

The Korean Version of the Neuropsychiatric Inventory: A Scoring Tool for Neuropsychiatric Disturbance in Dementia Patients

The Neuropsychiatric Inventory (NPI) is a standardized, validated, and reliable tool to assess neuropsychiatric derangements in dementia patients. The aim of this study is to develop the Korean version of the NPI (K-NPI) and to test its reliability and usefulness in dementia patients. The subjects were 49 normal controls and 92 patients with Alzheimer's disease (43), vascular dementia (32), frontotemporal lobar degeneration (11), and other causes (6). Their caregivers familiar with the subjects' everyday behavior were interviewed with the K-NPI. In a subgroup (29/141) of the caregivers, the K-NPI was repeated for test-retest reliability, average of 23.1 days after the initial test. Prevalence rates of 12 behavioral domains in dementia patients were comparable to those of the original NPI; apathy was the most common and hallucination was the least common behavior. Total K-NPI scores correlated positively with dementia severity assessed with the Korean Mini-Mental State Examination. Test-retest reliabilities of frequencies and severities of all subscales were significantly high. Depression, anxiety, apathy, irritability, night-time behavior, and eating change were identified at very low rates in normal controls and were significantly less than those in dementia patients ($p < 0.001$). The K-NPI, whose reliability and competency are comparable to those of the original version, may be a reliable and useful tool for measuring neuropsychiatric disturbances in Korean dementia patients.

Key Words: Dementia; Alzheimer Disease; Dementia, Vascular; Frontotemporal Lobar Degeneration; Behavior

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INTRODUCTION

Neuropsychiatric disturbances are common manifestations of dementing disorders. Neuropsychiatric disorders may be the presenting manifestations of dementing disorders, appearing before cognitive alterations and heralding the onset of the brain disease (1, 2). Some behavioral changes have prognostic significance. Delusions, for example, are associated with more rapid decline of intellectual function in Alzheimer disease (AD) (3-5). Neuropsychiatric disturbances add burdens to caregivers and are a major cause of institutionalization of dementia patients (6-8). The neuropsychiatric aspects of dementia syndromes are often treatable with psychotropic medications (9). Neuropsychiatric manifestations change as the dementias progress, requiring reevaluation and implementation of new interventions in the course of the illness. Thus, neuropsychiatric features of dementias have important diagnostic, prognostic, and management implications.

Several tools are available to assess the behavior in dementia patients. The principal instruments currently in use include BEHAVE-AD (9), Neurobehavior Rating Scale (10), Columbia University Scale for Psychopathology in Alzheimer's disease (11), and Cornell Scale for Depression in Dementia (12). Cummings et al. (13) recently developed Neuropsychiatric Inventory (NPI) to assess the behavioral abnormalities in dementia patients. The NPI has been proven valid and reliable and has been used in clinical studies in North America (14). The NPI is a convenient instrument that evaluates both the frequency and the severity of abnormal behaviors including delusions, hallucinations, agitation, dysphoria, anxiety, euphoria, apathy, disinhibition, irritability and aberrant motor behavior, and neurovegetative changes including night time behavior and eating change.

The NPI has several advantageous features when compared with existing instruments. First, the screening question approach allows the clinician to focus on areas of psychopathology while not expanding time on unreward-

ing inquiries. Secondly, the NPI explores a wide range of psychopathology. In addition to behavioral domains that are assessed with other instruments (9-11), the NPI also assesses apathy, euphoria and irritability, which are the common behavioral changes accompanying dementia. Thirdly, the NPI is scored on the basis of information provided by the caregiver and thus avoids the problems inherent in asking questions to demented patients or observing behavior for only a restricted period of time.

To the best of our knowledge, standardized instruments for evaluating neuropsychiatric symptoms in dementia patients are not available in Korea yet. Thus, this study was to develop the Korean version of the NPI (K-NPI) and to test its usefulness and reliability in Korean dementia patients.

MATERIALS AND METHODS

Subjects

Patients consisted of 92 individuals with dementia evaluated at Samsung Medical Center or Inha University Hospital. Diagnostic work-ups included complete medical history, physical and neurological examinations, comprehensive neuropsychological testing, blood tests, and brain imaging with CT or MRI. The blood tests for screening medical causes of cognitive decline included hematology, chemistry, syphilis serology, vitamin B₁₂, folate, and thyroid function test. Forty three of these patients had Alzheimer Disease (AD), 32 had vascular dementia (VaD), 11 had frontotemporal lobar degeneration (FTLD), and six patients had other types of dementing disorders (3 dementia with parkinsonism, 1 progressive supranuclear palsy, 1 normal pressure hydrocephalus, and 1 head trauma). Patients with AD met the criteria of the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association for probable AD (15). Patients with VaD met the criteria for probable ischemic VaD proposed by the State of California Alzheimer's Disease Diagnostic and Treatment Centers (16). Patients with FTLD met the consensus on clinical diagnostic criteria (17). Three patients with dementia and parkinsonism were considered to have a degenerative disease but their diagnoses could not be specified.

To learn if behavioral problems change as dementia progresses, patients were divided into three groups based on their Korean Mini-Mental State Examination (K-MMSE) (18) scores (scores 0 to 10=severe; 11 to 20=moderate; 21 to 30=mild).

Control subjects were 49 spouses of either the patients admitted to neurology department (15/49) or the pa-

tients in neurology outpatient clinic (34/49) at Samsung Medical Center or Inha University Hospital. They did not have previous history of neurological or psychiatric disorders. Their scores on the K-MMSE were within the normal range of standards adjusted to age and level of education (19).

Caregivers providing behavioral information for the patients and the controls were a family member living with the subject or a relative seeing the subject 5 or more times a week. If the spouse of the subject had cognitive decline, the child of the subject was interviewed. The K-MMSE was administered within 1 week before or after the K-NPI was performed; in most subjects they were administered on the same day.

Translation of the NPI

The NPI was translated into Korean by a neurologist. The translated version went through two review processes, first by the behavioral neurology group at Samsung Medical Center consisting of 2 neurologists, 1 neuropsychologist and 2 speech-language pathologists and then passed to the 14 active members of Korean Dementia Research Group. Further changes were made after it was applied to 10 dementia patients. Then, the translated version was translated back to English by a bilingual (a Korean-American) non-medical person who was blinded to the original NPI. We made further changes by making comparison between the original NPI and the back-translated English version before deciding on the final K-NPI.

Administration of the K-NPI

Caregivers of the patients and the controls were interviewed with the K-NPI by the same procedures as previously described in the validation report of the original NPI (13). In each behavioral domain, the caregiver was presented with the screening question. The caregiver of the patient was asked if the patient's behavior had changed since the onset of the dementia and if the altered behavior has been present during the past month. Control interviewees were asked about the behavior that had occurred within the preceding 4 weeks and differed from the control subject's usual behavior.

If the answer to the screening question was negative, the interviewer proceeded to the next screening question. If the caregiver responded that abnormal behaviors were present in the past month, the behavioral domain was then explored with seven or eight subquestions that provided more detailed information about the neuropsychiatric disturbance. After the subquestions were answered, the caregiver was asked to rate the frequency of the

symptoms of that domain on a scale of 1 to 4 (1=less than once per week, 2=about once per week, 3=several times per week, 4=daily or continuously) as well as their severity (1=mild, 2=moderate, 3=severe).

The composite score (maximum=12) for each domain was calculated by multiplying the frequency by the severity. A total K-NPI score was calculated by adding 12 composite scores.

Test-retest reliability

Of the 141 caregivers participated in our study, 29 (22/29 from patient group and 7/29 from the control group) had repeat K-NPI for the test-retest reliability. Time interval between the initial test and the retest was 23.1 ± 7.4 days (range, 11-39 days). During the period between the test and the retest, dosage was not changed if the patients were given drugs that could modify their behavioral symptoms.

Statistical analysis

Comparison of age between the patient and the control group was conducted using the Student's *t*-test. For categorical or dichotomous variables (gender, informants), the chi-square test was used to test between-group differences. Cronbach's coefficient alpha was determined to assess the internal consistency reliability. For a better comparison of the change in behaviors as disease progresses and cognition declines, patients were divided into three groups based on their K-MMSE scores (scores 0 to 10=severe; 11 to 20=moderate; 21 to 30=mild). Total K-NPI score and mean composite (product of frequency \times severity; maximum=12) scores of each behavior were compared among the three K-MMSE groups via analysis of variance, and significance was established using the Tukey test. Comparison of severity score or frequency score of each behavior between the patient and the control group was conducted using the Student's *t*-test. Spearman correlation coefficients were generated for test-retest reliability calculations. For all tests, statistical significance was accepted at $p < 0.05$.

RESULTS

Demographics of patients, controls, and caregivers

The patients consisted of 44 men and 48 women and their mean age was 67.5 ± 9.7 yr (range, 38-85 yr). Their mean K-MMSE score was 17.5 ± 6.8 (range, 0-29). Behavioral information on the patients was obtained from 46 spouses, 43 children, and 3 others (2 paid caregivers

and 1 sister).

The 49 controls comprised 17 men and 32 women and their mean age was 66.9 ± 8.4 yr (range, 51-82 yr). The mean K-MMSE score of the control subjects was 26.3 ± 2.8 (range, 19-30). Caregivers providing behavioral information of the control subjects were 26 spouses and 23 children. There was no significant difference between the ages of the patients and the control subjects. Sex distribution and the type of the relationship of the informants to the subjects did not significantly differ between the patient and the control subjects.

Total K-NPI score and scores of the K-NPI subscales in patient group

Table 1 shows total K-NPI score and mean scores of the K-NPI subscales (frequency and severity) of the 92 patients. Also, it shows prevalence rate of each behavior. These data show that a wide range of psychopathology was present in the dementia patients. Apathy was the behavior most commonly recorded (77.2%); irritability/lability (59.8%), anxiety (56.5%), depression/dysphoria (45.7%), aberrant motor behavior (43.5%), and agitation/aggression (43.5%) were also frequently reported by caregivers. Hallucination (12%) was the least observed behavior and with the most restricted range of expression. Euphoria (16.3%) was the second least frequently observed behavior.

Internal consistency reliability

Cronbach's coefficient alpha was calculated to determine the internal consistency (internal consistency reliability) among the items from the 92 K-NPIs. Cronbach's alpha for overall reliability was 0.85. Cronbach's alpha was 0.81 for the frequency and 0.82 for the severity of individual items, establishing a high level of internal consistency reliability.

Relationship of behavioral changes to dementia severity

Total K-NPI scores and mean composite (product of frequency \times severity; maximum=12) scores of each behavior were compared among the three K-MMSE groups. Table 2 shows the number of patients, sex distribution and age of three K-MMSE groups. Their mean values of the K-MMSE and the total K-NPI scores are also shown. A one-way ANOVA showed that mean values for the total K-NPI scores were significantly different among three K-MMSE groups ($p = 0.003$). A Tukey test showed that the mean values of total K-NPI scores were significantly different between mild and severe dementia groups ($p < 0.01$) and between moderate and severe de-

Table 1. Prevalence of psychopathology and subscale scores (frequency and severity) of K-NPI in patients with dementia and controls

Subscale (Behavior)	Dementia patient (n=92)			Control (n=49)		
	Prevalence*	Frequency Mean (SD; range)	Severity Mean (SD; range)	Prevalence*	Frequency Mean (SD; range)	Severity Mean (SD; range)
1. Delusion	33.7%	0.87 (1.41; 0-4)	0.63 (1.02; 0-3)	0	0	0
2. Hallucination	12%	0.36 (1.01; 0-4)	0.24 (0.72; 0-3)	0	0	0
3. Agitation/Aggression	43.5%	1.27 (1.61; 0-4)	0.87 (1.13; 0-3)	0	0	0
4. Depression/Dysphoria	45.7%	0.95 (1.27; 0-4)	0.72 (0.91; 0-3)	22.4%	0.29 (0.58; 0-2) [†]	0.22 (0.42; 0-1) [†]
5. Anxiety	56.5%	1.39 (1.47; 0-4)	1.03 (1.08; 0-3)	16.3%	0.33 (0.83; 0-3) [†]	0.18 (0.44; 0-2) [†]
6. Euphoria/Elation	16.3%	0.40 (1.00; 0-4)	0.28 (0.70; 0-3)	0	0	0
7. Apathy/Indifference	77.2%	2.52 (1.67; 0-4)	1.75 (1.18; 0-3)	6.1%	0.06 (0.24; 0-1) [†]	0.06 (0.24; 0-1) [†]
8. Disinhibition	38.0%	0.93 (1.35; 0-4)	0.75 (1.04; 0-3)	0	0	0
9. Irritability/Lability	59.8%	1.48 (1.43; 0-4)	1.12 (1.08; 0-3)	4.1%	0.08 (0.40; 0-2) [†]	0.06 (0.32; 0-2) [†]
10. Aberrant motor	43.5%	1.49 (1.79; 0-4)	1.08 (1.31; 0-3)	0	0	0
11. Night-time behavior	26.1%	0.80 (1.46; 0-4)	0.59 (1.07; 0-3)	6.1%	0.16 (0.72; 0-4) [†]	0.06 (0.24; 0-1) [†]
12. Appetite/Eating	35.9%	1.34 (1.82; 0-4)	0.67 (1.00; 0-3)	4.1%	0.08 (0.45; 0-3) [†]	0.04 (0.20; 0-1) [†]
Total K-NPI score [‡]		29.86 (26.87; 0-109)			1.08 (1.62; 0-7) [†]	

*Percentage of subjects with each scorable psychopathology in each group

[†]Significantly different from patient group ($p < 0.001$)

[‡]Total K-NPI score calculated by adding 12 composite (product of frequency \times severity; maximum=12) scores

Table 2. Mean K-MMSE and K-NPI total scores for patients with mild (K-MMSE scores 21-30), moderate (K-MMSE scores 11-20), and severe (K-MMSE scores 0-10) dementia

	Mild	Moderate	Severe
No. of patients	31	40	13
Sex (M:F)	20:11	18:22	2:11
Age (yr)	64.4 (10.3; 38-79)*	70.7 (7.9; 52-85)	67.1 (10.9; 41-83)
K-MMSE score	24.3 (2.2; 21-29)	15.9 (2.8; 11-20)	6 (4.0; 0-10)
Total K-NPI score	20.6 (21.8; 0-85)	29.1 (29.3; 0-109)	50.6 [†] (23.7; 14-104)

*Mean (SD; range)

[†]Significantly different from mild ($p < 0.01$) and moderate group ($p < 0.05$)

mentia groups ($p < 0.05$).

To understand better the relationship of each behavioral change to cognitive decline, we analyzed the composite score (frequency \times severity) of each behavior within the three K-MMSE groups. A one-way ANOVA showed that the differences of mean composite scores among 3 K-MMSE groups were significant in three of 12 behavior domains (agitation, apathy, and aberrant motor behavior) (Fig. 1). Composite scores for apathy ($p < 0.01$) and aberrant motor behavior ($p < 0.01$) of the severe dementia group were significantly greater than those of mild and moderate dementia groups. The composite score for agitation behavior of the severe K-MMSE group was significantly greater than that of mild K-MMSE group ($p < 0.05$).

Scores of the K-NPI subscales in controls

Total K-NPI score and severity and frequency of each

subscale of controls are presented in Table 1. Also, the prevalence of each behavior in control subjects is shown in Table 1. Control caregivers rated zero in 6 of the 12 subscales of the K-NPI, which were delusion, hallucinations, agitation, euphoria, disinhibition, or aberrant motor behavior. On the other hand, subscales with scores above zero were depression, anxiety, apathy, irritability, night-time behavior, and appetite/eating change. Total K-NPI score and all severity and frequency scores of these subscales were very low and significantly less than those of the patients ($p < 0.001$). None of the subscale scores correlated significantly with the K-MMSE scores.

Test-retest reliability

Table 3 presents the test-retest reliability measures for the 12 K-NPI subscales. Test-retest reliabilities of the frequency and severity rating of all behavioral domains were significantly high; overall correlations were 0.63 for

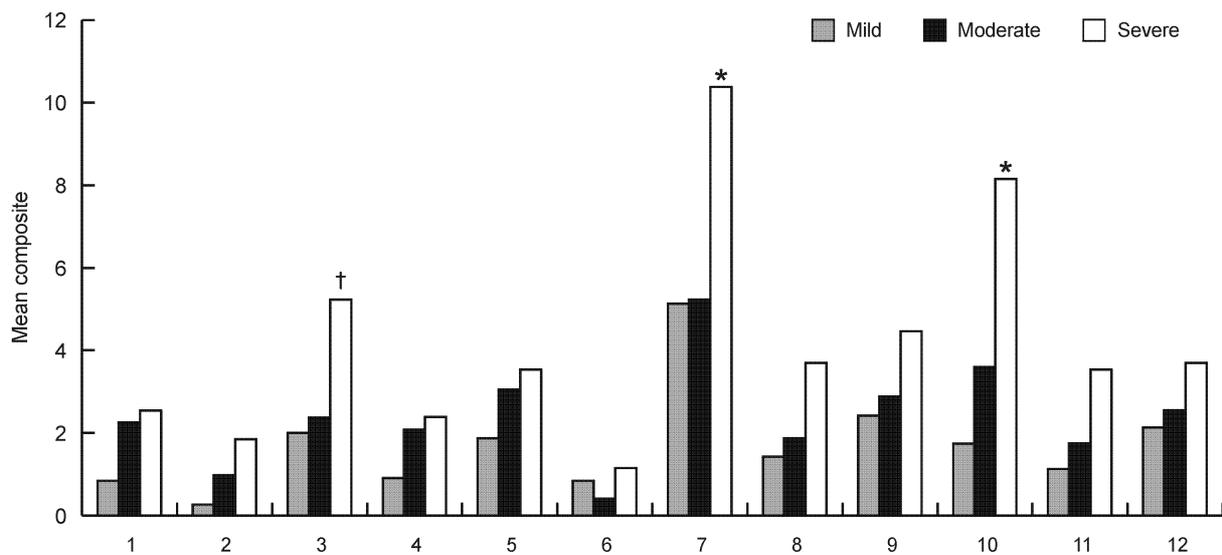


Fig. 1. Mean composite scores of the 12 K-NPI behaviors of the three K-MMSE groups. Numbers in abscissa represent behavioral domains as shown in Table 1 and 2. Mild, moderate and severe dementia according to K-MMSE scores (see text). *Items which were significantly different between the severe and the other cognitive groups ($p < 0.01$); †Item which was significantly different between the mild and the severe K-MMSE group ($p < 0.05$).

Table 3. Test-retest reliability (n=29)

Subscale (Behavior domain)	Test-retest	
	Frequency correlation* (p)	Severity correlation* (p)
1. Delusion	0.75 (<0.001)	0.78 (<0.001)
2. Hallucination	0.46 (0.012)	0.48 (0.008)
3. Agitation/Aggression	0.56 (0.002)	0.55 (0.002)
4. Depression/Dysphoria	0.59 (0.001)	0.55 (0.002)
5. Anxiety	0.59 (0.001)	0.66 (<0.001)
6. Euphoria/Elation	0.60 (0.001)	0.60 (0.001)
7. Apathy/Indifference	0.76 (<0.001)	0.75 (<0.001)
8. Disinhibition	0.53 (0.003)	0.50 (0.006)
9. Irritability/Lability	0.63 (<0.001)	0.69 (<0.001)
10. Aberrant motor	0.51 (0.005)	0.51 (0.005)
11. Night-time behavior	0.60 (0.001)	0.59 (0.001)
12. Appetite/Eating	0.43 (0.020)	0.47 (0.010)

*Spearman correlation coefficient

frequency ($p < 0.001$) and 0.64 for severity ($p < 0.001$).

DISCUSSION

The present study demonstrated that non-cognitive behavioral changes are ubiquitous in dementia patients. The range of psychopathology observed in dementia patients was wide. This contrasts with the findings in normal control subjects in whom changes in behavior were rare and of low intensity. Apathy was the most frequent behavioral change in dementia patients. This finding was consistent with the original validation study of patients with AD (13) and Japanese study of patients

with dementia of variable etiologies (20). Most scales for neuropsychiatric measurement in dementia patients such as BEHAVE-AD do not include alterations in personality, such as apathy and irritability. However, this study suggests that these are among the most common behavioral changes that occur in dementia patients. In the original validation study, euphoria was the behavior least frequently observed (13). In our study, however, hallucination was the least observed behavior and euphoria was the second least frequently observed behavior. The reason for this difference may be explained by the fact that whereas only patients with AD was recruited in the original study, patients with FTD were also included in our study, thereby contributing to higher prevalence of

euphoria than in the original study (21).

Total K-NPI scores increased significantly as dementia progressed. Of the 12 cognitive domains, agitation/aggression, apathy and aberrant motor behavior showed positive correlation with dementia severity. These findings are similar to those of previous study (22), although patient groups of our study were different from those of previous studies.

The test-retest reliability was high in most behavior symptoms in our dementia patients. However, there was relatively weak correlation in the frequency rating of hallucination ($p=0.012$), and frequency ($p=0.02$) and severity ($p=0.01$) of eating change. The lower test-retest reliability of these domains may reflect more variability in the behavior or relative difficulties for caregivers to reliably assess and report these behaviors. In the original validation study, the test-retest reliability of euphoria could not be assessed, for no patient was judged to be euphoric. Our study showed that even the test-retest reliabilities of severity and frequency of euphoria were high (all, $r=0.60$; $p=0.001$). Also, neuro-vegetative symptoms such as appetite/eating change and night-time behavior were not assessed in original validation study, for these two items were added after the validation study. Our study found that the test-retest reliabilities of severity and frequency of two neuro-vegetative symptoms were also significantly high.

In our study, the test-retest reliabilities of all measures except for the severity of anxiety, severity and frequency of apathy and irritability were slightly lower than those of the original study. The reason may be that whereas in the original study all informants were living with the patient, in our study informants were living with the patient or frequently taking care of the patient (above five times per week). Another account might be that all patients in the original study had AD, but in our study, many patients with VaD or dementia of other causes were included. Behaviors of patients with VaD or dementia of other causes may be much variable than those of AD. Thirdly, the time interval (23.1 days) between initial test and retest in our study was longer than that (21 days) in the original validation study (13).

Normal elderly in our study scored above zero in 6 of 12 domains but the mean scores of these domains were significantly lower than those of dementia patients ($p < 0.001$). Specifically, they scored 2 or less on depression subscale (severity \times frequency), 4 or less on anxiety, 1 or less on apathy, 4 or less on irritability, 4 or less on night-time, and 4 or less on appetite/eating. Therefore, elevation of the subscale score beyond these limits in normal elderly may indicate the presence of psychopathology.

Also, mere presence of delusion, hallucinations, agitation, euphoria, disinhibition, and aberrant motor behavior

should be considered abnormal. As in the original validation study, we did not establish cutoff scores or determine what score might correlate with a clinical diagnosis such as major depressive episode (Dysphoria scale), manic episode (Euphoria scale), or anxiety disorder (Anxiety scale). Thus, these categorical diagnoses must be made on the basis of clinical information complementary to that obtained with the K-NPI.

In summary, the K-NPI with its proven usefulness and reliability may be a useful tool for measuring neuropsychiatric disturbances of Korean dementia patients for clinical and research purposes.

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