Neuropsychiatric Symptoms in Parkinson's Disease Dementia Are Associated with Increased Caregiver Burden

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ABSTRACT

Objective Neuropsychiatric symptoms are common in Parkinson's disease dementia (PDD). Frequent and severe neuropsychiatric symptoms create high levels of distress for patients and caregivers, decreasing their quality of life. The aim of this study was to investigate neuropsychiatric symptoms that may contribute to increased caregiver burden in PDD patients.

Methods Forty-eight PDD patients were assessed using the 12-item Neuropsychiatric Inventory (NPI) to determine the frequency and severity of mental and behavioral problems. The Burden Interview and Caregiver Burden Inventory were used to evaluate caregiver burden.

Results All but one patient showed one or more neuropsychiatric symptoms. The three most frequent neuropsychiatric symptoms were apathy (70.8%) and anxiety (70.8%), followed by depression (68.7%). More severe neuropsychiatric symptoms were significantly correlated with increased caregiver burden. The domains of delusion, hallucination, agitation and aggression, anxiety, irritability and lability, and aberrant motor behavior were associated with caregiver stress. After controlling for age and other potential confounding variables, total NPI score was significantly associated with caregiver burden.

Conclusions The results of this study confirm that neuropsychiatric symptoms are frequent and severe in patients with PDD and are associated with increased caregiver distress. A detailed evaluation and management of neuropsychiatric symptoms in PDD patients appears necessary to improve patient quality of life and reduce caregiver burden.

Key Words Parkinson's disease; Motor symptoms; Dementia; Neuropsychiatric symptoms; Caregiver burden.
giver’s age, gender, health status, and caregiving duration also influence their quality of life and stress. Because many factors interact to independently or dependently influence caregiver burden and distress, this study asked whether neuropsychiatric and motor symptoms cause increased caregiver burden in the case of PDD. Neuropsychiatric symptoms and motor or cognitive dysfunction relating to caregiver burden were assessed using the Burden Interview (BI) and Caregiver Burden Inventory (CBI).  

**MATERIALS & METHODS**

**Patients**

This study was approved by the ethics committee of Seoul St. Mary's Hospital. Each patient provided written, informed consent prior to participating.

Forty-eight patients diagnosed with PDD at the movement disorder outpatient clinic of the university hospitals based on the UK Parkinson’s Disease Society Brain Bank clinical diagnostic criteria and the clinical diagnostic criteria for probable PDB were enrolled. Clinical information included age, gender, disease duration, history of hypertension, diabetes mellitus, heart disease, dyslipidemia, and current medication. Data from complete physical and neurological examinations, laboratory tests, and brain magnetic resonance imaging were obtained. Patients 1) with a previous stroke or other neurological and psychiatric disorders, 2) atypical PD or secondary Parkinsonism or 3) secondary causes of dementia were excluded.

All patients were on anti-parkinsonian medications. The levodopa equivalent daily dose was calculated as follows: dose of levodopa plus dose of dopamine agonists multiplied by equivalents (= 1 × levodopa dose + 0.75 × controlled release dose + 0.33 × entacapone + 20 × ropinirole dose + 100 × pramipexole + 10 × selegiline + 1 × amantadine). When enrolled in this study, all patients had been diagnosed for the first time with dementia. No PD patient had ever taken anti-dementia drugs, antipsychotics, antidepressants or anxiolytics prior to this study.

**Clinical evaluation**

Information on memory problems and other subjective cognitive deficits was obtained from caregiver interviews.

To assess neuropsychiatric symptoms, the Neuropsychiatric Inventory (NPI) was used. The NPI comprises sub-questions in 12 different categories covering four major neuropsychiatric symptom domains: mood, apathy, agitation, and psychosis. Symptom frequency was rated on a scale of 1 to 4, and severity was rated on a scale of 1 to 3. A composite score ranging from 1 to 12, defined as the product of frequency and severity, was calculated. In addition, NPI sub-scores for each patient were analyzed using five different clusters of neuropsychiatric symptoms: 1) few and mild neuropsychiatric symptoms (n = 19), 2) high scores on depression, anxiety, apathy and low scores on the other items (“mood” group, n = 9), 3) high scores on apathy and low scores on the remaining items including depression (“apathy” group, n = 7), 4) moderate or severe sub-scores on the majority of items including irritability and agitation items (“agitation” group, n = 11), and 5) high scores on hallucinations and delusions together with low scores on the majority of other items (“psychosis” group, n = 2).

The general cognitive status and dementia severity were evaluated using the Korean version of the Mini-Mental State Examination (MMSE) and the Clinical Dementia Rating (CDR) scale and Global Deterioration Scale. Parkinsonian motor symptoms were evaluated using the Unified Parkinson’s Disease Rating Scale (UPDRS) part III and the modified Hoehn and Yahr (H&Y) scale when patients were on medications. All patients were divided into tremor-dominant and akinetic rigid-dominant groups based on previous methods.

Caregiver burden was evaluated using BI and CBI. BI is a 22-item questionnaire used to measure caregiver stress caused by patient disabilities. Each item is scored from 0 to 4. Total score is calculated as the sum of all scores and ranges from 0 to 88. CBI is a 24-item multidimensional questionnaire comprised of 5 different subscales that quantify caregiver burden: 1) time-dependence burden: time spent on caregiving (items 1–5), 2) developmental burden: caregiver feelings during care (items 6–10), 3) physical burden: status of general health problems (items 11–14), 4) social burden: problems in the family and social life (items 15–19), and 5) emotional burden: negative feelings about the patient (items 20–24). Each individual item is scored from 0 to 4, the total score is the sum of all sub-scores and
ranges from 0 to 96. The responder for these questionnaires was selected from one of the family members using the following criteria: 1) being a relative of the patient and older than 18 years; and 2) serving as the primary caregiver and with an intimate knowledge of the patient that developed over time.

**Statistical analyses**

Demographics were described using the mean, standard deviation (SD), number, and percentage. Correlation analyses were conducted to evaluate the relationship between neuropsychiatric symptoms, other motor and cognitive features, and caregiver burdens. Independent-sample t-tests were used to compare caregiver burdens and neuropsychiatric symptoms between tremor- and akinetic rigid-dominant groups. Burden differences among NPI clusters were also compared using a one-way analysis of variance. Multiple linear regression analyses were performed to evaluate the effect of associated variables on caregiver burden. A *p* value < 0.05 was considered significant. Statistical analyses were performed using SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA).

**RESULTS**

Of the 48 patients, 28 were men and 20 women. Their mean age (± SD) was 74.7 ± 6.6 years and the mean duration of PD was 3.9 ± 4.4 years. Fourteen patients (29.2%) had diabetes, 21 (43.8%) had hypertension, 7 (14.6%) had heart disease, and 2 (4.2%) had an abnormal lipid profile. Eight patients were current smokers, 3 were ex-smokers, and 37 were non-smokers. The severity of parkinsonian motor and cognitive symptoms was as follows: mean UPDRS part III score, 28.1 ± 12.4; mean H&Y stage score, 2.4 ± 0.8; mean MMSE score, 19.8 ± 4.0; and mean CDR score, 1.1 ± 0.7 (Table 1). All patients were on anti-parkinsonian medications with levodopa only or with dopamine agonists, amantadine, entacapone or selegiline. The mean levodopa equivalent daily dose was 490.3 ± 318.6 mg.

With the exception of 1 patient, all presented with one or more neuropsychiatric symptoms. The most frequent neuropsychiatric symptoms were anxiety and apathy (70.8%), followed by depression (68.7%), nighttime behavior disorder (58.3%), and appetite change (47.9%). Delusion, hallucination, agitation and aggression, disinhibition, irritability and lability, and aberrant motor behavior were present in 20–40% of patients. Euphoria occurred relatively infrequently (8.3%).

The total NPI score did not differ between male and female patients (male vs. female = 24.4 ± 24.2 vs. 22.6 ± 24.3, *p* = 0.729), and we observed no associations with age (*r* = -0.004, *p* = 0.980), disease duration (*r* = 0.062, *p* = 0.678), levodopa equivalent daily dose (*r* = 0.032, *p* = 0.827) or MMSE score (*r* = 0.090, *p* = 0.542). However, the total NPI score did

**Table 1. Clinical and neuropsychological characteristics of patients**

| Variables                              | Mean ± SD       |
|----------------------------------------|-----------------|
| Age (yr)                               | 74.7 ± 6.6      |
| Sex, male (%)                          | 26 (58.3)       |
| Hypertension (%)                       | 21 (43.8)       |
| Diabetes mellitus (%)                  | 14 (28.2)       |
| Heart disease (%)                      | 7 (14.6)        |
| Dyslipidemia (%)                       | 2 (4.2)         |
| Current or ex-smoker (%)               | 11 (22.9)       |
| Disease duration (yr)                  | 3.9 ± 4.4       |
| UPDRS part III                         | 28.1 ± 12.4     |
| Hoehn and Yahr stage                   | 2.4 ± 0.8       |
| MMSE                                   | 19.8 ± 4.0      |
| CDR                                    | 1.1 ± 0.7       |
| GDS                                    | 3.8 ± 0.9       |
| Levodopa equivalent dose (mg)          | 490.3 ± 318.6   |
| Neuropsychiatric Inventory             | 23.6 ± 24.0     |
| Delusion                               | 1.2 ± 2.1       |
| Hallucination                          | 1.2 ± 2.5       |
| Agitation and aggression               | 1.9 ± 3.3       |
| Depression and dysphoria               | 2.4 ± 3.0       |
| Anxiety                                | 3.6 ± 4.4       |
| Euphoria                               | 0.5 ± 1.9       |
| Apathy                                 | 3.4 ± 3.8       |
| Disinhibition                          | 1.4 ± 2.9       |
| Irritability and lability              | 2.1 ± 3.4       |
| Aberrant motor behavior                | 1.7 ± 3.1       |
| Nighttime behavior disorder            | 2.6 ± 3.4       |
| Appetite change                        | 1.8 ± 2.5       |
| Beck Anxiety Inventory                 | 39.8 ± 12.8     |
| Beck Depression Inventory              | 19.4 ± 12.3     |
| Burden Interview                       | 37.8 ± 22.2     |
| Caregiver Burden Inventory             | 35.7 ± 23.0     |
| Time-dependence burden                 | 13.0 ± 6.2      |
| Developmental burden                   | 7.6 ± 6.4       |
| Physical burden                        | 6.2 ± 5.1       |
| Social burden                          | 4.4 ± 4.0       |
| Emotional burden                       | 4.5 ± 4.7       |

Data denoted the mean ± standard deviation or numbers with percentages in parenthesis. UPDRS: Unified Parkinson’s Disease Rating Scale, MMSE: Mini Mental Status Examination, CDR: Clinical Dementia Rating scale, GDS: Global Deterioration Scale.
correlate with CDR ($r = 0.444, p = 0.002$), H&Y stage score ($r = 0.326, p = 0.024$), and UPDRS part III ($r = 0.312, p = 0.031$).

All caregivers reported mild to moderate burdens, ranging from 0 to 79 using BI (mean: 37.8 ± 22.2) and 3 to 87 using CBI scores (mean: 35.7 ± 23.0). The mean CBI sub-scale scores were: time-dependence burden, 13.0 ± 6.2; developmental burden, 7.6 ± 6.4; physical burden, 6.2 ± 5.1; social burden, 4.4 ± 4.0; and emotional burden, 4.5 ± 4.7.

Neuropsychiatric symptoms correlated significantly with greater caregiver burden (Table 2). Delusion, hallucination, agitation and aggression, anxiety, irritability and lability, and aberrant motor behavior were associated with greater caregiver stress (Table 2 and 3). For the NPI clusters, caregivers of groups with irritability, agitation and psychotic symptoms (clusters 4 and 5), reported more severe stress or burden (Table 4).

Increasing age, longer disease duration, and lower MMSE scores did not affect caregiver burden. Burden correlated with more severe motor symptoms and cognitive dysfunction quantified using UPDRS part III and H&Y stage scores and CDR. Caregiver

### Table 2. Correlation between caregiver burden and neuropsychiatric parameters

| Variables                      | Burden Interview | Caregiver Burden Inventory |
|--------------------------------|------------------|---------------------------|
| Age                            | -0.121 (0.411)   | 0.100 (0.497)             |
| Disease duration                | 0.077 (0.804)    | 0.132 (0.370)             |
| UPDRS part III score           | 0.358 (0.012)*   | 0.265 (0.050)*            |
| Hoehn and Yahr stage           | 0.327 (0.023)*   | 0.417 (0.003)*            |
| MMSE                           | -0.011 (0.938)   | 0.085 (0.564)             |
| CDR                            | 0.515 (< 0.001)* | 0.421 (0.003)*            |
| GDS                            | 0.341 (0.018)*   | 0.365 (0.011)*            |
| Levodopa equivalent dose       | 0.098 (0.506)    | 0.085 (0.564)             |
| Beck Anxiety Inventory         | 0.378 (0.008)*   | 0.187 (0.203)             |
| Beck Depression Inventory      | 0.294 (0.043)*   | 0.149 (0.313)             |
| Neuropsychiatric Inventory     | 0.675 (< 0.001)* | 0.605 (< 0.001)*          |
| Delusion                       | 0.425 (0.001)*   | 0.503 (< 0.001)*          |
| Hallucination                  | 0.435 (0.002)*   | 0.367 (0.010)             |
| Agitation and aggression       | 0.472 (0.001)*   | 0.454 (0.001)             |
| Depression and dysphoria       | 0.363 (0.011)*   | 0.203 (0.166)             |
| Anxiety                        | 0.581 (< 0.001)* | 0.457 (0.001)             |
| Euphoria                       | 0.013 (0.932)    | 0.196 (0.182)             |
| Apathy                         | 0.409 (0.004)*   | 0.195 (0.185)             |
| Disinhibition                  | 0.510 (< 0.001)* | 0.447 (0.001)             |
| Irritability and lability      | 0.518 (< 0.001)* | 0.465 (0.001)*            |
| Aberrant motor behavior        | 0.438 (0.002)*   | 0.336 (0.020)*            |
| Nighttime behavior disorder    | 0.219 (0.135)    | 0.333 (0.021)*            |
| Appetite change                | 0.214 (0.144)    | 0.316 (0.029)*            |

Data denote $r$ ($p$ value) of the correlation. * $p < 0.05$, † $p < 0.01$. UPDRS: Unified Parkinson’s Disease Rating Scale. MMSE: Mini Mental Status Examination. CDR: Clinical Dementia Rating scale. GDS: Global Deterioration Scale.

### Table 3. Correlation between CBI sub-score and neuropsychiatric parameters

| Variables                      | CBI time-dependent burden | CBI developmental burden | CBI physical burden | CBI social burden | CBI emotional burden |
|--------------------------------|---------------------------|--------------------------|---------------------|------------------|---------------------|
| Delusion                       | 0.487 (< 0.001)*          | 0.520 (< 0.001)*         | 0.426 (0.003)       | 0.404 (0.004)     | 0.371 (0.010)*      |
| Hallucination                  | 0.353 (0.014)*            | 0.372 (0.009)*           | 0.239 (0.102)       | 0.286 (0.047)*    | 0.306 (0.034)*      |
| Agitation and aggression       | 0.403 (0.005)*            | 0.485 (< 0.001)*         | 0.418 (0.003)       | 0.314 (0.030)*    | 0.409 (0.004)*      |
| Depression and dysphoria       | 0.107 (0.469)             | 0.271 (0.063)            | 0.099 (0.504)       | 0.275 (0.059)     | 0.156 (0.292)       |
| Anxiety                        | 0.433 (0.002)*            | 0.486 (< 0.001)*         | 0.405 (0.004)       | 0.454 (0.001)     | 0.320 (0.026)*      |
| Euphoria                       | 0.061 (0.679)             | 0.223 (0.128)            | 0.180 (0.220)       | 0.275 (0.059)     | 0.237 (0.105)       |
| Apathy                         | 0.285 (0.050)*            | 0.155 (0.292)            | 0.300 (0.039)*      | 0.067 (0.650)     | 0.086 (0.554)       |
| Disinhibition                  | 0.452 (0.001)*            | 0.515 (< 0.001)*         | 0.432 (0.002)       | 0.286 (0.049)*    | 0.323 (0.025)*      |
| Irritability and lability      | 0.398 (0.005)*            | 0.499 (< 0.001)*         | 0.476 (0.001)       | 0.331 (0.022)*    | 0.409 (0.004)*      |
| Aberrant motor behavior        | 0.296 (0.039)*            | 0.417 (0.003)            | 0.293 (0.043)*      | 0.329 (0.022)*    | 0.277 (0.057)       |
| Nighttime behavior disorder    | 0.261 (0.073)             | 0.300 (0.035)*           | 0.448 (0.001)       | 0.296 (0.039)*    | 0.269 (0.065)       |
| Appetite change                | 0.277 (0.056)             | 0.320 (0.027)*           | 0.374 (0.009)       | 0.273 (0.061)     | 0.229 (0.118)       |

Data denote $r$ ($p$ value) of the correlation. * $p < 0.05$, † $p < 0.01$. CBI: Caregiver Burden Inventory.

### Table 4. Comparisons of caregiver burdens among NPI clusters

| Clusters | BI (n = 19) | CBI developmental burden (n = 16) | CBI physical burden (n = 13) | $p$ | Post-hoc tests |
|----------|-------------|----------------------------------|-------------------------------|-----|----------------|
| Cluster 1| 25.6 ± 18.6 | 10.5 ± 6.6                       | 4.8 ± 6.0                     | < 0.001 | Cluster 4, 5 > cluster 1 = cluster 2, 3 |
| Cluster 2| 25.9 ± 20.6 | 12.9 ± 8.0                       | 6.5 ± 8.0                     | < 0.001 | Cluster 4, 5 > cluster 1 = cluster 2, 3 |
| Cluster 3| 23.0 ± 9.0  | 11.8 ± 5.0                       | 5.4 ± 5.0                     | 0.005 | Cluster 4, 5 > cluster 1 = cluster 2, 3 |
| Cluster 4| 24.5 ± 10.5 | 10.5 ± 6.5                       | 4.8 ± 6.0                     | < 0.001 | Cluster 4, 5 > cluster 1 = cluster 2, 3 |
| Cluster 5| 25.0 ± 11.0 | 12.0 ± 7.0                       | 5.0 ± 7.0                     | 0.003 | Cluster 4, 5 > cluster 1 = cluster 2, 3 |

Data denote the mean ± standard deviation. Analyses were performed using one-way analysis of variance and LSD post-hoc tests were used for comparisons. BI: Burden Interview, CBI: Caregiver Burden Inventory, NPI: Neuropsychiatric Inventory.
burden tended to be greater for the akinetic rigid-dominant group, although there were no differences in neuropsychiatric symptoms between tremor-dominant and akinetic rigid-dominant groups with the exception of the apathy domain (Table 5).

Linear regression analyses revealed that NPI score associated independently with caregiver burden in patients with PDD, as measured using BI and CBI, regardless of age, gender, vascular risk factors, and motor and cognitive status (Table 6).

**DISCUSSION**

Parkinson's disease dementia patients included in this study presented with frequently occurring neuropsychiatric symptoms. All but one patient showed at least one or more neuropsychiatric symptoms. The frequency and severity of neuropsychiatric symptoms were similar to previous studies;[4] the most frequent and severe symptoms were apathy, anxiety, and depression. In contrast, euphoria was the rarest symptom.

A number of demographics and factors were associated with increased caregiver burden. Parkinsonian motor-symptom status or dementia severity in patients was associated with greater caregiver distress. However, neither patient age nor disease duration increased neuropsychiatric symptoms or family burden. This finding may be because the patients in this study had relatively short durations of PD: (3.9 ± 4.4 years) compared with a previous study (10.9 ± 7.7 years);[14] the shorter disease duration may cause selection bias, and it is therefore possible that the longer disease duration group was underrepresented.

Severe neuropsychiatric symptoms correlated with caregiver distress; caregivers reported greater burden as neuropsychiatric symptoms became more frequent and severe. Only euphoria, which was the most rare and mildest symptom, was not associated with caregiver burden. Both sub-items and scales for depression and anxiety (Beck Depression Inventory...)

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**Table 5.** Comparison of caregiver burden and neuropsychiatric parameters based on Parkinsonian motor phenotype

| Variables                        | Tremor-dominant (n = 20) | Akinetic rigid-dominant (n = 22) | p value |
|----------------------------------|--------------------------|----------------------------------|---------|
| Burden Interview                 | 31.8 ± 20.9              | 44.9 ± 22.0                      | 0.041*  |
| Caregiver Burden Inventory       | 30.5 ± 20.7              | 41.8 ± 24.5                      | 0.069   |
| Time-dependence burden           | 11.7 ± 6.6               | 14.5 ± 5.5                       | 0.127   |
| Developmental burden             | 6.3 ± 6.1                | 9.0 ± 6.6                        | 0.155   |
| Physical burden                  | 5.4 ± 5.0                | 7.1 ± 5.2                        | 0.244   |
| Social burden                    | 3.5 ± 2.9                | 5.6 ± 4.9                        | 0.062   |
| Emotional burden                 | 3.6 ± 3.6                | 5.6 ± 5.6                        | 0.155   |
| Neuropsychiatric Inventory       | 19.7 ± 20.4              | 28.3 ± 27.4                      | 0.218   |
| Delusion                         | 1.2 ± 2.1                | 1.2 ± 2.2                        | 0.987   |
| Hallucination                    | 1.2 ± 2.7                | 1.1 ± 2.3                        | 0.849   |
| Agitation and aggression         | 1.6 ± 3.2                | 2.1 ± 3.5                        | 0.594   |
| Depression and dysphoria         | 1.8 ± 2.5                | 3.1 ± 3.5                        | 0.173   |
| Anxiety                          | 3.5 ± 4.2                | 3.8 ± 4.7                        | 0.805   |
| Euphoria                         | 0.3 ± 1.2                | 0.8 ± 2.5                        | 0.366   |
| Apathy                           | 1.9 ± 2.1                | 5.1 ± 4.7                        | 0.007†  |
| Disinhibition                    | 1.1 ± 2.3                | 1.7 ± 3.5                        | 0.475   |
| Irritability and lability        | 1.5 ± 2.7                | 2.8 ± 4.0                        | 0.186   |
| Aberrant motor behavior          | 1.2 ± 2.4                | 2.3 ± 3.7                        | 0.250   |
| Nighttime behavior disorder      | 2.6 ± 3.3                | 2.5 ± 3.6                        | 0.909   |
| Appetite change                  | 1.7 ± 2.4                | 1.8 ± 2.7                        | 0.907   |

Data denote the mean ± standard deviation. *< 0.05, †< 0.01.

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**Table 6.** Associations of caregiver burden with demographics or neuropsychiatric variables based on linear regression analysis

| Variables                        | Burden Interview B (SE) 95% CI | Caregiver Burden Inventory B (SE) 95% CI |
|----------------------------------|-------------------------------|------------------------------------------|
| Age                              | -0.570 (0.467) -1.522, 0.361 | 0.050 (0.446) -0.858, 0.856              |
| Gender                           | 2.927 (5.816) -0.896, 14.760 | 2.582 (5.550) -8.710, 13.874            |
| Diabetes mellitus                | -3.136 (6.414) -16.185, 9.912 | -7.954 (6.121) -20.407, 4.498           |
| Hypertension                     | 8.069 (6.184) -4.513, 20.651 | 8.661 (5.902) -3.346, 20.668            |
| Heart disease                    | -4.218 (8.257) -21.018, 12.562 | -5.101 (7.860) -21.133, 10.931          |
| Dyslipidemia                     | 14.494 (13.579) -13.134, 42.121 | 15.639 (12.959) -10.726, 42.005         |
| Disease duration                 | 1.049 (0.703) -0.381, 2.479  | 1.449 (0.671) 0.084, 2.814*             |
| Hoehn & Yahr stage               | 3.459 (3.876) -4.427, 11.345 | 6.963 (3.699) -0.563, 14.489            |
| Levodopa equivalent dose         | 0.013 (0.010) -0.008, 0.033  | 0.010 (0.010) -0.010, 0.029             |
| Beck Anxiety Inventory           | 0.071 (0.275) -0.487, 0.630  | -0.143 (0.262) -0.896, 0.390            |
| Beck Depression Inventory        | -0.170 (0.259) -0.698, 0.358 | -0.305 (0.248) -0.809, 0.199            |
| MMSE                             | 0.814 (0.820) -0.853, 2.481  | 1.089 (0.782) -0.511, 2.671             |
| CDR                              | 1.488 (6.261) -11.250, 14.226 | -3.933 (5.975) -16.092, 8.220           |
| Neuropsychiatric Inventory       | 0.619 (0.151) 0.313, 0.926   | 0.758 (0.144) 0.466, 1.051†             |

Data denote the coefficient B and standard error (SE) of the correlation. *< 0.05, †< 0.01. MMSE: Mini Mental Status Examination, CDR: Clinical Dementia Rating scale.
frequency and severity of neuropsychiatric symptoms may not generalize to other populations; however, many cross-sectional studies have been performed and their outcomes accepted.\(^2\)\(^4\)

In conclusion, the results from this study confirm neuropsychiatric symptoms are frequent and severe in patients with PDD and that they are associated with increased caregiver distress. These data suggest that the detailed evaluation and management of neuropsychiatric symptoms in PDD patients may improve patient quality of life and reduced caregiver burden.

**Conflicts of Interest**

The authors have no financial conflicts of interest.

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**REFERENCES**

1. Aarsland D, Bønnick K, Alves G, Tynes OB, Pedersen KF, Ehrt U, et al. The spectrum of neuropsychiatric symptoms in patients with early untreated Parkinson's disease. J Neurol Neurosurg Psychiatry 2009;80:928-930.
2. Stella F, Banzato CE, Quagliato EM, Viana MA, Christofolletti G. Psychopathological features in patients with Parkinson's disease and related caregivers' burden. Int J Geriatr Psychiatry 2009;24:1158-1165.
3. Aarsland D, Bønnick K, Ehrt U, De Deyn PP, Tekin S, Emre M, et al. Neuropsychiatric symptoms in patients with Parkinson's disease and dementia: frequency, profile and associated care giver stress. J Neurol Neurosurg Psychiatry 2007;78:36-42.
4. Kulisevsy J, Pagonabarraga J, Pascual-Sedano B, García-Sánchez C, Girondel A; Trapecio Group Study. Prevalence and correlates of neuropsychiatric symptoms in Parkinson's disease without dementia. Mov Disord 2010;25:1889-1896.
5. Morley JE, Weintraub D, Mamikonyan E, Moberg PJ, Sidrowf AD, Duda JE. Olfactory dysfunction is associated with neuropsychiatric manifestations in Parkinson's disease. Mov Disord 2011;26:2051-2057.
6. Aarsland D, Larsen JP, Karlsen K, Lim NG, Tandberg E. Mental symptoms in Parkinson's disease are important contributors to caregiver distress. Int J Geriatr Psychiatry 1999;14:866-874.
7. Karlsen KH, Tandberg E, Aarsland D, Larsen JP. Health related quality of life in Parkinson's disease: a prospective longitudinal study. J Neurol Neurosurg Psychiatry 2000;69;584-589.
8. McKinlay A, Grace RC, Dalrymple-Alford JC, Anderson T, Fink J, Roger D. A profile of neuropsychiatric problems and their relationship to quality of life for Parkinson's disease patients without dementia. Parkinsonism Relat Disorders 2008;14:37-42.
9. Weintraub D, Moberg PJ, Duda JE, Katz IR, Stern MB. Effect of psychiatric and other nonmotor symptoms on disability in Parkinson's disease. J Am Geriatr Soc 2004;52:784-788.
10. Aarsland D, Larsen JP, Tandberg E, Laake K. Predictors of nursing home placement in Parkinson's disease: a popula-
Systematic review of levodopa dose equivalency reporting

Tomlinson CL, Stowe R, Patel S, Rick C, Gray R, Clarke CE.

1689-1707; quiz 1837.

Societal guidelines. Parkinsons Dis 2012;2012:190901.

Factors influencing quality of life in caregivers of people with Parkinson’s disease and implications for clinical guidelines. Parkinsons Dis 2012;2012:198901.

14. Schrag A, Horvis A, Morley D, Quinn N, Jahanshahi M. Caregiver burden in Parkinson’s disease is closely associated with psychiatric symptoms, falls, and disability. Parkinsonism Relat Disord 2006;12:35-41.

15. Ozdilek B, Gunal DJ. Motor and non-motor symptoms in Turkish patients with Parkinson’s disease affecting family caregiver burden and quality of life. J Neuropsychiatry Clin Neurosci 2012;24:478-483.

16. Morley D, Dummett S, Peters M, Kelly L, Hewitson P, Dawson J, et al. Factors influencing quality of life in caregivers of patients with Parkinson’s disease: A psychometric study. Acta Neurol Scand 2010;122:418-424.

17. Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. Gerontologist 1980;20:649-655.

18. Caserta MS, Lund DA, Wright SD. Exploring the Caregiver Burden Inventory (CBI): further evidence for a multidimensional view of burden. Int J Aging Hum Dev 1996;43:21-34.

19. Novak M, Guest C. Application of a multidimensional caregiver inventory: Gerontologist 1989:29:798-803.

20. Lai C, Luciani M, Morelli F, Galli F, Cappelluti R, Penco I, et al. Predictive role of different dimensions of burden of risk of complicated grief in caregivers of terminally ill patients. Am J Hosp Palliat Care 2014;31:189-193.

21. Gibb WR, Lees AJ. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson’s disease. J Neurol Neurosurg Psychiatry 1988;51:745-752.

22. Emre M, Aarsland D, Brown R, Burn DJ, Duyckaerts C, Mizuno Y, et al. Clinical diagnostic criteria for dementia associated with Parkinson’s disease. Mov Disord 2007;22:1689-1707; quiz 1837.

23. Tomlinson CL, Stowe R, Patel S, Rick C, Gray R, Clarke CE. Systematic review of levodopa dose equivalency reporting in Parkinson’s disease. Mov Disord 2010;25:2649-2653.

24. Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. Neurology 1994;44:2308-2314.

25. Bromnick K, Aarsland D, Larsen JP. Neuropsychiatric disturbances in Parkinson’s disease clusters in five groups with different prevalence of dementia. Acta Psychiatr Scand 2005;112:201-207.

26. Lewis SJ, Foltynie T, Blackwell AD, Robbins TW, Owen AM, Barker RA. Heterogeneity of Parkinson’s disease in the early clinical stages using a data driven approach. J Neurol Neurosurg Psychiatry 2005;76:343-348.

27. Tomlinson CL, Stowe R, Patel S, Rick C, Gray R, Clarke CE. Systematic review of levodopa dose equivalency reporting in Parkinson’s disease. Mov Disord 2010;25:2649-2653.

28. Comella CL, Nardone TM, Diederich NJ, Stubbins GT. Sleep-related violence, injury, and REM sleep behavior disorder in Parkinson’s disease. Neurology 1996;51:526-529.

29. Aarsland D, Alves G, Larsen JP. Disorders of motivation, sexual conduct, and sleep in Parkinson’s disease. Adv Neurol 2005;96:56-64.

30. Leroi I, Harshbettar V, Andrews M, McDonald K, Byrne EL, Burns A. Carer burden in apathy and impulse control disorders in Parkinson’s disease. Int J Geriatr Psychiatry 2012;27:160-166.

31. Global Parkinson’s Disease Survey Steering Committee. Factors impacting on quality of life in Parkinson’s disease: results from an international survey. Mov Disord 2002;17:60-67.

32. Leiknes T, Tysnes OB, Aarsland D, Larsen JP. Caregiver distress associated with neuropsychiatric problems in patients with early Parkinson’s disease: the Norwegian ParkWest study. Acta Neurol Scand 2010;122:418-424.

33. Burn DJ, Tröster AI. Neuropsychiatric complications of medical and surgical therapies for Parkinson’s disease. J Geriatr Psychiatry Neurol 2004;17:172-180.

34. Wada-Isoe K, Ohta K, Inamura K, Kitayama M, Nomura T, Yasui K, et al. Assessment of hallucinations in Parkinson’s disease using a novel scale. Acta Neurol Scand 2008;117:35-40.

35. Wint DP, Okun MS, Fernandez HH. Psychosis in Parkinson’s disease. J Geriatr Psychiatry Neurol 2004;17:127-136.

36. Weintraub D, Hurtig H. Presentation and management of psychosis in Parkinson’s disease and dementia with Lewy bodies. Am J Psychiatry 2007;164:1491-1498.