



## Regional update

## Gender differences in behavioral and psychological symptoms of patients with Alzheimer's disease



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## ABSTRACT

Behavioral and psychological symptoms of dementia (BPSD) in patients with Alzheimer's disease have a strong correlation with cognitive impairment and impairment in activities of daily living. Although recent studies have reported that gender may play a role in BPSD, this finding was not evident in several other studies. The present study classified patients with Alzheimer's disease into groups with mild and moderate dementia to examine the gender differences in BPSD in each group. We divided a total of 125 patients diagnosed with Alzheimer's disease according to the criteria of the fifth edition of the *Diagnostic and Statistic Manual of Mental Disorders* (DSM-5) into groups with mild and moderate dementia. Then we examined whether the groups showed differences in memory functions, activities of daily living, and BPSD depending on gender. Our results showed a significant gender difference in Depression/Dysphoria symptoms (BPSD) among the patients in the mild dementia group ( $t = -2.344, p < 0.05$ ), but there was no significant gender difference among the patients in the moderate dementia group. For both the mild and moderate dementia groups, there were no significant gender differences in memory functions and activities of daily living. The results of this study indicated that female patients with mild dementia are more vulnerable to depression than male patients. Future studies should more continuously examine a variety of factors that affect BPSD depending on the severity of Alzheimer's disease.

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## 1. Introduction

With the increasing aging of the population worldwide, the prevalence of neurodegenerative diseases among the elderly is also on the rise. Korea has continued to evolve toward an aging society since 2000 with the rapid increase of the elderly population, and the proportion of older individuals with neurodegenerative diseases has increased accordingly. In particular, dementia, one of the most common neurodegenerative diseases among the elderly, has emerged as a critical burden in societies. In 2010, the number of patients with dementia in Korea was estimated to be about 470,000, and this number is predicted to rise to 750,000 by 2020. It is important for the government to fund and support research for the prevention, treatment, and management of dementia.

Alzheimer's disease is the most common type of dementia. It is particularly common among adults aged 80 or older, with more

than 30% of the older adult population reported to have the disease (Ritchie and Lovestone, 2002). Alzheimer's disease is characterized by cognitive impairments in several domains, including memory, visuospatial, language, and executive functions (Badddeley et al., 2002; Commings and Benson, 1992; Zec, 1993). Furthermore, they face increasing difficulty with not only the most basic functions of life but also with other complex daily activities. Ultimately, patients with Alzheimer's disease progress to the point at which they cannot carry on an independent life. In addition, they also experience behavioral and psychological symptoms of dementia (BPSD) comprising a variety of non-cognitive symptoms, which undermine the quality of life of patients' caregivers and families and aggravate their psychological pain (Stern et al., 1997; González-Salvador et al., 2000; Steele et al., 1990).

BPSD is a term that refers to symptoms of disturbed perception, thought content, mood, behavior frequently occurring in patients with dementia, including hallucination, delusion, depression, euphoria, agitation, aggression, abnormal vocalization, wandering, over-activity, sexual disinhibition, sleep disturbances and apathy (Finkel and Burns, 2000). Although BPSD undoubtedly very commonly accompanies Alzheimer's disease, the prevalence of BPSD may depend on the progress of the disease, its demographic distribution, and the assessment scales utilized. For example,

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according to Tatsuru et al. (2012), while men are more prone to symptoms such as aggressiveness and diurnal rhythm disturbances than women, they are less likely to experience symptoms such as paranoia, delusional ideations, hallucinations, affective disturbances, anxiety, and phobias. Lovheim et al. (2009) also reported that men show more aggressive and regressive behaviors than women while women are more prone to depressive symptoms.

Meanwhile, other studies have also reported that the prevalence of BPSD may differ depending on the progress of the disease (Harwood et al., 2000; Lopez et al., 2003; Srikanth et al., 2005; Thompson et al., 2010). Lopez et al. (2003) stated that the mood symptoms of BPSD generally occur in the early stages of the disease, while psychotic symptoms and those related to anxiety and aggression occur during the middle and late stages of the disease. Hashimoto et al. (2014) reported that the progress of Alzheimer's disease is significantly correlated with BPSD scores.

As shown above, there have been a variety of studies conducted on BPSD in relation to gender and disease progress. In particular, the exploration of various factors that affect the prevalence of BPSD is significant in that it can boost the efficacy of therapeutic intervention and reduce costs by predicting presenting symptoms in accordance with demographic information, such as patients' age or gender, and disease progress. According to Lee et al. (2014), which was analyzed the Korean dementia patients as a whole, there were no significant gender differences in BPSD symptoms. It was not consistent with the result from the study of Lovheim et al. (2009), which reported more aggressive in male patients and more depressive symptoms in female. So this study was designed to examine gender differences in BPSD symptoms between subgroups based on severity (i.e., mild and moderate stage dementia) as the secondary analysis. We also looked on the relationship of general cognitive decline with memory function, activity of daily living (ADL), BPSD according to the severity of Alzheimer's disease.

## 2. Methods

### 2.1. Study subjects

The present study included 125 patients who visited the dementia clinic in the department of psychiatry at the Ilsan Paik Hospital for impaired memory. The patients were diagnosed with Alzheimer's disease based on the criteria of the fifth edition of the *Diagnostic and Statistic Manual of Mental Disorders* (DSM-5). The sample data for this retrospective, cross-sectional analysis was conducted from August 2013 to April 2015. This secondary analysis was done for the total 125 patients including 98 of previously reported study (Lee et al., 2014). 27 subjects who visited Ilsan Paik Hospital complaining memory impairment and diagnosed as Alzheimer's disease from September 2014 to April 2015 were also included in this analysis.

Patients meeting any of the following criteria were excluded from the study: 1) Patients diagnosed with dementia of a different type besides Alzheimer's disease; 2) patients with a history of head trauma or brain damage; 3) patients with other neurodegenerative diseases, such as Parkinson's disease or Huntington's disease; 4) patients with a history of drug abuse; 5) patients with medical problems that can affect cognition, such as thyroid dysfunction; and 6) patients with accompanying psychiatric disorders.

The subjects were divided into groups with mild dementia or moderate dementia based on the severity of impaired cognition measured by the Mini-Mental State Examination-Korean version (MMSE-K). Patients who scored 19 points or higher on the MMSE-K were classified as having mild dementia, and those who scored between 10 and 18 points were classified as having moderate dementia. This study was approved by the Institutional Review

Board (IRB) of the Inje University Ilsanpaik Hospital, and conformed to the Declaration of Helsinki.

### 2.2. Assessment scale

#### a Mini-Mental State Examination-Korean version (MMSE-K)

This tool was developed to measure the overall cognitive functions of older adults aged 60 or older, including time orientation, space orientation, memory registration, memory recall, attention and calculation, language function, and comprehension and judgment. The test comprises thirty questions worth one point each, and we used a modified scoring system depending on the subjects' education level.

#### • Construction Recall and Word List Delayed Recall/Recognition in CERAD-K

The Consortium to Establish a Registry for Alzheimer's Disease-Korean version (CERAD-K) is a tool developed to assess the diagnosis of dementia, and it is divided into neuropsychological assessment and clinical assessment. The neuropsychological assessment comprises a Verbal Fluency Test, MMSE-KC, Construction Praxis, Construction Recall, Word List Memory Test (Delayed Recall, Delayed Recognition), and Trail Making Test A, B. In the present study, we used the Construction Recall and Delayed Recall and Delayed Recognition Test of the Word List Memory Test to measure visual and linguistic memory. The Construction Recall Test assesses visual memory by instructing the subjects to copy four geometrical figures (circle, rhombus, overlapped squares, and regular hexahedron) and to recall and redraw them after an elapsed time. The Word Delayed Recall Test assesses delayed linguistic recall by presenting subjects with a list comprising ten words at two-second intervals and instructing them to recall the words after a delay. The Word Delayed Recognition Test assesses the degree to which subjects accurately recognize the target stimuli when the previous ten words are presented along with ten interference stimuli.

#### • The Korean Version of the Blessed Dementia Scale-Activities of Daily Living (BDS-ADL-K)

This is a scale developed to assess the activities of daily living of dementia patients by selecting the items related to daily living in the Dementia Rating Scale. It is included in the clinical assessment section of the CERAD-K, and it comprises eight items related to daily living and three items related to eating, bowel movements, and clothing habits. The total score is 17 points, and higher scores indicate undermined activities of daily living.

#### • Korean Neuropsychiatric Inventory (K-NPI)

This is a tool developed to assess the BPSD of dementia patients. It assesses the severity and frequency of patients' problem behaviors in a total of twelve fields (Delusions, Hallucinations, Agitation/Aggression, Anxiety, Euphoria/Elation, Apathy/Indifference, Disinhibition, Irritability/Lability, Aberrant Motor Behavior, Sleep/Nighttime Behavior, and Appetite/Eating Changes) as well as the stress of caregivers. The score may range from 0 to 144 points, and higher scores indicate more severe problem behaviors.

### 2.3. Statistics

The data for this study were analyzed using SPSS 18.0. First, we analyzed the demographic variables (age, education level, MMSE-K) of the patients in the mild and moderate dementia groups and

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