There is a growing awareness of the importance of behavioral and psychologic symptoms of dementia (BPSD) among patients with dementia. There are several reasons for this. First, BPSD are major sources of a caregiver’s burden and also the most important factor when considering the need for institutionalization of dementia patients. BPSD occur in about 90% of patients with dementia. Studies comparing the BPSD in the major types of dementia using unitary behavioral rating scales are limited. We studied BPSD in patients with four major types of dementias from a memory clinic.

**Background/Purpose:** Behavioral and psychologic symptoms of dementia (BPSD) are major sources of a caregiver’s burden and also the most important factor when considering the need for institutionalization of dementia patients. BPSD occur in about 90% of patients with dementia. Studies comparing the BPSD in the major types of dementia using unitary behavioral rating scales are limited. We studied BPSD in patients with four major types of dementias from a memory clinic.

**Methods:** We recruited patients with dementia from our memory clinic from January 2003 to February 2004. The Behavioral Pathology in Alzheimer’s Disease Rating Scale (BEHAVE-AD) was used to measure BPSD severity. Clinical Dementia Rating and Mini Mental State Examination were used to determine dementia severity.

**Results:** A total of 137 patients with four major types of dementia were recruited from 155 patients with dementia who attended the clinic during the study period. The main dementia types identified were Alzheimer’s dementia (AD) in 54.8%, vascular dementia (VaD) in 20.6%, frontotemporal dementia (FTD) in 8.4%, dementia with Lewy bodies (DLB) in 4.5%, and other dementias in 11.6%. BPSD were found in 92.0% of the patients but only 43.1% received psychotropic treatment. The relative risk of receiving psychotropic treatment for BPSD subscales paralleled the extent of caregivers’ burden as assessed by the BEHAVE-AD global rating. Type-specific BPSD, e.g., hallucination was identified for DLB, activity disturbances for FTD, anxiety and phobias for AD and affective disturbance for VaD.

**Conclusion:** A strategy of targeting type-specific BPSD may be beneficial, such as environmental stimulus control for DLB patients who are prone to have hallucinations, design of a pacing path for patients with FTD who need support for symptoms of wandering and emotional support for patients with VaD who are susceptible to depression. [J Formos Med Assoc 2006;105(7):556–562]

**Key Words:** Alzheimer’s dementia, behavior, dementia of Lewy bodies, frontotemporal dementia, psychologic symptoms, vascular dementia
elderly. Study of the nature, prevalence, clinical typing, staging of severity and use of medications in patients with BPSD is required to improve our ability to treat and to care for patients with different types of dementia. BPSD are seen in about 90% of patients with dementia. Among the various types of dementia, BPSD have been best studied in Alzheimer’s disease (AD). A review of 24 studies of psychosis involving more than 2200 patients found that delusion was reported in 11–73% of all patients. There are several reasons for such wide variation in the prevalence rates of delusion as well as other BPSD, but the most important is the lack of a consistent approach in defining and measuring BPSD. For example, lower rates (22%) of delusions in AD patients may be due to a sampling of BPSD occurring only in the 4 weeks prior to the interview. The most prominent aspect of frontotemporal dementia (FTD) is a profound change in personality and social conduct compared with the premorbid state. Verbal outbursts and inappropriate activities were more common among FTD than among AD patients. The most frequent BPSD in dementia with Lewy bodies (DLB) are visual hallucinations and delusions. Paranoid delusions have been reported to occur in up to 80% and hallucinations in up to 60% of patients with DLB. Vascular dementia (VaD) is associated with a high frequency of psychosis; delusions may occur in up to 50% of patients and VaD is also more likely to cause depression (45%) than AD (17%). However, previous studies have not compared BPSD among the major types of dementia using a unitary behavioral rating scale. This is very important since different behavioral rating scales might have different emphasis or weighting on various dimensions of BPSD. Furthermore, the appearance and distribution of BPSD and even the caregiver’s burden may be affected by many factors including different cultural backgrounds. This study obtained clinical information from patients with various major types of dementia from a single outpatient clinical population, some of whom received psychotropic medications for their BPSD.

**Methods**

**Subjects**

Patients with dementia attending a university hospital memory clinic between January 2003 and February 2004 were recruited. Patients with dementia or suspected dementia in the hospital were referred to the clinic for diagnosis and treatment, and to facilitate caregiver support through consultation and education. Patients who visited the memory clinic received a thorough history taking and comprehensive physical and neurologic examinations. Mental status examinations were also performed, which typically used a Mini Mental State Examination (MMSE) and/or a Cognitive Abilities Screening Instrument.

Neuroimaging, biochemical, and hematologic studies were performed to rule out treatable causes of dementia. In patients with atypical findings, further detailed neuropsychologic studies were performed to assess general and specific cognitive functions as well as psychiatric symptoms.

Patients were grouped according to the following diagnostic criteria: NINCDS-ADRDA criteria for AD; NINDS-AIREN criteria for VaD; McKeith et al’s consensus of diagnosis for DLB; and Neary et al’s criteria for FTD. The use of psychotropic medications was recorded. Those patients who failed to visit the memory clinic on a regular basis or had too few visits for adequate information gathering were excluded.

**Assessment**

After obtaining informed consent, the caregivers were interviewed with the Behavioral Pathology in Alzheimer’s Disease Rating Scale (BEHAVE-AD) to identify and to describe the BPSD of the patient in the past 3 months. The BEHAVE-AD is a 26-item observer rating scale containing seven subscales, each rated 0–3 as follows:

1. paranoid and delusional ideation;
2. hallucinations;
3. activity disturbances;
4. aggressiveness;
5. diurnal rhythm disturbance;
6. verbal outbursts;
7. inappropriate activities.

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6. verbal outbursts;
7. inappropriate activities.
(6) affective disturbance; and
(7) anxiety and phobias.

The 26th item is a global rating which can be used as an index of the caregiver’s burden due to the BPSD, in which 0 indicates “not at all troubling to the caregiver or dangerous to the patient”; and 3 indicates “severely troubling or intolerable to the caregiver or dangerous to the patient”. The Clinical Dementia Rating (CDR) was used to evaluate and to stage patients with dementia. MMSE was also administered to assess patient’s cognitive functions.

Data analysis

Gender distribution, CDR scores, and the global rating of the BEHAVE-AD were examined for differences among patients with four types of dementia using $\chi^2$ test. Differences in mean age and years of education among the four dementia types were analyzed using one-way ANOVA with Scheffé post hoc pairwise comparison. ANCOVA was performed with covariates of CDR scores and the ages among the four dementia types to determine differences among the adjusted BEHAVE-AD total scores and subscales, using Scheffé method for post hoc comparisons. Odds ratios of various subscales were also computed for relative risks of using psychotropic medications and for high caregivers’ burden (patients whose global ratings of BEHAVE-AD were 2 or 3). Spearman correlations were used to explore relations among total scores or subscales of the BEHAVE-AD, and for MMSE scores. All analyses were performed with SPSS version 8.0 (SPSS Inc, Chicago, IL, USA).

Results

A total of 137 patients with four major types of dementia out of 155 patients treated at the clinic during the study period were included (Table 1). The prevalence of different dementia types in these patients were AD 54.8%, VaD 20.6%, DLB 4.5%, and other dementias 11.6%. Patients in the heterogeneous category of “other dementias” were excluded from further analysis. There were no significant differences among patients with different dementia types in the distribution of sex ($\chi^2 = 47.83, p < 0.001$) and years of education ($F = 0.91, p = 0.439$). However, mean ages were significantly different among types ($F = 8.36, p < 0.001$). Scheffé post hoc tests revealed that patients with FTD were much younger than those with AD and VaD (both $p < 0.001$).

Scheffé post hoc tests also revealed a significant difference in MMSE score between patients with AD and FTD ($F = 7.73, p < 0.001$; Table 1). However, the presence of BPSD may have prohibited an adequate mental function test in some patients due to their uncooperative attitude. The high rate of failure to take or complete the MMSE,

| Table 1. Demographic and clinical characteristics of patients with dementia |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Diagnosis | AD (yr) | VaD (yr) | DLB (yr) | FTD (yr) | Total (yr) |
| Age at onset | 72.8 ± 9.1 | 75.1 ± 6.3 | 71.9 ± 5.9 | 61.8 ± 7.5 | 72.2 ± 8.9 |
| Number (F/M) | 85 (54/31) | 32 (18/14) | 7 (2/5) | 13 (6/7) | 137 (80/57) |
| Education (yr) | 6.8 ± 5.3 | 8.5 ± 5.7 | 7.6 ± 5.6 | 8.5 ± 5.4 | 7.4 ± 5.4 |
| CDR (1/2/3) | 43/37/5 | - | 0/4/3 | 5/1/7 | 52/52/33 |
| BEHAVE-AD† | 8.2 ± 2.1 | 13.5 ± 3.2 | 18.2 ± 4.4 | 9.7 ± 3.0 | 10.1 ± 3.9 |
| GBEHAVE-AD‡ | 0.75 ± 0.06 | 1.31 ± 0.07 | 1.86 ± 0.04 | 1.54 ± 0.1 | 1.01 ± 0.4 |
| MMSE§ | 16.0 ± 5.2 | 13.1 ± 6.3 | 8.0 ± 7.7 | 8.2 ± 6.6 | 14.7 ± 6.1 |
| Medication || 28 (32.9%) | 16 (50.0%) | 6 (85.7%) | 9 (69.2%) | 59 (43.1%) |

*ANOVA with Scheffé post hoc, $F = 8.36, p < 0.001$; † ANCOVA adjusted with covariates of CDR scores and ages with Scheffé post hoc, $F = 8.644, p < 0.001$ for BEHAVE-AD, and $F = 6.00, p < 0.001$ for GBEHAVE-AD; ‡ ANCOVA with Scheffé post hoc, $F = 7.73, p < 0.001$; †† $\chi^2 = 13.00, p = 0.005$. AD = Alzheimer’s disease; VaD = vascular dementia; DLB = dementia of Lewy bodies; FTD = frontotemporal dementia; C/D = clinical dementia rating; BEHAVE-AD = adjusted mean ± standard deviation of total scores; GBEHAVE-AD = adjusted mean ± standard deviation of global ratings of BEHAVE-AD; MMSE = mini mental state examination; Medication = percentages of patients receiving psychotropic medications.
especially in patients with DLB (57%) and FTD (33%), prevented further comparative analysis of MMSE data among groups.

The distribution of severity based on CDR scores among different types of dementia was not even ($\chi^2 = 47.83$, $p < 0.001$). Thus, further analyses of the total scores or subscales of BEHAVE-AD were done with adjusted ages and CDR scores.

The most frequent symptom dimension noted among the subscales was activity disturbances. More than two-thirds (67.2%) of patients had activity problems in which purposeless activity took the lead (48.9%) followed by wandering (43.8%) and inappropriate activities (30.7%). The second most frequent symptom dimension was paranoid and delusional ideation (62.0%) in which suspiciousness/paranoia (42.3%) was the most frequently encountered manifestation followed by the delusion that “people are stealing things” (40.1%). The third most frequent symptom dimension was anxiety and phobias (58.4%) with the most common anxiety arising from upcoming events (36.5%). The fourth most frequent symptom dimension was aggressiveness (48.2%) in which verbal outbursts (36.5%) were more frequent than physical threats or violence (16.1%). Affective disturbance (35.8%), either as tearful episodes (29.2%) or as depressed mood (21.2%), was also found in some patients. Hallucinations (30.7%), most frequently in the form of visual hallucinations or their verbal, physical or emotional responses (25.5%), were also not infrequently noted.

Clinical type-specific BPSD patterns were readily identified. DLB was associated with a high incidence of hallucinations (71.4%) and aggressiveness (71.4%), FTD with a high incidence of activity disturbances (92.3%), AD with a high incidence of anxiety and phobias (61.2%) and VaD with a high incidence of paranoid and delusional ideation (71.9%) and affective disturbance (46.9%; Table 2).

ANCOVA with adjusted CDR scores and ages revealed significant between-subject effects of BEHAVE-AD total scores ($F = 8.64$, $p < 0.001$) among different types of dementia (Table 1). Scheffé post hoc test indicated that these differences were greatest in DLB out of the four dementia types and also that those for VaD were higher than for AD and FTD (all $p < 0.001$). Further analysis of the subscale data disclosed significant differences in aggressiveness ($F = 11.10$, $p < 0.001$), activity disturbances ($F = 11.10$, $p < 0.001$), paranoid/delusional ideation ($F = 3.11$, $p = 0.017$), activity disturbances ($F = 7.09$ and $p < 0.001$; $F = 8.36$ and $p < 0.001$; $F = 11.10$ and $p < 0.001$. AD = Alzheimer’s disease; VaD = vascular dementia; DLB = dementia of Lewy bodies; FTD = frontotemporal dementia; % = incidence of subscales of BPSD in each subtype of dementia and in total number of patients; mean ± SD of subscales in different types of dementia and in total number of patients.

### Table 2. Relative incidence and adjusted subscales of BPSD among types of dementia

<table>
<thead>
<tr>
<th></th>
<th>AD</th>
<th>VaD</th>
<th>DLB</th>
<th>FTD</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paranoid/delusional ideation*</td>
<td>58.8%</td>
<td>71.9%</td>
<td>57.1%</td>
<td>61.5%</td>
<td>62.0%</td>
</tr>
<tr>
<td>Hallucinations†</td>
<td>2.5 ± 0.4</td>
<td>3.7 ± 0.7</td>
<td>4.7 ± 0.8</td>
<td>1.3 ± 0.1</td>
<td>2.8 ± 0.9</td>
</tr>
<tr>
<td>Activity disturbances‡</td>
<td>22.4%</td>
<td>46.9%</td>
<td>71.4%</td>
<td>23.1%</td>
<td>30.7%</td>
</tr>
<tr>
<td></td>
<td>0.8 ± 0.2</td>
<td>1.4 ± 0.3</td>
<td>4.4 ± 1.2</td>
<td>0.6 ± 0.1</td>
<td>1.1 ± 0.9</td>
</tr>
<tr>
<td>Aggressiveness§</td>
<td>62.4%</td>
<td>71.9%</td>
<td>57.1%</td>
<td>92.3%</td>
<td>67.2%</td>
</tr>
<tr>
<td></td>
<td>4 ± 0.4</td>
<td>1.6 ± 0.4</td>
<td>3.6 ± 0.9</td>
<td>3.2 ± 1.2</td>
<td>1.8 ± 0.9</td>
</tr>
<tr>
<td>Diurnal rhythm disturbances</td>
<td>34.1%</td>
<td>71.9%</td>
<td>71.4%</td>
<td>69.2%</td>
<td>48.2%</td>
</tr>
<tr>
<td>Affective disturbance</td>
<td>9 ± 0.4</td>
<td>3.1 ± 0.9</td>
<td>3.0 ± 0.9</td>
<td>2.2 ± 1.0</td>
<td>1.6 ± 1.1</td>
</tr>
<tr>
<td>Anxiety/phobias</td>
<td>28.2%</td>
<td>56.3%</td>
<td>42.9%</td>
<td>53.8%</td>
<td>38.0%</td>
</tr>
<tr>
<td></td>
<td>4 ± 0.0</td>
<td>0.9 ± 0.1</td>
<td>0.6 ± 0.0</td>
<td>0.8 ± 0.0</td>
<td>0.6 ± 0.2</td>
</tr>
<tr>
<td></td>
<td>36.5%</td>
<td>46.9%</td>
<td>28.6%</td>
<td>7.7%</td>
<td>35.8%</td>
</tr>
<tr>
<td></td>
<td>8 ± 0.1</td>
<td>1.1 ± 0.2</td>
<td>0.8 ± 0.1</td>
<td>0.3 ± 0.1</td>
<td>0.8 ± 0.2</td>
</tr>
<tr>
<td></td>
<td>61.2%</td>
<td>56.3%</td>
<td>57.1%</td>
<td>53.8%</td>
<td>58.4%</td>
</tr>
</tbody>
</table>

*ANCOVA of subscales adjusted for CDR scores and ages ($F = 3.11$, $p = 0.017$) for paranoid/delusional ideation; †$F = 7.09$ and $p < 0.001$; ‡$F = 8.36$ and $p < 0.001$; §$F = 11.10$ and $p < 0.001$. AD = Alzheimer’s disease; VaD = vascular dementia; DLB = dementia of Lewy bodies; FTD = frontotemporal dementia; % = incidence of subscales of BPSD in each subtype of dementia and in total number of patients; mean ± SD of subscales in different types of dementia and in total number of patients.
disturbances \((F = 8.36, \ p < 0.001)\), hallucinations \((F = 7.09, \ p < 0.001)\) and the paranoid/delusional ideation subscale \((F = 3.11, \ p = 0.017)\). Post hoc tests showed that the hallucinations subscale score was highest in the DLB group, followed by VaD. The activity disturbance subscale score was also highest in DLB followed by FTD, although the relative incidence of such behavior was highest in FTD. In contrast, FTD followed all other dementia types in scores both for affective disturbance and for anxiety/phobias subscales (both \(p < 0.001\)).

The mean total scores for the BEHAVE-AD were significantly different between patients receiving \((14.8 \pm 8.8)\) and not receiving \((6.5 \pm 6.4)\) psychotropic medications \((F = 41.44, \ p < 0.001)\). The relative risk of receiving psychotropic medications in symptom subscales represented by odds ratios were aggressiveness \((2.81)\), paranoid/delusional ideation \((2.24)\), hallucinations \((2.12)\), diurnal rhythm disturbance \((1.79)\), activity disturbances \((1.56)\), affective disturbance \((1.28)\), and anxiety/phobias \((1.07)\). Relative risk of high caregiver’s burden paralleled the risk of receiving psychotropic medications, with odds ratios in the order of aggressiveness \((17.57)\), paranoid/delusional ideation \((5.77)\), hallucinations \((4.26)\), diurnal rhythm disturbance \((4.00)\), activity disturbances \((2.64)\), affective disturbance \((1.85)\), and anxiety/phobias \((1.40)\).

MMSE scores showed significant negative correlations with subscales of the BEHAVE-AD including activity disturbances \((n = 105, \ \text{Spearman rho } r = -0.358, \ p < 0.001)\) and aggressiveness \((r = -2.59, \ p < 0.001)\) but not with the total score \((r = -0.155, \ p = 0.115)\). CDR was positively correlated with total BEHAVE-AD \((n = 137, \ \text{Spearman rho } r = 0.379, \ p < 0.001)\) as well as with subscales of aggressiveness \((r = 0.410, \ p < 0.001)\), activity disturbances \((r = 0.303, \ p < 0.001)\), and hallucinations \((r = 0.254, \ p = 0.003)\).

**Discussion**

FTD was characterized by much younger mean age of onset than AD and other types of dementia in this study, which is compatible with previous observations.\(^{21}\) The FTD patient with the earliest age of onset in this series was a 49-year-old male.

DLB accounts for only 4.5% \((7/155)\) of dementia cases in this study. Although this series of patients was from a memory clinic, its distribution might not represent the prevalence of dementia in the general population. A previous study in the UK found DLB to be the second most common pathologic cause of dementia, comprising 20% of autopsy cases.\(^ {22}\) An epidemiologic study in suburban London found that DLB accounted for 10.9% of all types of dementias.\(^ {23}\) These findings suggest the possibility of ethnic differences in the prevalence rate of DLB, but neuropathologic confirmation is required.

Although the manifestations of BPSD may be influenced by a variety of factors, they are primarily the results of underlying neurobiologic changes in the brain. Previous clinicopathologic correlation studies of BPSD had limited and inconclusive findings. Paranoid/delusional ideation has been related to a temporal dysfunction.\(^ {26}\) Neurobiologic studies of agitation and aggression uncovered several relationships. Functional imaging using \(^{18}\)F-fluorodeoxyglucose PET showed that agitation and disinhibition correlated with decreased frontal and temporal cortical metabolic rate.\(^ {27}\) The extent of white matter injury and the overall severity of the neuropsychiatric symptoms as well as severity and depression were also well correlated.\(^ {28}\) Left frontal lobe lesion has been proposed to be pathogenic for depression, especially the lesions of the left anterior frontal lobe.\(^ {29}\)

Previous studies found patients with AD often manifested motor behavior disturbance, aggressiveness, mood disturbances, and psychotic symptoms.\(^ {30–33}\) In this study, we found patients with AD had relatively increased incidence of anxiety and phobias. Transcultural or multiethnic studies suggested that these manifestations had ethnic, cultural, and social background dependencies.\(^ {30–32}\)
More apathy and depression were reported in western populations in contrast to more activity disturbances and aggressiveness in oriental patients. However, such comparisons may be confounded by differences in clinical populations including various severities or differences in professional backgrounds of the interviewers.

One of the main findings of this study was the delineation of subtype-specific patterns of BPSD. For example, hallucination had the highest incidence and severity in patients with DLB. Recurrent visual hallucination is typically well-formed and is one of the essential core features of DLB in the consensus criteria of McKeith et al. Activity disturbances were noted in almost all patients (92.3%) with FTD in this series, similar to a previous report. Nevertheless, the early appearance of impaired language function in FTD could prevent the expression of some BPSD such as affective disturbance, hallucinations or anxiety and phobias. On the other hand, affective disturbance was most frequently encountered in VaD (46.9%) in that nearly one out of two patients exhibited such problems.

Patients with DLB had the highest mean total scores of BEHAVE-AD, caregiver’s burden, and incidence of receiving psychotropic medications. On the contrary, VaD had the highest scores in several subscales such as aggressiveness, diurnal rhythm disturbances or paranoid/delusional ideation in addition to the aforementioned affective disturbance. VaD was not as aggressively treated as DLB and FTD. The discrepancy should be further elucidated. The presence of more caregiver-disturbing or stress-producing BPSD such as aggressiveness, paranoid/delusional ideation and hallucinations, was associated with more frequent prescription of psychotropic medications. This suggests that the main purpose of using psychotropic medications is to relieve the caregiver’s burden. In contrast, BPSD with lower odds ratios of high caregiver’s burden such as activity disturbances, affective disturbance and anxiety-phobias, could be more easily handled by nonmedication methods.

The relationship between BPSD and cognitive deficits, either in terms of cognition or functional status in patients with dementia, was not conclusive. However, psychotic symptoms, activity disturbances, and aggressiveness seemed to have an adverse effect on cognitive functions or vice versa.

Although this study included a total of 137 of 155 patients with dementia who visited a memory clinic during the study period, the numbers of some dementia types such as DLB and FTD remained small due to their comparatively low incidence. This is a major limitation of this study and should be kept in mind when considering possible generalization of the findings.

Conclusion

The study found the subtype-specific BPSD in different types of dementia including hallucination in DLB, activity disturbances in FTD, and affective disturbance in VaD. The relative risk of psychotropic medications was highly correlated with the severity of caregivers’ burden, indicating that caregivers’ burden prompted physicians to prescribe psychotropic medications for patients with dementia. Since nonpharmacologic interventions for BPSD are helpful for caregivers of patients with dementia, the need for different strategies of caregiving for patients with different types of dementia should be emphasized, including environmental stimulus control for DLB patients who are prone to having hallucinations, design of a pacing path for patients with FTD who need support for symptoms of wandering, and emotional support for patients with VaD who are susceptible to depression.

References


