

# Severity and prevalence of behavioral and psychological symptoms among patients of different dementia stages in Taiwan

SI-SHENG HUANG<sup>1</sup>, WEN-FU WANG<sup>2</sup>, YI-CHENG LIAO<sup>1</sup>

<sup>1</sup>Department of Psychiatry, Changhua Christian Hospital, Changhua, Taiwan.

<sup>2</sup>Department of Neurology, Changhua Christian Hospital, Changhua, Taiwan.

Received: 12/09/16 – Accepted: 05/24/17

DOI: 10.1590/0101-60830000000127

## Abstract

**Background:** To better understand the trends of behavioral and psychological symptoms of dementia (BPSD) over the disease progression is important to provide psychoeducation for dementia caregivers. **Objective:** This study examined the severity and occurrence of BPSD across the various degrees of the disease. **Methods:** This study was a cross-sectional design. Patients (N = 276) who had dementia from July 2001 to October 2008 were surveyed and assessed for dementia stage, using the clinical dementia rating scale (CDR). BPSD was evaluated using the Neuropsychiatric Inventory (NPI). We examined the differences between the severities and occurrence of the individual's BPSD among various CDR stages with the Kruskal-Wallis test and Chi-square test. **Results:** Delusion (p = 0.01), agitation/aggression (p = 0.033), apathy/indifference (p = 0.009), aberrant motor behavior (p < 0.001), nighttime behavior disturbances (p < 0.001), and eating abnormalities (p = 0.001) were significantly different among stages of dementia. The severity of BPSD became exacerbated over the course of the disease, and was highest in moderate (CDR = 2) or severe (CDR = 3) dementia. The occurrence of BPSD was highest when the CDR equaled 2 (97.5%). **Discussion:** The association of global (or certain) BPSD, across different stages of dementia, is a non-linear relationship. These findings suggest the importance of taking into account clinical dementia stage for managing BPSD.

Huang SS *et al.* / *Arch Clin Psychiatry.* 2017;44(4):89-93

**Keywords:** Behavioral and psychological symptoms of dementia, dementia, prevalence, severity, Taiwan.

## Introduction

The behavioral and psychological symptoms of dementia (BPSD) are common and serious problems that affect the quality of life for both patients with these symptoms, as well as their caregivers. BPSD present a major challenge in the medical management of patients, and are the major cause of institutionalization. After the onset of disease, more than 80% of demented patients exhibit at least one behavioral and psychological symptom, and no significant differences are observed in the prevalence between Alzheimer's disease (AD) and non-AD dementias<sup>1</sup>. Among the factors associated with caregiver distress, the patient's BPSD are most closely associated with caregiver burden<sup>2</sup>. Therefore, to better understand the trends of symptoms over the disease progression is important to provide psychoeducation for dementia caregivers in clinical practice.

The Neuropsychiatric Inventory (NPI)<sup>3</sup> was developed to assess psychopathology in dementia patients, and has been widely used in studies for dementia. It evaluates 12 BPSD, including delusions, hallucinations, agitation/aggression, dysphoria/depression, anxiety, euphoria/elation, apathy/indifference, disinhibition, irritability/lability, aberrant motor behavior, nighttime behavioral disturbances, and appetite and eating abnormalities. Many studies have investigated the prevalence of various BPSD as the dementia disorder progresses, using NPI. Apathy has seemed to become increasingly common as the dementia worsens<sup>4</sup>. Aggressive behavior and aberrant motor behavior have also been found to correlate with an increase in cognitive impairment<sup>5</sup>. Conversely, some studies have found a reduction of such behavior in the most severe stages<sup>6</sup>. There is no general agreement concerning hallucinations about whether there is a relationship between the level of cognitive impairment and BPSD<sup>4</sup> or not<sup>5,7</sup>. The studies on depressive symptoms in dementia have shown heterogeneous results. Some studies have found a decreased prevalence in severe dementia, while other studies have not found an association<sup>4,5,8</sup>. Some studies have found almost no correlation at all between BPSD and the level of cognitive impairment<sup>7,9</sup>.

In Taiwan, approximately 80% of the care for dementia patients is provided within the community by family members, and over half (56.6%) of main caregivers spend more than 8 hours per day caregiving<sup>10</sup>. Liu *et al.* reported a high prevalence of BPSD in Taiwanese patients with AD, and suggested that these symptoms were associated with cognitive deficits<sup>11</sup>. In a Taiwanese study, several clinical dementia stages<sup>10</sup> and more behavioral disturbances<sup>12</sup> were reported to be the associative factors of caregiver burden. Huang *et al.*<sup>13</sup> found that caregiver burden was significantly negatively correlated with CDR stages, and it was presumed that a patient with dementia was more difficult to take care of during the early and middle stage of disease, in which they had more BPSD. However, the investigation of the severity and prevalence of BPSD along the progression of the disease was scarce in Taiwan.

Our aim was to examine the severity and occurrence of BPSD across the different stages of the disease in Taiwan.

## Methods

### Subjects

This study used a cross-sectional design. In total, 276 patients with dementia who visited the memory clinic of a medical center in central Taiwan, from July 2001 to October 2008, were recruited. For the reliability of the data, we defined the criteria for dementia caregivers were (1) a relative (older than 18 years) who caring for the individual at least 4 hours per day; (2) being the primary caregiver and having intimate information of the patient over time. Subjects who fit the diagnostic criteria for dementia of the 4<sup>th</sup> edition of the Diagnostic and Statistical Manual of Mental Disorders<sup>14</sup> were recruited and assessed for their stage of dementia, using the clinical dementia rating scale (CDR)<sup>15</sup>. If the CDR revealed a score of 0.5, we further confirmed the clinical history, educational level, as well as the Mini-Mental State Examination (MMSE)<sup>16</sup> scores to validate the diagnosis of dementia. The diagnosis was made by two senior physicians (W.F.

Wang and Y.C. Liao). The CDR, NPI, and cognitive functions test of all patients were assessed by well-trained and qualified psychologists. The hospital has a standardized objective, evidence-based procedure to authorize psychologists to provide clinical services consistent with their qualifications. The trained researchers verbally administered the instruments to the subjects and recorded the answers according to standardized procedure of each measurement. Caregivers' backgrounds were collected at a single visit to the memory clinic. This study was conducted according to the Declaration of Helsinki, the regulation of clinical research in the country and was approved by the institutional review board of the medical center. Written informed consent was obtained from all subjects.

## Measures

The patients' BPSD were assessed using the NPI<sup>3</sup>, which was developed to measure psychopathology in people with dementia. The NPI includes 12 symptoms. The caregiver rated the frequency and severity of each symptom, using scores from 0 to 4 for frequency, and scores from 0 to 3 for severity. The NPI score for each BPSD was the product of the frequency and severity subscores (frequency multiplied by the severity). The total NPI score ranged from 0 to 144. The Cronbach's alpha coefficient of the Chinese version of the NPI was 0.76. The test-retest reliabilities of frequency and severity were significantly correlated, with the overall correlations being 0.85 for frequency ( $p < 0.001$ ), and 0.82 for severity ( $p < 0.001$ )<sup>17</sup>. The patients' clinical dementia stages were assessed with the CDR, and cognitive function with the Chinese version of the cognitive abilities screening instrument (CASI, C-2.0)<sup>18</sup>. The MMSE score in this study was derived from part of the CASI score.

## Data analysis

We used descriptive statistics to characterize the study population. Statistical analysis was performed using SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA). The assumption of a normal distribution of the variables was verified using the Kolmogorov-Smirnov test, which showed a violation. Therefore, we used the non-parametric test to evaluate the data. In addition to descriptive statistics, the differences of severity of BPSD (the product score of the frequency multiplied by the severity subscores of individual BPSD domain) among dementia stages (different CDR stages) were tested using the Kruskal Wallis test. Furthermore, we examined the differences on the occurrence rate of BPSD among different stages of dementia with a Chi-square test. For all analyses, the probability level used to indicate statistical significance was set at  $p < 0.05$ .

## Results

A total of 276 patients were recruited. The mean age was  $79.70 \pm 7.20$  years old. One hundred and eighty nine of 276 (68.5%) patients were female. The diagnosis of the patients comprised 167 cases of AD (60.5%), 70 cases of vascular dementia (25.4%), 25 cases of dementia due to multiple etiologies (9.0%), and 14 cases of dementia due to other general medical conditions (5.1%). Table 1 shows the characteristics of patients with dementia grouped by CDR in this study.

Table 2 lists the mean scores of the individual NPI domain, the product of the frequency and severity subscores (frequency multiplied by the severity), according to CDR stage in patients with dementia. The NPI total score resulted in a statistically significant difference among the different stages of dementia ( $p < 0.001$ ), and scores were highest when the CDR equaled 3. By the individual NPI domain, delusion ( $p = 0.01$ ), agitation/aggression ( $p = 0.033$ ), apathy/indifference ( $p = 0.009$ ), aberrant motor behavior ( $p < 0.001$ ), nighttime behavior disturbances ( $p < 0.001$ ), and appetite and eating abnormalities ( $p = 0.001$ ) had statistically significant differences among the different stages of dementia. These BPSD became worse

and worse over the disease course, and the product subscores were significantly higher in the moderate (CDR = 2) or severe (CDR = 3) stages, compared to the very mild (CDR = 0.5) stage of dementia.

Table 3 shows the percentage of the presence of each BPSD in different stages of dementia patients. The occurrence of BPSD (97.5%) was highest when the CDR equaled 2. There was a statistically significant difference in the occurrence rate among the stages of dementia. Considering each BPSD, the occurrence rate of delusion, apathy/indifference, aberrant motor behavior, nighttime behavior disturbances, and eating abnormalities was significantly different among the stages of dementia. The highest occurrence of delusion was 53.2% when the CDR equaled 2; apathy/indifference was 55.6%, when the CDR equaled 3; aberrant motor behavior was 48.1%, when the CDR equaled 3; nighttime behavior disturbances was 70.4%, when the CDR equaled 3; and appetite and eating abnormalities was 41.8%, when the CDR equaled 2. In group 1 (CDR = 0.5), the highest occurring symptom was depression (40.0%); in group 2 (CDR = 1), the highest occurring symptom was depression (47.2%); in group 3 (CDR = 2), the highest occurring symptoms were delusion and nighttime behavior disturbances (53.2%); in group 4 (CDR = 3), the highest occurring symptom was nighttime behavior disturbances (70.4%).

## Discussion

Although the number of subjects was small in the later stage group of dementia (CDR = 4), we included the sample in the analysis in an attempt to illustrate the trend of severity and prevalence of BPSD, from very early to later stages of dementia. The results of this study revealed that severity of BPSD was associated with different stages in dementia. The highest severity of global BPSD was seen in severe dementia (CDR = 3), and decreased in severity when CDR equaled 4. Considering individual BPSD, delusion, agitation/aggression, apathy/indifference, aberrant motor behavior, nighttime behavior disturbances, and appetite and eating abnormalities were significantly different among stages of dementia. The highest severity of the above symptoms was seen at the moderate (CDR = 2) or severe (CDR = 3) stage of dementia. The occurrence of BPSD was highest at the moderate stage of dementia (CDR = 2). By each BPSD, the occurrence rate of delusion, apathy/indifference, aberrant motor behavior, nighttime behavior disturbances, and eating abnormalities were significantly different among the stages of dementia. The occurrence rate of these BPSD was highest at the moderate (CDR = 2) or severe stage (CDR = 3) of dementia.

The severity of some BPSD has demonstrated that they are associated with the dementia stages. Hashimoto *et al.*<sup>19</sup> reported that seven of the 12 BPSD domains assessed by NPI revealed increased severity as dementia progressed. However, these results were only present for the patients in the very early stages (CDR = 0.5) to middle stages (CDR = 2) of dementia. The severity of seven BPSD domains included: delusion, hallucination, agitation, apathy, irritability, aberrant motor behavior, and sleep disturbance; and, all were highest at the moderate stage of dementia. These results did not find BPSD in later stages of dementia (CDR = 3 or 4). In the present study, the severity of delusion, agitation, apathy, aberrant motor behavior, nighttime behavior disturbances, and eating abnormalities were found to be statistically significantly different across the dementia stages. Indeed, as shown in Table 2, their NPI scores increased as the CDR progressed to the second stage. However, the severity of agitation and apathy continuously increased as the disease progressed to stage 4 of dementia. The severity of delusion was highest at stage 2 of dementia, and gradually lessened afterward; the severity of aberrant motor behavior and nighttime behavior disturbances was highest at stage 3, and attenuated afterward. The longitudinal changes in symptom severity did not always result in a positive correlation with dementia severity, according to present study.

Some studies suggested that there was no difference in prevalence of BPSD among the stages of dementia<sup>7,9</sup>. Our study found that the prevalence of delusion, apathy/indifference, aberrant motor behavior,

**Table 1.** Demographic and clinical characteristics of patients with dementia according to disease severity

	CDR					All	P
	0.5	1	2	3	4		
N (%)	55 (19.9)	106 (38.4)	79 (28.6)	27 (9.8)	9 (3.3)	276 (100)	
Age (years)	75.84 ± 6.27	79.57 ± 7.33	82.06 ± 6.56	80.96 ± 7.40	80.44 ± 7.11	79.70 ± 7.20	< 0.001 <sup>a</sup>
Gender (female, %)	36 (65.5)	70 (66.0)	56 (70.9)	21 (77.8)	6 (66.7)	189 (68.5)	0.766 <sup>b</sup>
Education (years)	4.71 ± 4.84	3.63 ± 4.17	3.08 ± 4.37	2.52 ± 3.79	1.33 ± 2.65	3.50 ± 4.34	0.066 <sup>a</sup>
Diagnosis (AD, %)	43 (78.2)	62 (58.5)	42 (53.2)	15 (55.6)	5 (55.6)	167 (60.5)	0.049 <sup>b</sup>
MMSE	20.17 ± 4.17	15.28 ± 4.57	10.07 ± 4.90	3.91 ± 3.32	1.40 ± 2.61	13.56 ± 6.69	< 0.001 <sup>a</sup>
CASI	66.53 ± 17.13	48.63 ± 17.93	29.07 ± 16.54	15.20 ± 17.32	3.60 ± 10.47	41.96 ± 24.33	< 0.001 <sup>a</sup>

<sup>a</sup> Analysis of variance (ANOVA); <sup>b</sup> Chi-square test; Values are n (%) or the mean ± SD.

CDR: Clinical Dementia Rating Scale; AD: Alzheimer’s Disease; MMSE: Mini-Mental State Examination; CASI: Cognitive Abilities Screening Instrument.

**Table 2.** Mean scores of individual NPI domains of the product subscores (frequency multiplied by the severity) according to dementia severity (CDR score), mean (SD)

	CDR					All	P <sup>a</sup>	Post hoc <sup>b</sup>
	0.5	1	2	3	4			
Delusion	1.15 (2.67)	1.84 (3.31)	3.32 (4.12)	3.00 (3.75)	1.33 (4.00)	2.22 (3.59)	0.01	0.5 < 2; 0.5 < 3; 1 < 2; 2 > 4
Hallucination	0.67 (1.70)	1.02 (2.57)	1.90 (3.53)	2.41 (3.66)	2.00 (4.24)	1.37 (2.96)	0.051	0.5 < 2; 0.5 < 3; 1 < 3
Agitation/aggression	0.78 (2.32)	1.33 (2.70)	2.38 (3.55)	2.41 (3.51)	3.33 (5.29)	1.69 (3.14)	0.033	0.5 < 2; 0.5 < 3
Dysphoria/depression	1.44 (2.80)	2.07 (3.41)	2.56 (3.82)	1.41 (2.85)	0.44 (0.73)	1.96 (3.34)	0.245	
Anxiety	1.05 (2.26)	1.63 (3.22)	2.42 (3.85)	2.59 (3.74)	1.44 (3.97)	1.83 (3.36)	0.455	
Euphoria/elation	0.04 (0.19)	0.03 (0.17)	0.47 (1.82)	0.44 (2.31)	0 (0)	0.20 (1.23)	0.175	1 < 2
Apathy/indifference	1.18 (2.66)	1.70 (3.20)	2.53 (3.52)	3.52 (4.02)	4.00 (6.00)	2.09 (3.46)	0.009	0.5 < 2; 0.5 < 3; 1 < 3
Disinhibition	0.67 (2.08)	0.66 (2.08)	1.10 (2.68)	1.19 (2.40)	0.11 (0.33)	0.82 (2.27)	0.464	
Irritability/Lability	1.22 (2.81)	1.80 (3.28)	2.32 (3.84)	2.89 (3.82)	2.67 (5.29)	1.97 (3.50)	0.361	
Aberrant motor behavior	0.33 (1.26)	1.47 (3.19)	3.08 (4.28)	3.04 (3.93)	1.33 (3.04)	1.85 (3.50)	< 0.001	0.5 < 1; 0.5 < 2; 0.5 < 3; 1 < 2; 1 < 3
Nighttime behavior disturbances	1.36 (2.51)	1.98 (3.30)	3.63 (4.33)	5.56 (5.01)	3.33 (5.29)	2.72 (3.94)	< 0.001	0.5 < 2; 0.5 < 3; 1 < 2; 1 < 3
Appetite and eating abnormalities	0.65 (1.80)	1.80 (3.43)	2.78 (4.00)	2.96 (4.09)	0 (0)	1.91 (3.47)	0.001	0.5 < 2; 0.5 < 3; 1 < 2; 2 > 3; 2 > 4; 3 > 4
NPI total score	10.55 (13.70)	17.33 (20.42)	28.48 (21.75)	31.41 (17.82)	20.00 (16.87)	20.63 (20.55)	< 0.001	0.5 < 1; 0.5 < 2; 0.5 < 3; 1 < 2; 1 < 3

<sup>a</sup> P values refer to the Kruskal-Wallis test; <sup>b</sup> Comparison of NPI symptoms between different dementia stages. The column lists the CDR stages that have significant differences in NPI scores. NPI: Neuropsychiatric Inventory; CDR: Clinical Dementia Rating Scale.

**Table 3.** Occurrence of each behavioral and psychological symptoms of dementia according to the disease stage

Variables	CDR					All (n = 276)	P <sup>a</sup>	Post hoc <sup>b</sup>
	0.5 (n = 55)	1 (n = 106)	2 (n = 79)	3 (n = 27)	4 (n = 9)			
Delusion	15 (27.3)	37 (34.9)	42 (53.2)	14 (51.9)	1 (11.1)	109 (39.5)	0.004	0.5 < 2
Hallucination	11 (20.0)	26 (24.5)	28 (35.4)	12 (44.4)	2 (22.2)	79 (28.6)	0.086	
Agitation/Aggression	10 (18.2)	31 (29.2)	31 (39.2)	11 (40.7)	3 (33.3)	86 (31.2)	0.089	
Dysphoria/Depression	22 (40.0)	50 (47.2)	39 (49.4)	8 (29.6)	3 (33.3)	122 (44.2)	0.357	
Anxiety	16 (29.1)	37 (34.9)	29 (36.7)	11 (40.7)	2 (22.2)	95 (34.4)	0.744	
Euphoria/Elation	2 (3.6)	3 (2.8)	8 (10.1)	1 (3.7)	0 (0)	14 (5.2)	0.190	
Apathy/Indifference	11 (20.0)	33 (31.1)	34 (43.0)	15 (55.6)	3 (33.3)	96 (34.8)	0.009	0.5 < 3
Disinhibition	9 (16.4)	18 (17.0)	17 (21.5)	8 (29.6)	1 (11.1)	53 (19.2)	0.530	
Irritability/Lability	15 (27.3)	39 (36.8)	31 (39.2)	12 (44.4)	2 (22.2)	99 (35.9)	0.435	
Aberrant motor behavior	6 (10.9)	29 (27.4)	34 (43.0)	13 (48.1)	2 (22.2)	84 (30.4)	< 0.001	0.5 < 2; 0.5 < 3
Nighttime behavior disturbances	18 (32.7)	39 (36.8)	42 (53.2)	19 (70.4)	3 (33.3)	121 (43.8)	0.003	0.5 < 3; 1 < 3
Appetite and eating abnormalities	9 (16.4)	29 (27.4)	33 (41.8)	11 (40.7)	0 (0)	82 (29.7)	0.003	0.5 < 2
Any BPSD	41 (74.5)	90 (84.9)	77 (97.5)	26 (96.3)	7 (77.8)	234 (87.6)	0.001	0.5 < 2; 1 < 2

<sup>a</sup> P values refer to Chi-square test; <sup>b</sup> Post hoc analysis of comparison for each NPI symptoms between different dementia stage. The column lists the CDR stages that have significant differences; values are n (%). CDR: Clinical Dementia Rating Scale.

nighttime behavior disturbances, and eating abnormalities was significantly different among the stages of dementia. Using 10 items of the NPI, Piccininni *et al.*<sup>20</sup> reported that only aberrant motor activity produced a statistically significant increase in NPI scores from a mild to severe degree of the disease; they also confirmed a clear trend of increased frequencies of disease severity in delusions and hallucinations. Symptoms of nighttime behavior disturbances and eating abnormalities were not mentioned in their study. These differing results, which may have been caused by both nighttime behavior disturbances and eating abnormalities, were not included in the 10-item NPI. Furthermore, in this study, hallucination symptoms occurred most frequently in those with severe dementia (CDR = 3); the p value equaled 0.086. Although the NPI is the most widely used measurement for BPSD, it still retains some shortcomings. For instance, the NPI is based on caregiver's observations that are obtained during a clinical interview, and does not allow for the clinician's judgment to be factored into the assessment. Non-professional caregivers may overlook some symptoms and signs of hallucinations or other BPSD. This may produce a bias in the study, and likely result in different findings between the current study and the others.

Our findings on the prevalence of BPSD showed a significant difference between the various stages of dementia. In general, the highest rate of occurrence was noted in stage 2 or 3 of dementia, and the lowest rate of occurrence was seen in more severe stages of dementia. We suggested that the association of global (or certain) BPSD (concerning severity and prevalence), across different stages of dementia, is a non-linear relationship. This finding is consistent with the study of Lövheim *et al.*<sup>21</sup>, in which the correlation between some BPSD and the level of cognitive impairment was found to be significant and non-linear, and the highest prevalence rates occurred at the middle stages of dementia. Lövheim *et al.*<sup>21</sup> confirmed that the factor of passiveness had an almost linear correlation to the level of cognitive impairment. The aggressive behavior, wandering behavior, restless behavior, verbally disruptive/attention-seeking behavior, regressive/inappropriate behavior, hallucinatory symptoms, and depressive symptoms had the highest prevalence of middle-stage dementia and non-linear correlation. The use of a different scale (the Multi-Dimensional Dementia Assessment Scale, MDDAS<sup>22</sup>) in Lövheim *et al.*'s study may offer new information, although it has limited comparability. In comparing the MDDAS with the NPI, passiveness may partly correspond to apathy; aggressive behavior corresponds to delusion, wandering and restless behaviors correspond to aberrant motor behavior; verbally disruptive/attention-seeking behavior may partially correspond to nighttime behavior disturbances; and, some descriptions of restless behaviors may correspond to eating abnormalities in the NPI. In a similarity seen in both studies, some symptoms, like delusion, aberrant motor behavior, nighttime behavior disturbances, and eating abnormalities, showed the highest severity and occurrence when CDR was 2 or 3, and lessened at later stages of dementia. Divergently, and unlike Lövheim *et al.*'s results, we found that the prevalence of apathy was highest when CDR equaled 3, and it decreased at stage 4 of CDR. The occurrence rate of apathy did not show an increasing trend as dementia progressed. Because the subjects of the stage 4 group were few in number, statistical power may have been limited. The occurrence rates of depression and hallucinations were relatively stable and were not significantly different among the stages of dementia in our study. However, a slightly decreased occurrence rate was still noted for both symptoms at later stages of dementia. The relatively smaller sample size in stage 3 and 4 may have restricted the ability to generalize our results. Because of the patients' reduced speech, communication ability, and motor function, caregivers may have had difficulty interpreting symptoms (such as delusion) in later stages of dementia. Furthermore, motor functions were affected, and this may have contributed to the reduced prevalence of certain behavioral disturbances, such as aberrant motor behavior, nighttime behavior disturbances, and eating abnormalities at that stage.

Our study identified a high frequency and severity of depression in the very early stage (CDR = 0.5) of dementia patients, similar to previous findings<sup>23</sup>. It is possible that symptoms are associated with pathological changes in regions of the brain associated with its pathogenesis. There is evidence of increased neuropathological changes within the hippocampus in AD patients who suffer from depression<sup>24</sup>. An alternative explanation is that depression in dementia patients is an emotional reaction to the decline of cognitive function in the early stage of dementia. People with memory problems have a high risk of psychological distress and depressive symptoms as a result of the situation<sup>25</sup>. Compared with the relatively stable prevalence and severity of depression and anxiety, there was a progressive prevalence of apathy, delusion, aberrant motor behavior, nighttime behavior disturbances, and eating abnormalities symptoms, from the very early to middle stages of dementia. For example, structural atrophy and functional deficits in medial and frontal regions associated with motivation and reward mechanisms of the brain may account for the increased prevalence of apathy as the disease progresses<sup>26</sup>. This is supported by previous results, in which apathy increased with increased severity of memory deficits<sup>27</sup>, or global cognitive impairment<sup>9</sup>.

This study had several limitations in terms of data generalization. First, because only the patients from community were recruited in this study, the difference between people accommodated from community and long-term institutions on the occurrence of BPSD<sup>28</sup> could not be compared in this study. Second, we included subjects with AD and non-AD. We were unable to differentiate the effects between different dementia subtypes, which may have produced differential effects on BPSD; although, there was no significant difference in severity and prevalence between AD and non-AD dementias in some studies<sup>1,29</sup>. Third, nighttime behavior disturbances and eating abnormalities were not included in the 10-item NPI. The evaluation instrument that assessed BPSD restricted the generalization of results among studies. Fourth, the symptoms present in the patients tended to fluctuate; the probability that a person's symptom occurred at certain time-point during the cognitive decline was probably higher. The prevalence rates were likely further affected by the fact that these BPSD may have been higher and more severe in a hospital-based study sample than a community population. Fifth, the relatively small sample size of the stage 4 dementia group may have limited the analysis and restricted the representativeness.

In summary, the severity and occurrence of BPSD are different in various stages of dementia. The highest severity of global BPSD occurred at the severe stage dementia (CDR = 3), and decreased at the later stage of dementia (CDR = 4). The severity and prevalence of delusion, apathy, aberrant motor behavior, nighttime behavior disturbances, and eating abnormalities were different among stages of dementia. The clinicians should take into account clinical dementia stage in managing BPSD and offering psychoeducation toward caregivers in clinical practice.

## Acknowledgements

We acknowledge the contribution of the entire memory clinic team. We thank the patients and clinical staff of our hospital. There is no conflict of interest in this study.

## References

1. Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, DeKosky S. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. *JAMA*. 2002;288:1475-83.
2. Lim YM, Son GR, Song JA, Beattie E. Factors affecting burden of family caregivers of community-dwelling ambulatory elders with dementia in Korea. *Arch Psychiatr Nurs*. 2008;22:226-34.
3. Cummings JL. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. *Neurology*. 1997;48:10-6.

4. Selbaek G, Kirkeveld O, Engedal K. The prevalence of psychiatric symptoms and behavioural disturbances and the use of psychotropic drugs in Norwegian nursing homes. *Int J Geriatr Psychiatry*. 2007;22:843-9.
5. Shimabukuro J, Awata S, Matsuoka H. Behavioral and psychological symptoms of dementia characteristic of mild Alzheimer patients. *Psychiatry Clin Neurosci*. 2005;59:274-9.
6. Holtzer R, Tang MX, Devanand DP, Albert SM, Wegesin DJ, Marder K, et al. Psychopathological features in Alzheimer's disease: course and relationship with cognitive status. *J Am Geriatr Soc*. 2003;51:953-60.
7. Lam LC, Leung T, Lui VW, Leung VP, Chiu HF. Association between cognitive function, behavioral syndromes and two-year clinical outcome in Chinese subjects with late-onset Alzheimer's disease. *Int Psychogeriatr*. 2006;18:517-26.
8. Craig D, Mirakhor A, Hart DJ, McIlroy SP, Passmore AP. A cross-sectional study of neuropsychiatric symptoms in 435 patients with Alzheimer's disease. *Am J Geriatr Psychiatry*. 2005;13:460-8.
9. Spalletta G, Baldinetti F, Buccione I, Fadda L, Perri R, Scalmana S, et al. Cognition and behaviour are independent and heterogeneous dimensions in Alzheimer's disease. *J Neurol*. 2004;251:688-95.
10. Fuh JL, Wang SJ, Liu HC, Wang HC. The caregiving burden scale among Chinese caregivers of Alzheimer's patients. *Dement Geriatr Cogn Disord*. 1999;10:186-91.
11. Liu CY, Wang PN, Lin KN, Liu HC. Behavioral and psychological symptoms in Taiwanese patients with Alzheimer's disease. *Int Psychogeriatr*. 2007;19:605-13.
12. Lee SH, Wu SC. Determinants of burden and depression among family caregivers. *Nursing Research*. 1998;6:57-67 (In Chinese).
13. Huang SS, Liao YC, Wang WF, Lai TJ. The Factors Associated with Burden of Caring Patients with Dementia: A Memory Clinic Based Study. *Taiwanese Journal of Psychiatry (Taipei)*. 2012;26:96-104.
14. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders. 4th ed. (DSM-IV). Washington DC: American Psychiatric Association, 1994.
15. Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. *Br J Psychiatry*. 1982;140:566-72.
16. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189-98.
17. Fuh JL, Liu CK, Mega MS, Wang SJ, Cummings JL. Behavioral disorders and caregivers' reaction in Taiwanese patients with Alzheimer's disease. *Int Psychogeriatr*. 2001;13:121-8.
18. Lin KN, Wang PN, Liu CY, Chen WT, Lee YC, Liu HC. Cutoff scores of the cognitive abilities screening instrument, Chinese version in screening of dementia. *Dement Geriatr Cogn Disord*. 2002;14:176-82.
19. Hashimoto M, Yatabe Y, Ishikawa T, Fukuhara R, Kaneda K, Honda K, et al. Relationship between Dementia Severity and Behavioral and Psychological Symptoms of Dementia in Dementia with Lewy Bodies and Alzheimer's Disease Patients. *Dement Geriatr Cogn Disord Extra*. 2015;5:244-52.
20. Piccininni M, Di Carlo A, Baldereschi M, Zaccara G, Inzitari D. Behavioral and psychological symptoms in Alzheimer's disease: frequency and relationship with duration and severity of the disease. *Geriatr Cogn Disord*. 2005;9:276-81.
21. Lövheim H, Sandman PO, Karlsson S, Gustafson Y. Behavioral and psychological symptoms of dementia in relation to level of cognitive impairment. *Int Psychogeriatr*. 2008;20:777-89.
22. Sandman PO, Adolfsson R, Norberg A, Nystrom L, Winblad B. Long-term care of the elderly. A descriptive study of 3600 institutionalized patients in the county of Vasterbotten, Sweden. *Compr Gerontol A*. 1988;2:120-32.
23. Di Iulio F, Palmer K, Blundo C, Casini AR, Gianni W, Caltagirone C, et al. Occurrence of neuropsychiatric symptoms and psychiatric disorders in mild Alzheimer's disease and mild cognitive impairment subtypes. *Int Psychogeriatr*. 2010;22:629-40.
24. Rapp MA, Schnaider-Beeri M, Grossman HT, Sano M, Perl DP, Purohit DP, et al. Increased hippocampal plaques and tangles in patients with Alzheimer disease with a lifetime history of major depression. *Arch Gen Psychiatry*. 2006;63:161-7.
25. Simard M, Hudon C, Van Reekum R. Psychological distress and risk for dementia. *Curr Psychiatry Rep*. 2009;11:41-7.
26. Nowrangi MA, Lyketsos CG, Rosenberg PB. Principles and management of neuropsychiatric symptoms in Alzheimer's dementia. *Alzheimers Res Ther*. 2015;7:1-10.
27. Robert PH, Berr C, Volteau M, Bertogliati-Fileau C, Benoit M, Guerin O, et al. Importance of lack of interest in patients with mild cognitive impairment. *Am J Geriatr Psychiatry*. 2008;16:770-6.
28. Cheng TW, Chen TF, Yip PK, Hua MS, Yang CC, Chiu MJ. Comparison of behavioral and psychological symptoms of Alzheimer's disease among institution residents and memory clinic outpatients. *Int Psychogeriatr*. 2009;21:1134-41.
29. Thompson C, Brodaty H, Trollor J, Sachdev P. Behavioral and psychological symptoms associated with dementia subtype and severity. *Int Psychogeriatr*. 2010;22:300-5.