT-NCD, the reason remains uncertain. One possibility is that the imaging features of cortical atrophy, hypoperfusion and hypometabolism are not prominent in the cases of earlier onset.

Second, we reviewed the symptomatic features that cognitive function was relatively preserved in the early stages. The results of cognitive tests of probable bvFT-NCD were as follows: MMSE, 21.3 ± 1.4 (n = 8); ADAS, 15.8 ± 3.2 (n = 4); and those for unclassified bvFT-NCD were as follows: MMSE, 21.9 ± 2.3 (n = 7); ADAS 11.1 ± 2.2 (n = 4); the difference between the two groups was not statistically significant. As aforementioned, cognitive functions were relatively preserved in both cases, and cognitive characteristics are not the supporting evidence to exclude unclassified bvFT-NCD from bvFT-NCD.

Third, we will consider the differential diagnoses based on DSM-5, which lists the following diseases that should be differentiated from bvFT-NCD: NCD due to AD, NCD with Lewy bodies, NCD due to Parkinson's disease, vascular NCD, progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), primary mental disorders such as major depression, bipolar disorders and schizophrenia, and other medical conditions including metabolic disturbances, nutritional deficiencies and infection.

Regarding the differentiation from NCD due to AD, the DSM-5 provides the following explanation: "10–30% of patients presenting with a syndrome suggestive of major or mild FT-NCD are found at autopsy to have AD pathology. This occurs more frequently in individuals who present with progressive dysexecutive syndromes in the absence of behavioral changes or movement disorder, or in those with the logopenic variant."[1] It has been suggested that bvFT-NCD is difficult to differentiate from AD, especially the frontal variant of AD,[5,6] merely by clinical manifestation, and the possibility cannot be ruled out that post-mortem examination would reveal the AD pathology in these cases. As for neuroimaging evidence, four cases of unclassified bvFT-NCD underwent SPECT brain scan, and none presented the characteristic brain blood flow patterns of AD. In addition, the patterns were inconclusive in all four of the cases without SPECT images.

Regarding NCD with Lewy bodies and NCD due to Parkinson's disease, the DSM-5 provides the following explanation: "In major or mild NCD with Lewy bodies core and suggestive features of Lewy bodies must be present. In major or mild NCD due to Parkinson's disease spontaneous parkinsonism emerges well before the cognitive decline."[1] In the present series, differentiation in such cases is thus rather easy, because the cases of unclassified bvFT-NCD have few findings suggestive of NCD with Lewy bodies or NCD due to Parkinson's disease.

Next, the DSM-5 mentions that bvFT-NCD can be differentiated from vascular NCD based on a history

of cerebrovascular event(s) and findings of clinical neuroimaging with consideration paid to executive ability and behavioral changes.[1] In the present study, neuroimaging tests were carried out in all eight patients, and the possibility of vascular NCD could be ruled out.

Regarding PSP and CBD, the DSM-5 only mentions the possibility of overlapping PSP, CBD and motor neuron disease.[1] As frontotemporal lobar degeneration encompasses a wide spectrum of clinical entities, including PSP and CBD,[7,8] differentiation can be difficult if the cases show some features of motor neuron disease. However, the eight cases of unclassified bvFT-NCD did not have characteristic clinical features of motor neuron disease. Thus, they are unlikely to be diagnosed as PSP and/or CBD.

As to mental disorders, the DSM-5 mentions that the development of progressive neurocognitive difficulties will help to differentiate bvFT-NCD from primary mental disorders, such as major depression, bipolar disorders or schizophrenia.[1] In clinical practice, bvFTD is frequently misdiagnosed as primary mental disorder at onset,[9] and consequently, differentiation requires longitudinal follow up. The present cases of unclassified bvFT-NCD did not meet the criteria of major depression, bipolar disorder or schizophrenia, but they should be followed to confirm the presence or absence of progressive neurocognitive difficulties.

The DSM-5 simply mentions that treatable physical causes of NCD can be differentiated by careful medical evaluation.[1] The Department of Psychiatry at NCGG carries out blood examinations to evaluate patients for conditions including metabolic disturbances, nutritional deficiencies and infection, in addition to electrocardiography, and abdominal and chest X-ray. These tests are carried out for all patients, including cases diagnosed with bvFT-NCD. Thus, the possibility of physical causes of NCD can be ruled out.

Neurodevelopmental disorders might be listed for differential diagnosis from bvFT-NCD, although the DSM-5 is not currently taking these disorders into account. Some of the neurodevelopmental disorders have the possibility to show characteristic symptoms similar to bvFT-NCD, such as deficit of social communication, excessive repetitive behaviors and restricted interests. Because the neurodevelopmental disorders typically manifest early in the developmental period, the aforementioned symptoms sometimes cause impairments of social, academic and occupational functioning. In all of the eight cases of unclassified bvFT-NCD, no historical information such as failure to meet standards of personal independence and social responsibility in their youth was taken.

Finally, neuroimaging features were considered. The images of all the cases of the present study were interpreted by a psychiatric specialist (KF) and radiological specialists. The DSM-5 describes the neuroimaging features characteristic of bvFT-NCD as follows: "both frontal lobes (especially the medial frontal lobes) and the anterior temporal lobes are atrophic," and "functional imaging demonstrates hypo perfusion and/or cortical hypometabolism in the corresponding brain regions, which may be present in the early stages in the absence of structural abnormality."[1] None of the present cases that were diagnosed with unclassified bvFT-NCD showed the characteristic representation. One of the cases that was diagnosed as having probable bvFT-NCD (patient 7; Table 3) showed the characteristic pattern on MRI morphological imaging, but not on SPECT functional imaging. It is not known why this case showed such discrepant morphological and functional images.

As described here, unclassified bvFT-NCD can be considered to fulfil the diagnostic criteria of bvFT-NCD from a cross-sectional and clinical perspective, although the possibilities of AD and mental disorders cannot be ruled out. For differentiation from AD and/or mental disorders, longitudinal observation or post-mortem examination should be carried out. The combined application of more recent diagnostic imaging technologies,[8,10,11] cerebrospinal fluid examination[12] and electroencephalographic examination[13] might assist in the differentiation. To establish clinical diagnostic criteria for unclassified bvFT-NCD, accumulation of cases and evidence will be required, along with longitudinal observation using various diagnostic technologies and post-mortem examination.

Disclosure statement

The authors declare no conflict of interest.

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2 抑うつ

Point

- 「うつ」に関して，うつ病，うつ症状，うつ状態などまぎらわしい術語が多い。その違いを整理した。高齢者では身体疾患合併，薬物の影響により「うつ状態」になりやすい。
- 高齢者におけるうつ症状の評価にはGDS15が汎用されている。
- 認知症とうつは合併しやすく，区別が難しいが，認知症ではアパシーを伴うことが多く，その違いを知って対応することが必要である。うつとアパシーの評価方法としては「やる気スコア」が有用である。アルツハイマー型認知症以外にレビー小体型認知症においても高率にうつ状態を併発する。
- 虚弱高齢者はうつ状態を呈することが多いが，それ以外の精神症状も併発している。状態をよく観察，評価して対応する。不急不要な薬剤中止，現段階で最も重大な身体・精神病態から対応すること，生活・介護などで最も影響のある症状から治療することなどが求められる。

1 「うつ」とは何を指しているか

初めにしばしば混同される「うつ病」と「うつ症状」，「うつ状態」について簡単に説明しておく。英語表記ではすべて「depression」と表現されるが，日本語になると語尾がついてそれぞれ少しずつ違う意味合いを表すのでまぎらわしい。

高齢者のうつ病に関しては別章にて詳述されるが，うつ病は，さまざまな精神機能の中で気分・感情が主に障害される疾患の1つである。診断基準として汎用されるDSM-IV-TRにおいて「大うつ病」と記述されている一群が典型的な病像であり，「うつ病」というと大うつ病をさすことが多い。「うつ病」には抑うつ気分，喜びの喪失，自責感といった精神症状に加えて，全身倦怠感，体重減少あるいは増加といった身体症状がほとんど常に伴っていることが特徴である。つまり，「うつ病」とは単純な精神疾患というよりも心身相関的病態である。

「うつ症状」は抑うつ気分などうつ病にみられる精神症状を指して使用されることが多く，うつ病と必ずしも一致しない。近親者の死に対する悲哀反応としても出現するし，うつ病の診断を満たさない状態でもうつ症状を示す。「うつ状態」はいろいろな使われ方をされているがここでは，「うつ病以外の精神，身体疾患および薬物使用に随伴したうつ症状群」とする[1]。神経疾患である脳血管障害やパーキンソン病においても抑うつ気分，精神運動抑制などを認めるが，神経とは直接関連しないような身体疾患においてもうつ状態を合併しやすい疾患は多い（表1）[2]。また，薬物によりうつ状態が惹起されることもしばしば経験される（表2）[3]。

表1 うつ状態を合併しやすい身体疾患

内分泌疾患	下垂体障害，甲状腺機能障害，副甲状腺機能低下症，副腎皮質機能障害，機能低下症
代謝性疾患	糖尿病，慢性腎不全（透析患者），電解質異常
神経疾患	脳血管障害，パーキンソン病，多発性硬化症，筋萎縮側索硬化症
心疾患	本態性高血圧，虚血性心疾患，うっ血性心不全
消化器疾患	消化性潰瘍，膵臓疾患，潰瘍性大腸炎，過敏性腸症候群，肝疾患
腫瘍性疾患	膵がん，肺がん，乳がん，慢性リンパ性白血病
感染症	インフルエンザ，結核，肺炎
膠原病	全身性エリテマトーデス，慢性関節リウマチ
産婦人科	産後（産後うつ病），月経前困難症，更年期障害
その他	外科手術後，悪性貧血，喘息，アトピー性皮膚炎，慢性疼痛，頭痛

（文献2，p143-50を参考に作成）

表2 うつ状態を引き起こす薬物例

降圧薬	β遮断剤，メチルドパ，レセルピン，クロニジン，カルシウム拮抗薬，ジギタリス製剤
ステロイド製剤	
βインターフェロン製剤	
抗炎症薬	コデイン，オピオイド，インドメタシン，COX-2阻害薬
抗パーキンソン薬	ドーパ製剤，アマンタジン，ブロモクリプチン
ベンゾジアゼピン系抗不安薬	ジアゼパム（セルシン®）など
抗精神病薬	クロルプロマジン（ウインタミン®）など

（文献3，p13-33より改変）

2 高齢者におけるうつ症状の評価方法

うつ症状の有無や重症度を評価することは，うつ病の診断，治療のためだけでなく，合併する身体疾患の治療を行う上でも重要な情報である。臨床場面における高齢者うつ症状の評価としてよく用いられるのがgeriatric depression scale（GDS）である。30の質問項目に「はい/いいえ」で答えてもらう自記式検査法であり，うつ状態の有無を判定するスクリーニングとして有用である。30項目は煩雑なため15項目による短縮版（GDS15）が汎用される（表3）[4]。GDS15において5項目以上該当する場合，うつ状態が疑われ，11点以上では重症であると考えられる。ただし，GDSが高値であることが直ちに「うつ病」であることを意味するわけではない。上記のように診断基準に合う様々な病態が存在するかどうかを評価する必要がある。

そのほかに，うつ症状の重症度の判定にはハミルトンうつ病評価尺度（HAM-D：Hamilton rating scale for depression），モントゴメリー－アスバーグうつ病評価尺度（MADRS：Montgomery-Asberg depression rating scale）が用いられる。

表3 GDS15

1	自分の生活に満足していますか。	はい / **いいえ**
2	これまでやってきたことや興味があった多くを，最近やめてしまいましたか。	**はい** / いいえ
3	自分の人生はむなしいものと感じますか。	**はい** / いいえ
4	退屈と感じることがありますか。	**はい** / いいえ
5	普段は気分のよいほうですか。	はい / **いいえ**
6	自分に何か悪いことが起こるかもしれないという不安がありますか。	**はい** / いいえ
7	あなたはいつも幸せと感じていますか。	はい / **いいえ**
8	自分は無力と感じることがよくありますか。	**はい** / いいえ
9	外に出て新しい物事をするより，家に中にいるほうが好きですか。	**はい** / いいえ
10	ほかの人に比べて記憶力が落ちたと感じますか。	**はい** / いいえ
11	今生きていることは，素晴らしいことと思いますか。	はい / **いいえ**
12	自分の現在の状態はまったく価値のないものと感じますか。	**はい** / いいえ
13	自分は活力が満ちあふれていると感じますか。	はい / **いいえ**
14	今の自分の状況は希望のないものと感じますか。	**はい** / いいえ
15	ほかの人はあなたより恵まれた生活をしていると思いますか。	**はい** / いいえ

うつ症状の答え（太字）を1点として計算。
評価基準：0～4 うつ症状なし；5～10 軽度のうつ病；11～ 重度のうつ病

（文献4より改変）

3 認知症とうつ・アパシー

うつ病は抑うつ気分，精神運動抑制などから認知症に類似の症状を示すことが知られており仮性痴呆（認知症）と呼ばれてきた。うつ気分がひどくなったために本来できるはずの思考，行動がとれなくなった状態である。したがって，治療が奏効すればもとの行動や思考ができるようになる。不眠や「自分はもうダメになった，悪いのは自分だ」などの自分を責めるような言動，悲しいなどの訴えがある場合はうつ状態にあると考えられる。症状および検査における鑑別点を表に示した（表4）[5]。しかしながら実際の臨床場面では，両者の区別が困難であることが多い。

認知症患者を診察する上で注意すべき重要なポイントとして，アパシー（無気力，自発性低下とほぼ同義）がある。認知症に伴う精神症状として抑うつと診断されている例の多くはアパシーである。抑うつに伴う精神運動抑制とアパシーが混同されやすいが，アパシーを抑うつと誤って安易に抗うつ剤を投与するとふらつきや転倒などを引き起こし，日常生活動作能力（ADL）の低下が進んでしまうこともありうる。本人，家族からの問診で自責感，悲哀，睡眠障害，感情不安定性などがあった場合はうつ症状が疑われる。一方，アパシーでは感情の動きに乏しく，無欲・無関心が前景に出る点で異なっている（表5）。アパシーの評価方法としては「意欲の指標」[6]など様々なものがあるが，うつとの鑑別には岡田らの「やる気スコア」が有用である（表6）[7]。上記のGDSとやる気スコアを同時に測定し，比較することで，アルツハイマー型認知症